The NHLS is a proud recipient of the 2015 European Quality Award.
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Foreword

In the past year the National Health Laboratory Service (NHLS) continued to strengthen its mandate for teaching, training and research in conjunction with its academic partners and through its research centres. The NHLS continues to work closely with its academic partners and stakeholders to facilitate and deliver pathology training and research activities towards improvement of the diagnostic service platform. Vocational training for registrars and intern medical scientists is provided in the following disciplines: Anatomical Pathology, Chemical Pathology, Haematology, Human Genetics, Immunology, Medical Microbiology and Medical Virology.

This Academic Review includes activities achieved by NHLS staff members on joint appointments (dual appointments by the NHLS and each university) with the academic partners and acknowledges the much valued contribution achieved through this distinctive relationship. A formal relationship exists between the NHLS and the following academic partners:

- The University of Cape Town
- The University of the Free State
- The University of KwaZulu-Natal
- The University of Limpopo
- The University of Pretoria
- Stellenbosch University
- The University of the Western Cape
- The University of the Witwatersrand
- Sefako Makgatho Health Sciences University
- Walter Sisulu University.

The demerger of the university of Limpopo from the now Sefako Makgatho Health Sciences University resulted in the introduction of a new medical school. The relationship between the NHLS and the academic partners is cemented in the overarching Umbrella Agreement and individual Bilateral Agreements. These agreements continue to provide the framework for governance structures, joint staff establishments, financial arrangements and uninterrupted and equitable access to both the academic and service platforms.

Our academics are locally and internationally acknowledged for their teaching, research, leadership and community service activities and achievements. The NHLS is not only leading the way in South Africa and the Southern African Development Community (SADC), but our academic footprint is rapidly expanding beyond the region.

The close relationship with our academic partners enables the NHLS and universities to produce skilled and dedicated health professionals in pathology. The NHLS has the statutory responsibility to train pathologists, medical scientists, technologists and technicians for the country as a whole. The teaching training and research mandates are carried seamlessly through integrated support programmes with our academic partners.

This report indicates the wealth of research output achieved through this collaboration. It also highlights activities supported through the NHLS academic centres. Together, the NHLS – including the National Institute of Communicable Diseases (NICD) and National Institute for Occupational Health (NIOH) – and the universities boast a truly impressive research output, as is evident by the amount of grant funding received, the number of peer-reviewed publications and presentations at local and international congresses, and the translation of research into national policies and operational improvements.
The future is filled with challenges and the 2016/17 year will continue with the prioritisation of key objectives. These include, but are not limited to:

1. A comprehensive review of the Academic Pathology Platform with the view of developing a detailed strategy and implementation plan on an enhanced and optimised platform
2. Improved registrar and intern scientists’ recruitment and retention drive
3. Improved registrar pass rate
4. Improving the equity profile of students
5. Translation of research into operational efficiencies
6. Translation of research to influence national policies.

In conclusion, I would like to express my sincere gratitude for the excellent contributions of our academic partners. I am looking forward to exciting developments and prosperous co-operation in the years ahead.
### Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AASLD</td>
<td>American Association for the Study of Liver Diseases</td>
</tr>
<tr>
<td>ACS</td>
<td>Acute coronary syndromes</td>
</tr>
<tr>
<td>ACSR</td>
<td>AIDS Cancer Specimen Repository</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>AKN</td>
<td>Acne keloidalis nuchae</td>
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<tr>
<td>AM</td>
<td>Acral melanoma</td>
</tr>
<tr>
<td>AMC</td>
<td>AIDS Malignancy Consortium</td>
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<tr>
<td>AML</td>
<td>Acute myeloid leukaemia</td>
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<tr>
<td>ANDEMA</td>
<td>African Network for Improved Diagnostics, Epidemiology and Management of Common Infectious Agents</td>
</tr>
<tr>
<td>ARV</td>
<td>Anti-retroviral</td>
</tr>
<tr>
<td>ASAP</td>
<td>African Strategies for the Advancement of Pathology</td>
</tr>
<tr>
<td>ASC</td>
<td>Adipose-derived mesenchymal stromal cell</td>
</tr>
<tr>
<td>ASC-US</td>
<td>Atypical squamous cells of undetermined significance</td>
</tr>
<tr>
<td>ASLM</td>
<td>African Society for Laboratory Medicine</td>
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<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guérin</td>
</tr>
<tr>
<td>BER</td>
<td>Base excision repair</td>
</tr>
<tr>
<td>BHSc</td>
<td>Bachelor of Health Science</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>BRCA</td>
<td>Breast cancer (gene)</td>
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<td>BSc</td>
<td>Bachelor of Science</td>
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<td>BSI</td>
<td>Bloodstream infections</td>
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<td>BSL</td>
<td>Biological safety level</td>
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<td>BV</td>
<td>Bacterial vaginosis</td>
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<td>CAH</td>
<td>Congenital adrenal hyperplasia</td>
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<td>CANSA</td>
<td>Cancer Association of South Africa</td>
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<td>CAP</td>
<td>College of American Pathologists</td>
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<td>CAPRISA</td>
<td>Centre for the AIDS Programme of Research in South Africa</td>
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<td>CAVD</td>
<td>Collaboration for AIDS Vaccine Discovery</td>
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<td>CBH</td>
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<td>CBTBR</td>
<td>Centre of Excellence for Biomedical TB Research</td>
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<tr>
<td>CCHF</td>
<td>Crimean–Congo haemorrhagic fever</td>
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<tr>
<td>CCMT</td>
<td>Comprehensive Care Management and Treatment</td>
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<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
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<td>CDC-GDD</td>
<td>Centers for Disease Control and Prevention – Global Disease Detection</td>
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<tr>
<td>CEQAS</td>
<td>Cytogenetic External Quality Assessment Services</td>
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<td>CF</td>
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<td>CFAR</td>
<td>Centers for AIDS Research</td>
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<td>CMID</td>
<td>Clinical Microbiology and Infectious Diseases</td>
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<td>Charlotte Maxeke Johannesburg Academic Hospital</td>
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<td>CML</td>
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<td>CMMR-D</td>
<td>Constitutional Mismatch Repair Deficiency</td>
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<td>Colleges of Medicine of South Africa</td>
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<td>CMV</td>
<td>Cytomegalovirus</td>
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<td>CNS</td>
<td>Central Nervous System</td>
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<td>COBES</td>
<td>Community-based education and service</td>
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<td>CPD</td>
<td>Continuing Professional Development</td>
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<td>CPUT</td>
<td>Cape Peninsula University of Technology</td>
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<tr>
<td>CRF</td>
<td>Complex circulating recombinant form</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
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<tr>
<td>CT</td>
<td>Chlamydia trachomatis</td>
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<td>CVM</td>
<td>Cervical vaginal microbiome</td>
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<td>Acronym</td>
<td>Full Form</td>
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<td>DAFF</td>
<td>Department of Agriculture, Forestry and Fisheries</td>
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<tr>
<td>DBS</td>
<td>Dried blood spots</td>
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<td>DCTB</td>
<td>Differentially culturable tubercle bacteria</td>
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<td>DD</td>
<td>Developmental delay</td>
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<tr>
<td>DFG</td>
<td>Deutsche Forschungsgemeinschaft</td>
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<td>DGM</td>
<td>Dr George Mukhari</td>
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<td>DGMC</td>
<td>Donald Gordon Medical Centre</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<td>DoH</td>
<td>Department of Health</td>
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<td>DRC</td>
<td>Democratic Republic of Congo</td>
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<td>DST</td>
<td>Department of Science and Technology</td>
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<tr>
<td>DTHF</td>
<td>Desmond Tutu HIV Foundation</td>
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<tr>
<td>DTM&amp;H</td>
<td>Diploma in Tropical Medicine and Hygiene</td>
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<td>DTRA</td>
<td>Defence and Threat Reduction Agency</td>
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<td>DTTC</td>
<td>Desmond Tutu TB Centre</td>
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<td>EBV</td>
<td>Epstein Barr virus</td>
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<td>ECDC</td>
<td>European &amp; Developing Countries Clinical Trials Partnership</td>
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<td>EFI</td>
<td>European Federation of Immunogenetics</td>
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<td>EGK</td>
<td>Electronic gatekeeping</td>
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<td>EID</td>
<td>Early infant diagnosis</td>
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<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
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<td>EPTB</td>
<td>Extrapulmonary tuberculosis</td>
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<td>EQA</td>
<td>External quality assurance</td>
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<td>ESBL</td>
<td>Extended-spectrum beta-lactamases</td>
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<td>ESR</td>
<td>Erythrocyte sedimentation rate</td>
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<td>EU</td>
<td>European Union</td>
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<tr>
<td>EV</td>
<td>Enterovirus</td>
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<td>EVD</td>
<td>Ebola Viral Disease</td>
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<td>FA</td>
<td>Fanconi anaemia</td>
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<td>FBC</td>
<td>Full blood count</td>
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<tr>
<td>FCPath</td>
<td>Fellowship of the College of Pathologists of South Africa</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FH</td>
<td>Familial hypercholesterolaemia</td>
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<tr>
<td>FISH</td>
<td>Fluorescent in situ hybridisation</td>
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<td>FNAB</td>
<td>Fine needle aspiration biopsies</td>
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<tr>
<td>FNB</td>
<td>Fine needle aspiration</td>
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<td>FRC</td>
<td>Faculty Research Council</td>
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<td>FRCPath</td>
<td>Fellowship of the Royal College of Pathologists</td>
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<tr>
<td>FSASP</td>
<td>Federation of South African Societies of Pathology</td>
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<tr>
<td>FT MTB</td>
<td>FluoroType MTB</td>
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<tr>
<td>GAP</td>
<td>Global Alliance for Progress</td>
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<tr>
<td>GARPEC</td>
<td>Global Antibiotic Resistance Prescribing in Children</td>
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<tr>
<td>GC MS</td>
<td>Gas chromatography mass spectrometry</td>
</tr>
<tr>
<td>GDM</td>
<td>Gestational diabetes mellitus</td>
</tr>
<tr>
<td>GEMP</td>
<td>Graduate Entry Medical Programme</td>
</tr>
<tr>
<td>GET</td>
<td>Global Emerging Pathogens Treatment</td>
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<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>GGE</td>
<td>Gradient gel electrophoresis</td>
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<tr>
<td>GHRC</td>
<td>Global HIV Vaccine Research Consortium</td>
</tr>
<tr>
<td>GIRNS</td>
<td>Global Influenza Response Networks Surveillance</td>
</tr>
<tr>
<td>GIT</td>
<td>Gastro-intestinal tract</td>
</tr>
<tr>
<td>GMO</td>
<td>Genetically modified organisms</td>
</tr>
<tr>
<td>GNB</td>
<td>Gram-negative bacilli</td>
</tr>
<tr>
<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>GSH</td>
<td>Groote Schuur Hospital</td>
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<tr>
<td>GvHD</td>
<td>Graft-versus-host disease</td>
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<tr>
<td>H3Africa</td>
<td>Human Heredity and Health: Africa</td>
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<td>HAART</td>
<td>Highly active antiretroviral therapy</td>
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<td>HAI</td>
<td>Healthcare-associated infection</td>
</tr>
<tr>
<td>HAIG</td>
<td>HIV Activation and Inflammation Group</td>
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<td>HAND</td>
<td>HIV-associated neurological disease</td>
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<td>HAV</td>
<td>Hepatitis A virus</td>
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<td>HBOCS</td>
<td>Hereditary Breast and Ovarian Cancer Syndrome</td>
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<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
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<td>HCV</td>
<td>Hepatitis C virus</td>
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<tr>
<td>HCW</td>
<td>Healthcare workers</td>
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<td>HD</td>
<td>Huntington's disease</td>
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<td>HDL</td>
<td>High-density lipoprotein</td>
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<td>HEU</td>
<td>HIV-exposed, uninfected</td>
</tr>
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<td>HEV</td>
<td>Hepatitis E virus</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<tr>
<td>HIVAN</td>
<td>Human immunodeficiency virus-associated nephropathy</td>
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<tr>
<td>HLA</td>
<td>Human leukocyte antigen</td>
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<tr>
<td>HOD</td>
<td>Head of Department</td>
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<tr>
<td>HOPE</td>
<td>HIV Outreach Programme and Education</td>
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<td>HPCSA</td>
<td>Health Professions Council of South Africa</td>
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<td>HPgV</td>
<td>Human pegivirus</td>
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<td>HPLC</td>
<td>High-performance liquid chromatography</td>
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<td>HPP</td>
<td>HIV Pathogenesis Programme</td>
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<td>HPV</td>
<td>Human papillomavirus</td>
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<td>HSV</td>
<td>Herpes simplex virus</td>
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<td>HTA</td>
<td>Health Technology Assessment</td>
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<td>IALCH</td>
<td>Inkosi Albert Luthuli Central Hospital</td>
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<td>IBRO</td>
<td>International Brain Research Organisation</td>
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<td>ICU</td>
<td>Intensive care unit</td>
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<tr>
<td>ID</td>
<td>Infectious diseases</td>
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<tr>
<td>IDM</td>
<td>Institute of Infectious Disease and Molecular Medicine</td>
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<tr>
<td>IND</td>
<td>Investigative new drug</td>
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<tr>
<td>INR</td>
<td>International Normalised Ratio</td>
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<tr>
<td>IPC</td>
<td>Infection prevention and control</td>
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<tr>
<td>IRT</td>
<td>Inhibitor Resistant Temoniera</td>
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<tr>
<td>ISBER</td>
<td>International Society for Biological and Environmental Repositories</td>
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<tr>
<td>ITP</td>
<td>Immune thrombocytopenic purpura</td>
</tr>
<tr>
<td>IUC</td>
<td>Institutional University Cooperation</td>
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<tr>
<td>IUD</td>
<td>Intrauterine device</td>
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<td>JAK</td>
<td>Janus kinase</td>
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<td>KEH</td>
<td>King Edward VIII Hospital</td>
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<td>KIDCRU</td>
<td>Children's Infectious Diseases Clinical Research Unit</td>
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<td>KWE</td>
<td>Keratolytic winter erythema</td>
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<td>KZN</td>
<td>KwaZulu-Natal</td>
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<tr>
<td>LAMP</td>
<td>Loop-mediated isothermal amplification</td>
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<tr>
<td>LC/-MS/MS</td>
<td>Liquid Chromatography tandem Mass Spectrometry</td>
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<td>LDL</td>
<td>Low-Density Lipoprotein</td>
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<td>LFA</td>
<td>Lateral flow assay</td>
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<td>LFT</td>
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<td>LIPG</td>
<td>endothelial lipase</td>
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<td>LIS</td>
<td>Laboratory information system</td>
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<td>LNG</td>
<td>Levonorgestrel-releasing</td>
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<td>Acronym</td>
<td>Description</td>
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<td>LP</td>
<td>Lactase persistence</td>
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<td>LPA</td>
<td>Line-probe assays</td>
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<td>LSHTM</td>
<td>London School of Hygiene &amp; Tropical Medicine</td>
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<tr>
<td>LTI</td>
<td>Laboratory for Tissue Immunology</td>
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<td>MALDI MSI</td>
<td>Matrix-assisted laser desorption ionisation mass spectrometry imaging</td>
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<td>MALDI-TOF-MS</td>
<td>Matrix-assisted laser desorption/ionisation time of flight mass spectrometry</td>
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<td>MBRT</td>
<td>Molecular Biosciences Research Thrust</td>
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<td>MeCRU</td>
<td>Mecri Clinical Research Unit</td>
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<td>MEEI</td>
<td>Massachusetts Eye and Ear Infirmary</td>
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<td>MGH</td>
<td>Massachusetts General Hospital</td>
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<td>MGIT</td>
<td>Mycobacteria Growth Indicator Tube</td>
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<td>MIBE</td>
<td>Measles inclusion body encephalitis</td>
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<tr>
<td>MIC</td>
<td>Minimum inhibitory concentration</td>
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<td>MLPA</td>
<td>Multiplex ligation-dependant probe amplification</td>
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<td>Multilocus sequence typing</td>
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<td>Masters in Medicine</td>
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<td>MMRU</td>
<td>Molecular Mycobacteriology Research Unit</td>
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<td>MoU</td>
<td>Memorandum of understanding</td>
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<td>MRC</td>
<td>Medical Research Council</td>
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<td>MRSAs</td>
<td>Methicillin-resistant Staphylococcus aureus</td>
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<td>MS</td>
<td>Mass Spectrometry</td>
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<td>Multiple sclerosis</td>
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<td>MSc</td>
<td>Masters in Science</td>
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<td>MSM</td>
<td>Men who have Sex with Men</td>
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<tr>
<td>MT</td>
<td>Medical technologist</td>
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<td>MTBC</td>
<td>Mycobacterium tuberculosis complex</td>
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<td>National Academic Pathology Committee</td>
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<td>NEQAS</td>
<td>National external quality assurance</td>
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<td>Non-governmental Organisation</td>
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<td>National Health Insurance</td>
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<td>National Health Laboratory Service</td>
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<tr>
<td>NIAAA</td>
<td>National Institute on Alcohol Abuse and Alcoholism</td>
</tr>
<tr>
<td>NICD</td>
<td>National Institute for Communicable Diseases</td>
</tr>
<tr>
<td>NIH</td>
<td>National Institute of Health</td>
</tr>
<tr>
<td>NIH, USA</td>
<td>National Institutes of Health (USA)</td>
</tr>
<tr>
<td>NIOH</td>
<td>National Institute for Occupational Health</td>
</tr>
<tr>
<td>NMAH</td>
<td>Nelson Mandela Academic Hospital</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>NNRTI</td>
<td>Non-nucleoside reverse transcriptase inhibitor</td>
</tr>
<tr>
<td>NPP</td>
<td>National Priority Programmes</td>
</tr>
<tr>
<td>NRF</td>
<td>National Research Foundation</td>
</tr>
<tr>
<td>NTBRL</td>
<td>National Tuberculosis Reference Laboratory</td>
</tr>
<tr>
<td>NTM</td>
<td>Nontuberculous mycobacteria</td>
</tr>
<tr>
<td>OGTT</td>
<td>Oral glucose tolerance test</td>
</tr>
<tr>
<td>OLP</td>
<td>Oral lichen planus</td>
</tr>
<tr>
<td>OWSD</td>
<td>Organization for Women in Science for the Developing World</td>
</tr>
<tr>
<td>PAS</td>
<td>Periodic acid-Schiff</td>
</tr>
<tr>
<td>PBL</td>
<td>Problem-based learning</td>
</tr>
<tr>
<td>PCOS</td>
<td>Polycystic ovary syndrome</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
</tr>
</tbody>
</table>
SUSHI  Simultaneous Ultrasensitive Subpopulation Staining/Hybridization In Situ
TAD  Tshwane Academic Division
TALE  Transcription activator-like effector
tAT  Turnaround time
TB  Tuberculosis
TBC  To be confirmed
TbH  Tygerberg Hospital
TBP  Teaching Biology Project
THRIp  Technology and Human Resources for Industry Programme
TIA  Technology Innovation Agency
TLSG  Tygerberg Lymphoma Study Group
TMP  Teaching Mathematics Programme
TREAT TB  Technology, Research, Education and Technical Assistance for Tuberculosis
TSP  Teaching Sciences Programme
TWG  Technical Working Group
UCT  University of Cape Town
UEC  Urea, electrolytes and creatinine
UFS  University of the Free State
UKZN  University of KwaZulu-Natal
UL  University of Limpopo
URC  University Research Committee
URF  Unique recombinant form
USA  United States of America
USAf  Universities South Africa
USAID  US Agency for International Development
UWC  University of the Western Cape
V3SWG  Viral Vector Vaccines Safety Working Group
VAP  Ventilator-associated pneumonia
VL  Viral load
VLIR  Vlaamse Interuniversitaire Raad
WB  Whole blood
WHO  World Health Organization
WHO AFRO  WHO African Regional Office
Wits  University of the Witwatersrand
WNV  West Nile virus
WSU  Walter Sisulu University
XDR-TB  Extensively Drug-Resistant Tuberculosis
ZDV  Zidovudine
ZN  Ziehl-Neelsen
ZRU  Zoonosis Research Unit
Anatomical Pathology

Head: Prof. Dhirendra Govender

1. ABOUT THE DIVISION

The Anatomical Pathology Division provides comprehensive diagnostic histopathological, cytopathological and autopsy services to Groote Schuur Hospital (GSH), Red Cross War Memorial Children’s Hospital (RCCH), Somerset and Victoria Hospitals, which belong to the University of Cape Town’s academic hospital. It provides diagnostic services to approximately half of the Western Cape public health service including 2 Military Hospital in Wynberg. There are separate South African National Accreditation System (SANAS) laboratories at Groote Schuur (histopathology and cytopathology) and RCCH. Diagnostic services are also offered to the University of Cape Town Private Academic Hospital and consultative and referral services to the National Health Laboratory Service (NHLS) and private laboratories in East London, Port Elizabeth, Cape Town, Durban and Pietermaritzburg.

Table 1: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Profession</th>
<th>Pathologist</th>
<th>Medical Doctors</th>
<th>PhD Scientists</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>26</td>
<td>23</td>
<td>60</td>
<td>61</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

The GSH histopathology laboratory received 30 933 surgical pathology cases (including many cases with multiple specimens), the cytopathology laboratory processed 66 944 cases, of which 58 177 were cervical smears and 8 767 were non-gynaecological cases. The Fine Needle Aspiration (FNA) Clinic performed 138 FNA procedures. The electron microscopy unit at GSH processed 425 specimens and the immunohistochemical laboratory performed 21 514 tests. During the reporting period 86 adult autopsies were performed. The foetal and perinatal service at GSH examined 26 foetuses and 725 placentas.

The RCCH histopathology service included paediatric patient referrals from Western Cape and Eastern Cape. This laboratory received a total of 3 063 specimens which included paediatric cases and muscle biopsies. A consultative service for muscle biopsies is based at RCCH; during the reporting period 237 muscle biopsies were processed. The electron microscopy unit at RCCH processed 378 specimens. A total of 35 paediatric autopsies were conducted. The laboratory processed 265 non-gynaecological cytology samples and 107 inter-operative frozen sections were performed.

Pathologists and registrars participated in 50 clinicopathological meetings per month held at GSH and the RCCH.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Staff members teach Anatomical Pathology to MBChB undergraduates during semesters 3–5 in an integrated, problem-orientated (case-based) course, with computer-based tutorials and small-group teaching (i.e. museum and mortuary demonstrations). A major revision of the anatomical pathology teaching to MBChB students was undertaken during the Language of Medicine course and additional revisions were made during 2015. New tutorials make use of the upgraded Pathology Learning Centre at the Medical School. A limited number of students gain access to a special study module in anatomical pathology in semester 4, which is currently the best and earliest opportunity of attracting future anatomical pathologists into the discipline.

Third year BSc (occupational therapy) and BSc (physiotherapy) students are taught by anatomical pathology consultants as an integral part of the clinical sciences course for the allied health sciences.

3.2. Postgraduate

There are 12 registrars and three supernumerary registrars. There were three PhD, two MSc and 19 MMed students during the reporting period. Two registrars were successful in the FCPath (Anat) Part 2 examination in 2015/16.

Prof. D Govender, Associate Prof. K Pillay and Associate Prof. R Naidoo continued their lecture and tutorial contribution in the BSc (Honours) cancer module.
### Table 2: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>20</td>
<td>12 (11)</td>
<td>6</td>
</tr>
</tbody>
</table>

() – indicates the number of individuals who sat for exams out of all the final year trainees

### 4. RESEARCH ACTIVITIES

The main research focus is in the field of molecular pathology pertaining to diseases that are common in South Africa and the Western Cape. These include various cancers, in particular those affecting disadvantaged population groups. The major research focus since the establishment of the research laboratory has been breast cancer, gastrointestinal cancer and lymphoma. Cancer research includes studies related to the use of matrix-assisted laser desorption/ionisation time of flight mass spectrometry (MALDI-TOF-MS) to identify proteins and peptides in formalin fixed paraffin embedded cancer tissue. In addition, the use of MALDI imaging mass spectrometry is being investigated to identify proteomic patterns and their distribution directly in tissue. Other research areas include tuberculosis, cardiomyopathy and foetal-alcohol syndrome.

#### 4.1. Research Projects

**Project Title:** Investigation of microRNA expression in thyroid carcinoma among South African patients  
Researchers: N Mokhesi, Associate Prof. R Naidoo, Prof. D Govender, Prof. C Dandara and Associate Prof. I Ross  
Funding: SAMRC

**Project Title:** Expression Levels of microRNA-127 in a cohort of HIV-positive and HIV-negative Diffuse Large B-Cell Lymphoma  
Researchers: C Olivier, Associate Prof. R Naidoo and Prof. D Govender  
Funding: Nautilis Fishing

**Project Title:** Investigating the relationship between miRNA expression and Epithelial Mesenchymal Transition in colorectal cancer  
Researchers: A Jaca, Associate Prof. R Naidoo and Dr M Locketz  
Funding: NRF

**Project Title:** Identifying children with Constitutional Mismatch Repair Deficiency (CMMR-D) syndrome in the expanding Lynch syndrome population in Cape Town  
Researchers: Dr A Wessels, Associate Prof. K Pillay and Prof. R Ramesar  
Funding: NHLS Research Trust

**Project Title:** The role of stem cells and the WNT signalling pathway in renal cell carcinoma  
Researchers: Dr S Madlala, Prof. D Govender and Dr R Roberts  
Funding: NHLS Research Trust

**Project Title:** Differentiating follicular thyroid carcinoma from the follicular variant of papillary thyroid carcinoma  
Researchers: Dr TN Rikhotso, Prof. D Govender and Dr M Otto  
Funding: NHLS Research Trust (pending)

#### 4.2. Grant Funding

- National Research Foundation (NRF)  
- Cancer Association of South Africa (CANSA)  
- NHLS Research Trust.

### 5. RESEARCH OUTPUT

#### 5.1. Journal Publications


### 5.2. Conference Presentations

#### Oral Presentations


6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

- The Registrar Training Programme was recognised for its excellence by the Health Professions Council of South Africa (HPCSA), ranking amongst the top five specialist training programmes in the UCT Faculty of Health Sciences.
- Dr Hue-Tsi Wu was admitted by examination to the Fellowship of the Royal College of Pathologists (FRCPath), United Kingdom.
- Dr M Locketz was the Chair of the Young Pathologist Slide Seminar for the SA IAP annual congress 2015.
- Dr K Pillay was promoted *ad hominem* to Associate Professor.
Chemical Pathology

Head: Prof. David Marais

1. ABOUT THE DIVISION

Chemical Pathology integrates diagnosis, training and research in a platform comprising laboratories in Groote Schuur Hospital (GSH), the Red Cross War Memorial Children’s Hospital (RCCH), and the Falmouth Building at the University of Cape Town. There is an overlap with clinical pathology training and research when the registrars rotate through chemical pathology. The National Health Laboratory Service (NHLS) at C17 in GSH comprises chemical pathology, haematology, immunology, allergology, virology and microbiology. It provides routine diagnostic services, as well as a clinical trials service, to the local teaching hospital, other Western Cape provincial healthcare facilities, and the University of Cape Town Private Academic Hospital. The staff at GSH includes Dr F Omar, Dr P Fortgens and Dr H Vreede whose involvement in other activities is relieved by the part-time appointment of Dr C Hudson. Prof. G van der Watt is based at the Red Cross Hospital laboratory.

The GSH C17 laboratory is a highly automated laboratory, accredited by the South African National Accreditation System (SANAS). Analyses are undertaken on automated instruments using the Cobas 6000 platform, which was successfully installed in the previous year. Specialised tests available include protein and lipoprotein electrophoresis (semi-automated Sebia Minicap and Hydrasys systems), various manual assays and immunoassays. The radioimmunoassays include active renin, aldosterone, 17-hydroxyprogesterone, acetylcholine receptor autoantibody, and 11-deoxycortisol. The molecular laboratory genetic testing repertoire includes metabolic diseases, pharmacogenetics, androgen receptors and some mitochondrial genes. Inherited metabolic disease assays are done at the RCCH laboratory. Gas chromatography with mass spectrometry detection is used. Additional investigation is done in the Falmouth Building, including establishing primary fibroblast lines. These and other samples, especially in lipidology, are investigated further and it is hoped to expand the repertoire of diagnostic tests as the need arises for patient care and research.

Table 3: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>PhD Scientist</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>5</td>
<td>1</td>
<td>15</td>
<td>22</td>
<td>22</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

The laboratories try to solve clinical problems as they arise. The loss of staff as well as financial constraints has limited capacity but fibroblast cultures, spectrophotometric, fluorometric, some radio-isotope and chromatographic studies can still be undertaken. Special investigations include: 7-dehydrocholesterol, pyruvate kinase, blood cyanide and Niemann Pick C disease by filipin staining of fibroblasts. Genetic work-up includes sterol biosynthetic errors (mevalonate kinase deficiency, Smith-Lemli-Opitz syndrome). Dyslipoproteinaemias are worked up by electrophoresis for dysbetalipoproteinaemia and LpX, whereas genetic investigations include the Low-Density Lipoprotein (LDL) receptor, apolipoprotein B100 for binding defects and PCSK9. Apolipoprotein E genetics is also done.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Staff members perform undergraduate and postgraduate teaching in chemical pathology. Registrars rotate between the different sections within the laboratories at the GSH and RCCH hospitals to obtain skills and experience across the discipline. They receive weekly tutorials on basic biochemistry, methodology, management, lipidology, and molecular medicine. Journal discussions in chemical pathology are supplemented with endocrinology seminars, ward attendances, and post-clinic meetings in lipidology. The chemical pathology registrar (Dr M Ndlovu) was joined by a second registrar (Dr E Theron) in the previous year but resigned in September. She was replaced by Dr J Cole. In January Dr J Rusch joined the division as the third registrar. There were no applicants for the intern scientist training that was advertised in the last week of December. Dr Omar is the course convenor for clinical pathology which involved Dr Bosman, Dr Erasmus, Dr Swanepoel and Dr Swart. The toxicology training is undertaken by Dr van der Watt, supported by Dr Fortgens and Dr Omar.

Table 4: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
3.1. Other Training Information

A course in deoxyribonucleic acid (DNA) analysis is offered in the Falmouth Laboratory and proved popular for its third year. Full day courses in lipidoanalysis have been delivered at other centres.

4. RESEARCH ACTIVITIES

The diagnostic work provides information on various disorders in the region and serves as the starting point for research to best serve the country. There is much demand to introduce progress made overseas to this country. Of particular interest is inherited metabolic disease, including mitochondrial disorders. Local experience differs from experience abroad due to the different composition of the local population. Glutaric aciduria type 1 and galactosaeemia are established as founder effects in the black population and there are also indications of mitochondrial disease. Lipidoanalysis expertise and research spans electrophoresis, thin layer chromatography and genetics of familial hypercholesterolaemia and dysbetalipoproteinaemia. The latter subject attracted a visit for collaboration in research from the University of Utrecht.

4.1. Research Units/Study Groups Linked to the Department

Support from the Medical Research Council Cape Heart Group came to an end but provided necessary information on severe disorders of lipoprotein metabolism, which now needs to be translated into practice. The Medical Research Council (MRC) support for research into complement deficiency, undertaken by Dr P Owen, now retired, and Dr A Orren is also nearing completion. This was undertaken in collaboration with the Allergology Division of Internal Medicine under the leadership of Prof. Paul Potter.

4.2. Research Projects

Research projects for MMed qualifications require much time in preparation and ethics approval as well as fund raising, and generally require more than a year for completion.

| Project title | Genetic dyslipidaemias at the Groote Schuur Hospital Lipid Clinic, with an emphasis on familial hypercholesterolaemia and dysbetalipoproteinaemia |
| Researchers | Ms G Solomon, Ms B Ratanjee, Prof. AD Marais and the Lipid Clinic staff |
| Funding | MRC Cape Heart Group |
| Duration | January 2009–March 2015 |

| Project title | Hyperalphalipoproteinaemia due to endothelial lipase (LIPG) deficiency |
| Researchers | Dr J Cole, Dr DM Blackhurst, Prof. AD Marais and lipid clinic collaborators |
| Funding | MRC Cape Heart Group 2012–2014 |
| Duration | January 2013–September 2015 |

| Project title | Direct analysis in real time time-of-flight chromatography and mass spectrometry for identification of metabolic disease |
| Researchers | Dr DM Blackhurst, Mr D Kok, Dr G van der Watt, Dr F Omar, Dr P Fortgens, Ms S Meldau and Prof. AD Marais |
| Funding | Soft funds, awarded NHLS Research Trust in 2015. Transfer is awaited to continue this project |
| Duration | January 2013–December 2016 |

| Project title | Growth factors (including FGF23) and hormonal responses in patients with renal failure |
| Researchers | Dr N Erasmus, Dr F Omar and renal unit collaborators |
| Funding | Project grant to renal unit |
| Duration | 2012–2015 |

| Project title | The N-acetyl transferase 2 gene haplotype and single nucleotide prevalences in the local mixed ancestry population |
| Researchers | Dr C Swart, Dr F Omar and Prof. AD Marais |
| Duration | October 2013–on-going |
4.3. Grant Funding

- The NRF Trust award will support metabolic disease investigation using a novel chromatography technique.

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Book Chapters


5.3. Conference Presentations

**Oral Presentations**

Marais AD. Diagnosis of dyslipidaemias and dyslipoproteinaemias. NHLS PathReD meeting, Johannesburg, 16 April 2015.

Wolmarans KH, Brice BC, Firth JC, Marais AD, Blom DJ. Paediatric Lipidology Presentation, the UCT/Red Cross Hospital Experience. 12th Lassa Congress, Bloemfontein, 16–19 April 2015.


Solomon GAE, Ratanjee BD, Wolmarans KH, Brice BC, Barron JK, Jooste RJ, Blom DJ, Marais AD, Departments of Medicine and Clinical Laboratory Science, University of Cape Town, Groote Schuur Hospital, National Health Laboratory Service and MRC Cape Heart Group. Heterozygous familial hypercholesterolaemia (FH): The Groote Schuur Hospital Lipid Clinic experience. Lipids and Atherosclerosis Society of Southern Africa Congress, Bloemfontein, 19 April 2015.


**Invited speakers**


Prof. Marais was invited to participate in the 17th International Symposium on Atherosclerosis in Amsterdam in May 2015 as well as the PathReD Congress in Johannesburg in April 2015.

A presentation was delivered by Dr F Omar at the 2015 American Association for the Study of Liver Diseases (AASLD) annual meeting in San Francisco.

**Abstracts and/or Poster Presentations**


6. ADDITIONAL INFORMATION

Dr G van der Watt was promoted *ad hominem* to Associate Professor and Dr F Omar was promoted to senior lecturer by the University of Cape Town for the contributions to service, teaching and research. Dr H Vreede took over from Dr J Naiker as head of the Chemical Pathology Expert Committee and also contributed to the development of TrakCare. Dr F Omar and Prof. van der Watt participated in the College of Pathology examinations. Dr P Fortgens participated in the production of the NHLS National Pathology Handbook Working Group.

The constraints on staff and funding during the review period limited research and coverage programmes.
Haematology

Head: Prof. Nicolas Novitzky

1. ABOUT THE DIVISION

Haematology provides a comprehensive diagnostic service to the hospital and offers specialised tests for the diagnosis of haematological malignancies to the Division of Haematology and Department of Radiation Oncology. It receives samples from about 300 external locations, which include the Red Cross War Memorial Children’s Hospital (RCCH), as well as referrals from Tygerberg Hospital, regional laboratories e.g. Worcester, Vredenburg, Paarl, as well as from the Garden Route and the Eastern Cape (George, Knysna, Port Elizabeth and East London). The Molecular Haematology Unit also offers specialised services to clinicians in private practice, including oncologists from Constantiaberg MediClinic, Panorama MediClinic and Melomed. The laboratory continues to maintain its SANAS accreditation, in line with international standards.

Pathologists and registrars participate in lectures, practical lectures and examinations for undergraduate medical students at the University of Cape Town (UCT). Haematopathology, clinical pathology and clinical haematology registrars undergo experiential training in the laboratory under the supervision of the consultant pathologists following the requirements of the College of Pathologists.

The UCT Leukaemia Unit remains an accredited research grouping that continues to provide a home for science students and pathology registrars undertaking research projects in blood diseases.

Table 5: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>PhD Scientist</th>
<th>Technologists</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>1</td>
<td>17</td>
<td>23</td>
<td>23</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

The haematology section of the laboratory has been SANAS accredited for 12 years, and was most recently inspected in March 2016.

This laboratory received samples from about 300 locations, which include those in terms of memorandums of understanding (MoUs): Mowbray Maternity, Vanguard, Mitchell’s Plain and Hanover Park, as well as private laboratories and clinics. More than 100 clinics refer samples for ante-natal or antiretroviral (ARV) testing. Both the molecular service and flow service provide critical specialised testing to state facilities in the Eastern Cape and several private clinics in the Western Cape.

The Molecular Haematology Unit added two new validated tests during the review period, namely the CALR exon 9/MPL exon 10 mutations in myeloproliferative neoplasms test and the TERC and TERT mutations in aplastic anaemia test, adding to the continued growth of this important testing platform. The molecular unit has consistently shown a 20–35% growth over the last seven years:

![Molecular Haematology test](image)
3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The division participates in the teaching of both undergraduate and postgraduate students. Registrars and consultants participate in undergraduate training in MBCHB semester 4, facilitating various modules and focusing on blood disorders.

At the postgraduate level, training is provided to Masters and PhD science students in cell and molecular biology, as well as postgraduate training in haematopathology for medical graduates. Clinical haematology registrars train in the laboratory as part of their specialist certification. In addition, within the Department of Clinical and Laboratory Sciences, three divisions participate in the training for clinical pathology trainees. Experiential teaching and microscope tutorials are offered to registrars in haematopathology. Journal clubs, seminars and group teaching are provided to haematopathology, clinical haematology and general medical registrars.

Interdepartmental meetings are held with academic staff from Tygerberg Hospital and the Red Cross War Memorial Children’s Hospital (RCCH). Faculty members from the division also regularly contribute to the teaching programmes of the human biology section, as well as to the departments of Internal Medicine and Clinical and Laboratory Sciences.

Specific molecular haematology training is also provided to registrars through the Haem/Clin Haem Pathology Registrar Molecular Training Programme, which is offered on a yearly basis for both UCT and Stellenbosch University based registrars. The course consists of a series of 10 lectures and a three day practical session, followed by a short assessment.

In 2015 the Division of Haematology introduced The Biology of Blood module into the Bachelor of Science Medical Honours Course, having identified that there was a lack of basic haematology teaching in the curriculum. The module is aimed at providing students with knowledge on the formation and functions of blood components and describes the structure of organs and tissues of importance to these processes. Students are introduced to the molecular basis of certain haematological malignancies including leukaemias, lymphomas and multiple myeloma, as well as pathophysiology, diagnosis, available treatment and minimal residual disease monitoring. This course involves teaching by both NHLS and UCT staff. In 2017, the second module will be introduced into the programme which will be aimed at explaining to students what is meant by biotechnology, the production and use of recombinant antibodies for therapy, gene therapy, the production and use of transgenic animals, and a brief insight into biotechnology companies. Once these two modules are established into the BSc Medical Honours programme, a full Haematology Honours programme will be introduced into the existing BSc Medical Honours course.

Table 6: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th>Qualification/Course</th>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFPath and Cert Clin Haem</td>
<td>6*</td>
<td>4*</td>
<td>3*</td>
<td>75%</td>
</tr>
<tr>
<td>PhD</td>
<td>1</td>
<td>1</td>
<td>Awaiting thesis review</td>
<td></td>
</tr>
<tr>
<td>BSc Hons module: Biology of Blood</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>100%</td>
</tr>
<tr>
<td>Haem/Clin Haem Registrar Molecular Training Programme</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Includes one Clinical Haematology Registrar

Trainees/Registrars

- Dr Ruth Gopie passed part I Haematology, 2015
- Dr Celeste Swart passed MMed Clin Path part I Haematology, 2015
- Dr Michelle Bosman passed MMed part I Haematology Clin Path, March 2016
- Kirsty Wienand submitted her PhD, December 2015.

4. RESEARCH ACTIVITIES

The UCT Leukaemia Unit was established more than ten years ago within the clinical and laboratory divisions of haematology, to foster research into haematological malignancies as a seamless grouping of bench-to-bedside researchers. The unit has been reviewed twice and approved by the UCT University Research Committee (URC). It will continue focusing on the areas of haemopoietic stem cell biology and stem cell transplant immunology. The research laboratory is well equipped to support undergraduate and postgraduate pathology and science students. Dr S Mowla and Dr K Shires have continued expanding the molecular and cellular research interests in haematological malignancies, normal and malignant haematopoiesis, detection of minimal residual disease in patients with leukaemia, cellular therapies and haematopoietic stem cell transplantation. In addition, in collaboration with Prof. A Wonkam from Human Genetics, the molecular mechanisms that modify the expression of HbF in patients with sickle cell anaemia are being studied.
There is a solid collaboration with the clinical service that resulted in combined projects in the field of plasma cell disorders, lymphoproliferative disorders and acute leukaemias. Registrars are completing mini dissertations and studying the clinico-pathological correlation in HIV-associated malignancies.

Dr S Mowla’s research is aimed at understanding the link between HIV infection and the development of HIV/AIDS-related non-Hodgkin’s lymphomas (NHLs) such as diffuse Large B-cell Lymphoma and Burkitt’s Lymphoma. The pathogenesis of HIV-associated NHLs involves a complex interplay of biological factors, including the emerging role of HIV encoded proteins, viral induced microRNAs and other oncogenic signalling pathways. Current projects include characterising the effect observed of HIV proteins Nef and Tat on the expression of oncogenic c-MYC and the DNA modifying enzyme activation-induced cytidine deaminase, two key cellular factors involved in the pathogenesis of lymphomas. The role that microRNAs may play in the oncogenic process is also being investigated.

Dr K Shires’ research focuses on the development of novel assays to detect and monitor minimal residual disease in haematological malignancies, specifically focusing on multiple myeloma. This research involves the identification of unique aberrant molecular signatures in multiple myeloma, advanced cell biology techniques to understand the link of markers to pathogenesis and the development of sensitive detection strategies including both multiplex real-time PCR and flow cytometric approaches.

4.1. Research Units/Study groups Linked to the Department

The UCT Leukaemia Unit is a URC-accredited research grouping with a focus on haematological malignancies and stem cell transplantation immunology. MSc and PhD students are trained in cellular and molecular biology techniques while participating in research projects. Members include N Novitzky, K Shires, S Mowla, J Opie, E Beltchev, M Ntobongwana, L Phillips, N Mashigo, C du Toit and E Verburgh.

4.2. Research Projects

**MMed Project title:** HIV-associated Hodgkin lymphoma at GSH, Western Cape  
**Principal investigator:** Dr L Swart  
**Supervisor:** Dr J Opie, Co-supervisor: Prof. N Novitzky  
**Expected end date:** December 2016

**MMed Project title:** Burkitt lymphoma/leukaemia at GSH, Western Cape  
**Principal investigator:** Dr A Koller  
**Supervisor:** Dr J Opie, Co-supervisor: Prof. N Novitzky  
**Expected end date:** December 2016

**MMed Project title:** Paediatric acute myeloid leukaemia (AML): The Red Cross War Memorial Children’s Hospital experience  
**Principal investigator:** Dr R Freeks  
**Supervisor:** Prof. N Novitzky  
**Expected end date:** December 2016

**MMed Project title:** Establishing locally derived reference intervals for full blood count parameters and white cell differential counts in the Western Cape region of South Africa  
**Principal investigator:** Dr A De Koker  
**Supervisor:** Dr J Opie, Co-supervisor: Dr A Bird (WPBTS)  
**Expected end date:** December 2017

**MMed Project title:** Diagnostic molecular markers in South African Ph chromosome negative Myeloproliferative Neoplasms  
**Student:** Dr R Gopie  
**Supervisor:** Dr K Shires  
**Expected end date:** December 2017

**PhD Project title:** The use of MAGE C1 to determine the malignant cell phenotype in Multiple Myeloma  
**Student:** K Wienand  
**Supervisor:** Dr K Shires  
**Submitted:** December 2015
Project title: Immune reconstitution following allogeneic stem cell transplantation
Researchers: N Novitzky, G Davidson and R Abdullah

Project title: Pathogenesis of HIV-associated NHLs. Characterising the effect of HIV proteins Nef and Tat on the expression of oncogenic c-MYC and the DNA modifying enzyme activation-induced cytidine deaminase
Researcher: S Mowla

4.3. Grant Funding
- Funding obtained during this period: NRF and MRC
- Funding obtained by Dr Karen Shires during this period only: NHLS Research Trust, MRC, AstraZeneca Research Trust and University of Cape Town Equipment Fund.

5. RESEARCH OUTPUTS

5.1. Journal Publications


5.2. Conference Presentations

Oral presentations
Wienand K, Shires K (2015). The use of Mage C1 and flow cytometry to determine and monitor the malignant cell type in multiple myeloma. 20th World Congress on Advances in Oncology and 18th International Symposium on Molecular Medicine, Athens, Greece, October 2015.

Poster presentations
Novitzky N, Pillay D, Thomas V, Hendricks M, Davidson A. Alemtuzumab is effective for the prevention of GvHD in patients with Fanconi’s Anaemia undergoing HLA identical stem cell transplantation. SASCeTS meeting, Johannesburg, 13–14 November 2015.


5.3. Plenary Talks
Prof. Nicolas Novitzky:
- Invited speaker at the opening of the Igazi Paediatric Oncology Unit at the Port Elizabeth Provincial Hospital, 01 April 2015.
- Invited speaker at the 5th EBM Training Course. Title: Stem cell transplantation in developing countries: Challenges and special needs. Marrakech, Morocco, May 2015.
- Invited speaker for the International Society of Paediatric Oncology (SIOP) meeting. Title: Stem cell transplantation for sickle cell anaemia. Cape Town, 06 October 2015.
• Invited speaker at the AMGEN DR Scientific Retreat. Title: Management of Refractory ITP. Johannesburg, 17–18 October 2015.
• Invited speaker for the UCT Paediatric Refresher course. Title: Transplantation in symptomatic haemoglobin disorders. Cape Town, 11 February 2016.

Dr Jessica Opie:
• Invited speaker for the UCT FCP Refresher course. Title: Haematology for the FCP Part I examination. Cape Town, May 2015.
• Invited speaker for oral plenary presentation, Indian Ocean Rim Laboratory Haematology Congress. Title: Coagulation Conundrums in HIV. Perth, Australia, October 2015.

Dr Karen Shires:

6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

Dr K Shires was invited to attend the AstraZeneca Research Trust awards evening in March 2016, in recognition of a successful funding application.

7. ADDITIONAL INFORMATION

Table 7: Test volumes April 2015–February 2016

<table>
<thead>
<tr>
<th>Test type</th>
<th>Number of tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full blood counts, differentials and fluid cell counts</td>
<td>277 538</td>
</tr>
<tr>
<td>Reticulocyte counts</td>
<td>1 926</td>
</tr>
<tr>
<td>ESR</td>
<td>8 026</td>
</tr>
<tr>
<td>Malaria</td>
<td>376</td>
</tr>
<tr>
<td>Routine coagulation tests</td>
<td>57 015</td>
</tr>
<tr>
<td>Blood grouping tests and antibody screens</td>
<td>35 892</td>
</tr>
</tbody>
</table>
Human Genetics

Head: Prof. Raj Ramesar

1. ABOUT THE DIVISION

The Division of Human Genetics has a strong clinical presence in most of the major disciplines (medicine, paediatrics, obstetrics/gynaecology, oncology, surgery and psychiatry). This has led to research projects based on the burdens of disease in each of these disciplines, which usually have the objective of identifying the biological basis of the disease. The research findings are translated into the molecular and cytogenetic tests which are offered through the National Health Laboratory Service (NHLS) molecular and cytogenetic diagnostic laboratories, located in the business unit at Groote Schuur Hospital (GSH). These tests are useful for accuracy of diagnosis (i.e. molecular for heterogeneous conditions), as well as for predictive testing, where this may be indicated e.g. the extensive colorectal cancer project, with the Department of Surgery.

The division’s strong research programme is underpinned by training of BSc(Med)(Hons), MSc and PhD students. At any given time there are about 40 postgraduates in the division (more than 30 of whom are Masters, PhDs and post-doctorates). The division strives to be at the cutting edge of research, which currently involves microarray-based genome-wide association studies, as well as next-generation sequencing for some of the common chronic disorders which form the greater burden of disease in South Africa. Recognising the promise of genetics and genomics in medicine, the department also hosts a Masters level training programme in genetic counselling.

Table 8: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>PhD Scientist</th>
<th>MSc Scientist</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
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</thead>
<tbody>
<tr>
<td>Total</td>
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<td>6</td>
<td>3</td>
<td>14</td>
<td>16</td>
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</tbody>
</table>

2. DIAGNOSTIC SERVICE

The human genetics diagnostic laboratories are based in the NHLS Business Unit at Groote Schuur Hospital, and serve as a national referral centre for a range of molecular and cytogenetic diagnostic tests, with the main focus for 2015/16 being on clients. Several systems were improved within the laboratory to streamline processes and increase the quality of results. Some of these included appointing supervisors to the different benches, who are responsible for turnaround time, changes in processes, updating standard operating procedures (SOPs) and training.

The division won second prize in the NHLS National Annual Awards in the category Best Academic Laboratory. This prize money has been put towards team building. SANAS accreditation was renewed following the audit without any non-conformances. The division also performed well in its external quality control programme, which covers all types of samples and testing procedures – the division achieved 100% for all chromosome analysis and fluorescent in situ hybridisation (FISH) challenges. Six members of staff attended the Southern African Society for Human Genetics (SASHG) 2015 with five poster presentations. Staff went on various training courses offered by the NHLS. Staff were also involved in the training of Honours students, intern medical technologists, experiential students, registrars, intern scientists, scientists, medical students, etc. The goal for 2016/17 is to investigate the feasibility of microarray technologies in the diagnostic environment. This will follow from a research study which forms part of an MSc project.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The division is the headquarters of the African Society of Human Genetics, which has been pivotal to the emergence of the Human Heredity and Health: Africa (H3Africa) research programme (www.H3Africa.org) which is funded by the National Institutes of Health (NIH, USA) and the Wellcome Trust (UK). This programme, apart from developing an impressive network of well-supported genomics and human health projects on the continent, has the objective of large-scale education and training, pertaining to genomics and bioinformatics. Prof. Raj Ramesar is involved with three of the projects, (i) as co-Principal Investigator on the Genetics of Schizophrenia in the Xhosa people, (ii) as co-investigator on the Genetics of Rheumatic Heart Disease, and (iii) The Burden, spectrum and etiology of type 2 diabetes in sub-Saharan Africa. Prof. Ambroise Wonkam is Principal Investigator on the project Exploring Perspectives on Genomics and Sickle Cell Public Health Interventions.

In the 2013/14 the MSc in Genetic Counselling was re-instated, taking into account the need to produce cadres of health professionals who are aligned with the anticipated outcome of research in African genomics and the implementation of genetics and genomics in the health care programmes of the continent.
The division houses the African Genome Education Institute (AGEI), which is an NGO whose task it is to make science accessible to the public. In this regard the AGEI raises funds and supports two major activities: (i) the Darwin Seminars, which are quarterly evening seminars for the public in the areas of genomics, anthropology and evolution, and which attract a full house of 200–250 attendees, and (ii) the Teaching Biology Project (TBP) [http://www.teachingbiologyproject.org.za], which is a programme aimed at teachers from previously disadvantaged high schools. The programme hosts about 80 teachers every quarter, in a week long residential programme at Bishops High School (Rondebosch), during school recess, for a programme of lectures and workshops intensively covering material in and related to their curriculum. This is going to expand to a Teaching Sciences Programme (TSP) and Teaching Mathematics Programme (TMP) in the near future.

Table 9: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>40</td>
<td>15</td>
<td>15</td>
<td>100%</td>
</tr>
</tbody>
</table>

4. **RESEARCH ACTIVITIES**

The division has contributed significantly to the understanding of the molecular genetic basis of a wide range of hereditary disorders in South Africa. This research, which is usually done in the UCT laboratories and is funded by e.g. the resident MRC Human Genetics Research Unit, or the lay support group, Retina South Africa, has provided the basis for sustainable diagnostic services in the NHLS laboratory at GSH.

The research niches which have been explored because of a high level of clinical expertise and interest, include neurodegenerative conditions (this includes Huntington disease and cerebellar ataxias); genetics of retinal degenerative diseases, genetics of colorectal cancers; pharmacogenomics; genetics of bipolar disorder and schizophrenia, and more recently the genetics of sickle cell disease and thalassemia.

The current niche being explored is the analysis of African genomes using state-of-the-art genome-wide analysis in order to understand the predisposition to common chronic disorders such as diabetes and neuropsychiatric conditions – notably bipolar disorder and schizophrenia. Each of the projects is designed at Masters, and notably at PhD level. While aimed at understanding the basis of diseases, the objective is also to produce diagnostic testing of relevance to the clinic. A major area of exploration currently is the genetic dissection of severe adverse drug reactions for common conditions. Two of the notable diseases/drugs include: (i) cancer and cisplatin (with hearing impairment as the adverse event), and (ii) cancer and anthracycline (where the adverse drug reaction is cardiotoxicity). A range of pharmacogenetic projects pertinent to antiretrovirals is being conducted by Prof. Collet Dandara.

4.1. Research Units/Study Groups linked to the Department

**Research Unit:** MRC Human Genetics Research Unit  
**Director:** Prof. Raj Ramesar  
**Short description:** The goal of the unit is to undertake research into the genetic basis of diseases important in South Africa, while at the same time focusing on creating genomics-research capacity for the country.

**Research Programme:** PharmacoGenomics International (pGENI)  
**Regional Representative:** Prof. Raj Ramesar  
**Short description:** The objective of this programme is to contribute pharmacogenomic data of the local populations to this international research initiative, so that the genomic variants responsible for the metabolism and processing of drugs are taken into account in future drug designs, as well as for present design of essential drug lists for emerging countries. This would be for the purpose of optimising effectiveness of prescribed drugs, as well as minimising adverse drug events.

4.2. Research Projects

**Project Title:** Genetics of inherited retinal degenerative disorders  
**Principal Investigator:** Prof. Raj Ramesar, Prof. Jacquie Greenberg  
**Funding:** Retina South Africa  
**Duration:** 1994–Continuing

**Project Title:** Genetics of neurodegenerative disorders and stem cells  
**Principal Investigator:** Prof. Jacquie Greenberg  
**Funding:** National Research Foundation  
**Start Date:** 2000
<table>
<thead>
<tr>
<th>Project Title</th>
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<tbody>
<tr>
<td>Principal Investigator</td>
<td>Prof. Raj Ramesar</td>
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<tr>
<td>Funding</td>
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<tr>
<td>Start Date</td>
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<table>
<thead>
<tr>
<th>Project Title</th>
<th>Genetics of schizophrenia in the Xhosa people</th>
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</thead>
<tbody>
<tr>
<td>Co-principal Investigator</td>
<td>Prof. Raj Ramesar</td>
</tr>
<tr>
<td>Principal Investigator</td>
<td>Prof. Dan Stein, UCT: Psychiatry</td>
</tr>
<tr>
<td>Funding</td>
<td>National Institute of Mental Health, NIH, USA</td>
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<table>
<thead>
<tr>
<th>Project Title</th>
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<tr>
<td>Principal Investigator</td>
<td>Prof. C Dandara</td>
</tr>
<tr>
<td>Funding</td>
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</tr>
<tr>
<td>Start Date</td>
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<table>
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<tr>
<th>Project Title</th>
<th>Exploring perspectives of genomics of sickle cell public health interventions</th>
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<tr>
<td>Principal Investigator</td>
<td>Prof. Ambroise Wonkam</td>
</tr>
<tr>
<td>Funding</td>
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<table>
<thead>
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<th>Genetics of colorectal cancer</th>
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<tr>
<td>Principal Investigator</td>
<td>Prof. Raj Ramesar</td>
</tr>
<tr>
<td>Collaborator</td>
<td>Prof. Paul Goldberg, Surgery, UCT/GSH</td>
</tr>
<tr>
<td>Funding</td>
<td>CANSA and the MRC Human Genetics Research Unit</td>
</tr>
<tr>
<td>Start Date</td>
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</table>

### 4.3. Grant Funding
- Medical Research Council, SA
- National Institutes of Mental Health, NIH, USA
- National Institutes of Health, USA
- National Research Foundation
- Retina South Africa

### 5. RESEARCH OUTPUT

#### 5.1. Journal Publications


5.2. Research Translated to Diagnostic Technology, Policy or Service

Genetics of colorectal cancers, neurodegenerative disorders and muscular dystrophies are currently implemented into the NHLS diagnostic laboratories at the Groote Schuur Business Unit.
Immunology

Head: Prof. Clive Gray

1. ABOUT THE DIVISION

The Division of Immunology at the University of Cape Town/GSH, NHLS Coastal Branch, is involved with a range of activities from histocompatibility to clinical immunology diagnostic testing to identify the mechanisms of infectious disease immunity and translational clinical research on human immunodeficiency virus (HIV) and tuberculosis (TB). The Laboratory for Tissue Immunology (LTI) is responsible for human leukocyte antigen (HLA) class I and class II typing for solid organ and bone marrow/stem cell matching. This is the only laboratory in South Africa, and in Africa, to have European Federation of Immunogenetics (EFI) accreditation to perform HLA typing, cross-matching and anti-HLA antibody identification. The Clinical Immunology and Allergy Laboratory performs routine diagnostic testing for autoimmune diseases and identification of allergens causing adverse reactions ranging from minor symptoms to life threatening anaphylaxis. Basic research in the allergy section has focused on T cell cytokine responses to allergens, as well as the application of novel assays to identify sensitivity profiles, which complements the diagnostic laboratory. Basic mechanisms of TB disease are being investigated in the academic laboratories, especially looking at novel therapeutic interventions. HIV immunology research is focused on mucosal immunity in neonates and in adolescent males to understand aspects of host susceptibility to infection. There is a teaching component in the medical undergraduate syllabus providing immunology lectures from years 1–3 in the MBChB undergraduate syllabus. Online learning through Immunopaedia (www.immunopaedia.org.za) supplies added material for undergraduates and postgraduates. Postgraduate immunology through the BSc Honours in Infectious Disease and Immunology programme and Research Immunology cater for more advanced basic and clinical immunology.

Table 10: Total number of NHLS staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>PhD Scientist</th>
<th>BSc Honours</th>
<th>Technologists</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
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<td>5</td>
<td>8</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

2.1. Laboratory for Tissue Immunology

The Laboratory for Tissue Immunology, Division of Immunology is the only EFI accredited facility in Africa and successfully passed inspection in November 2015 as part of the ongoing EFI accreditation. This enables the laboratory to confirm and report HLA matching between donors and unrelated recipients at class I and II loci at high resolution who are awaiting bone marrow transplants. The laboratory works closely with the South African Bone Marrow Registry. The laboratory also offers histocompatibility testing and performs HLA class I and II antibody identification along with single antigen antibody assays for both living-related and cadaveric donor solid organ transplantation; molecular HLA typing at low and high resolution (class II only) for bone marrow and solid organ transplants and for disease associations. Over the past year, over 6 500 HLA typings have been performed. There are approximately 400 patients on the active Renal Waiting List and about 40 candidates awaiting other organs. The following table shows the number of tests performed over the past year:

Table 11: Histocompatibility Statistics

| Renal Recipients HLA Typed | 421 |
| Renal Donors HLA Typed | 388 |
| Cardiacs, Liver, Soft Tissue HLA typed | 45 |
| Cadaver Donors | 38 |
| Bone Marrow Patients | 457 |
| Bone Marrow Donors | 797 |
| Unrelated Bone Marrow Donors | 180 |
| DNA Low Resolution (2-digit) | 8 430 |
| DNA High Resolution (4-digit) | 1 233 |
| HLA-B*27 | 239 |
| HLA-B15* | 78 |
| Class I ID Screen + Single Antibody Assay | 1 792 |
| Class II ID Screen + Single Antibody Assay | 1 306 |
2.2. Clinical Immunology and Allergy

Over the past year, 23,832 diagnostic tests were performed in the Clinical Immunology and Allergy Laboratory. Of these assays, 18,451 were for the detection of autoantibodies, which aid clinicians in the diagnosis of autoimmune diseases and 5,381 for allergy investigations.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Table 12: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>31</td>
<td>10</td>
<td>6</td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

- Investigating TNFRp75 in acute M. tuberculosis infection: contribution of neutrophils and alveolar macrophages in host immune protection has been initiated and is ongoing.
- The project investigating the interaction between neurons and T cells and the potential mechanisms that influence host immunity against CNS-TB has been started and is ongoing.
- The toxicity profile of earlier reported novel phenothiazines as anti-tuberculosis compounds has been started and is being investigated.
- The study on the role of neuron specific TNF in tuberculosis has been completed and the data published.
- A study on the role of Bacillus Calmette–Guérin (BCG) vaccination in malaria infection has been initiated and is ongoing.
- A study investigating the interaction of dendritic cells and T cells in CNS-TB have been started and is ongoing.
- A study entitled A Novel Dual Animal Pre-clinical Platform: Accelerating HIV Vaccine Product Development in South Africa is ongoing.
- Factors affecting HIV susceptibility in the male adolescent genital tract. Findings show that asymptomatic sexually transmitted infections cause immune activation in the inner foreskins before medical male circumcision.
- Innate, Adaptive and Mucosal Immune Responses in HIV-1 Exposed Uninfected Infants: A Human Model to Understand Correlates of Immune Protection – New-born infants are being recruited from HIV-infected mothers to identify factors in breast milk that can inhibit HIV in vitro and to identify whether exclusive breast-feeding or mixed feeding impacts on infant immunity by measuring immunogenicity to polio, BCG and rotavirus vaccines.

4.1. Research Units/Study Groups Linked to the Department

Prof. Gordon Brown, Aberdeen University, Scotland. Collaborator on The role of C-type Rectin receptor ClecF8/Clec4D in host immunity against M. tuberculosis.

Dr Gerald Chege, Virology, UCT. Collaborator on A Novel Dual Animal Pre-clinical Platform: Accelerating HIV Vaccine Product Development in South Africa.

Dr Anwar Jardine, Department Chemistry, UCT. Collaborator on Evaluating the toxicity and anti-mycobacterial efficacy of 10H-phenothiazine N-propylsulphonate derivatives, C3 and C4 in a small animal model of tuberculosis.

Prof. Dirk Lang, Department Human Biology, UCT. Collaborator on Neuron T cell interaction during CNS-TB.

Prof. Dale Greiner, University of Massachusetts. Collaborator on A novel dual animal pre-clinical platform: Accelerating HIV vaccine product development in South Africa.

Prof. Michael Brehm, University of Massachusetts. Collaborator on A novel dual animal pre-clinical platform: Accelerating HIV vaccine product development in South Africa.

Prof. S Magez, Vrye University, Belgium. Collaborator on Assessment for vaccine efficacy for malaria and tuberculosis in a co-infection setting relevant for disease endemic sub-Saharan African regions.

Prof. VFJ Quesniaux, Pro B Ryffel, CNRS, France. Collaborator on Understanding TNF/TNFR and IL-1/IL-1R associated mechanisms of host pathogen relationships and innate and adaptive immune responses to tuberculosis.

Prof. Anna-Lise Williamson, Virology, UCT/NHLS. Collaborator on Novel HIV vaccine candidates for South Africa.
### 4.2. Research Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Co-Principal Investigator</th>
<th>Funding</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Innate, adaptive and mucosal immune responses in HIV-1 exposed uninfected</td>
<td>Clive Gray</td>
<td>Canadian Institutes of Health Research, 01044-000</td>
<td>2011–2018</td>
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<tr>
<td>Infants: A human model to understand correlates of immune protection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ART and risk of preterm delivery in a rural high HIV prevalence area</td>
<td>Clive Gray</td>
<td>National Institutes of Health, 1R01HD080385-01</td>
<td>2015–2019</td>
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<tr>
<td>The impact of maternal HIV exposure on infant immunity and responses to vaccination</td>
<td>Clive Gray</td>
<td>National Research Foundation Grant, #92770</td>
<td>2014–2016</td>
</tr>
<tr>
<td>Incentive funding for rated researchers</td>
<td>Clive Gray</td>
<td>National Research Foundation (South Africa)</td>
<td>2016–2021</td>
</tr>
<tr>
<td>Dendritic cells in CNS-TB</td>
<td>Muazzam Jacobs</td>
<td>National Research Foundation (South Africa)</td>
<td>2015–2017</td>
</tr>
</tbody>
</table>
Project Title: Neurotuberculosis – Training for the future
Principal Investigator: JJ Jacobs
Funding: National Research Foundation (South Africa)
Duration: 2015–2017

Project Title: Mycobacterium tuberculosis infection of neurons and its immune regulatory potential on T cells
Principal Investigator: Muazzam Jacobs
Funding: Medical Research Council

Project Title: Understanding TNF/TNFR and IL-1/IL-1R associated mechanisms of host pathogen relationships and innate and adaptive immune responses to tuberculosis
Principal Investigator: Muazzam Jacobs
Funding: National Research Foundation (South Africa)
Duration: 2013–2017

Project Title: Incentive funding for rated researchers
Researcher: Muazzam Jacobs
Funding: National Research Foundation (South Africa)
Duration: 2013–2017

Project Title: Evaluating the toxicity and anti-mycobacterial efficacy of 10H-phenothiazine N-propylsulphonate derivatives, C3 and C4 in a small animal model of tuberculosis
Principal Investigator: Muazzam Jacobs
Funding: University of Cape Town: RCIPS Concept Fund C12-004
Duration: 2013

Project Title: HIV-TB in humanised mice
Principal Investigator: Muazzam Jacobs
Funding: National Research Foundation (South Africa)
Duration: 2012–2014

Project Title: Investigating the role of brain neuronal-derived tumour necrosis factor in protective immunity against M. tuberculosis infection
Principal Investigator/Primary applicant: Muazzam Jacobs
Funding: Medical Research Council (South Africa)
Duration: 2011–2013

Project Title: Assessment for vaccine efficacy for malaria and tuberculosis in a co-infection setting relevant for disease endemic sub-Saharan African regions
Co-Principal Investigator: Muazzam Jacobs
Funding: National Research Foundation (South Africa)
Duration: 2011–2013

4.3. Grant Funding
National Research Foundation (South Africa); Medical Research Council (South Africa); University of Cape Town; Research Contracts and Intellectual Property Services (RCIPS) Concept Fund; National Health Laboratory Service; Canadian Institutes of Health Research; National Institute of Health; European and Developing Countries Clinical Trials Partnership (EDCTP) Strategic Primer; National Institutes of Health.
5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

Invited speaker: Muazzam Jacobs – TNF-TNFR signalling in host immune responses against tuberculosis; Sun Yat Sen University, China. 22 June 2015.


Poster Presentations


Medical Microbiology

Head: Prof. Mark Nicol

1. ABOUT THE DIVISION

The Division of Medical Microbiology (www.medmicro.uct.ac.za) encompasses a tertiary diagnostic microbiology service, provided by Groote Schuur Hospital (GSH), a research programme based at the hospital, as well as at the Health Sciences Campus and a postgraduate training programme.

The aim is to conduct research that is relevant to the infectious disease burden in South Africa, particularly tuberculosis, pneumonia and drug-resistant pathogens and including a specific focus on identifying cost-effective and appropriate diagnostic solutions for important infectious diseases in South Africa.

The division participates in the teaching of undergraduate medical students and has been spearheading an initiative to develop e-learning tools for pathology. The division supports a small training programme for registrars in medical microbiology, clinical pathology and infectious diseases, and has an MSc and PhD postgraduate programme. The division also contributes to the training of medical technologists and has an intern medical scientist training programme registered with the HPCSA.

Table 13: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Profession</th>
<th>Pathologist</th>
<th>PhD Scientist</th>
<th>Technologists</th>
<th>Support</th>
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<td>5</td>
<td>23</td>
<td>5</td>
<td>35</td>
<td>36</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The NHLS GHS Microbiology Laboratory continues to provide high quality diagnostic services to eight hospitals, as well as to surrounding clinics, processing an average of 40 000 tests a month. This includes a full range of diagnostic services for tuberculosis, including Xpert MTB/RIF, culture, genotypic and phenotypic drug susceptibility testing, as well as molecular testing for resolution of discrepant rifampicin susceptibility results. The laboratory acts as a referral centre for George, providing both diagnostic testing for challenging isolates, as well as consultative support and advice.

Clinical liaison services are provided to clinicians from the Western and Eastern Cape and intensive care unit and antibiotic stewardship ward rounds are attended on a weekly basis in various hospitals. Hospital and provincial management are assisted with infection control matters and advice on the appropriate use of laboratory services.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The division is actively involved in teaching undergraduate medical students, as well as in ongoing curriculum design and review. A particular focus has been the development of an e-learning approach to support and strengthen undergraduate teaching. Teaching activities include lectures, tutorials and practicals. Members contribute to the intercalated molecular medicine course, offered to 3rd year medical students to prepare them for BSc (Hons) and a future research career. The division has an active postgraduate programme, including training at Masters and doctoral level. The division contributes microbiology modules to the Honours programme, as well as to the MSc in Forensic Science.

Table 14: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Qualification</th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
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</table>
4. RESEARCH ACTIVITIES

Research within the department is focused on infectious diseases in South Africa, particularly on the epidemiology, pathogenesis and microbiological diagnosis of such diseases. Research niches include childhood pneumonia; the origin and evolution of the human microbiome in early childhood; the impact of the microbiome on child health; novel diagnostics for meningitis and leptospirosis; the development and assessment of novel diagnostics for tuberculosis, including point-of-care tests; and drug discovery for *Mycobacterium tuberculosis*.

4.1. Research Units/Study Groups linked to the Department

**MRC/NHLS/UCT Molecular Mycobacteriology Research Unit (MMRU)**

*Director: Prof. V Mizrahi*

The MMRU has positioned itself at the front end of TB drug discovery, with a focus on investigating those aspects of *M. tuberculosis* physiology of greatest relevance to TB drug discovery, namely metabolic vulnerability, drug permeation, resistance, persistence and tolerance. In addition, in close collaboration with local and international partners, a platform has been established for routine compound screening against *M. tuberculosis* under a variety of growth conditions *in vitro*. The unit comprises senior scientists, postdoctoral fellows, and postgraduate students, and participates in several major TB drug discovery consortia. Since 2011, the MMRU has been based within the Division of Medical Microbiology and the Institute of Infectious Disease and Molecular Medicine (IDM) where it constitutes the UCT node of the DST/NRF Centre of Excellence for Biomedical TB Research.

4.2. Research Projects

**Project Title:** TB-CHILD: Tuberculosis Collaborating Centre for Child Health  
*Principal Investigators:* Prof. M Nicol (NHLS/UCT), Prof. H Zar (UCT)  
*Funding:* Medical Research Council  
*Short Description:* This consortium aims to evaluate a range of novel molecular and immunological tests for their performance in the diagnosis of tuberculosis in children.

**Project Title:** REPORT-TB: Evaluation of the accuracy of Xpert Ultra for the diagnosis of tuberculosis in children  
*Principal Investigators:* Prof. M Nicol (NHLS/UCT), Prof. H Zar (UCT), Prof. J. Starke (Baylor College of Medicine)  
*Funding:* NIH (USA)  
*Short Description:* This study aims to evaluate the accuracy of Xpert Ultra for the diagnosis of tuberculosis in children.

**Project Title:** Optimising health systems to improve delivery of decentralised care for patients with drug resistant tuberculosis  
*Principal Investigators:* Prof. M Nicol (NHLS/UCT), Dr H Cox (UCT), Prof. M Moshabela (Africa Centre), Dr K Kielman (Queen Margaret), Prof. K Milisana (UKZN), Prof. A Grant (LSHTM)  
*Funding:* UK MRC/Wellcome Trust  
*Short Description:* This study looks at health system factors associated with successful implementation of decentralised care for patients with MDR-TB.

**Project Title:** The Drakenstein Child Health Study  
*Principal Investigators:* Prof. M Nicol (NHLS/UCT), Prof. H Zar (UCT), Dr M Kaba (UCT), Dr E du Toit (UCT), Dr L Ah Tow-Edries (UCT), Dr L Robberts (NHLS/UCT), Dr V Allen (UCT), Dr C Moodley, Mr F Dube (UCT), Mrs S Abdulgader (UCT), Ms F Patel (UCT), Mrs S Africa (UCT), Mrs S Claassen-Weitz (UCT), Ms M Ngwarai (UCT)  
*Funding:* Bill and Melinda Gates Foundation, Carnegie Foundation, Wellcome Trust  
*Short Description:* This study is a collaboration between the department of Paediatrics and Child Health, and Medical Microbiology at UCT. From the Drakenstein sub-district in the Western Cape, 1 139 mother-infant pairs were enrolled and are being followed up over the first five years of life. The primary aim of the study is to evaluate the aetiology and risk factors for the development of pneumonia and other lung illness in the first two years of life.

**Project Title:** The effect of early childhood exposure to environmental organisms on the development of wheezing in young children  
*Principal Investigators:* Prof. M Nicol (NHLS/UCT), Dr M Kaba (UCT), Dr L Ah Tow (UCT), Mrs M Duyver (UCT), Dr E du Toit (UCT), Prof. H Zar (UCT)  
*Funding:* Bill and Melinda Gates Foundation, Carnegie Foundation, Wellcome Trust
Short Description: The aim is to examine whether high levels of exposure to environmental organisms (fungi, bacteria) influence the onset of childhood wheezing. Home dust samples are being collected antenatally, at six and 12 months, using electrostatic dust collectors and evaluated by next-generation sequencing to determine bacterial and fungal diversity.

Project Title: The stool microbiota and its relationship to allergy and wheezing
Principal Investigators: Prof. M Nicol (NHLS/UCT), Dr M Kaba (UCT), Mrs S Claassen-Weitz (UCT), Prof. H Zar (UCT), Ms M Ngwarai (UCT)
Funding: Bill and Melinda Gates Foundation, Carnegie Foundation, Wellcome Trust
Short Description: The aim is to identify the diversity and main components of the stool microbiota of infants and mothers over a two-year period at one-month intervals. This information will be related to the development of wheezing illness. Stool samples are being collected from infants and mothers at birth and monthly thereafter until two years of age. DNA will be extracted and the diversity will be measured using a next-generation sequencing approach.

Project Title: Nasopharyngeal microbiome and pneumonia in young children from Drakenstein sub-district, South Africa
Principal Investigators: Prof. M Nicol (NHLS/UCT), Prof. H Zar (UCT), Mrs S Claassen-Weitz (UCT), Dr E du Toit (UCT)
Funding: Bill and Melinda Gates Foundation, Carnegie Foundation, NIH
Short Description: The aim of this study is (i) to investigate longitudinally the nasopharyngeal microbiome of a birth cohort of 500 infants (sampled two-weekly over a two-year period), (ii) to determine the nasopharyngeal pathogens associated with near-term progression to pneumonia in childhood during the first two years of life, and (iii) to study the microbial diversity in infants sampled using metagenomic approaches.

Project Title: BREATHe study
Principal Investigators: Prof. M Nicol (NHLS/UCT), Prof. R Ferrand (LSHTM), Prof. J Oyvind (Tromso), Prof. L Corbett (LSHTM)
Funding: GLOBVAC
Short Description: To conduct a randomised controlled trial of azithromycin for HIV-infected adolescents with chronic lung disease.

Project Title: The epidemiology and genetic characteristics of extended-spectrum beta-lactamase and carbapenemase-producing bacteria in apparently healthy children, South Africa
Principal Investigators: Prof. M Nicol (NHLS/UCT), Dr M Kaba (UCT), Dr C Moodley, Mr R Manhenze (UCT), Prof. H Zar (UCT)
Funding: Bill and Melinda Gates Foundation, University of Cape Town, Carnegie Foundation, Wellcome Trust
Short Description: This study is nested within the Drakenstein Child Health Study and the aim is to study the epidemiology and genetic characteristics of extended-spectrum beta-lactamas (ESBL) and carbapenemase-producing bacteria in the stool of apparently healthy South African children.

Project Title: Staphylococcus aureus carriage in apparently healthy children, South Africa
Principal Investigators: Prof. M Nicol (NHLS/UCT), Mrs S Abdulgader (UCT), Prof. H Zar (UCT), Dr L Robberts (NHLS/UCT)
Funding: Bill and Melinda Gates Foundation, University of Cape Town, Organisation for Women in Science in the Developing World
Short Description: This study is nested within the Drakenstein Child Lung Health Study. The aim of the study is to investigate the longitudinal patterns of S. aureus nasopharyngeal colonisation in the first year of life, including co-colonisation with other bacterial and viral colonisers/pathogens of the upper respiratory tract.

Project Title: Development of a real-time assay for the diagnosis of meningitis in children
Principal Investigators: Dr C Bamford (UCT/NHLS), Dr E du Toit (UCT), Mr J Khumalo (UCT), Dr R Muloiwa (UCT), Dr B Eley (UCT), Dr D Hardie (UCT)
Funding: NHLS Research Trust
Short Description: This is a study of the use of molecular diagnostic methods to improve the detection of the common bacterial and viral causes of community-acquired meningitis in children in South Africa. Being independent of culture, molecular methods may be of particular value in patients who have received prior antibiotic therapy. Use of molecular methods may significantly reduce unnecessary antibiotic treatment and hospitalisation.
Project Title: Characterisation of *Mycobacterium tuberculosis* complex isolates with discordant rifampicin susceptibility test results detected in a routine TB laboratory in Cape Town

Principal Investigator: Dr N Beylis (NHLS/UCT)

Other Investigators: Mr Y Ghebrekristos (NHLS), Dr V Allen (UCT), Dr JM Wojno (NHLS/UCT), Prof. M Nicol (NHLS/UCT)

Funding: NHLS research Trust

Short Description: This study aims to characterise the discrepant rifampicin results for *Mycobacterium tuberculosis* by rpoB sequencing and rifampicin MIC testing.

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Project Title: Validation of a real-time PCR assay for detection of leptospirosis

Principal Investigators: Dr PR Naicker (NHLS/UCT), Dr C Moodley (NHLS/UCT), Dr A Scobie (PHE), Dr L Robberts (NHLS/UCT), Dr M Chand (PHE), Dr C Arnold (PHE), Dr N Shetty (PHE), Prof. M Nicol (NHLS/UCT)

Funding: TBC

Short Description: This study aims to validate and assess the clinical utility of a real-time PCR assay for the diagnosis of acute leptospirosis using blood and urine samples from patients presenting to Groote Schuur Hospital and local referring hospitals in Cape Town, South Africa.

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Project Title: Molecular epidemiology and characterisation of *Clostridium difficile* isolates obtained from Groote Schuur Hospital, Brooklyn Chest Hospital and DP Marais SANTA Hospital 2014/15

Principal Investigators: Prof. S Reid (UCT), Dr B Kullin (UCT), Dr J Wojno (NHLS/UCT), Dr L Robberts (UCT)

Funding: Centre for Opportunistic and Hospital Acquired Infections, National Institute for Communicable Diseases

Short Description: The project provides molecular epidemiological typing of hospital acquired *C. difficile* isolates for the infection control service at Groote Schuur Hospital and characterises antimicrobial resistance and strain typing.

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Project Title: *Haemophilus influenzae* colonisation patterns in young children from Drakenstein sub district, South Africa

Principal Investigators: Dr L Ah Tow (UCT), Prof. M Nicol (NHLS/UCT), Ms F Patel (UCT), Prof. H Zar (UCT)

Funding: Bill and Melinda Gates Foundation, NIH

Short Description: This study aims (i) to longitudinally describe colonisation patterns of *Haemophilus influenzae* in children within the first two years of life, (ii) determine the proportion of infants and mothers who have beta-lactam resistant HI, and the type of resistance present, BLPAR, BLNAR, gBLNAR and, or BLPACR, (iii) to longitudinally analyse the association and relationship between nasopharangeal colonisation of HI, *S. aureus*, *S. pneumoniae* and *M. catarrhalis*, and (iv) to determine the risk factors associated with HI colonisation in children.

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Project Title: Molecular epidemiology and characterisation of *Clostridium difficile* isolates obtained from Groote Schuur Hospital 2014/15

Principal Investigators: Dr L Robberts (NHLS/UCT), Dr B Kullin (UCT), Prof. O Perovic (NICD)

Funding: Centre for Opportunistic and Hospital Acquired Infections, National Institute for Communicable Diseases

Short Description: The project provides real-time molecular epidemiological typing of hospital acquired *C. difficile* isolates for the infection control service at Groote Schuur Hospital and characterises antimicrobial resistance and strain typing.

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Project Title: Characterisation of carbapenem non-susceptible gram negative bacterial clinical isolates from the Western Cape

Principal Investigators: Dr L Robberts (NHLS/UCT), Dr C Moodley (NHLS/UCT), Dr D Rip (NICD/UCT), Prof. O Perovic (NICD)

Funding: Centre for Opportunistic and Hospital Acquired Infections, National Institute for Communicable Diseases

Short Description: This regional surveillance programme received carbapenem non-susceptible clinical isolates obtained from routine microbiological investigation of infection from the Western Cape NHLS laboratories to confirm and characterise resistance determinants.

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Project Title: Development of a real-time polymerase chain reaction (PCR) assay for detection of shiga toxin-producing *Escherichia coli* in stool specimens received for community acquired diarrhoea investigation

Principal Investigators: Dr L Robberts (NHLS/UCT), B Kalule (UCT), Prof. M Nicol (NHLS/UCT)

Funding: NHLS Research Trust

Short Description: The study aims to develop a real-time PCR targeting shiga toxin genes from stool specimens received at NHLS GSH Microbiology Laboratory for community acquired diarrhoea investigations.
Project Title: Evaluation of a Panfungal polymerase chain reaction (PCR) assay for the detection and identification of medically important fungi, isolated in a diagnostic laboratory
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr S Ntuli (NHLS/UCT), Dr C Bamford (NHLS/UCT), Prof. M Nicol (NHLS/UCT)
Funding: TBC
Short Description: Laboratory confirmation of deep fungal infections is important, as the clinical features may mimic those of other common opportunistic infections, resulting in delayed diagnosis and inappropriate treatment, sometimes with fatal consequences. Molecular methods, such as PCR and DNA sequence analysis, have been used to improve the detection of fungal infections. The study aims to validate a pan-fungal PCR, coupled with DNA sequence analysis, for the identification of fungal isolates in a routine diagnostic laboratory.

Project Title: Evaluation of the utility of a new, in-house PCR assay for the detection of Bordetella species in clinical samples, routinely sent to the NHLS Microbiology Diagnostic Laboratory at Groote Schuur Hospital.
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr J Wojno (NHLS/UCT), Prof. M Nicol (NHLS/UCT)
Funding: NHLS Research Trust
Short Description: A new in-house PCR assay will be evaluated to screen for the presence of Bordetella DNA in clinical samples coupled with an assessment of the yield of routine culture. The results obtained will be compared to the existing routine PCR assay performed at the National Institute for Communicable Diseases (NICD) reference laboratory in Sandringham, South Africa.

Project Title: The Pneumococcus Urinary Antigen Test Kit: Use in the laboratory for the presumptive diagnosis of pneumococcal bacteraemia
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr H Tootla (NHLS/UCT), Dr C Bamford (NHLS/UCT), Prof. M Nicol (NHLS/UCT)
Funding: TBC
Short Description: To determine the accuracy of the BinaxNOW Streptococcus pneumoniae Antigen Card test in a laboratory setting to provide a rapid presumptive diagnosis of pneumococcal bacteraemia immediately when the organism is suspected of being the causative agent of infection.

Project Title: Occurrence of a novel plasmid-mediated, colistin resistance mechanism (mcr-1), in South African Enterobacteriaceae with colistin resistance
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr C Bamford (NHLS/UCT), Mr R Moonieya, Prof. M Nicol (NHLS/UCT)
Funding: TBC
Short Description: This study aims to provide novel insight into the occurrence of the plasmid-mediated colistin resistance gene, mcr-1, in selected South African bacterial isolates displaying phenotypic resistance to colistin.

Project Title: The accuracy of extended spectrum beta-lactamase detection in South African laboratories using the Vitek 2 Gram-negative susceptibility card AST-N255
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr C Bamford (NHLS/UCT), Ms AL Young, Prof. M Nicol (NHLS/UCT)
Funding: TBC
Short Description: This study aims to provide novel insight into the occurrence of the plasmid-mediated colistin resistance gene, mcr-1, in selected South African bacterial isolates displaying phenotypic resistance to colistin.

Project Title: Evaluation of a commercial real-time PCR assay for the detection of carbapenemase-producing, gram negative isolates at Groote Schuur Hospital
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr D Rip (NHLS/UCT)
Funding: TBC
Short Description: A commercial qRT-PCR kit for the detection of carbapenemase-producing Gram-negative bacteria will be evaluated in comparison with the current in-house conventional assay.

Project Title: Retroactive screening of Klebsiella pneumoniae for carbapenemase-producing genes
Principal Investigators: Dr C Moodley (NHLS/UCT), Dr L Robberts (NHLS/UCT)
Funding: NICD Grant Funding
Short Description: This project will look at K. pneumoniae isolates collected from bloodstream infections, from numerous locations within South Africa, for two years (2010–2012). Utilising high-throughput DNA extraction, approximately 200 isolates with reduced susceptibility to the carbapenems will be screened with real-time PCR for the presence of commonly occurring carbapenemase encoding genes, as well as those that are infrequently observed. Genes encoding porins and membrane components required for antibiotic resistance will also be investigated using PCR and DNA sequence analysis. Isolates which have been shown to carry any resistance-determinants of interest will be analysed using functional enzyme hydrolysis, to elucidate the functional contribution to resistance by each gene.

Project Title: Moraxella catarrhalis in the nasopharynx of young children from Drakenstein sub-district, South Africa
Principal Investigators: Dr V Allen (UCT), Prof. M Nicol (NHLS/UCT), Dr L Ah Tow (UCT), Prof. H Zar (UCT)
Funding: Bill and Melinda Gates Foundation, NIH
Short Description: This study aims (i) to longitudinally describe the colonisation pattern of M. catarrhalis in children within the first two years of life, (ii) to investigate the strain diversity of M. catarrhalis, (iii) to identify the risk factors (such as smoking, siblings, breastfeeding and day-care attendance) associated with M. catarrhalis colonisation, (iv) to longitudinally describe the association of M. catarrhalis with other members (S. pneumonia, H. influenza and possibly S. aureus) of the nasopharyngeal microbial community, and (v) to identify the presence of the genes (BRO-1 and BRO-2) responsible for beta-lactamase production and to quantify the percentage of each isotype in the population.

Project Title: Nasopharyngeal carriage and antibiotic resistance patterns of Gram-negative bacilli (GNB) in infants
Principal Investigators: Dr M Kaba (UCT), Dr L Ah Tow (UCT), Mrs S Africa (UCT), Prof. M Nicol (NHLS/UCT), Prof. H Zar (UCT)
Funding: Bill and Melinda Gates Foundation, NIH, Wellcome Trust
Short Description: This study aims (i) to longitudinally investigate the nasopharyngeal carriage rate and antimicrobial susceptibility patterns of GNB colonising children under the age of 2 years, (ii) to identify risk factors associated with nasopharyngeal carriage of GNB as well as the acquisition of multidrug resistant GNB, (iii) to determine the genetic relatedness of GNB isolates from mother-infant pairs, and (iv) to determine whether nasopharyngeal colonisation of GNB is associated with the subsequent development of pneumonia in the cohort.

Project Title: Development and optimisation of a molecular-based method for the detection of Helicobacter pylori
Principal Investigators: Dr M Kaba (UCT), Dr L Ah Tow (UCT), Ms P Mahlobo (NRF intern) (UCT)
Funding: NRF funding
Short Description: This study aims (i) to optimise two conventional PCR protocols for the detection of H. pylori, using H. pylori genomic DNA, (ii) to design and optimise a real-time PCR protocol (targeting the glmM gene) for the detection of H. pylori, using H. pylori genomic DNA, (iii) to optimise culture conditions for H. pylori, using an ATCC strain, and (iv) to screen clinical samples (such as stool and biopsy) for the presence of H. pylori by both culture and molecular based methods.

Projects – MRC/NHLS/UCT Molecular Mycobacteriology Research Unit
Project Title: Target identification and validation in new TB drug discovery
Principal Investigators: Prof. V Mizrahi (UCT/NHLS), Associate Prof. DF Warner (UCT)
Funding: NRF (South Africa), MRC (South Africa), Bill and Melinda Gates Foundation (USA), European Union FP7
Short Description: In collaboration with local and international research groups, the antimycobacterial activity of novel small-molecules derived from chemical screens and other compound sources are being evaluated, as well as using hits as probes in target identification and validation analyses.

Project Title: The development of new tools for TB drug discovery
Principal Investigators: Prof. V Mizrahi (UCT/NHLS), Associate Prof. DF Warner (UCT)
Funding: NRF (South Africa), MRC Strategic Health Innovation Partnerships (SHIP) (South Africa), Bill and Melinda Gates Foundation (USA), European Union FP7
Short Description: In these studies, genetic methods are being used to develop new tools and bioreporters for application in TB drug discovery and development programmes.
Project Title: Understanding drug permeation in *M. tuberculosis*
Principal Investigators: Prof. V. Mizrahi (UCT/NHLS), Associate Prof. DF Warner (UCT)
Funding: NRF (South Africa), MRC (South Africa), Howard Hughes Medical Institute (USA), NIH (USA)
Short Description: A combination of molecular genetics and omics methods is being applied to determine the factors that influence drug permeation in *M. tuberculosis* and which might be exploited in TB drug discovery and development programmes.

Project Title: Mechanisms of DNA repair, replication and mutagenesis in mycobacteria
Principal Investigators: Associate Prof. DF Warner (UCT), Prof. V. Mizrahi (UCT/NHLS)
Funding: NRF (South Africa), MRC (South Africa), Howard Hughes Medical Institute (USA), NIH (USA)
Short Description: An integrated genetic, biochemical and physiological approach has been applied to investigate the molecular mechanisms underlying DNA metabolism in *M. tuberculosis*. The rationale underlying the work is that these processes are intricately associated with some of the defining features of mycobacterial pathogenesis, such as the slow growth rate of the bacillus and its ability to acquire multi-drug resistance by chromosomal mutagenesis.

Project Title: The role of vitamin B₁₂ in mycobacterial metabolism
Principal Investigators: Associate Prof. DF Warner (UCT), Prof. V. Mizrahi (UCT/NHLS)
Funding: NRF (South Africa), MRC (South Africa), Howard Hughes Medical Institute (USA)
Short Description: The biosynthesis and transport of vitamin B₁₂ in *M. tuberculosis*, and the role of vitamin B₁₂-dependent enzymes and metabolic regulation in mycobacterial metabolism and pathogenesis are being investigated.

Project Title: Mechanisms of stress adaptation and antibiotic tolerance in mycobacteria
Principal Investigators: Associate Prof. DF Warner (UCT), Prof. V. Mizrahi (UCT/NHLS)
Funding: NRF (South Africa), MRC (South Africa)
Short Description: This project aims to investigate mechanisms of stress adaptation and antibiotic tolerance in *M. tuberculosis* by focusing on candidate genes that have been implicated in these processes.

Project Title: The impact of drug resistance-associated mutations on mycobacterial physiology
Principal Investigators: Associate Prof. DF Warner (UCT), Prof. V. Mizrahi (UCT/NHLS)
Funding: NRF (South Africa), MRC (South Africa)
Short Description: It is expected that mutations implicated in resistance to frontline anti-TB drugs might impact key physiological processes in *M. tuberculosis*. This project aims to investigate the impact of drug resistance on mycobacterial metabolism and, in turn, the host-pathogen interaction.

Project Title: Replisome dynamics in *M. tuberculosis*: linking persistence to genetic resistance
Principal Investigators: Associate Prof. DF Warner (UCT), Prof. V. Mizrahi (UCT/NHLS), Dr Roger Woodgate (NICHD, USA)
Funding: NIH (USA), MRC (South Africa)
Short Description: The predicted role of a major *M. tuberculosis* stress response pathway, the so-called ‘SOS response’, is being investigated with respect to providing the functional link between the formation of antibiotic-tolerant ‘persister’ cells and the subsequent emergence of genetically drug-resistant mutants during extended antibiotic treatment.

Project Title: Genomic investigations of transmission and microdiversity in a high TB-HIV burden setting
Principal Investigators: Associate Prof. DF Warner (UCT), Dr Keren Middelkoop (UCT)
Funding: Bill and Melinda Gates Foundation (USA)
Short Description: This study utilises whole-genome sequencing to determine the degree of genotypic heterogeneity in aerosolised *Mycobacterium tuberculosis* (MTB) populations isolated under clinical conditions.
5. RESEARCH OUTPUT

5.1. Journal Publications


AnnuAl AcAdemic Review RepoR t 2015/16
AcAdemic Aff AiRs, ReseAR ch And QuAlity AssuRAnce


Medical Virology

Head: Prof. Carolyn Williamson

1. ABOUT THE DIVISION

The Division of Medical Virology contributes to the diagnosis, treatment, prevention and eradication of viral diseases in South Africa through a diagnostic laboratory service together with a dynamic research programme. The Virology Diagnostic Laboratory is a SANAS accredited facility within the NHLS, and is located at GSH. It provides service to both GSH and RCCH, and serves as a regional reference centre providing a clinical and diagnostic service to local teaching hospitals and surrounding public health clinics.

Research within the division focuses on human papillomavirus (HPV), HIV and major co-infections, virus discovery and vaccinology. Research is performed within the Institute of Infectious Diseases and Molecular Medicine and in the GSH NHLS diagnostic laboratory. In HIV prevention, transmission and pathogenesis, the division has contributed to the understanding of the role of viral determinants in eliciting broadly cross-neutralising antibodies; HIV superinfection; the impact of mucosal inflammation and other sexually transmitted co-infections on HIV transmission risk; T cell immunity to HIV and HIV vaccine and microbicide development. Application of next-generation sequencing technology has resulted in the discovery of novel HPVs and other viruses as well as further characterisation of the cervical microbiome. There has also been research on BCG and poxviruses as vaccine vectors. The diagnostic laboratory is involved in a variety of operational research projects to detect new potential pathogens in diagnostic samples; evaluate point-of-care technology for HIV viral load and early infant diagnosis; and to determine the epidemiology of hepatitis E in the Western Cape.

The division contributes to undergraduate teaching and plays a major role in postgraduate training and currently hosts 34 postgraduate students (registered for BMed Hons, MSc, PhD or Postdoctoral degrees).

Table 15: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist</th>
<th>PhD Scientist</th>
<th>South African*</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
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<td>1</td>
</tr>
<tr>
<td>White</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
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<tr>
<td>South African*</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

2.1. Medical Virology Diagnostic Laboratory, Groote Schuur Hospital

Head: Associate Prof. Diana Hardie

The SANAS accredited diagnostic laboratory provides a wide range of virology diagnostic assays for the public sector health facilities in the Western Cape. The laboratory serves as the referral laboratory for primary and secondary facilities in the province to provide critical serology and molecular diagnostic tests, including HIV viral load and early infant diagnosis for the priority programme. The laboratory serves the needs of tertiary academic hospitals such as Groote Schuur Hospital and Red Cross War Memorial Hospital in highly specialised assays for complex academic settings.

It is one of the leading laboratories in the country in terms of range of molecular diagnostic tests offered. The three key focus areas of virology molecular assays, based on the local disease burden and clinical expertise are: diagnostic tests for opportunistic pathogens in HIV infected patients and transplant recipients; multiplex PCR for the diagnosis of respiratory tract infections; and molecular diagnosis and monitoring of viral hepatitis and hepatitis B and C drug resistance testing.

The laboratory also actively participates in optimisation of public health programmes. The diagnostic laboratory staff works closely with the provincial Department of Health, Department of Public Health at University of Cape Town, National Institute of Communicable Disease and the NHLS National Priority Programmes on several surveillance and operational quality improvement collaborations.
Dr Stephen Korsman leads the national coverage programme for virology at UCT which supports the laboratories in the Eastern Cape and parts of Western Cape. Telephonic and electronic support has been provided. In-person outreach was limited in the past year by financial constraints within the NHLS. George NHLS laboratory was visited by a pathologist on one occasion. Visits to the Eastern Cape did not occur, and substantial support was provided telephonically and by e-mail.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The division is responsible for semester 3-5 undergraduate teaching in the discipline of medical virology which includes problem-based learning (PBL) facilitation, lectures and computer-based tutorials. The division contributes to the Molecular Medicine BSc/MBChB/PhD intercalated programme. In terms of postgraduate training, staff in the division participate in the teaching and training of registrars, intern technologists, technicians and intern medical scientists in the discipline of molecular biology and virology. In addition, there is a large teaching programme for BSc Honours, MSc and PhD students.

Table 16: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Qualification</th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSc Med Hons</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>100%</td>
</tr>
<tr>
<td>MSc</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>16%</td>
</tr>
<tr>
<td>Registrars</td>
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<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PhD</td>
<td>17</td>
<td>5</td>
<td>1</td>
<td>5.8%</td>
</tr>
<tr>
<td>All</td>
<td>29</td>
<td>10</td>
<td>5</td>
<td>17%</td>
</tr>
<tr>
<td>South African</td>
<td>19</td>
<td>9</td>
<td>4</td>
<td>21%</td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

4.1. Research Projects

Project Title: Novel HIV vaccine candidates for South Africa
Investigators: Prof. A-L Williamson, Dr R Chapman, Dr N Douglass, Dr G Chege, E Margolin, M van Diepen, P Ximba, S Galant
Collaborators: Prof. Edward Rybicki, Prof. Lynn Morris
Funding: MRC-SHIP
Short Description: Novel Env vaccines based on modified and chimeric proteins as well as expression using plant-based production and poxvirus systems are being produced and tested.

Project Title: HIV vaccines based on HIV-1C Mosaic Gag
Principal Investigators: Prof. A-L Williamson, Dr R Chapman, Dr N Douglass, Dr T Jongwe
Funding: National Institutes of Health (NIH), NRF
Short Description: The immunogenicity of HIV subtype C mosaic Gag antigen designed by Fischer et al. (2007), was tested using three different vaccine platforms namely a novel DNA vaccine backbone, BCG and modified vaccinia Ankara. Future work will include vaccinating in conjunction with antibody-generating mosaic immunogens or boosting with HIV-1C Env protein.

Project Title: Optimisation of rBCG as an HIV vaccine vector
Principal Investigators: Prof. A-L Williamson, Dr R Chapman, S Chetty
Funding: NIH, NRF
Short Description: BCG, the tuberculosis vaccine, is being developed as a potential HIV vaccine vector. Wild type, ΔpanCD, pfo and a combination ΔpanCDpfo strains of BCG expressing HIV-1 subtype C Gag. Modified rBCG vaccines containing (gag) primed for increased vaccine specific T cell functionality as compared to the wild type strain.

Project Title: Sequence analysis of human papillomaviruses
Investigators: Prof. A-L Williamson, Dr T Meiring, Prof. EP Rybicki, Dr ZZA Mbulawa, A Murahwa
Funding: PRF, NRF and NHLS Trust
Short Description: Next-generation sequencing (NGS) technologies have opened up the opportunity to directly examine viral diversity in clinical specimens. Novel HPV types have been identified using this technology and are presently being characterised.
Project Title: An investigation of the interaction of the genital microbiome with human papillomavirus (HPV)
Investigators: Prof. A-L Williamson, Dr T Meiring, H Onywera
Funding: CANSA and NRF
Short Description: While studies at UCT have linked HPV, HIV and the immune milieu, no studies have been done on the impact of the total genital microbiota on HPV. The bacterial microbiota of the female genital tract is known to protect the vagina from pathogens. The cervical vaginal microbiome (CVM) is being studied and components found to be related to HPV infection.

Project Title: Investigation of GeneXpert human papillomavirus performance
Investigators: Prof. A-L Williamson, Dr ZZ A Mbulawa
Collaborators: Prof. C Firnhaber (Right to Care), C Chibwesha (Right to Care), T Wilkin (Weill Cornell Medical College, New York), B Goeieman (Right to Care)
Funding: South African Research Chairs Initiative of the Department of Science and Technology and National Research Foundation; Weill Cornell Medical College Division of Infectious Diseases and USAID PEPFAR (674-A-00-08-00007-00), PHE ZA.09.0265 South Africa
Short Description: This study investigated the performance of Cepheid Xpert HPV assay in South African human immunodeficiency virus (HIV)-infected women and compared its performance with that of Hybrid Capture-2 (hc2). Xpert is a promising screening test in HIV-infected women, that performs similarly to hc2.

Project Title: The natural history of oral HPV infection in South African heterosexual activity couples
Investigators: Prof. A-L Williamson, Dr ZZ A Mbulawa
Collaborators: Prof. D Coetzee
Funding: South African Research Chairs Initiative of the Department of Science and Technology and National Research Foundation and Poliomyelitis Research Fund
Short Description: HPV genotyping was performed in cervical, penile and buccal cells of 662 women and men using Roche linear array HPV genotyping assay. The high oral-genital concordance in couples suggests that there was oral-genital contact. The increasing rate of oral sex especial in adolescents may increase the oral HPV prevalence and lead to increase oral cancer in our communities.

Project Title: Comprehensive Antibody Vaccine Immune Monitoring Consortium (CA-VIMC). Collaboration for AIDS Vaccine Discovery (CADV)
Principal Investigator: Dr D Montefiori, Duke University, USA
SA Principal Investigator: Prof. C Williamson
UCT Investigators: C Rademeyer, R Thebus, J Marais
Funding: Bill and Melinda Gates Foundation
Short Description: HIV-1 functional Env genes and infectious molecular clones from South Africa have been cloned and characterised, in preparation for the next phase 2b/3 HIV vaccine trials. The clones have been evaluated for genetic and antigenic diversity of HIV-1 strains currently circulating in this region, and to ascertain how well the strains are represented by current vaccine immunogens and reference reagents.

Project Title: Vaccine-mediated effects on immunological, viral and clinical factors in HIV breakthrough infections
Principal Investigators: Prof. C Williamson
Co-investigator/ collaborators: Dr D Chopera (UCT); Prof. L Morris (NICD)
Funding: Strategic Health Innovation Partnerships (SHIP). Medical Research Council (MRC) and Bill and Melinda Gates Foundation
Short Description: Vaccine-mediated effects on neutralising responses and viral sequences are being investigated through the evaluation of breakthrough infections from vaccine trials in South Africa. This study is likely to provide critical insights into understanding the mechanism of action of vaccines, optimisation of future HIV vaccine candidates, as well as contribute substantially towards understanding the effect of vaccination on the natural history of HIV infection.
Project Title: Broad neutralising HIV antibodies, adjuvants and immunogens
Principal Investigators: Prof. C Williamson (UCT), Prof. P Moore (NICD)
Co-investigator /collaborators: Dr C Anthony (UCT)
Funding: Strategic Health Innovation Partnerships (SHIP). Medical Research Council (MRC)
Short Description: An effective HIV vaccine needs to elicit broadly cross-neutralising antibodies (bNAbs), able to neutralise diverse HIV strains from across the world. These kinds of antibodies develop in ~20% of infected people, though normally after two to three years of infection. The aim is to learn lessons from infected people who naturally made broadly cross-neutralizing antibodies (bNAbs), and translate these into immunogens. To achieve this, viral deep sequencing of defined epitopes are being performed to identify viral variants that contribute to the development of breadth. This project is being done in collaboration with Prof. P Moore who is characterising broadly neutralising antibodies from people with breadth.

Project Title: Biostatistical, computational biology, and mathematical modelling for the assessment of immune correlates of protection in the HVTN 701 and 702 efficacy trials in South Africa
Principal Investigator: Dr P Gilbert, HIV Vaccine Trials Network (HVTN), USA
SA Principal Investigator: Prof. C Williamson
UCT Investigator: M Logan
Funding: Bill and Melinda Gates Foundation
Short Description: The purpose of this project is to enhance biostatistical, computational biological, and mathematical modelling research for assessing correlates of vaccine efficacy in randomised clinical trials conducted in the Republic of South Africa.

Project Title: Risk assessment of HIV infected to HIV infected transplantation in South Africa
Principal Investigator: Prof. E Muller
SA Principal Investigator: Prof. C Williamson
UCT Investigators: Dr P Selhorst, C Combrinck
Funding: National Institute of Allergy and Infectious Diseases, NIH
Short Description: This project is examining clinical and virological factors in HIV-infected kidney transplants from deceased donors into HIV infected recipients namely: determining the incidence, extent, and nature of donor-to-recipient HIV-SI in HIV-infected-to-HIV-infected renal transplants; quantifying recipient’s virus infiltration into the graft kidney; and investigating virus compartmentalisation in kidney epithelium.

Project Title: Timing of establishment of the HIV latent reservoir in subtype C infected women
Principal Investigator: Prof. C Williamson (UCT); Prof. R Swanstrom, UNC, USA
UCT Investigators: Dr M-R Abrahams, W Nevondo
Funding: National Institute of Allergy and Infectious Diseases, NIH
Short Description: This project aims to characterise the genetic diversity of the latent reservoir of HIV subtype C infected individuals as a function of time, to determine when the latent viral reservoir is established, and to determine how immune activation influences the viral composition of the reservoir.

Project Title: Viruses in CSF of HIV patients with acute and chronic neurological syndromes detected by new generation sequencing
Investigators: Dr H Smuts; Associate Prof. D Hardie
Funding: Poliomyelitis Research Foundation (PRF)
Short Description: A next-generation sequencing (NGS) pilot study was undertaken to identify viruses in cerebrospinal fluid (CSF) of HIV-infected patients presenting with a range of neurological symptoms. Human pegivirus (HPgV) – previously known as GBV-C – was detected in 4/8 HIV-associated neurological disease (HAND) patients. The viral load and genetic characteristics of baseline and 6-month paired blood and CSF samples of HPgV-positive samples are currently being investigated.

Project Title: Molecular characterisation of measles viruses from brain of patients with measles inclusion body encephalitis (MIBE) and sub-acute sclerosing pan encephalitis (SSPE)
Investigators: Associate Prof. D Hardie; Dr H Smuts
Funding: Poliomyelitis Research Foundation (PRF)
Short Description: Molecular characterisation has revealed that both MIBE and SSPE viruses are closely related to the epidemic virus, but have mutations to key structural proteins. A striking difference between MIBE and SSPE viruses is in the matrix protein. The sequence of this gene in MIBE viruses is largely preserved, while it is highly mutated in SSPE. The matrix protein is critical to enable virus budding and it is hypothesised that this finding provides evidence that the mode of measles viral spread in the CNS is fundamentally different in these two brain diseases. This hypothesis is under investigation.

Project Title: Molecular surveillance of non-poliovirus enterovirus infections in patients with viral meningitis and respiratory illness
Investigators: Dr H Smuts, Associate Prof. D Hardie, Dr S Korsman
Funding: Poliomyelitis Research Foundation (PRF)
Short Description: There is minimal recent data on the changing prevalence and seasonality of enteroviral species and serotypes in the Cape Town community. Screening of enterovirus-positive respiratory and CSF samples from hospitalised patients for the four different enterovirus species/serotypes, A, B, C and D will be undertaken over a three-year period to identify these changes as well as disease associations. Over a 15 month period from June 2014 to September 2015, 3 360 respiratory samples were received at the Virology Molecular Diagnostic Laboratory for respiratory virus screening of which in 442 (17.4%) were enterovirus (EV) positive. Co-infection with up to 5 other respiratory viruses was common. EV-B species were most commonly detected (23%) followed by EV-A (7.5%) and EV-C (1.4%). The role of enterovirus serotypes as a cause of central nervous system (CNS) disease, including meningitis/encephalitis and neonatal sepsis, was also investigated. Over a 21 month period (January 2014– September 2015) 54 CSF samples from patients were found to be EV positive. In 23 patients with a diagnosis of meningitis 11 different EV serotypes were identified – Echovirus- 6, -7, -9, -14, -18, -30, -33, Coxsackie B3, Coxsackie A9 and enterovirus A71.

Project Title: Can hepatitis E virus (HEV) be found in food products of swine origin in Cape Town?
Investigators: Dr S Korsman, J Bloemberg, M Brombacher, A Giuricich, R Halley-Stott, Dr M Kaba
Short Description: To determine the prevalence of HEV in pig meat purchased at shops in the Cape Town area.

Project Title: Can evidence of hepatitis E virus infection be found in pigs in the Cape Town Metropole?
Funding: Polio Research Foundation, NHLS Research Trust
Investigators: Dr S Korsman, M Andersson, J Grewar, L van Helden, Prof. W Preiser
Short Description: To search for serological and molecular evidence of pigs slaughtered in Cape Town for human consumption. Preliminary seroprevalence is 32% (n=429 tested until now). Seroprevalence appears to be different between farms of origin. This suggests that pig-derived food products may be a source of local hepatitis E infection, and that meat from certain farms may be a higher risk. Attempts to detect viral RNA are ongoing.

Project Title: Seroprevalence of hepatitis E virus (HEV) in Western Cape, South Africa
Investigators: RG Maddern, S Wallace, Prof. M Sonderup, Dr S Korsman, T Chivese, B Gavin, A Edem, R Govender, N English, C Kajiyama, O Lutchman, AA van der Eijk, SD Pas, HR Dalton, Prof. W Spearman
Short Description: To determine the seroprevalence of HEV IgG in hospital patients in Cape Town. A seroprevalence of 29.1% (21.9% age-adjusted) was found, which was similar in three defined racial groups and individuals with and without HIV. Seroprevalence in children was very low with a rapid increase in early adulthood. The only risk factor for seropositivity on multivariate analysis was pork consumption (p<0.001, OR 2.052 (1.39-3.03). A diagnosis of hepatitis E should be considered in any patient presenting with hepatitis in Cape Town, irrespective of travel history, age, or racial group.

Project Title: Analysis of cytomegalovirus (CMV) UL97 drug resistance mutations
Investigators: Dr N Nkosi, Dr S Korsman, Dr H Smuts, Associate Prof. D Hardie, Dr N Hsiao
Funding: NHLS Research Trust
Short Description: Ganciclovir is widely used in the solid organ and stem-cell transplant setting in South Africa. Following the development of an in-house assay, the prevalence of CMV UL97 DRM secondary to ganciclovir use amongst immune-suppressed populations in Cape Town was documented. Six mutations from 39 (15%) individuals were identified, namely L595S, H520Q, C592G, M460V, D605E and Q449K. These findings suggest CMV disease despite ganciclovir therapy may be associated with the presence of UL97 mutations in our setting. The prevalence and clinical outcomes thereof need to be better documented.
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<tr>
<th>Project Title</th>
<th>Funding</th>
<th>Short Description</th>
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<tr>
<td>Characterising the antiretroviral resistance and clinical profiles of mother-child pairs involved in in-utero human immunodeficiency virus (HIV) transmission. Investigators: Dr N Nkosi, Dr Z Valley-Omar, Dr M Kroon, Dr N Hsiao</td>
<td>Polioymelitis Research Foundation (PRF)</td>
<td>This study aims to describe the prevalence and nature of transmitted drug resistance among neonates born to HIV positive mothers with antiretroviral exposure.</td>
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<td>Evolution of HIV early infant diagnosis and the impact of birth testing in the Western Cape</td>
<td>None</td>
<td>The requests and results of HIV PCR for early infant diagnosis in the Western Cape were reviewed through analysis of laboratory information system data. The uptake of routine early infant diagnosis (EID) testing following the birth testing was found to be suboptimal as &lt;50% of infants with negative birth PCR returned for routine EID testing.</td>
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<td>Classification of HIV virological failure using whole blood vs plasma viral load</td>
<td>Global fund/Alere Health Care</td>
<td>Whole blood (WB) collection and testing through either dried blood spots (DBS) or point-of-care viral load (VL) assays are potential solutions to the logistical challenges around delivering VL service to remote areas. However, variability was noted between the different WB VL assays with difficulties assigning a uniform threshold across all platforms to accurately predict virological failure of plasma samples, reflecting the differences in sample treatment/processing (DBS vs fresh blood samples) and sample input volume.</td>
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<tr>
<td>Hepatitis A seroprevalence in South Africa. Are we in epidemiological transition?</td>
<td>Polioymelitis Research Foundation, NHLS Research Trust</td>
<td>It is hypothesised that South Africa is in an epidemiological transition of Hepatitis A virus infection from a childhood to infection of adolescence and young adults. In this study we conduct a pilot cross-sectional study in the Western Cape Province aimed at assessing the Hepatitis A seroprevalence at various ages. We anticipate our findings will provide key direction towards future introduction of Hepatitis A vaccine in South Africa’s EPI.</td>
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<tr>
<td>A GIFT (Genital Inflammation Test) for HIV prevention</td>
<td>MRC SHIP</td>
<td>Sexually transmitted infections (STIs) and bacterial vaginosis (BV) cause inflammation in the female genital tract that is associated with increased risk of HIV infection. STIs and BV are a huge burden in developing countries like South Africa, particularly in women at high risk of HIV infection, and are thus a major cause of genital inflammation in these populations. These investigators and others have shown that STIs and BV are often asymptomatic. Therefore, although women with asymptomatic STIs have genital inflammation and are at increased risk of HIV (and reproductive complications), these women are not being treated. There is an urgent need for novel, accurate and inexpensive POC tests to identify women with asymptomatic STIs/BV who have subclinical inflammation and are therefore at increased risk of HIV infection. The feasibility is being investigated using a combination of three cytokine biomarkers as predictors of the presence of an STI or BV when measured in genital secretions, to develop a POC test device to identify women who have asymptomatic infections. A prototype lateral flow test device is currently being developed. In parallel, the markers have been validated in three different cohorts of women from South Africa (Cape Town and Durban) and Kenya. This test aims to reduce the prevalence of STIs and BV and HIV risk in South African women. A provisional patent for this test has been filed, and patent review will take place in May 2016.</td>
</tr>
<tr>
<td>Hormone-induced mucosal susceptibility and HIV risk in South African adolescents</td>
<td>NIH R01 (MRC-NIH)</td>
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Mechanism of HPV-associated genital wart persistence and recurrence in HIV-infected women in South Africa

Associate Prof. J-A Passmore

Principal Investigator: Prof. A-L Williamson (UCT)

Funding: Poliomyelitis Research Foundation

Short Description: Women with persistent HPV infections are at the highest risk of cervical disease progression and cancer. Identifying co-factors associated with HPV persistence is therefore important in the fight to prevent HPV-associated disease progression. One of the most significant co-factors for HPV persistence and accelerated disease progression is infection with HIV. The aim of this study was to compare the prevalence and persistence of HPV types associated with genital warts in HIV-infected and uninfected women; and to compare NK and T cell functional and phenotypic properties from HPV-associated genital warts from HIV-infected and HIV-uninfected women. HIV+ women had significantly lower frequencies of CD4 T cells in warts and blood. HIV+ women tended to have lower frequencies of NK cells with capacity to kill cancerous cells in both blood and warts than HIV- women. Wart NK cells from HIV+ women expressed significantly lower mediators of killing (CD107a) and produced less inflammatory cytokines to activate the rest of the immune system. Highly active antiretroviral therapy (HAART) status did not improve NK cell functionality.

HPV prevalence during HIV infection in women using intrauterine devices (IUDs)

Principal Investigator: Associate Prof. J-A Passmore

Co-investigator: Prof. A-L Williamson (UCT)

Funding: Poliomyelitis Research Foundation

Short Description: IUDs are greatly underutilised in South Africa with less than 1% of women currently using this contraceptive method. Although the Copper T and the levonorgestrel-releasing IUD (LNG-IUD) are available to South African women, the LNG-IUD is mostly employed in the private sector. IUDs have been shown to consistently decrease the risk of endometrial cancer in women. However very little is known about how IUDs affect the progression of HPV infections and cervical cancer. A systemic review has suggested that the use of IUDs does not alter HPV infections, but it may decrease the development of cervical disease. It is thought that IUDs defend against carcinogenesis and HPV infection by inducing a moderate inflammatory response in the endometrium and cervix. The aim of this study was to determine whether copper IUD or LNG-IUD use by HIV-infected women leads to more prevalent or persistent HPV infections, and the role that genital inflammation plays in this setting in a double-blinded randomised control trial. HPV typing and cytokine measurement have been completed in cervicovaginal lavages from all samples from enrolment, three and six months post-insertion of the IUDs. The study is ongoing and will continue into 2017.

Role of vaginal bacteriophages in emergence of bacterial vaginosis (BV) and modulating the microbiome: Controllable viral strategies to decrease risk for HIV infection in women

Principal Investigator: Associate Prof. J-A Passmore

Co-investigators: Dr H Jaspan, Dr R Froissart

Funding: Poliomyelitis Research Foundation

Short Description: Bacterial vaginosis (BV) is characterised by a disruption of the female vaginal bacterial microbiome that is typified by a replacement of most commensal and protective bacteria belonging to Lactobacillus spp. with other less protective pathogenic commensal bacteria. Probably because of the vaginal inflammation caused by bacteria associated with BV, this condition increases susceptibility to sexually transmitted infectious viral or microparasitic agents, including HSV-2, and enhances the risk of HIV acquisition by 60%. Critically, what causes the shift between a healthy genital microbiome to a pathogenic vaginal microbiome that is symptomatic of BV is unknown. Bacteriophages are common viruses that target many bacterial species and have been implicated in molding the gut bacteriome in humans. The aim of this study was to evaluate the role of bacteriophages in the depletion of Lactobacillus spp. that occurs during the development of BV. It was hypothesised that fluctuation of healthy vaginal bacterial composition to an unhealthy one like bacterial vaginosis is associated with the presence of bacteriophages targeting commensal vaginal Lactobacilli spp. A panel of commensal Lactobacilli isolates is currently being built for this study of bacteriophage host tropism. The study is ongoing.
5. RESEARCH OUTPUT

5.1. Journal Publications


5.2 Conference Presentations


Williamson A-L. Global pre-clinical data and new vaccine concepts in a meeting on “Considerations for a Pan-African HIV Vaccine Development Agenda” hosted by HIV Vaccine Enterprise as part one of their meetings on “Timely Topics in HIV/Vaccines”. Kigali, Rwanda. 16–17 March 2015.

5.3 Poster Presentations


Anatomical Pathology

Head: Dr Jacqueline Goedhals

1. ABOUT THE DEPARTMENT

The Department of Anatomical Pathology provides histopathology services to the Free State and performs immunohistochemistry for the Northern Cape. Cytology services are provided to the Free State and Northern Cape provinces and specimens are also received from Gauteng. A post mortem service was provided to the Free State and was predominantly utilised by the Universitas Academic Complex. A specialised fetal and neonatal post mortem service was available to hospitals in the Free State and Northern Cape.

The department is involved in teaching undergraduate and post graduate medical students and occupational therapy and physiotherapy students.

Table 17: Total number of staff per profession and highest qualification

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2. DIAGNOSTIC AND CLINICAL SERVICES

The department provided a diagnostic surgical pathology service to provincial hospitals in the Free State and a cytopathology service to hospitals and clinics in the Free State and Northern Cape. Cytology specimens were also received from Gauteng. Over 16 000 surgical cases and 90 805 cytology specimens were evaluated and 55 autopsies were performed. The department also performed immunohistochemical stains for the anatomical pathology laboratory in Kimberley, Northern Cape. A frozen section service was available at Universitas Hospital and technologists were available to assist with on-site cytology diagnoses in theatres at Universitas as well as to fetch renal biopsies at the state and private hospitals in Bloemfontein.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate Teaching

The department presented a module on general pathology to second year medical students and seventeen sessions on systemic pathology, which were integrated into system modules, were delivered to second and third year medical students. A short course on general pathology was offered to third year physiotherapy and occupational therapy students.

3.2. Postgraduate Teaching

Daily departmental and interdepartmental meetings were held including problem slide discussions, cytology cases, tutorials and Journal Club meetings. There were six anatomical pathology registrars. Dr D Zaharie, a neuropathologist from the University of Stellenbosch and NHLS gave a short course to the anatomical pathology registrars in February 2016 on brain, muscle and nerve biopsies.

Table 18: Total number of trainees per qualification category and rates of successful completion/pass rates

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Table 19: Number of final year trainees who graduated or completed their training programme

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*Indicates number of trainees who successfully completed their programme (n) over the total number of trainees who were in their final year of training i.e. MMed – 4th year; Intern Scientist – 2nd year, MSc – 3rd year, PhD – 5th Year).

# Intern Scientist and Registrars indicates those who successfully completed their board examinations/assessments

Table 20: Total number of trainees per year of training

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</table>

4. RESEARCH ACTIVITIES

The Department of Anatomical Pathology is in an ongoing collaboration with the Department of Cardiothoracic Surgery on a project entailing the decellularisation of cardiac tissue.

Members of the department attended a number of congresses and courses during the year including the 38th Annual Postgraduate Medicine Course in Renal Biopsy in Medical Diseases of the Kidneys in New York; the 26th European Congress of Pathology in Serbia; the XXXVII International Paediatric Pathology Association Advanced Course in Paediatric Pathology in France; and the International Academy of Pathology Congress in Johannesburg.

Dr R Ecker, CEO of TissueGnostics GmbH visited the department and presented a talk entitled ‘Tissue cytometry and tissue sociology – new concepts to look at cells and cellular interaction in cancer tissue’.

4.1. Research Projects

Project Title: Determining the mutation frequency and prognostic import of POLE proofreading domain mutations in uterine carcinosarcomas

Investigators: Dr J Goedhals in collaboration with Dr T Bosse from the Netherlands

Project Title: Next-generation sequencing of paragangliomas and phaeochromocytomas

Investigators: Dr J Goedhals and Dr L Maree in collaboration with the Department of Surgery, University of the Free State

4.2. Grant Funding

The Zoonosis Research Unit (ZRU), together with the following partners, was awarded funding from the African Network for Improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA) project:

- University Teaching Hospital, University of Bouake, Cote d’Ivoire
- National Laboratory of Agricultural Development/Central Laboratory of Animal Pathology, Cote d’Ivoire
- National Institute for Biomedical Research, Kinshasa, Democratic Republic of Congo (DRC)
5. RESEARCH OUTPUTS

5.1. Journal Publications


5.2. Conference Presentations

M Venter was invited to talk entitled A One health approach to tract zoonotic neurological arboviruses in South Africa at the South African Equine Veterinary Association Conference, Stellenbosch, 16 February 2015.

Gouveia De Almeida AP(1,2,3), Ferreira CAC(1,2,3), Mixão VDP(1,2), Marques Novo MTL(1,2,3), Palmeiro Calado MM(1,2,3), Pires Gonçalves LA(1,2,3), Duarte Belo SM(1,2,3). First molecular identification of mosquito vectors of Dirofilaria immitis in continental Portugal. (1)Medical Parasitology Unit, Medical Parasitology and Microbiology Unit-UPMM, (2)Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, (3)Zoonosis Research Unit, Faculty of Health Sciences, University of Pretoria, Portugal. (11)International Public Health and Biostatistics Unit. 7th European Mosquito Control Association, Valencia, Spain, February 2015. Abstract book p. 83, paper 5.7 Oral presentation.

Prof. Venter was an invited speaker at the Informal Consultation on RSV using the Global Influenza Response Networks Surveillance (GIRNS) platform, World Health Organisation, Geneva Switzerland 25-27 March 2015.


Braack L. Research undertaken by the University of Pretoria Centre for Sustainable Malaria Control. SADC Annual Malaria Managers Meeting. Johannesburg, 26–28 August 2015.


Prof. M Venter participated in the Pandemic Influenza Preparedness (PIP) framework advisory group technical working group on the sharing of Influenza genetic sequence data, WHO HQ, Geneva.


5.3. Technical consultations/policies

- M Venter participated in the writing of the testing guidelines for dangerous and emerging viruses in Africa with the WHO AFRO while spending a month at the WHO AFRO offices as Centers for Disease Control and Prevention (CDC) liaison for the Ebola outbreak, January 2015.
- WHO Advisor on using the influenza surveillance network for other respiratory virus surveillance, specifically respiratory syncytial virus (RSV), March 2015.
- M Venter attended a high level WHO meeting on Building global health security beyond Ebola, Cape Town, 13–15 July.
- Prof. M Venter participated in the PIP Framework Advisory Group TWG on the sharing of influenza genetic sequence data, WHO HQ, Geneva.

5.4. Conference Organiser

Haematology and Cell Biology

Head: Prof. Marius J Coetzee

1. ABOUT THE DEPARTMENT

Prof. Chris Viljoen has taken special care with the BMedSc (Hons) students to develop them into postgraduate students. A PhD was awarded in December 2015. Two senior registrars will be writing their College exams in 2016. The department is looking forward to welcoming two supernumerary registrars who will join the department in 2016. Another PhD student is set to graduate at the end of 2016. One of the consultants is working hard on a PhD in thrombosis and haemostasis.

The formation of separate Academic and Pathology divisions (or sections) within the department has been successful. Prof. Chris Viljoen heads the Academic Division and has been promoted to full Professor with effect from 01 January 2016.

2. DIAGNOSTIC AND CLINICAL SERVICES

Over 143,710 groups of tests were done. Doctors shared in seeing 2,551 patients at the Haematology Clinic, and 272 patients at Kimberley Hospital. The International Normalised Ratio (INR) Clinic saw 6,564 patients. Two Point-of-Care (POC) INR devices and a blood film stainer were assessed for the Health Technology Assessment (HTA) Unit.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

One intern was able to register as a medical scientist with the HPCSA, and two others have submitted their portfolios. Two registrars are set to sit their FCPath Part II in 2016.

4. RESEARCH ACTIVITIES

The Department is focusing on haemostasis, genetically modified organisms (GMO) and related topics, optimising the diagnosis and monitoring of haematological malignancies.

4.1. Research Units/Study Groups Linked to the Department

The Special Haemostasis Laboratory under Prof. Muriel Meiring is entering into a cost recovery service level agreement with the NHLS in order to optimise the use of both the University of the Free State (UFS) and NHLS equipment.

The GMO Testing Facility under Prof. Chris Viljoen is offering chronic myeloid leukaemia transcript level quantification and will also enter into a cost recovery service level agreement with the NHLS. The Unit is affiliated to Eurofins GeneScan. It delivers a popular GMO testing service and is looking into herbicide residues in food.

4.2. Research Projects

Current projects

- Thrombotic thrombocytopenic purpura in HIV (Mr Roodt, Dr Janse van Rensburg, Dr Joubert and Prof. Meiring).
- Hereditary haemorrhagic telangiectasia in the Free State and Northern Cape (NHLS Research Trust Grant) (Prof. Coetzee).
- An audit on the use of blood products in adult patients in Kimberley Hospital Complex (Dr Joubert).
• Comparison of the antigen levels and activities of ADAMTS13, Von Willebrand factor and plasminogen in the different blood products currently available in South Africa for the treatment of thrombotic thrombocytopenic purpura (Dr Anneke van Marle, Dr Jaco Joubert).
• Development of a Von Willebrand factor propeptide assay (TIA Seed Fund) (Prof. Meiring).
• Development of a ADAMTS13 auto-antibody assay (BMedSc (Hons) project) (Prof. Meiring).
• ADAMTS13 auto-antibodies in HIV-associated TTP (NRF) (Ms MM Khemisi, Prof. Meiring).
• Characterisation of a tissue factor inhibitor (TIA Seed Fund) (Mr J Vermeulen, Prof. Meiring).
• Bleeding parameters in adults on long-term valproic acid treatment (PhD, collaboration with Neurology) (Prof. Meiring).
• Development and implementation of a real-time reverse transcriptase polymerase chain reaction assay to detect the intron 22 inversion in severe haemophilia A patients (Dr Janse van Rensburg, Dr GM Marx and Mr JF Kloppers).
• Food authenticity with regard to meat and meat derived ingredients in processed foods (Prof. Viljoen, Ms Sreenivasan, Ms Booysen).
• Presence of glyphosate in genetically modified food products (Prof. Viljoen, Ms Sreenivasan, Mr Koortzen).
• The application of external quality controls for BCR-ABL monitoring using the GeneXpert (Prof. Viljoen, Ms du Plessis, Ms Sreenivasan).
• The completion of bone marrow request forms (Prof. Coetzee and medical students).
• The appropriateness of serological test requests for autoimmune disorders at an academic hospital (Prof. Coetzee and medical students).
• An evaluation of medical interns’ knowledge of warfarin (Dr Joubert and a medical student).
• An evaluation of the in vitro effects of streptokinase on the coagulation profile and fibrinolytic system of Papio ursinus (BMedSc (Hons) project) (Dr Joubert).

Completed projects

• Evaluation of two POC testing instruments for measuring a patient’s INR. NHLS Health Technology Assessment Unit (BMedSc (Hons) project) (under Dr Joubert).
• Evaluation of a Hematek 3000 system for the NHLS Health Technology Unit of the NHLS (Dr van der Linde).
• The effect of rooibos tea extracts on blood coagulation, (BMedSc (Hons) project), (Dr Walter Janse van Rensburg, Johan de la Rey).
• Validation of an ADAMTS13 antigen assay (BMedSc (Hons) project), (Ms S Myeni, Prof. Meiring).
• Thrombogenicity and endothelialisation of decellularised baboon arteries (MSc project), (Ms MM Khemisi, Prof. Meiring).
• Thrombotic potential in patients undergoing kidney biopsies (Collaboration with Nephrology), (Prof. Meiring).
• Detection of calreticulin mutations in patients suspected of having a myeloproliferative disorder (BMedSc (Hons) project), (Dr André de Kock).
• Comparison of whole blood and Trizol stabilised samples for the quantification of BCR-ABL on the GeneXpert, (Honours project under Prof. Viljoen and Ms du Plessis).
• Screening for monogenic forms of hypertension in a black population of the Free State, (MMedSc project by Ms T Smith under supervision of Prof. Viljoen).

4.3. Grant Funding

• South African Medical Research Council (MRC)
• National Research Foundation (NRF)
• NHLS Research Trust
• Technology Innovation Agency (TIA) Seed Fund
• UFS Interdisciplinary grants.

5. RESEARCH OUTPUT

5.1. Journal Publications


Janse van Rensburg WJ. Comparison of common platelet receptors between the chacma baboon (Papio ursinus) and human for use in pre-clinical human-targeted anti-platelet studies. Platelets. Published online: 11 Nov 2015, DOI:10.3109/09537104.2015.1095878.


5.2. Conference Presentations

National conferences
- Papers: n/a
- Posters: 2

International conferences
- Papers: n/a
- Posters: 3

6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

- Prof. Chris Viljoen NRF C3
- Prof. Muriel Meiring NRF C2
- At the 2015 Faculty Research Forum, Dr Jaco Joubert won the Kerneels Nel Medal for Joubert J, Joubert S, Raubenheimer J, Louw V. The long-term effects of training interventions on transfusion practice: A follow-up audit of red cell concentrate utilisation at Kimberley Hospital, South Africa. Transfusion and Apheresis Science 2014; 51(3): 25–32. He also won the prize for the Best Junior Educational Poster.
- Prof. Chris Viljoen won the Best Laboratory Poster (Senior category) for A perspective on GM detection in South Africa.
- Dr Leriska Haupt was the runner-up for the Best Junior Clinical Paper with Determination of functional iron deficiency status in haemodialysis patients at Pelonomi Hospital and Kimberley Hospital Complex.
- Jan-G Vermeulen was the runner-up for the Best Junior Laboratory Paper for The in vitro refolding a human derived single chain variable fragment against tissue factor, Jan-G Vermeulen, SM Meiring, FJ Burt, E van Heerden.
- Dr Leriska Haupt won the third prize for the Really Short Registrar Research Presentations in July 2015.
- Dr Jaco Joubert was one of two young South Africans invited to attend the Achieve Haemophilia Theory Programme, 16–18 November 2015, Baveno/Milan, Italy.
- Prof. Chris Viljoen and Prof. Muriel Meiring received R40 000 each as part of the National Research Foundation (NRF) Incentive Programme Funds in 2015.

7. ADDITIONAL INFORMATION

Prof. Coetzee is currently the Pathology Representative for the Universitas Academic Business Unit as well as the Chair of the Haematology Expert Committee.
Human Genetics

Head: Prof. Magda Theron

1. ABOUT THE DIVISION

The division is a SANAS-accredited service provider, and participates in international external quality programmes to ensure quality assurance. It provides a genetics healthcare platform to the Northern Cape and parts of the Free State. It also provides a prenatal service on samples including peripheral blood, products of conception, chorionic villus sampling and skin biopsy. Aneuploidy fluorescent in situ hybridisation (FISH) offers the benefit of a 24-hour turnaround time in high-risk pregnancies, while cell culturing provides a much deeper insight into the presence of abnormalities.

The molecular genetics laboratory is the national facility for the screening of familial breast cancer and also provides an international service to various parts of the African continent. The cytogenetics laboratory serves as the national referral unit for the diagnosis of Roberts’s syndrome and Fanconi anaemia. The laboratories primarily render a comprehensive diagnostic service to the Universitas Hospital, 3 Military Hospital, Pelonomi Regional Hospital, National District Hospital, Kimberley Hospital, Orpington Hospital, Bungen Hospital, Tsepong Hospital and surrounding clinics and various private pathology firms. Comprehensive genetics encompassed four sub-disciplines, molecular genetics, molecular cytogenetics (or fluorescent in situ hybridisation), cytogenetics and clinical genetics.

Mutation screening in the molecular genetic laboratory is mostly PCR-based and population-directed. The division provides diagnostic screening for inherited breast cancer and referrals throughout South Africa and the African continent are diagnosed. The FISH laboratory renders a prenatal and postnatal screening programme based on microdeletions and common chromosomal aneuploidies. The cytogenetic laboratory provides a prenatal and postnatal laboratory service for congenital and acquired chromosomal abnormalities. Cytogenetic analysis plays a major role in the diagnosis, prognosis and treatment of acquired genetic aberrations associated with haematological malignancies. Traditional cytogenetic analysis is performed on peripheral blood, bone marrow, amniotic fluid, products of conception and skin fibroblasts.

2. DIAGNOSTIC AND CLINICAL SERVICES

Haematological malignancies are diagnosed by both karyotyping and FISH. Different cell culture methods, synchronisation and time frames, have been introduced to provide the best quality of service with the most suitable turnaround times. Specific FISH probes are used to identify the presence of micro rearrangements to provide for personalised medicine. The molecular platform is polymerase chain reaction (PCR)-based and provides excellent quality and sensitivity for genetic testing. The introduction of real-time, high resolution melting equipment to the diagnostic and research platform ensures more cost efficient and sensitive molecular testing. This screening method also excludes the sequencing of negative samples and allows for high throughput analysis. Introduction of the multiplex ligation probe analysis has been implemented on the molecular diagnostic platform. This test method is now being validated on the cytogenetics platform, especially in dysmorphic patients, and will close the gap between molecular and cytogenetic diagnosis.

The analysis of solid tissue in paraffin-embedded slides provides for genetic testing also in post-mortem samples.

Table 23: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>PhD Scientists</th>
<th>MSc Scientists</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
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3. TEACHING AND TRAINING

3.1. Undergraduate Teaching

The division offers postgraduate training programmes for Masters degree, MMedSc (Human Genetics) and doctorates (PhD) in human genetics. At present six Masters students are registered for postgraduate studies. The intern medical scientist programme is very active and the facility is accredited by the Health Professions Council of South Africa (HPCSA) as a registered internship provider. Three intern medical scientists successfully completed training. Only one of these positions is funded by the NHLS.

Table 24: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
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<tr>
<th></th>
<th>Total Number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of Successful Completions</th>
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<td>All</td>
<td>6</td>
<td>3</td>
<td>-</td>
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</table>
4. RESEARCH ACTIVITIES

4.1. Research Projects

**Project Title:** Familial breast cancer in South Africa

**Principal investigator:** Five research projects on the molecular screening of familial breast cancer genes, *BRCA1* and *BRCA2*, in the diverse South African are undertaken under the supervision of Dr NC van der Merwe: (i) The molecular screening of familial breast cancer patients in the Indian population of South Africa, (ii) Molecular screening of familial breast cancer patients of Mixed ancestry/Coloured population of the Western Cape, (iii) Screening for large genomic rearrangements within the African, Indian and Mixed population of South Africa, screening the diverse South African population for mutations within the moderate susceptibility genes (iv) PALB2 and (v) BLM.

**Collaborators:** Prof. WD Foulkes, MD – Medical Geneticist – Department of Oncology and Molecular Genetics, McGill University, Montreal Canada; Dr G Chong PhD – Department of Oncology and Molecular Genetics, McGill University, Montreal Canada; Prof. EN Imyanitov, MBChB – Department of Tumour Growth Biology, Petrov Institute, St Petersburg, Russia; Dr I Buccamazza, MBChB – Surgeon – Head of Breast Unit, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa; P Moeti, MMSc Human Genetics – Post Graduate student, Division of Human Genetics, University of the Free State, Bloemfontein, South Africa; HMVE Combirink, MMSc Human Genetics – Post Graduate student, Division of Human Genetics, University of the Free State, Bloemfontein, South Africa; J Oosthuizen, MMSc Human Genetics – Medical Scientist at NHLS Division of Human Genetics, Bloemfontein, South Africa.

**Description:** The familial breast cancer genes *BRCA1* and *BRCA2* play a role in transcription, DNA repair of double-stranded breaks and recombination. Mutations in these genes account for about 40% of inherited breast cancer families and more than 80% of familial breast and ovarian cancer families. Screening of patients for a breast cancer genetic predisposition provides a unique opportunity to prevent the effects of the disease in more than a single person, for it is applicable to all related immediate family members. The goal of an effective national genetic screening programme is therefore to determine the presence of a deleterious mutation within an affected breast cancer patient, followed by intervention in susceptible family members before irreversible damage occurs. In order to identify susceptible family members, the breast cancer patient herself has to be fully screened for the major genes that might play a role in the individual’s DNA damage response pathway such as *BRCA1* and *BRCA2*. The presence of disease-causing mutations in these role players might impair genome stability control and may therefore contribute to familial breast cancer overall.

The research performed by this group in collaboration with others over the past 15 years has resulted in the identification of the first founder mutations present within the Afrikaner population (Reeves et al. 2004), the Coloured/Xhosa population from the Western Cape (van der Merwe et al., 2012) and the South African Indian and the Black African populations (van der Merwe et al. 2014). These results have laid the foundation for all familial breast cancer testing within South Africa, as the knowledge of the prevalence of these mutations in a specific population is necessary to provide accurate genetic counselling and clinical management.

The molecular screening of familial breast cancer patients in the Indian population of South Africa involved a variety of mutation screening techniques including the protein truncation test, high resolution melting analysis and first generation DNA sequencing. Nine different pathogenic mutations (from a total of 50 families) have been identified and characterised. Five of the disease-causing mutations were detected within *BRCA1* (BRCA1 185delAG,p.Leu22_Glu23LeuValfs; c.191G>A,p.Cys64Tyr; c.1360_1361delAG,p.Ser454Terfs; c.3593T>A,p.Leu1198Ter; c.5365_5366delGCinsA,p.Ala1789_Ile1790LeuTrpfs) with four in *BRCA2* (c.5279C>G,p.Ser1760Ter; c.5563C>G,p.Ser1855Ter; c.5563C>G,p.Ser1855Ter; c.8754+1G>A and c.9435_9436delGT,Val3145_Phe3146=fs). Three unrelated families were carriers of the splice site mutation found within *BRCA2* exon 21. No large rearrangements were detected. All these mutations were specific to the Afrikaner population (Reeves et al., 2012) and the South African Indian and the Black African populations (van der Merwe et al. 2014). These results have laid the foundation for all familial breast cancer testing within South Africa, as the knowledge of the prevalence of these mutations in a specific population is necessary to provide accurate genetic counselling and clinical management.

Molecular screening for large genomic rearrangements within the African, Indian and Mixed populations of South Africa. This MMSc project involved optimisation of the multiplex ligation probe analysis technique used for the screening for larger rearrangements within the familial BC genes, and then subsequent screening of 100 African, Indian and Coloured BC patients for this type of mutation. The research is being conducted on breast cancer patients tested negative for the presence of the smaller deletions/duplications/single base changes within *BRCA1* and *BRCA2* genes. Although none of the patients proved to carry this type of mutation, the technique was optimised and validated for use on the diagnostic platform in the NHLS Human Genetics laboratory. More than 100 breast cancer patients representing the Coloured
population from the Western Cape were screened for mutations within the familial breast cancer genes. Three recurrent mutations have been characterised. These will be tested for possible founder effects by performing haplotype analysis. Once status as founders has been confirmed this will be included in the molecular spectrum of the current diagnostic platform (population-based testing).

The possible involvement of two other candidate genes in the pathogenicity of breast cancer has been investigated. The moderate susceptibility genes, PALB2 and BLM, involve screening BRCA-negative breast cancer patients for mutations within these moderate impact genes. This study is focusing on the screening of 60 patients representing the Black, Indian and Coloured populations. The aim is the identification of potential disease-causing mutations that might explain the presence of breast cancer in these families, as the disease could not be traced to either BRCA1/2. These genes are associated with a chromosomal instability disorder, Bloom syndrome, and have not revealed in the plethora of elucidation such as PALB2, because it was previously postulated that mutations in BLM do not have much of an effect. This has been proven incorrect as mutations within this gene have been detected for BRCA negative breast cancer patients from Russia, Belarus and the Ukraine, and were found to increase an individual’s lifetime risk of BC six-fold, at least in the Slavic population.

During the period 2015/16, two NRF interns have been hosted within the Division of Human Genetics. Their training period of 12 months has been a great success as not only have they grown into independent researchers, they have contributed on various levels to the functionality of the laboratory.

5. RESEARCH OUTPUT

5.2. Conference Presentations

The work of this group has been presented at local, national and internal forums.

Oosthuizen J, Djee BK, Moeti PJ, Van der Merwe NC (2015a). Challenges and limitations observed during MLPA optimisation. 48th Faculty Research Forum of the Faculty of Health Sciences, Bloemfontein, South Africa.

Combrink HMVE, Oosthuizen J, Moeti PJ, Van der Merwe NC (2015b). Characteristics of hereditary breast cancer in the Indian population of South Africa. 48th Faculty Research Forum of the Faculty of Health Sciences, Bloemfontein, South Africa.


Attendance of the BRCA challenge meeting hosted by the Human Variome Project, held at UNESCO Paris, France, 12–13 June 2015.

6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

- Member of the Institutional Pathology Committee
- Member of National Academic Pathology Committee
- Board member of the Medical and Dental Board, Health Professions Council of South Africa
- Chair of the Medical Science Committee, Medical and Dental Board, Health Professions Council of South Africa
- Executive member of the Medical and Dental Board, Health Professions Council of South Africa
- Chair of the Medical Science Committee, Medical and Dental Board of the Health Professions Council of South
- Chair of Genetics Expert Committee
- Chair of the Medical Science Expert Committee
- Member of the Science Committee of the University of the Free State
- Chair of the Continual Professional Education Committee of the University of the Free State.
Medical Microbiology and Virology

Head: Prof. AA Hoosen

1. ABOUT THE DEPARTMENT

The department’s research focus areas are:

- Vector-borne and zoonotic viruses research  
  Head of research group: Prof. FJ Burt
- Human papilloma virus research  
  Head of research group: Prof. FJ Burt
- Human immunodeficiency virus research  
  Head of research group: Dr D Goedhals
- Molecular epidemiology of outbreak-causing bacteria  
  Primary investigator: Mrs A van der Spoel van Dijk.

Undergraduate and postgraduate training is provided for technicians (microbiology, virology, TB, clinical pathology); technologists (microbiology, virology, clinical pathology); science students (BSc Honours, MSc, PhD); undergraduate physiotherapy, occupational health, optometry, and medical students; and medical specialist training for medical microbiology, medical virology and infectious diseases.

2. DIAGNOSTIC AND CLINICAL SERVICES

The department provides a 24-hour microbiology and virology diagnostic and consultation service to Universitas and National hospitals. Telephonic consultation for clinical support is provided to Pelonomi Hospital as well as to the rest of the Free State and Kimberley. Information is provided on request to medical practitioners and health care workers. Ward rounds are conducted with clinicians.

Table 25: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Medical Doctors</th>
<th>PhD Scientists</th>
<th>MSc Scientists</th>
<th>Technologists</th>
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<th>South African</th>
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3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate Teaching

All undergraduate lectures are presented in English and Afrikaans, except where indicated otherwise.

Undergraduate teaching includes:

- MBBch II and III: MURI 2724, MCAR 2724, MRES 3714, MGEM 2724, MNER 3714, MGAS 2724, (Systemic infections): Co-ordinators Dr MD Morobadi and Dr K Baba
- Optometry III: SYPM 3704 (3rd year)
- Allied Health Students: PTCS 3704 (Physiotherapy); OCTS 3704 (Occupational Therapy).

3.2. Postgraduate Teaching

Postgraduate students enrolled

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<td>MMed</td>
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| PhD          | 2 (Micro)  
  4 (Virology) |
| MMedSc       | 1 (Micro)  
  5 (Virology) |
| BMedSc (Hons)| 6 (Micro and Virology) |
Postgraduate students qualified

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Technologists Trained

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<td>Laboratory assistants</td>
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Table 26: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
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<th>Percentage of successful completions</th>
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<tbody>
<tr>
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</tbody>
</table>

3.4. Other Training Information

Technicians and medical technologist training is shown above. This training is done in-house for technicians (TB, microbiology, virology and clinical pathology) and with the Central University of Technology for Medical Technologists.

4. RESEARCH ACTIVITIES

4.1. Research Units/Study Groups Linked to the Department

Medical Virology

**Vector-borne and Zoonotic Viruses Research Group**

**Head of Research Group:** Prof. FJ Burt

Research focuses on characterising humoral and cellular immune responses in patients with Crimean-Congo haemorrhagic fever (CCHF) virus and other arboviruses of medical significance, epitope discovery for vaccine development, development of molecular and serological assays for detection of arboviruses and other neglected diseases; and evaluation of vaccines against CCHF and yellow fever viruses.

**Human Papilloma Virus Research Group**

**Head of Research Group:** Prof. FJ Burt

The research group focuses on the identification and characterisation of human papillomavirus associated with recurrent laryngeal papillomas and head and neck cancers.

**Human Immunodeficiency Virus Research Group**

**Head of Research Group:** Dr D Goedhals

Collaborators: Dr JC Jansen van Vuuren, Dr D Steyn (Department Internal Medicine, UFS), Dr C Seebregts (MRC), Dr T de Oliveira (Africa Centre, UKZN), Dr J Frater, Prof. R Phillips (University of Oxford, UK)

The research group focuses on HIV drug resistance genotyping and surveillance in the public sector treatment programme and immunological studies including T cell function and viral adaptation in AIDS.

Medical Microbiology

**Molecular Epidemiology of Outbreak Causing Bacteria Group**

**Primary Investigator:** Mrs A van der Spoel van Dijk

Collaborators: Dr N Ismail (NICD), Dr S Omar (NICD), Dr H Said (NICD), Dr A-M Dyrhala Reese (University of Bergen), Dr L Rigouts (Institute of Tropical Diseases, Belgium) The research focuses on the detection of genes involved in the development of resistance to drugs used for the treatment of tuberculosis, the genotypes of strains circulating in the Free State and the diagnostic application thereof.
4.2. Research Projects

Vector-borne and Zoonotic Viruses Research Group

Head of Research Group: Prof. FJ Burt

Project Title: Immune responses in survivors of Crimean-Congo haemorrhagic fever and evaluation of candidate vaccines
Funding: Poliomyelitis Research Foundation, NHLS Research Trust, NRF/DST Research Chair

Project Title: Tick-borne and mosquito-borne pathogens in humans in southern Africa
Funding: NHLS Research Trust, University of the Free State, NRF/DST Research Chair

Project Title: Development and evaluation of novel vaccines for medically significant arboviral diseases
Funding: NHLS RT

Human Papilloma Virus Research Group

Head of Research Group: Prof. FJ Burt

Project Title: Human papillomavirus in head and neck neoplasms
Funding: NRF

Human Immunodeficiency Research Group

Head of Research Group: Dr D Goedhals

Project Title: A longitudinal comparison of HIV quasi specie populations in patients before commencing HAART and after failing HAART using a next generation deep sequencing approach
Funding: Poliomyelitis Research Foundation

Project Title: Characterisation of T cell responses to the non-structural proteins of the M segment in survivors of CCHF virus infection
Funding: NHLS Research Trust

Project Title: Development of in-house molecular assays and evaluation of the GeneXpert MTB/RIF assay for the rapid detection of extrapulmonary tuberculosis
Funding: NHLS Research Trust

Molecular epidemiology of outbreak causing bacteria group

Head of Research Group: Mrs A van der Spoel van Dijk

Project Title: Monitoring of drug resistance, drug resistance determinants and molecular epidemiology of Mycobacterium tuberculosis isolates in the Free State Province, South Africa

Project Title: Detection of mutations involved in resistance to Pyrazinamide, Fluoroquinolones and Diaryquinolines in MDR strains of Mycobacterium tuberculosis in the Free State and the best methods to detect resistance

Project Title: Tuberculosis in adolescents aged 10–19 in the Free State Province

Project Title: Detection of the CTX-M gene in Escherichia coli isolates from patients in the Universitas Hospital in Bloemfontein

Project Title: Molecular identification of Methicillin resistant Staphylococcus aureus in Universitas Hospital, Bloemfontein

Project Title: Characterising carbapenem – nonsusceptible isolates of Klebsiella pneumonia found at the Universitas Hospital

Project Title: The occurrence, detection and reporting of rifampicin resistance and presence of gene mutations affecting fitness in Mycobacterium strains from the Free State Province, South Africa: Implications in MDRTB and XDRRTB cases

4.3. Grant Funding

Burt FJ

- Received funding under the Sweden (STINT)/South Africa (NRF) Science and Technology Research Collaboration
- R500 000 grant received from NHLS for research project: Vaccine strategies for medically significant arboviruses, for 2016
- Received funding from Polio Research Foundation for research project: Innate signalling induced by CCHF virus proteins and Hazara virus as a model for CCHF virus.
Goedhals D

- Received funding from the Poliomyelitis Research Foundation for research project: Characterisation of T cell responses to the nonstructural proteins of the M segment in survivors of CCHF virus infection.

5. RESEARCH OUTPUT

5.1. Journal Publications

Full-length articles


Chapter in book


5.2. Conference Presentations

<table>
<thead>
<tr>
<th>International congresses</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>International invited speaker</td>
<td>3</td>
</tr>
<tr>
<td>National congress presentations</td>
<td>18</td>
</tr>
<tr>
<td>National congresses invited chair</td>
<td>3</td>
</tr>
<tr>
<td>National congresses invited speaker</td>
<td>3</td>
</tr>
<tr>
<td>Regional and local congress presentations</td>
<td>11</td>
</tr>
</tbody>
</table>

6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

48th University of the Free State, Faculty of Health Sciences Research Forum Bloemfontein, 27–28 August 2015:

- First prize in the senior laboratory division: Goedhals D, Paweska JT, Burt FJ. Identification of Novel T cell epitopes on Crimean-Congo haemorrhagic fever virus and confirmation of long-lived memory T Cell responses


- School of Medicine Researchers under 35 winner: Sokhela CM. Restriction method for detecting low level rifampicin resistance in *Mycobacterium tuberculosis*

4th Annual Free State Department of Health Provincial Research Day, Bloemfontein, 12-13 November 2015:

- Best Paper for Operational Research: Arendse T. Investigating an outbreak of Streptococcus pyogenes in a surgical ward at Universitas Academic Hospital, Bloemfontein, Free State

- Best Novice Paper: Van der Spoel van Dijk A. (Collected as supervisor for Medical Students Research project). Multidrug resistant (MDR) tuberculosis amongst adolescents in the Free State

Prestige Scholars Programme:

- Dr D Goedhals was appointed to the Vice-Chancellor’s Prestige Scholars Programme of the University of the Free State

Research Chair:

- The South African Research Chair in Vector-borne and zoonotic diseases research, hosted by the University of the Free State, funded by the Department of Science and Technology and administered by the NRF, was awarded to Prof F Burt. The work of the research chair is to investigate medically significant vector-borne and zoonotic viruses currently circulating; to define associations between these viruses and specific disease manifestations that have previously not been described in our region; to increase awareness of these pathogens; and to further the understanding of host immune responses, which should facilitate development of novel treatments or vaccines and drug discovery.

7. ADDITIONAL INFORMATION

The UFS Council confirmed the establishment of a Virology Division within the Department of Medical Microbiology.
Chemical Pathology

Head: Dr V Gounden

1. ABOUT THE DEPARTMENT

The Department of Chemical Pathology provides a 24-hour diagnostic and consultative service for the academic complex and is a referral centre for the entire KwaZulu-Natal (KZN) province for specialist tests. Consultative services and coverage across KZN are provided by three consultant chemical pathologists at the Academic complex and one at the Midlands complex.

The department participates in undergraduate and postgraduate training at the University of KwaZulu-Natal (UKZN). It trains specialists in chemical pathology and currently has five registrars and one intern medical scientist in training. The department provides in-service teaching and training to student medical technologists and technicians registered for both chemical and clinical pathology.

<table>
<thead>
<tr>
<th>Total number of staff per profession and highest qualification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologist MSc Scientist Technologists Technicians Support South African Total</td>
</tr>
<tr>
<td>All 4 1 19 14 15 53 54</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The total workload for the period 2015/16 for King Edward VIII Hospital (KEH) Laboratory was 955 515 tests, and for Inkosi Albert Luthuli Central Hospital (IALCH) the workload was close to 2 million tests.

The KEH Laboratory has been SANAS-accredited since July 2014. Installation of new chemistry analysers are planned by mid-2016. The IALCH Laboratory received SANAS accreditation in February 2016 following an initial audit in October 2015. This was achieved by the laboratory despite the loss of the HOD in the period before the audit and with no quality assurance supervisor since 2014.

The laboratory complex was also audited by the NHI National Core Standards Team in March 2015 and the chemistry laboratory as well as the other laboratories in the complex received a score of 100%.

Technical Staff shortages continue to be a challenge. The laboratory was able, during this period, to set up the 25 hydroxy vitamin D assay on its Liquid Chromatography tandem Mass Spectrometry (LC-/MS/MS) analyser. This improved turnaround times for this test, as previously it had been a send-away test, and introduced testing for Vitamin D on a more analytically sensitive and specific platform. It is the only laboratory currently in the NHLS to provide Vitamin D analysis on LC-MS/MS.

The laboratory continued with the BioRad Unity Connectivity Programme and participates in various external quality assurance programmes, such as Thistle, Royal College of Pathologists of Australia (RCPA) and National External Quality Assessment Service (NEQAS), throughout the year.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1 Undergraduate

The department contributed to lectures, student assessments, and to the content of the curriculum for medical students at the Nelson R Mandela School of Medicine. Pathologists from the department are involved in co-ordination of blocks, setting of examination questions and review of examination papers.

3.2 Postgraduate

Registrars in chemical pathology participate in a four-year MMed course which covers theoretical and practical training and includes submission of a research project. Training provided to registrars includes regular tutorials, case and calculation discussions, essay writing practice and regular wet-practical sessions. Registrars are assigned to different bench rotations and are involved in diagnostic service delivery. They also contribute to monitoring and troubleshooting of internal quality control and external quality assessment schemes, as well as in-laboratory method evaluations.

Registrars are involved in the teaching of medical students, technologists and technicians. The department also provides teaching for other specialty postgraduate students and is accredited to train intern medical scientists.
Technologists and Technicians

The department provides in-service teaching and training to student medical technicians and technologists registered for chemical pathology and clinical pathology.

Professional Development

The department conducts academic meetings that include case presentations, seminars and journal reviews twice weekly and has engaged in educational activities for clinicians with regard to requesting tests.

Table 26: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>17</td>
<td>14 (Tech)</td>
<td>10(Tech)</td>
</tr>
</tbody>
</table>

No registrars wrote part 2 exams during this period.

4. RESEARCH ACTIVITIES

4.1. Research Units/Study Groups Linked to the Department

Project Title: MANAGE Study
Principal Investigator: Dr B Biccard
Sub-Investigator: Dr P Naidoo
Short Description: The MANAGE clinical trial is a multicentre international study. It is co-ordinated by the Population Health Research Institute (PHRI) in Canada and commenced at IALCH in April 2014 and managed by the pre-operative research group led by Prof. Biccard. The aim of the trial is to investigate the usefulness of Dabigatran and Omeprazole following post-operative cardiovascular damage in non-cardiovascular surgery. To date, 65 patients have been recruited. Several biochemical markers are reviewed in the routine management of these patients. Additional testing is co-ordinated via the MANAGE team.

Project Title: VISION Study
Principal Investigator: Dr B Biccard
Sub-Investigator: Dr P Naidoo
Short Description: The Vascular events In non-cardiac Surgery patients cOhort evaluatioN study (VISION) is a multinational observational cohort study evaluating major vascular events in patients undergoing non-cardiac surgery. This study aims to determine an optimal clinical model to predict major peri-operative cardiovascular adverse events. It will also determine the extent of postoperative troponin leak, the proportion of postoperative myocardial infarctions that would have been missed without troponin analysis, and the long-term prognostic implications of a postoperative troponin leak. This study includes an international collaboration of anaesthetists, cardiologists, surgical disciplines and chemical pathologists. The IALCH Chemical Pathology Laboratory provided support for 24 hour Troponin T analysis. Study recruitment and sample analysis has been completed. Data collation, analysis and write-up are currently being completed.

Project title: Primary hypertension prevalence and risk factors in Grade XII learners in Durban, South Africa
Principal Investigator: Prof. R Bhimma
Sub Investigator: Dr V Gounden
Short Description: The project is being co-ordinated by the Paediatric and Adult Nephrology departments at IALCH/UKZN. The purpose of this study is to determine the prevalence of hypertension, and define its contributing risk factors in Grade XII learners in Durban, South Africa.

4.2. Research Projects

Project title: Dropper cap evaluation for Thermo Fischer controls (Pathologist: Dr RS Sirkar)

Project Title: Evaluation of common paediatric creatinine based glomerular filtration rate (GFR) estimating equations in African children in KwaZulu-Natal (Registrar: Dr Y Rampursat)
5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

National


International


6. WORKSHOPS ATTENDED/SKILLS TRAINING

- Good QC practices in the context of ISO 15189 – 03 June 2015 attended by registrars, pathologists and technologists from the department
- CMSA Examiner’s Workshop – 11 March 2016
- Teaching and Learning – Problem based learning – 18 February 2016
- Teaching and learning – Assessments – 25 February 2015
Medical Microbiology

Head: Prof. K P Mlisana

1. ABOUT THE DEPARTMENT

The KwaZulu-Natal Academic Complex consists of laboratories at both Inkosi Albert Luthuli Central Hospital (IALCH) and King Edward VIII Hospital (KEH) and is the provincial referral laboratory for bacteriological, fungal and mycobacterial identification and susceptibility testing. All joint staff microbiologists are incorporated into the staff complement of the academic complex, which has boosted service, research and the training capacity of the department. A well-structured and consistent consultative microbiology service, including regular visits and telephonic consultations, is provided to all larger KZN hospitals with ICU wards.

The research focus areas of the department include TB (diagnostics, drug resistance and paediatric TB), STIs and other multidrug resistant microorganisms. Within UKZN, closer research collaborations have been established with the Centre for the AIDS Programme of Research in South Africa (CAPRISA), Neurology Department, Paediatrics Department and School of Health Sciences. External collaborations include the Microbiology Department, UCT and Emory University (USA).

The department is involved in the teaching and training of both undergraduate and postgraduate students.

| Table 27: Total number of staff per profession and highest qualification |
|-------------------------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| Professional | Pathologist | Med Doctors | MSc | BSc | Technologists | Support | South African* | All |
| Black | 2 | 6 | - | - | 1 | 3 | 33 | 45 | 45 |
| Coloured | - | - | - | - | - | - | - | - | - |
| Indian | 10 | 7 | 3 | 2 | 11 | 6 | 39 | 39 |
| White | 1 | - | - | - | 1 | - | 2 | 2 |
| Other | 1 | - | - | - | - | - | 1 | 1 |
| South African* | 14 | 12 | 3 | 3 | 15 | 39 | 86 | 86 |
| Total | 14 | 13 | 3 | 3 | 15 | 39 | 87 | 87 |

2. DIAGNOSTIC SERVICE

A 24 hour microbiology service is provided by the laboratories within the academic complex. The repertoire of tests includes bacteriology, mycology and mycobacteriology and the laboratory strives to produce high quality, rapid and clinically relevant results to enhance patient management. Both phenotypic and genotypic identification and susceptibility testing are offered. The IALCH Microbiology Laboratory serves as a reference laboratory for the identification and susceptibility testing of isolates, including fungi, from laboratories throughout KZN.

The IALCH Tuberculosis (TB) Laboratory is the only culture facility in KZN, offering drug susceptibility testing of 1st and 2nd line anti-TB drugs for the province. The monthly average number of TB cultures and auramine stains that are processed at IALCH is 11,000 and 2,750 respectively. The laboratory currently offers GeneXpert testing for extrapulmonary TB (EPTB) specimens which has expedited the diagnosis of EPTB. The molecular TB facility performs Hain Line-probe assays (LPA) for identification and drug susceptibility of Mycobacterium tuberculosis. MTBDRsl LPA is performed in selected cases of smear positive or culture positive samples to assist in the diagnosis of extensively drug-resistant tuberculosis (XDR-TB). The identification of non-tuberculous mycobacteria using LPA is offered on request to a pathologist. Pathologists provide consultative services to clinicians on a daily basis and participate in a range of activities within the different hospitals including ICU ward rounds, Infection Control meetings and Pharmacy and Therapeutics Committees, etc.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Undergraduate and postgraduate students from UKZN as well as technicians and technologists in training from Durban University of Technology and Mangosuthu University of Technology receive teaching and training by the department.

3.1. Undergraduate UKZN students

Over 50 microbiology lectures and practical sessions are given to approximately 250 undergraduate medical students in the first three years of the MBChB programme. Most of the microbiology teaching occurs in the 3rd year during a six-week infectious disease module. A medical microbiology module is also offered to third year BMedSc students in the second semester. This course includes didactic lectures and laboratory practical sessions.
Basic microbiology lectures are delivered to health sciences students comprising predominantly audiology and physiotherapy students.

### 3.2. Postgraduate UKZN students

Honours students from UKZN receive lectures on advanced microbiology and immunobiology during the year. The department oversees the Microbial Pathogenesis module. Research projects are also conducted in the department and are supervised by the pathologists.

A comprehensive training programme encompassing theory and practical aspects of medical microbiology is offered to MMed registrars, intern medical scientists and fellows in infectious diseases. Registrar training comprises daily informal teaching at the bench and bedside as well as formal tutorials. In addition, registrars are involved in external quality assurance (EQA) programmes and have mock theory and practical examinations throughout the year.

A module on Sexually Transmitted Infections is taught to students enrolled for a postgraduate Diploma in the Clinical Management of HIV/AIDS (UKZN).

#### 3.3. Technologists and Technicians

The laboratory is accredited to provide experiential training to medical technologists and to train medical technicians. A weekly CPD programme is conducted for all staff members.

#### 3.4. Professional Development

Two senior registrars passed the FCPath (Micro) examination in October 2015 and another successfully completed MMed. Nine of 23 students who enrolled for the BMedSc (Honours) programme conducted research projects that were supervised by pathologists within the department.

One intern medical scientist completed training and one is in the final year of training.

Table 28 below demonstrates the category of students trained and the number trained in each department. Students include undergraduates and postgraduates.

#### Table 28: Category of students trained per department

<table>
<thead>
<tr>
<th>Category</th>
<th>Routine microbiology</th>
<th>TB laboratory</th>
<th>Mycology laboratory</th>
<th>Molecular laboratory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registrars (junior)</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Intern Scientists</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Experiential students</td>
<td>16</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Intern medical technologists</td>
<td>6</td>
<td>38</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Intern medical technicians</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Student Medical technologists</td>
<td>-</td>
<td>2</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Medical technicians</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Student Medical technologists</td>
<td>-</td>
<td>-</td>
<td>34</td>
<td>-</td>
</tr>
<tr>
<td>Medical technologists</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>BSc Honours</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29</strong></td>
<td><strong>45</strong></td>
<td><strong>45</strong></td>
<td><strong>13</strong></td>
</tr>
</tbody>
</table>

#### 3.5. Postgraduates

Interdepartmental academic meetings include weekly journal presentations, seminars, infectious disease case presentations and monthly research updates on projects related to the department.

Two junior registrars passed the MMed Part 1 examination in February 2015. Two senior registrars passed the FCPath (Micro) examination in October 2015 and a third completed her MMed project resulting in three newly qualified pathologists at the end of 2015. Two of these consultants could not be appointed into the department as there was only one vacant position.

Eleven students who enrolled for the BMedSc (Honours) programme conducted research projects that were supervised by pathologists within the department. Two fellows (paediatricians), registered for the diploma in infectious diseases, were trained. Two intern medical scientists were in training in 2015 and one completed and has now enrolled for a Masters degree within the department.
A Medical Microbiology module comprising lectures on antimicrobials and antimicrobial susceptibility testing was given to Honours students (Infection Prevention and Control).

The table below shows the number of postgraduate trainees per category that have completed/are still in training.

Table 29: Number of postgraduate trainees per category that completed/are still in training

<table>
<thead>
<tr>
<th>Total Number of trainees</th>
<th>Still in training</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intern Scientists</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>BSc Honours</td>
<td>9</td>
<td>-</td>
<td>9</td>
<td>100%</td>
</tr>
<tr>
<td>Registrars (junior)</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>100%</td>
</tr>
<tr>
<td>Registrars (senior)</td>
<td>5</td>
<td>5</td>
<td>-</td>
<td>100%</td>
</tr>
<tr>
<td>MMed</td>
<td>9</td>
<td>5</td>
<td>3 (+ 1 resignation)</td>
<td>75%</td>
</tr>
<tr>
<td>PhD</td>
<td>10</td>
<td>9</td>
<td>1 (MMed project completed)</td>
<td>100%</td>
</tr>
<tr>
<td>All</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>100%</td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

The Department continues to benefit from close research collaborations with CAPRISA (UKZN) resulting in various publications and joint grant applications. New collaborations have been established with the University of Cape Town, Medical Microbiology Department, and the collaborations with Emory University (USA) for two protocols, namely transmission of HIV-Associated XDR TB in SA (TRAX) and SHOUT study (The Survival and HIV Outcomes in MDR-TB) continue. The department collaborates with the MRC in a study testing the accuracy, sensitivity and specificity of the Loop-mediated Isothermal Amplification (LAMP) assay for detection of pulmonary M. tuberculosis (TB) infection.

To date, the research focus of the department has been on rapid diagnostic tests for TB, antimicrobial resistance testing, testing of potential antituberculosis compounds, proteomic profiling using sophisticated MALDI-TOF MS systems and biomarker analysis. Currently the department has undertaken research looking at non-molecular, rapid methods for drug susceptibility testing of MTB, viz, Resazurin (REMA) and a commercial Sensititre microplate assay. To address the challenges associated with TB paucibacillary samples like cerebrospinal fluid (CSF), research is in progress investigating novel methods to detect femtomole levels of MTB in CSF to improve laboratory diagnosis of TB meningitis.

4.1 Research Units/Study Groups Linked to the Department

Proof-of-Concept Study: Changing the STI care model to reduce genital inflammation and HIV risk
Research Group: CAPRISA, UKZN
Funder: NIH
Principal Investigator: Dr N Garrat, UKZN
Co-investigator: Prof. K Mlisana
Aim of the Study: To determine if a new model of enhanced STI management can reduce genital tract inflammation and HIV risk
Short Description: This study will explore whether an innovative, enhanced programme of STI management will result in a higher cure rate and lower recurrence rate, with a subsequent reduction in genital inflammatory cytokines and hence HIV risk. This proof-of-concept study will identify individuals with STIs using an innovative, point-of-care (POC) diagnostic test, an automated, cartridge-based nucleic amplification assay (GeneXpert) for the simultaneous detection of Neisseria gonorrhoeae (NG) and Chlamydia trachomatis (CT). Following POC diagnosis, participants will be treated immediately with appropriate therapy under direct supervision, giving the participants the same treatment to take home for their sexual partners (expedited partner therapy).

Study Title: The Survival and HIV Outcomes in MDR-TB (SHOUT)
Research Group: The Emory-Einstein TB Research Group
Funder: US National Institutes for Health
Emory Principal Investigator: N Gandhi (NIH PI)
UKZN Principal Investigator: K Mlisana
UKZN Co-investigator: P Moodley
Short Description: This study is a prospective, observational cohort examining the relative contributions of HIV-co-infection, antiretroviral therapy, and TB strain type to survival and treatment outcomes in patients with MDR-TB. The primary outcome is to determine if a difference in survival exists between patients who are HIV negative and HIV positive, in an era when ARVs are generally widely available. Secondary outcomes examine differences in culture conversion, MDR TB outcomes, adverse events, and adherence between the two groups. The rates of virologic failure and HIV resistance that develop on treatment will also be examined.

Study Title: Transmission of HIV-associated XDR TB in South Africa (TRAX)
Research Group: The Emory-Einstein TB Research Group
Funder: US National Institutes for Health
Emory Principal Investigator: N Gandhi (NIH PI)
UKZN Principal Investigator: P Moodley
UKZN Co-investigator: K Mlisana
Short Description: Objectives of the study are: i) to measure the proportion of new XDR TB cases which develop due to primary transmission and to determine risk factors for developing XDR TB through primary transmission; and ii) to determine transmission patterns of XDR TB using molecular genotyping, epidemiologic, and social network analysis, and to identify the persons and locations most prominently associated with XDR TB transmission.

4.2 Research Projects

Project Title: Laboratory detection of rifampicin low level resistance in MTB
NHLS Investigators: NR Dlamini, KP Mlisana
Funding: NHLS Research Trust (Research Advancement Grant)
Duration: 2015–2017

Project Title: Empiric antimicrobial therapy for probable versus directed therapy for possible ventilator associated pneumonia in critically injured patients
NHLS Investigator: Y Ramsamy
Collaborator (UKZN): DJJ Muckart
Funding: Still pending
Duration: 2014–2015

Project Title: Comparison of the E Test and Agar dilution methods for the antibiotic susceptibility testing of Neisseria gonorrhoeae
NHLS Investigators: KP Mlisana, M Pillay
Funding: Centre of Excellence for HIV Prevention – CAPRISA

Project Title: Prevalence of extended spectrum beta-lactamase-producing E. coli and K. pneumoniae in a KwaZulu-Natal (KZN) Referral Hospital
NHLS Investigator: N Naidoo, M Pillay, KP Mlisana
Funding: Not required
Duration: 013–2015

Project Title: Rapid diagnosis of tuberculous meningitis: Detection of tuberculostearic acid in cerebrospinal fluid
NHLS Investigators: K Mlisana, M Pillay, YM Coovadia
Co-investigators: A Bhigjee, P Govender
Funding: NHLS Research Trust
Duration: 2014–2015
<table>
<thead>
<tr>
<th>Project Title</th>
<th>NHLS Investigators</th>
<th>Co-investigators</th>
<th>Funding</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory screening and prevalence of carbapenemase-producing enterobacteriaceae isolates from Inkosi Albert Luthuli Central Hospital</td>
<td>SL Maphumulo (MMED Project), K Swe Swe-Han, KP Mlisana</td>
<td></td>
<td>None</td>
<td>2014–2016</td>
</tr>
<tr>
<td>Causes of meningitis in era of HIV</td>
<td>P Ramjathan (MMED Project), KP Mlisana, Y Coovadia</td>
<td></td>
<td>Not required</td>
<td>2013–2015</td>
</tr>
<tr>
<td>A retrospective analysis of fungal infection in a renal unit at a central referral hospital Durban, KwaZulu-Natal</td>
<td>A Khumalo (MMED Project) and K Swe Swe-Han</td>
<td></td>
<td>Not required</td>
<td>Jan 2014–Dec 2016</td>
</tr>
<tr>
<td>A prospective laboratory based study. Comparing the resazurin microtitre plate assay and sensititre mycotb plate method to the conventional indirect agar dilution drug susceptibility method</td>
<td>P Jaglal (MMED Project), M Pillay, KP Mlisana</td>
<td></td>
<td>UKZN Grant</td>
<td>2014–2016</td>
</tr>
<tr>
<td>Effect of the capsular material of <em>Cryptococcus neoformans</em> on the interplay between microglial cells and neutrophils</td>
<td>P Bhola (PhD project)</td>
<td>W Sturm (Supervisor)</td>
<td>UKZN grant and NHLS Research Trust</td>
<td>2013–2016</td>
</tr>
<tr>
<td>A novel standardised approach to the treatment and management of significant Acinetobacter species infection in KZN</td>
<td>K Swe Swe-Han (PhD project), KP Mlisana (Co-supervisor) and K Baba (Co-supervisor)</td>
<td>M Pillay (Supervisor)</td>
<td>UKZN grant and MEPI grant</td>
<td>2013–2016</td>
</tr>
</tbody>
</table>

4.3 Miscellaneous Projects

- Comparative evaluation of Eswab system with the Amies agar swab transport system.
- The prevalence of inhA/katG mutations in drug resistant Mycobacterium isolates in South Africa.
- Performance of the SD TB Ag MPT64 rapid assay for detection of *Mycobacterium tuberculosis* complex from contaminated and non-contaminated cultures in liquid and solid media.
- Diagnosis of tuberculosis meningitis in the human immunodeficiency virus era.
- A prospective study to evaluate stewardship, surveillance and prudent antimicrobial use as interventions to curb the emergence of MDRO.
• Spectrum of organisms and outcome of neonatal infections in HIV exposed and unexposed newborns at a tertiary care hospital in KZN (ongoing).
• Retrospective laboratory-based study on the microbial causes of culture positive meningitis at King Edward VIII Hospital (ongoing).

PhD Projects – Ongoing
• A novel standardised approach to the treatment and management of significant Acinetobacter species infection in KwaZulu-Natal: Dr KSS Han.
• Utility of Nybomycin against Mycobacterium tuberculosis: Dr A Niehaus.
• Effect of the capsular material of Cryptococcus neoformans on the interplay between microglial cells and neutrophils: Dr P Bhola.

MMed Projects (Current)
• A retrospective analysis of fungal infection in a Renal Unit at a central referral hospital in Durban, KwaZulu-Natal.
• Comparison of the resazurin microtitre plate assay (REMA) and the Sensititre Mycobt plate method to the conventional indirect drug susceptibility test using the agar dilution method.
• Sexually transmitted infections among men who have sex with men.
• Evaluation of the BioFire FilmArray BCID panel for identification of organisms and antimicrobial resistance genes from positive blood cultures.
• Laboratory screening and prevalence of carbapenemase producing enterobacteriaceae isolates from Inkosi Albert Luthuli Central Hospital (IALCH).
• Prevalence of Apsergillus species in HIV negative and HIV positive patients in KwaZulu-Natal.

5. TRAINING AND RESEARCH OUTPUT

5.1 Postgraduate Degrees Attained
• 1 PhD
• 1 Masters degree
• 2 passed FCPath (Micro) in Oct 2015
• 5 MMed completed in 2015
• 2 MMed Part 1 (Departmental Examination) – passed in 2015
• 1 Completed Intern Medical Scientist.

5.2 Journal Publications


Ramsamy Y, Muckart DJ, Bruce J, Han KSS, Misana K. Culture shock – To treat or not to treat. Am J Respir Crit Care Med. 2015; 191:A4057.

Ramsamy Y, Muckart DJ, Bruce J, Han KSS, Misana K. Balance of probabilities – Directed or empiric therapy for ventilator associated pneumonia (VAP)? Am J Respir Crit Care Med. 2015; 191: A4346.


5.3 Conference Presentations

**International Conferences: 2015**

**Oral Presentations**

Dr KSS Han. *Concerns on Pathogen Resistance and Public Health regarding MDR Acinetobacter sepsis vs synergy results of combination drugs susceptibility.* 1st International Caparica Conference in Antibiotic Resistance.

Dr Khine Swe Han. *The prevalence of Carbapenem Resistant Gram Negative Bacteria (CRGNB) and Methicillin Resistant Staphylococcus aureus (MRSA) in a central referral hospital, Durban, South Africa between 2010–2014.* Antibiotics Conference, September 2015, USA.

Posters: 5 (Unable to present four posters due to financial constraints)


- Ramsamy Y, Muckart DJJ, Bruce JL, Han KSS, Mlisana K. Balance of probabilities – Directed or empiric therapy for ventilator associated pneumonia (VAP).
- Ramsamy Y, Muckart DJJ, Han KSS, Mlisana K. Be narrow minded … Resistance to treatment is not futile.
- Ramsamy Y, Muckart DJJ, Bruce JL, Han KSS, Mlisana K. Culture shock – To treat or not to treat *A. baumannii* isolates in patients with suspected VAP in a trauma intensive care unit.


Mahabeer P. Drug-resistant Tuberculosis in children less than five years old with culture positive *Mycobacterium tuberculosis*. International Congress on Infectious Diseases (ICID), India, March 2016.

**National Conferences 2015**

**Oral Presentations**


Pillay M. Performance of the SD TB Ag MPT64 rapid assay for detection of *M. tuberculosis* complex from cultures grown in liquid and solid media. PathRed Conference.

Mlisana K. Laboratory challenges and successes in management of a Diphtheria outbreak in KZN. FIDSSA Conference.

Dlamini N. Drug resistant TB in KwaZulu-Natal: Trends over four years. FIDSSA Conference.


Mahomed S. Challenges in the interpretation of discordant molecular and phenotypic TB results. FIDSSA Conference.

Naidoo N. Sepsis syndrome in a case of prosthetic valve endocarditis caused by *Acinetobacter baumannii*. FIDSSA Conference.

**Poster Presentations**

Naidoo N. Antimicrobial susceptibility testing of *Nocardia spp* in KZN. PathRed Conference.

Mahabeer Y. Causes of nosocomial bacteraemia in intensive care units at a tertiary hospital in Durban. FIDSSA.

Mahabeer Y. First report of neonatal bacteraemia caused by *bla*<sub>ESBL</sub> *Raoultella ornitholytica*. FIDSSA.

Han KSS. The role of synergy tests in determining effective antibiotic combinations in the treatment of patients infected with *Acinetobacter baumannii*. FIDSSA.

Mahabeer P. Serotype distribution and Ampicillin susceptibility of *Haemophilus influenzae* associated with non-invasive infections. FIDSSA.

Han KSS. A rare case of Nocardia species causing mastoiditis and right extradural empyema in a patient with HIV infection in ENT unit at a central referral hospital, KZN. FIDSSA.
Virology

Head: Dr Pravi Moodley

1. ABOUT THE DEPARTMENT

A toll-free hotline for all Virology queries in KZN was set up in collaboration with CAPRISA, as part of the Advanced Clinical Care for HIV and TB. The department also participated in the HPCSA accreditation visits for the Medical Undergraduate Curriculum in May 2015.

Table 30: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Medical Doctors</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>Student Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>4</td>
<td>1</td>
<td>13</td>
<td>13</td>
<td>16</td>
<td>52</td>
<td>53</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

HIV PCR testing (Table 31) increased considerably due to the introduction of birth testing as part of Early Infant Diagnosis (EID). The number of HIV viral load tests decreased considerably since the establishment of HIV Viral Load testing at other Laboratories in KZN. All the viral serology enzyme-linked immunosorbent assays (ELISAs) for HIV, HAV, HBV, HCV, Rubella, Cytomegalovirus (CMV), Epstein-Barr virus, HSV 1/2 and toxoplasma serological markers are done in KZN routinely. These tests (Table 31) continue to increase due to more requests for HBV from the clinics in the Comprehensive Care Management and Treatment (CCMT) Programme. All the viral PCR (Table 31) testing in KZN for CMV, VZV, HSV, Parvovirus, Respiratory Viruses and Enteroviruses is also done. These more sophisticated PCR assays replaced the conventional virus isolation which is no longer offered as a diagnostic service, and all have passed all quality assurance verifications before being offered.

Table 31: Trends in diagnostic service workload: 2010–2015

<table>
<thead>
<tr>
<th></th>
<th>2011/12</th>
<th>2012/13</th>
<th>2013/14</th>
<th>2014/15</th>
<th>2015/16</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV Viral Loads</td>
<td>188 512</td>
<td>155 287</td>
<td>93 068</td>
<td>161 806</td>
<td>220 047</td>
</tr>
<tr>
<td>HIV PCR</td>
<td>103 424</td>
<td>85 866</td>
<td>133 541</td>
<td>115 691</td>
<td>159 753</td>
</tr>
<tr>
<td>Viral Serology</td>
<td>338 113</td>
<td>306 072</td>
<td>404 105</td>
<td>360 915</td>
<td>420 706</td>
</tr>
<tr>
<td>Viral PCR</td>
<td>6 985</td>
<td>5 872</td>
<td>11 809</td>
<td>1 483</td>
<td>6 053</td>
</tr>
<tr>
<td>HIV Drug Resistance</td>
<td>28</td>
<td>234</td>
<td>172</td>
<td>74</td>
<td>312</td>
</tr>
</tbody>
</table>

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Three medical technology students passed in March 2015 and one in September 2015. Seven students are currently registered and being prepared for the March 2017 examinations. An average of 15 undergraduate science students is taught in their final year BSc (Biomedical Science) per year with an annual pass rate of 100% in previous years. The pass rate in 2015 was 10 of 15 students. There are currently 31 students registered. An average of 200 undergraduate medical students is taught in the first three years of the curriculum. The department plays a much more intensive role in this programme, especially in third year.

Table 32: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

4. RESEARCH COVERAGE

Coverage was improved in KZN by providing services to Ngwelezane, Empangeni, Edendale PMMH and RKK Laboratories. Quality improvement sessions regarding EID were also provided at IALCH and Prince Mshiyeni Memorial Hospital (PMMH). The department is involved in the eThekwini District Health HIV/TB QUALITY Improvement Programme, and also provided a session in the KZN Polio Eradication Workshop. Sessions were presented on HIV drug resistance and HIV viral load suppression rates in KZN as part of the CAPRISA Advanced Clinical Care workshops for each of the 11 Health Districts in KZN.
4.1. Research Projects

**Project Title:** Aptamer Conjugated hybrid nanoparticles for targeted delivery of an antiretroviral drug to the lymph nodes  
**Collaborator:** Prof. T Govender (UKZN)  
**Funding:** NHLS Research Trust

**Project Title:** Impact of HIV, antiretroviral therapy and TB genotype on survival in MDR and XDR TB in a HIV positive adult South African cohort  
**Collaborators:** N Gandhi and his team from Emory University School of Medicine and K Misana. (NHLS, UKZN)  
**Funding:** NIH (non-IND study)

**Project Title:** Transmission of HIV-associated XDR TB in South Africa (TRAX)  
**Collaborators:** N Gandhi and his team from Emory University School of Medicine and K Misana (NHLS, UKZN)  
**Funding:** National Institute of Allergy and Infectious Diseases (NIH non-IND study)

**Project Title:** KwaZulu-Natal HIV drug resistance surveillance study  
**Collaborators:** Y Moosa (UKZN); V Marconi and his team from Emory University School of Medicine, Atlanta, Georgia, USA; D Kuritzkes (Harvard University School of Medicine, Boston, Massachusetts, USA); with researchers from University of Colorado, Denver, and Centers for Disease Control, Atlanta, Georgia, USA  
**Funding:** National Institute of Allergy and Infectious Diseases (non-IND study)

**Project Title:** Inhibition of HIV-1 encapsidation by targeted poly-ribonucleotide decoys: A novel nanoparticle approach  
**Principal Investigator:** R Parboosing – PhD project  
**Collaborator:** G Kruger (UKZN)  
**Funding:** Discovery Foundation and NRF

**Project Title:** Zidovudine (AZT) resistance in pregnant patients enrolled in the dual therapy arm of the Prevention of mother-to-child transmission (PMTCT) programme  
**Principal Investigator:** R Samuel – PhD project  
**Collaborators:** R Paredes (IrsiCaixa Retrovirology Laboratory, Barcelona, Spain) and M Gordon (HPP, UKZN)  
**Funding:** NHLS Research Trust and MRC

**Project Title:** Targeted delivery of HIV-1 integrase inhibitors using nanoparticles  
**Principal Investigator:** L Singh – PhD project  
**Collaborator:** Prof. T Govender (Catalysis and Peptide Research Unit, UKZN).  
**Funding:** NRF and NHLS Research Trust

**Project Title:** The importance of tissue compartmentalization during cytomegalovirus disease.  
**Principal Investigator:** Dr K Govender – PhD project  
**Collaborator:** Prof. D Pillay (Africa Centre, UKZN)  
**Funding:** Discovery Foundation, NHLS Research Trust

**Project Title:** Hepatitis B Virus variants in HBV mono-infected and HIV/HBV co-infected patients in a high dual infection setting  
**Principal Investigator:** Dr N Msomi – PhD project  
**Collaborator:** Dr M Gordon (HPP, UKZN)

**Project Title:** HIV-1 transmitted drug resistance and clinical implications of minority variants on treatment outcome, in patients initiating antiretroviral treatment and followed-up over a two-year period, in KwaZulu-Natal  
**Principal Investigator:** B Chimukangar – PhD project  
**Collaborators:** Dr P Moodley and Dr R Samuel (Virology), Dr K Naidoo (CAPRISA), Prof. T de Oliveria (Africa Centre)  
**Funding:** Africa Centre and CAPRISA
4.2. Grant Funding

- Dr R Parboosing – awarded NHLS Research Trust funding for Aptamer-functionnalised carbosilane dendrimers to reactivate HIV-1 latency (R500 000, 2016)
- Dr R Parboosing – awarded UKZN College of Health Sciences Competitive Grant for nanotechnology-based solutions for infectious diseases (Co PI, R1 500 000)
- Dr R Parboosing – awarded UKZN NanoHealth Initiative funding for Aptamer Conjugated Hybrid Nanoparticles for Targeted Delivery of Antiretroviral Drugs to the Lymph Nodes (Co PI, R250 000)
- Dr R Parboosing allocated one NRF Internship Programme for 2016
- Dr R Parboosing awarded NRF Thuthuka Programme funding for Inhibition of HIV-1 Encapsidation by targeted poly-ribonucleotide decoys: A novel nanoparticle approach (R280 000 annually 2013–2016)
- Miss L Singh awarded NHLS Research Trust for Targeted delivery of HIV-1 integrase inhibitors using nanoparticles (R250 000.00) and NRF Thuthuka Programme award (R248 000 annually 2017–2019)
- Dr R Samuel awarded MRC self-initiated grant for Zidovudine (AZT) resistance in pregnant patients enrolled in the dual therapy arm of the PMTCT programme (R190 000 annually 2013–2016)
- Mr B Chimukangara awarded CAPRISA/Africa Centre fund for HIV-1 transmitted drug resistance and clinical implications of minority variants on treatment outcome, in patients initiating antiretroviral treatment and followed-up over a two-year period, in KwaZulu-Natal (R370 000 2016–2017).

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

**Oral Presentations**


**Poster Presentations**

Anatomical Pathology

Head: Prof. NM Bida

1. DIAGNOSTIC SERVICES

1.1. Existing Diagnostic Services

The Department of Anatomical Pathology provides surgical pathology, autopsy pathology and cytopathology service to the Dr George Mukhari Hospital/Sefako Makgatho Health Sciences University Academic Complex, as well as some regional health facilities in Gauteng, Limpopo, Mpumalanga and North West provinces. The histologic diagnostic services include:

- Routine histology slides
- Special histochemical stains
- Immunocytochemical stains
- Immunofluorescence.

The electron microscopy unit is available for use by the department. The laboratory was fully accredited by the South African National Accreditation System in 2014 without any non-conformances noted. The number of histology cases registered increased from 13 759 in 2014 to 16 671 in 2015. This was an increase of 21%. There was a 9.5% increase in the number of cytology registrations from 83 802 in 2014 to 91 800 in 2015. Common routine special stains such as Ziehl-Neelsen (ZN) and Periodic acid-Schiff (PAS) are being introduced in the cytology laboratory. During the current reporting period a total of 46 autopsies was performed in the laboratory.

1.2. New Diagnostic Services

Direct immunofluorescence was introduced to support diagnostic services. The infrastructure of the Fine Needle Aspiration (FNA) Clinic is completed and started functioning in the second semester of 2015. The process of introducing enzyme histochemistry in the evaluation of muscle biopsies is advanced and it is envisaged that this will be in place before the end of this year.

2. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

2.1. Undergraduate

The consultancy staff is responsible for undergraduate teaching in anatomical pathology to MBChB students during their third year of study. This is done by way of lectures, practicals and tutorials.

The lecture hall previously used for student demonstrations is earmarked for revamping, together the mortuary. Until this is accomplished, mounted wet organ specimens or digital images will be used instead. Demonstrations for autopsy students will start once the new mortuary is fully refurbished.

Anatomical pathology is also taught to third-year BDS students from the Dental Faculty (first semester only). Some rationalisation of these curricula is being sought to alleviate the teaching burden.

The department is involved in formal lectures, by registrars, to the Allied Health Sciences Group, which includes Occupational Therapy, Dietetics, Radiography and Physiotherapy in the first half of the year. All allied Health Sciences students.

The whole class tutorial hall, fitted with microscopes, is being refurbished and may be ready for use by the middle of 2016.

2.2. Postgraduate

- There are currently eight resident registrars in the department in various years of study.
- A comprehensive training programme is in place and was recently fully accredited by the HPCSA.
- Dr N Ntsangani joined the department in November 2012, passed Fellowship of the College of Pathologists of South Africa (FCPath) (Part 1) in August 2014, and is now a senior registrar.
- Dr A Sokhulu joined the department in January 2014 as a transfer from Tshwane Academic Division (TAD) and obtained FCPath (Part 1) in April 2015. She is now a senior registrar.
- Dr B Bapela joined the department from TAD and has now successfully passed FCPath (Part 1) examinations, and is a senior registrar.
• Dr L Nevondo joined the department in July 2014 and is currently preparing to sit for the primary examinations.
• Dr O Dudikova joined the department in August 2014.
• Dr F Masha joined the department in July 2015.
• Dr T Mogashane joined the department in July 2015.
• Dr T Maleka joined the department in January 2016.
• Dr B Ratlabala qualified as an Anatomical Pathologist in May 2014, having obtained an MMed (Anatomical Pathology).
• The department runs a compressive formative assessment regularly to monitor progress in training. These formative assessments are also used in the first six months to give guidance in terms of the fitness of candidates to continue in their careers.
• From time-to-time non-resident registrars from the Department of Forensic Pathology, as well as Oral Pathology, rotate through the Department of Anatomical Pathology for one year as part of their training.

Technical Staff
Staff numbers have increased through the appointment of one medical technician and two student technicians to assist in the histology section of the department. Cytotechnologists are still required to deal with the high volume of work. One cytotechnologist successfully passed the September 2014 examinations.

Two laboratory assistants have written final examinations and results are awaited. A number of medical technicians will be trained to assist in the laboratory since there is a great shortage of student medical technologists and a shortage of qualified medical technologists.

Human Resources

Consultant Staff
• There are five full-time consultant pathologists in the department, viz. Prof. Bida (HOD), Dr MJ Chokoe, Dr BM Ratlabala, Dr M Muller and Dr T Motlagomang.
• Drs M Muller and T Motlagomang joined the department in July 2015.
• Prof. E Lancaster is appointed on a three-day per week session basis.
• One consultant post is vacant and it is envisaged that this will be filled in the second semester of 2016, after the mid-year examinations, through the placement of newly qualified staff for their two-year work-back plan.

Registrars
There are currently eight resident registrars in the department and one rotating registrar from the Oral Pathology Department.

Auxiliary Staff
One additional audio typist was appointed early in the year.

3. RESEARCH PROJECTS
Research is ongoing and a dedicated room for research is being developed to ensure optimal functioning. A research committee meets once a month to develop research ideas. The following research projects are under way:

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researchers</th>
<th>Short Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>The prevalence of HPV in conjunctival lesions of a HIV positive cohort</td>
<td>Ms L Mhlongo, Prof. NM Bida, Dr L Lebello</td>
<td>Conjunctival precancerous and cancerous lesions have dramatically increased in bedrock of HIV. HPV has been linked to many cancers in the setting of HIV. HPV has also been mooted to be involved in the precancerous and cancerous conjunctival lesions, especially in low socio-economic countries. The study seeks to investigate the prevalence and genotypes of HPV in conjunctival lesions.</td>
</tr>
<tr>
<td>HPV genotypes in atypical squamous cells of undetermined significance (ASC-US) lesions of the uterine cervix</td>
<td>Dr N Ntsangani, Prof. Bida, Dr L Lebello</td>
<td>HPV involvement is now well established in cervical precancerous and cancerous lesions. In about 20% of cervical smears examined during routine cervical pap smears using conventional methods, ASC-US is diagnosed. The role of risk categorisation of HPV involvement in these lesions remains uncertain, further confounding the management of such patients. The study seeks to determine the prevalence of HPV in ASC-US and risk categorisation in order to inform management and treatment.</td>
</tr>
</tbody>
</table>
**Project Title:** Prevalence of pathologic lesions of the implantation site in post-partum haemorrhage in Dr George Mukhari Academic Hospital

**Researchers:** Dr M Bapela, Prof. NM Bida, Dr Sitheme

**Short Description:** Lesions of intermediate trophoblasts are rarely reported as a cause of postpartum bleeding, probably due to under-reporting. The study seeks to examine the actual frequency of these lesions, and address causes of the under-reporting.

In collaboration with other departments, such as virology, research is being conducted in the area of HPV as part of the FLIR project jointly with the University of Antwerp, Belgium.

**Project Title:** The prevalence of human papillomavirus infections in ano-rectal cancers at the Dr George Mukhari Academic Hospital from 2005 to 2012

**Researchers:** M Kwinika, Dr L Lebello, Prof. NM Bida

**Short description:** HPV involvement in ano-rectal cancerous lesions has been reported. HPV types in different histological types has however not been thoroughly investigated. The study seeks to examine risk categorisation of HPV by histological types of ano-rectal cancers.

Prof. NM Bida participates in the following ongoing national research projects:

- National prostate cancer guidelines, funded by the MRC to establish a national cancer registry
- HPV in the Men who have Sex with Men (MSM) cohort in the North-West in collaboration with Microbiological Pathology.

The department also participates in the Rheumatic Heart Study in collaboration with the University of Cape Town.

At the school of pathology, a molecular cell pathology unit is being established as a training and research unit.

## 4. RESEARCH OUTPUT

### 4.1 Journal Publications


Becker JHR, Koto MZ, Matsevych OY, Bida NM. Haemangiopericytoma/solitary fibrous tumour of the greater omentum. *SAJS.* 2014; 52 (4) 325–329.

### 4.2 Conference Presentations


NM Bida. Cervical cancer screening – Pathologist’s perspective. 3rd WAKA HPV Africa Symposium, Kinshasa, DR Congo, 2-4 December 2015.

All staff attended BushPath.

**Professional Development**

- Eight registered for MMed in anatomical pathology
- One registered for MSc in anatomical pathology
- Four cytology medical technologists – one wrote in March 2015, one is writing in September 2015 and the other two are writing in March 2016
- One histology medical technologist is writing in March 2016
- Student histology medical technicians.
Chemical Pathology

Head: Prof. AyeAye Khine-Wamono

1. ABOUT THE DEPARTMENT

The Department of Chemical Pathology forms part of the essential 24 hour laboratory service provided to the Dr George Mukhari (DGM) Academic Hospital and provides specialised biochemical testing for various specialist clinics operated at this hospital by the clinical departments. The department trains chemical pathology registrars for MMed and FCPath degrees, medical science students for BSc (Hons), MSc and PhD degrees and Medical Technologist students for the internships for their Professional Board registration. The department is in collaboration with clinical departments at DGM Academic Hospital such as Family Medicine, Internal Medicine and Cardiology and Pediatrics for inter-departmental research programmes. Through these platforms, the departmental research capacity is built. Registrar teaching is also in collaboration with these clinical departments in order to enhance integration with clinical perspectives in learning.

Table 33: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Total</th>
<th>Pathologists</th>
<th>Med Doctors (registrars)</th>
<th>Technologists</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3</td>
<td>3</td>
<td>15</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The laboratory is staffed by 15 qualified technologists of whom two are supervisors and one is a laboratory manager. The laboratory comprises one core laboratory with two automated integrated chemistry and immunoassay analysers running 35 assays including HBA1C, tumour markers, endocrine profiles and therapeutic drug monitoring and small serum proteins. In addition, five POC testing machines for blood gas analysis at the five emergency units of the hospital and one POCT machine for cardiac markers at the casualty section, are managed by the laboratory technologists, and tests billed by NHLS. There is also a special chemical pathology laboratory where manual tests are performed including serum and urine protein electrophoresis and immunofixation, Lipid electrophoresis, CSF protein electrophoresis, metabolic screening (first tier), thin layer chromatography, porphyrin screening, occult blood screening and drug of abuse screening. The hospital is a training and referral hospital and has been organised into specialist clinics such as diabetic, endocrine and metabolic (adult and paediatric), hypertension, cardiology and lipid, gastroenterology, medical oncology and myeloma clinics. Referral consultations from the regional laboratories of Limpopo, North West and Gauteng North are also covered by this department.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department consists of three senior lecturers and two junior lecturers who present the chemical pathology module to undergraduate medicine students. The lecturers also provide integrated theme-based lectures to the same students from year 2 to year 5. Tutorials in the form of case discussions are provided in small group facilitation learning platforms to the final year medical students. The department trains Chemical Pathology registrars and currently holds four posts which are all filled. In addition, the medical science stream is training students enrolled for BSc (Hons), MSc and PhD in Chemical Pathology. Currently two Hons, three Masters and one PhD student are in the programme. Both MMed and MedSci programmes are HPCSA accredited for two years. Undergraduate Chemical Pathology is accredited by the council for five years.

The department was awarded the best department for non-clinical undergraduate teaching in 2015 for the third successive year. The programme includes weekly journal presentations, weekly academic seminars and weekly case discussions. Other inter-departmental seminars include weekly integrated pathology seminars and monthly Endocrine case discussions with the Department of Pediatrics.

Activities include training of medical technologists (MTs), MT interns and students on the current SOPs. In addition, MT students and interns are given lectures by the pathologists and senior technologists on laboratory practices, methods and principles, quality assurance, health and safety and basic chemical pathology of diseases in preparation for Board Examinations.

Table 34: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total Number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>7*</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

*One Masters student left the programme to transfer to another degree
3.1. Other Training Information

The HOD facilitates sessions in the workshops for Health Science Education programme, given by the university for staff development. These workshops take place throughout the year at different times in order to accommodate the clinical teaching staff. Other capacity-building exercises are presented on-line, using emails provided to the laboratory managers, supervisors and QA officers in the regions of Limpopo, North West and Gauteng North. These are in the areas of quality assurance and laboratory management.

4. RESEARCH ACTIVITIES

The department is currently involved in Nyaope research in which the street drug Nyaope mixtures are analysed for the School of Public Health.

The second project with which the department is busy relates to the metabolomics of chronic renal disease and insulin resistance via disturbed lipid metabolism. Nuclear magnetic resonance (NMR) and gas chromatography mass spectrometry (GC MS) methods for the metabolites are being developed. The department is collaborating with the departments of Chemistry (Sefako Makgatho Health Sciences University), Human Metabolomics (North West University) and the University of Alabama, USA.

4.1. Research Units/Study Groups Linked to the Department

- Myeloma study group
- Metabolomics study group in lipid and carbohydrate disorders
- Genetic testing of primary hyperlipidaemias
- Nutritional deficiency syndromes in HIV AIDS patients (Belgian study group).

4.2. Research Projects

Completed Masters Projects

Project Title: Impact analysis of the cost-effectiveness and clinical outcome of delayed sample separation of patient samples referred from remote clinics to Dr George Mukhari Academic Hospital laboratory for routine biochemical analysis
Investigator: Dr B Phiri (MMed)
Supervisors: Dr K Mentz, Dr AA Khine
Progress: The Study is completed and a mini-dissertation is ready for submission. The candidate is preparing for her final CMSA examination in August.
Funding: NHLS Research Trust

Project Title: Evaluation of Capillaries Flex II automated electrophoresis system in early diagnosis of multiple myeloma and related monoclonal gammopathies
Investigator: Sarah Mosima Pheeha
Progress: Thesis submitted to external examiners
Funding: IlEx SA (Sebia)

Project Title: Identification of CytoGlobulins in various clinical conditions at Dr George Mukhari Academic Hospital
Investigator: NM Tshilande
Progress: Thesis submitted to external examiners
Funding: Departmental funding

Ongoing Projects

Project Title: Use of N-terminal pro b-type natriuretic peptid (NT proBNP) in diagnosing and treatment monitoring of patients with congestive heart failure at Dr George Mukhari Academic Hospital
Investigator: Dr T Mapheto (MMed)
Supervisors: Dr KB Sedumedli, Prof. P Mntla (Cardiology)
The project is ongoing. Although no monetary funding was obtained, a test kit was secured from Roche and specimens have been stored for testing. Estimated completion of the project is September 2015. The student is preparing for the MMed intermediate examination in June.

**Funding:**
Roche Diagnostics SA

**Project Title:**
Relationship between average plasma glucose from home monitoring glucometer and from calculation using HBA1C in patients attending diabetic clinic at Dr George Mukhari Academic Hospital

**Investigator:**
Dr K Thobye (MMed)

**Supervisors:**
Prof. AA Khine, Prof. S Mda (Pediatric Endocrinology)

**Progress:**
Ethics has approved the project and patient recruitment will start in July when the student finishes the MMed intermediate examination.

**Funding:**
NHLS Research Trust

**Project title:**
Fatty acid metabolites in the development of insulin resistance in patients with chronic kidney disease

**Investigator:**
SJ Nwetjana (PhD study)

**Supervisors:**
Prof. AA Khine, Ms L Bekker, Prof. N Agyei (SMU Chemistry Department)

**Progress:**
Awaiting ethics approval

**Funding:**
In the process of applying to NHLS Research Trust

**Project title:**
Lactate and pyruvate ratio in the whole blood using UV spectrophotometer; application in tissue hypoxia

**Investigator:**
W Dube – for BSc (Hons)

**Supervisors:**
Prof. AA Khine, Ms L Bekker

**Progress:**
Awaiting ethics approval

**Funding:**
Departmental budget

**Project Title:**
Prevalence of B12 deficiency in HIV exposed patients

**Investigator:**
Dr KB Sedumedi (Independent research)

**Collaborators:**
Dr W Kangawaza (Internal Medicine)

**Progress:**
Ongoing

**Funded:**
Belgian study

**Project Title:**
Molecular basis of primary dyslipidaemias in patients attending Dr George Mukhari Academic Hospital

**Investigator:**
Dr AA Khine (PhD research)

**Supervisors:**
Prof. L Hay (Medunsa), Prof. D Marais (UCT)

**Progress:**
Recruitment and laboratory testing ongoing

**Funded:**
NHLS Research Trust

### 5. RESEARCH OUTPUT

#### 5.1. Journal Publications


Khine AA, Mokwena KE. Drug interactions in Nyaope mixture; A challenge for withdrawal treatment programmes and rehabilitation. (Submitted to *African Journal of Alcohol and Drug Abuse Studies*)

Machaka L, Khine AA. Factors associated with geophagia in pregnant women seen at Dr George Mukhari Academic Hospital and trace metals levels in their blood and urine. (Submitted to *Journal of Africa Health Sciences*)
5.2. Conference Presentations

**Poster Presentations**


Duma Z. Turner syndrome and its variants screened at Dr George Mukhari NHLS Cytogenetics Laboratory. PathRed Congress, 24 April 2015.

Tshilande N. Cryoglobulinemia associated with various clinical conditions at Dr George Mukhari Academic hospital. PathRed Congress, 24 April 2015.

**Oral Presentations**


Khine AA. Burden of dyslipidemias in South African black population seen at Dr George Mukhari Academic Hospital: 12 month retrospective audit. PS Africa Congress, Cape Town, 23–24 March 2016.

5.3. Research Translated to Policy

The audit for total prostate specific antigen (PSA) cut-off and its utility for detection of early prostate cancer is under way and will be published soon.

5.4. Research Translated to Diagnostic Technology

- Validation of High Performance Liquid Chromatography and UV detection in determination of vitamin D variants
- Validation of sample pre-treatment process with mercaptoethanol and fluidil in specimens with co-migration of immunoglobulin bands in multiple myeloma patients is at the manuscript preparation stage.

6. ACADEMIC AND RESEARCH/RECOGNITION HONOURS AWARDS

- Best teaching department award for MBChB programme 2015, honoured by the SMU.
Haematological Pathology

Head: Prof. V Moodley

1. ABOUT THE DEPARTMENT

Haematological Pathology offers a comprehensive 24-hour diagnostic service to the Dr George Mukhari (DGM) Academic Hospital. It also serves as a referral centre to the surrounding hospitals and clinics and provides diagnostic services to the Medunsa Clinical Research Unit.

Within the discipline, there is a strong focus placed on offering a quality service within the shortest possible turnaround time (TAT). The continuous and concerted effort made by staff to improve service delivery and TAT was evident in the laboratory continuing to meet the set TAT target for the CD4 test which forms part of the National Priority Programmes (NPP), as well as successfully maintaining SANAS accreditation. The discipline is actively involved in the teaching and training of both undergraduate and postgraduate students, as well as intern medical scientists, technologists and technicians.

Table 35: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4</td>
<td>15</td>
<td>4</td>
<td>23</td>
<td>23</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

Overall test volumes have increased by 0.5% in the last year to 365 648.

The ongoing involvement of consultants and registrars in the adult haematology ward and Outpatient Clinic has resulted in stronger working relationships between the clinical and pathology disciplines. Active participation in the paediatric haematology/oncology ward rounds continues, further consolidating the working relationship with these disciplines.

A Stat Laboratory was introduced to service care wards, intensive care units, oncology services, theatres, casualty and trauma units at DGM Academic Hospital. The introduction of this unit has translated into improved service delivery with shorter turnaround times.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Haematological Pathology is actively involved in the teaching and training of medical (MBChB) students. The teaching of haematology as a fully integrated subject for second and third-year MBChB students, as part of the practice of medicine curriculum, is well received. The teaching is also extended as a selective to fourth-year medical students. Weekly tutorials offered to sixth-year medical students as a pilot were a great success and have thus become a permanent teaching and learning opportunity in the curriculum. In 2016, as a new initiative, haematology is being offered to fifth-year medical students with the focus placed on laboratory testing. Thus exposure to the discipline of Haematology in the undergraduate MBChB programme will be from the second to the sixth year. The introduction of these new initiatives has resulted in further appreciation of the subject by undergraduate medical students.

MMed, intern medical scientists, MSc, BSc (Hons), medical technology and technician students are taught and trained. The discipline is highly committed towards ensuring that the highest standards of academic excellence are maintained. An inclusive practical and theoretical training programme is in place for registrars in haematology over a four-year period. All registrars who wrote both primary and final College of Medicine (Haematology) examinations in the last year have successfully passed. The discipline is also involved in training registrars from internal medicine, paediatrics and chemical pathology. In addition, BSc (Hons) and Masters programmes are presented. The discipline provides in-service teaching and training to both haematology and clinical pathology student medical technologists and technicians, as well as to intern medical scientists.

Table 36: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>16</td>
<td>8</td>
<td>6</td>
<td>75%</td>
</tr>
</tbody>
</table>

*These include the clinical medical technology students
3.1. Other Training Information
The discipline underwent successful accreditation by the HPCSA of its postgraduate MMed programme in February 2015.

4. RESEARCH ACTIVITIES

In addition to the research focus on enhancing service delivery, other areas of research activity include haematological aspects of HIV, as well as haematological malignancies, particularly multiple myeloma.

4.1. Research Projects

**Project Title:** Nucleotide sequence determination to identify possible DNA changes in a single locus profile mismatch in short tandem repeat of specimens sent for DNA profiling  
**Investigator:** Ms Y Harris  
**Supervisor:** Prof. DJ Welgemoed

**Project Title:** The usefulness of CD200 as a diagnostic and a prognostic marker in the immunophenotyping of mature B-cell neoplasms and acute myeloid leukaemias in patients seen at Dr George Mukhari Academic Hospital over a six-month period  
**Investigator:** Dr AM Pooe  
**Supervisor:** Dr RK Rankapole  
**Co-Supervisor:** Prof. V Moodley

**Project Title:** Parvovirus B19 prevalence in bone marrows of patients with cytopenias at Dr George Mukhari Academic Hospital  
**Investigator:** Dr AN Dlova

**Project Title:** Investigation of the morphological and immunophenotypic changes in bone marrow specimens of human immunodeficiency virus infected patients at Dr George Mukhari Academic Hospital, Ga-Rankuwa  
**Investigator:** Mr TL Moeketsi  
**Supervisor:** Prof. V Moodley  
**Co-supervisor:** Dr AN Dlova

**Project Title:** A comparative analysis of the use of liquid monoclonal reagents and DuraClone™ dried monoclonal reagents in the immunophenotypic investigation of suspected plasma cell dyscrasias at Dr George Mukhari and Steve Biko Academic hospitals  
**Investigator:** Dr J Alant  
**Supervisor:** Prof. V Moodley  
**Co-supervisor:** Prof. R Pool

4.2. Research Funding

NHLS Research Trust

5. RESEARCH OUTPUT

5.1. Publications

5.2. Conference Presentations

Poster Presentations

Van der Linde R, Moodley V, Sedumedi KB, Ndlovu W. Establishing if soluble transferrin receptor and/or serum hepcidin is superior to serum ferritin when determining the iron status of patients with anaemia of inflammation at Dr George Mukhari Academic Hospital over a six-month period. PathRed Congress, Emperors Palace, Johannesburg, South Africa. 14–16 April 2015.

Mahapa RSG, Dlova AN. The effect of electronic gatekeeping on the detection of pathology based on leucocyte differential counts and peripheral blood smears by the Department of Haematological Pathology at Dr George Mukhari tertiary laboratory in 2011 and 2012. Sefako Makgatho Health Sciences University Research Day, Pretoria, South Africa. 25–27 August 2015.

Lekabe JM, Rankapole RK. Establishing a reference range for the neutrophil count in healthy black adults living in the community served by the Dr George Mukhari Academic Hospital, Ga-Rankuwa, South Africa. Sefako Makgatho Health Sciences University Research Day, Pretoria, South Africa. 25–27 August 2015.

Sibandze DF, Moodley V, Rankapole RK. The evaluation of the efficacy of the plastic tubes versus glass tubes in the determination of the ABO and Rhesus blood grouping at Dr George Mukhari Academic Unit of the National Health Laboratory Services, Ga-Rankuwa. Sefako Makgatho Health Sciences University Research Day, Pretoria, South Africa. 25–27 August 2015.

5.3. Research translated to Diagnostic Technology, Policy or Service

- The research performed assessing the usefulness of CD200 in immunophenotyping translated into service delivery improvement where this monoclonal antibody has been added to the current protocols.
Microbiology

Head: Prof. M Nchabeleng

1. ABOUT THE DEPARTMENT

1.1. Teaching and Training

The Department of Microbiology teaches Medical Microbiology to the following undergraduate students: MBChB II and III (whole-year course); BDS III (semester); BCur (semester); and BSc Diet (semester). There is a postgraduate training component for registrars, PhD, MSc, BSc Honours and intern scientist students.

1.2. Research

The department has four focus areas, namely, tuberculosis, sexually transmitted infections (STIs), antimicrobial resistance/infection prevention and control, and contract research. For contract research, the two clinical trial units established in the department, namely: Mecru Clinical Research Unit (MeCRU) and Setšhaba Research Centre (SRC) continue to be involved in HIV prevention clinical trials at national and international levels.

Table 37: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologists</th>
<th>MSc Scientists</th>
<th>Technologists</th>
<th>Technicians</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 till June, then 1</td>
<td>1</td>
<td>-</td>
<td>18</td>
<td>10</td>
<td>1</td>
<td>32</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The department renders microbiology services for Dr George Mukhari (DGM) Academic Hospital and the surrounding clinics; it serves as a referral laboratory for some parts of Limpopo, North West and Mpumalanga Provinces. It also serves as a referral laboratory for TB cultures for the regional laboratories. The total volume of work increased by 6% from 280 330 in 2014/2015 to 297 180 in 2015/2016. SANAS accreditation was maintained, using ISO15189. The department continues to support infection prevention and control (IPC) activities and the Pharmacy and Therapeutic Committee of DGM Academic Hospital.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

During 2015, the department conducted a bi-annual workshop on the management of STIs for healthcare workers (HCW) from the surrounding clinics/district hospitals in the area and Tshwane District.

Table 38: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Technologists</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technologists</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Technicians</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>Registrars</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>All</td>
<td>11</td>
<td>7</td>
<td>4</td>
<td>57</td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

The collaboration between the University of Antwerp and the University of Limpopo (UL) through the Vlaamse Interuniversitaire Raad Institutional University Cooperation partnership (VLIR-IUC) is continuing with phase 2 for another five years. The areas of interest this time focus on sexually transmitted infections with special interest in human papilloma virus (HPV). Through this, the department collaborates with other departments in the institution, especially the Departments of Virology and Obstetrics and Gynaecology. HPV research includes testing for sub-Saharan countries.

For contract research, the two clinical trial units established in the department (MeCRU and SRC) continue to be involved in several clinical trials including HIV prevention strategies. MeCRU started exploratory studies into the group of Men who have Sex with Men (MSM), which has been a neglected group in the area.
4.1. Research Units/Study Groups Linked to the Department

UL-SMU/VLIR Collaboration: Prof. M Nchabeleng and University scientists (Dr MC le Roux, L Nemarude and B de Villiers)

Collaboration between UL/SMU and researchers at the University of Antwerp in the area of selected STIs, focussed on specific groups, including women attending the termination of pregnancy clinic (TOP) and MSM. This was the first year of phase 2 of the programme.

Project Title: HIV and Selected STI pathogens in Men Who Have Sex with Men (MSM) in the area North West of Pretoria.
Researchers: Prof. M Nchabeleng
Collaborators: Dr Mathebula (MeCRU), Dr M Le Roux (Microbiology), Ms L Nemarude (Microbiology), Dr Lebelo (Virology), Prof. G Selabe (Virology), Prof. M Bida (Anatomical Pathology), Prof. Raubenheimer (Oral Pathology – Dentistry) and MeCRU team.
Funding: VLIR, MeCRU sponsors for staffing
Short Description: To determine the prevalence, types and factors associated with HPV related precancerous and cancerous lesions, HIV and other STIs in the MSM population residing in the North West part of Pretoria.

4.2. Contract Research Collaboration

The two clinical research units are collaborating with national and international groups in the following clinical trials:

Project Title: A phase III, multi-centre, randomised controlled trial to assess the safety and effectiveness of the vaginal microbicide 1% Tenofovir Gel in the prevention of human immunodeficiency virus Type 1 infection in young women, and to examine effects of the microbicide on the incidence of herpes simplex virus Type 2 infection
Researchers: M Nchabeleng*, K Ahmed
Co-workers: MeCRU Team
SRC Team Sponsors: FACTS – DAIDS, DST, DoH and Bill and Belinda Gates Foundation
Duration: October 2011–June 2015 (completed)

Project Title: A phase II randomised double-blind, placebo-controlled trial to evaluate the immunogenicity and safety of a therapeutic recombinant biologically active HIV-1 Tat protein vaccine in HIV-infected, anti-Tat negative, ARV-treated adult volunteers
Researchers: Prof. M Nchabeleng and MeCRU team
Sponsors: ISS (Italian Government)

4.3 Research Projects (Self-Initiated)

Completed Projects

Project Title: Bacterial contamination of re-processed rigid laryngoscope blades and handles at DGMA Hospital
Researcher: Dr O Khobo-Mpe – Department of Anaesthetics
Co-worker: Dr MBR Maloba (Microbiology)
Student: Dr A Fourie (MMed – Anaesthetics)

Project Title: Prevalence of bacterial vaginosis in pregnant women and identification of microbes associated with a history of adverse pregnancy outcomes at DGM Academic Hospital using standard and polymerase chain reaction assays
Researchers: M le Roux, M Nchabeleng
Co-workers: Prof. TS Monokoane and Dr Sethale (Obstetrics & Gynaecology)
Student: Dr MR Ditsele (MMed)

Project Title: Tetracycline resistance among ureaplasmas isolated from women presenting for termination of pregnancy at the DGM Academic Hospital
Researchers: B de Villiers, M le Roux
Student: LM Ngobeni (MSc)
Project Title: The microbiology of the normal flora and management of neutropenic patients in a paediatric oncology ward at the DGM Academic Hospital
Researchers: M Nchabeleng, B de Villiers
Student: KP Lekoma (MSc)

Project Title: Investigation of Group B streptococci vaginal infection in women receiving termination of pregnancy at Dr George Mukhari Academic Hospital
Researcher: M le Roux
Student: M Mafunise (BSc Hons)

Project Title: Chlamydia trachomatis infection among women receiving termination of pregnancy at DGM Academic Hospital
Researchers: LA Nemarude, M le Roux
Student: M Thsilande (Hons)

Project Title: Investigation of non-tuberculous mycobacteria by genotype mycobacterium assay and 16s Ribosomal ribonucleic acid (rRNA) sequence analysis at the NHLS-Tertiary Laboratory
Researchers: NA Makhado, C Maluleka
Student: T Raidhani

Ongoing Projects

Project Title: Prevalence of sexually transmitted diseases in women receiving termination of pregnancy at Dr George Mukhari (DGM) Academic Hospital
Researchers: Dr MC le Roux (R), Ms B de Villiers
Co-workers: TS Monokoane (Obstetrics and Gynaecology)
Students: Several on different aspects of the project

Project Title: Genotypic diversity of Mycobacterium tuberculosis strains and association of isoniazid resistance with MDR TB at Dr George Mukhari tertiary laboratory
Student: AM Mhlongo (PhD)*
Supervisors: M Nchabeleng*, Dr G Selabe

Project Title: Characterisation of mycobacterial strains from clinical specimens of patients with tuberculosis at the Dr George Mukhari Tertiary laboratory, South Africa
Student: NA Makhado* (PhD)
Supervisors: B de Jong (Antwerp), M Nchabeleng*

Project Title: Comparison of lipopolysaccharides and outer membrane protein profiles of Pseudomonas aeruginosa isolates from selected wards at DGM Academic Hospital
Researchers: M Nchabeleng*, B de Villiers
Student: RM Mokgatla* (MMed)

Project Title: Discordancy of rifampicin susceptibility in mycobacterium complex isolates from Dr George Mukhari tertiary laboratory
Researchers: N Makhado, M Nchabeleng
Student: G Shkwambane-Ntlemo* (MMed)

Project Title: Characterisation of Staphylococcus aureus isolates from children with atopic dermatitis at DGM Academic Hospital
Researchers: Prof. Motswanaedi (Dermatology), M Nchabeleng*, B de Villiers
Student: B Ncube* (MMed)
Project Title: Prevalence and molecular analysis of *Mycoplasma genitalium* strain isolated from pregnant women at DGM Academic Hospital. Researchers: MC le Roux, B de Villiers

Student: M Mafunise (MSc)

Project Title: An evaluation of the validity of three molecular assays for the detection of drug resistant *Mycobacterium tuberculosis* at DGM Tertiary Laboratory, using the phenotypic BACTEC MGIT 960 as the gold standard

Researchers: NA Makhado*, C Maluleka*

Students: Raidani T (MSc)

Project Title: Characterisation of *rpoB* gene mutations from the clinical samples of *Mycobacterium tuberculosis* at DGM tertiary laboratory

Researchers: NA Makhado*, B de Jong (Antwerp)

Student: Matabane E (MSc)

* Indicates an NHLS employee

4.4. Grant Funding

- NHLS Research Trust
- SMU/VIIR Research Funds
- Individual sponsors for contract research.

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

Poster Presentations

Nchabeleng M*, Jiyane E, Nemarude L. Susceptibility profile and serotype of clinical *Cryptococcus* isolates at Dr George Mukhari Tertiary Laboratory. Pathology Research and Development Conference (PathRed) – April 2015.

Mafunise M, Le Roux MC, de Villiers BE, Monokoane TS. Investigation of Group B *Streptococci* vaginal colonisation in women receiving termination of pregnancy at DGM Academic Hospital. 6th FIDSSA Conference.


Raidani T, Makhado NA*, Maluleka C*. Investigation of non-tuberculous mycobacteria by genotype mycobacterium assay and 16S rRNA sequence analysis at the NHLS Tertiary Laboratory. 6th FIDSSA Conference.


All posters presented outside the institution were also presented on the SMU Research Day.

* Indicates NHLS employees
Oral Presentations

Le Roux MC, Matabane KH, Ditsele RMM*, Monokoane TS*. Bacterial vaginosis and genital pathogens in pregnant women. 6th FIDSSA, Drakensberg, KZN.

Le Roux MC. Mycoplasma genitalium: Role in disease and implications for syndromic management. (Plenary speaker). 6th FIDSSA Conference, Drakensberg, KZN.


* Indicates NHLS employees

6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

- MC le Roux: Selected as secretary South African Society for STIs.

7. ADDITIONAL INFORMATION

Prof. M Nchabeleng:

- Moderator for FCPath (UKZN); Examiner – MMed (UFS); Discipline representative for CMSA Council
- At SMU, serves on Higher Degrees Committee, Institutional Forum and Chairs Academic Planning Committee for MBChB 3.

Dr C Maluleka:

- Part of Infection Prevention and Control Committee and outbreak response team of DGM Academic Hospital
- Outreach Presentations:
  - Infection prevention and control to the new DGM Academic Hospital interns
  - Infection prevention and control quarterly presentations to new registrars in the main ICU.

Dr SG Mahlangu: Left the institution in July 2015

- Served on the school ethics committee
- Served on Pharmacy and Therapeutic Committee of DGM Academic Hospital.
Anatomical Pathology

Head (Acting): Dr Cinzia Campaini

1. ABOUT THE DEPARTMENT

The Department of Anatomical Pathology provides service and academic coverage. Service is delivered to the Northern Gauteng hospitals and clinics, as well as Mpumalanga. The academic component covers relevant teaching to both undergraduate and postgraduate medical students and the Allied Health Sciences of the University of Pretoria.

Table 39: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologists</th>
<th>Registrars</th>
<th>Med Scientists</th>
<th>Technologists</th>
<th>Student Technologists</th>
<th>Technicians</th>
<th>Student Technicians</th>
<th>Support</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>4</td>
<td>1</td>
<td>21</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>16</td>
<td>63</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

A diagnostic service is provided in histo- and cyto-pathology to Northern Gauteng and Mpumalanga. Post mortem services are rendered to the larger hospitals of Northern Gauteng. Medical staff are available for consultation to clinical colleagues and for consultations from private laboratories. A 24-hour emergency service is rendered to SBAH and Kalafong.

Overall figures for the year show 25,297 histopathology cases and 104,951 cytology cases. The breakdown for the cytology number yields 96,658 gynaecological, 5,120 non-gynaecological and 3,173 Fine Needle Aspirate cases. A total of 75 post mortems were performed.

An electron microscopy service is provided and 157 cases were done, of which roughly a third were from the private sector.

The immunohistochemistry laboratory performed 19,760 stains, some of which were requested from the private sector.

A fluorescent in situ hybridisation (FISH) service is in place, and PCR is planned for which funding will have to be sought.

The laboratories are SANAS accredited.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate Teaching

Teaching is provided to the medical students and the students of Occupational Therapy, Physiotherapy and Radiography. The teaching is inclusive of theory and practical post mortem and histopathology exposure where possible and appropriate.

3.2. Postgraduate Teaching

Teaching to postgraduates, besides those within the department, includes rotating registrars from Oral Pathology and Forensic Pathology, as well as from other departments e.g. Internal Medicine.

Table 40: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>All</th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>67%</td>
</tr>
</tbody>
</table>

(Current number of registrars is 4, with 2 having joined only recently)

4. RESEARCH ACTIVITIES

Due to severe staff shortages research has been very limited. Research on the presence of HPV in conjunctival squamous cell carcinoma in HIV positive individuals is ongoing. Assistance and participation in research projects from other departments is taking place. Registrar project supervision is done.
5. RESEARCH OUTPUT

5.1. Journal Publications


Chemical Pathology

Head: Prof. Tahir Pillay

1. ABOUT THE DEPARTMENT

The Department of Chemical Pathology is situated in the University of Pretoria and the core diagnostic laboratory is located at Steve Biko Academic Hospital (SBAH). The department has an academic and a research training programme. The Honours and Masters training programme in chemical pathology has been in existence for many years and fulfils a growing need for the training of scientists in the discipline of chemical pathology/clinical biochemistry. It is the only such active programme available in South Africa. The BSc (Hons) degree course has been offered by the Department of Chemical Pathology since 1998, with senior medical scientists in the department serving as programme co-ordinators. The department also trains specialists in chemical pathology and there are currently six registrars in training. Registrars acquire clinical experience from dealing with the core diagnostic laboratory, attending ward rounds, clinics and clinical meetings in the hospital and through active liaison with the clinicians in all the departments. The department has a number of active research programmes in the areas of molecular genetics, cell biology and molecular modelling. The training philosophy of the department is directed towards developing specialists who can bridge the gap between the bench to the bedside and who understand chemical pathology in detail and with insight into clinical diagnosis and management.

Table 41: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologists</th>
<th>PhD Scientists</th>
<th>Technologists</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4</td>
<td>1</td>
<td>11</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The Department of Chemical Pathology provides diagnostic pathology services to the SBAH, Tshwane District, and Weskoppies Hospitals and 60 clinics in the Pretoria region. In addition to providing after-hours laboratory services to Mamelodi Hospital, the laboratory receives referrals from private and NHLS laboratories nationwide.

For the period 2015/16, the total workload was 2 484 169 tests, representing a 30% increase over the previous year and an income of R83 109 329.

Albumin-corrected calcium reporting was discontinued in March 2015 in line with international trends based on published studies and a local study. Haloperidol referrals were discontinued in March 2015 due to low test volumes. A new, improved HDL method was successfully validated on behalf of the NHLS Health Technology Assessment Unit and introduced in September 2015. Thyroglobulin, Theophylline, Gentamycin and Amikacin testing were discontinued in November 2015 due to low test volumes and are referred to the NHLS and private laboratories.

The turnaround times (TAT) for routine urea, electrolytes and creatinine (UEC), liver function tests (LFTs) and cardiac troponin I (excluding work referred in from external sites) were 6.04, 6.80 and 8.68 hours respectively. Technical staff shortages (50% shrinkage in two years), in concert with the increased test volumes, continue to be a challenge and have had an impact on TAT. Results are medically validated remotely (after hours) by the registrars which helped to improve TAT. The introduction of auto-verification on TrakCare in the future and further automation of analytical processes will improve workflow and TAT.

The laboratory was inspected by SANAS in February 2016 and its accreditation was re-instated. The laboratory participates in further external quality assurance programmes (Thistle, RCPA and NHLS) with performance throughout the year being good, i.e. above target of 90% conformance (98.7%, 91.4% and 97.0% conformance respectively). The laboratory enrolled the two Beckman Coulter Automated analysers for chemistry and immunochemistry separately on the RCPA EQA programme during the current year in compliance with SANAS recommendations from the 2015 accreditation assessment.

The current automated chemistry and immunochemistry instruments will be replaced with Abbott Architect ci8200 instruments that have been installed and are undergoing evaluation following a protracted tender process that was concluded in September 2015. These new analysers will be integrated with the laboratory information system (LIS) via middle-ware software to assist in sample management and improvement of workflow as well as data management. A new bench top HbA1c Variant II HPLC instrument is due for installation following conclusion of a tender that was awarded to Bio-Rad in February 2016. This instrument will be linked to the existing TrakCare LIS and will assist in improvement of TAT for the HbA1c test.
3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

During the review period, chemical pathology consultants presented a total of 35 lectures to MBChB students. Lectures focused on pathophysiology and laboratory investigation of a wide range of disorders grouped under the following teaching blocks: Homeostasis, Diseases of Childhood, Abdomen and Breast, Traumatology and Genito-urinary Disorders. The Diagnostic Laboratory Medicine and Imaging block (GNK 689) has been chaired by a chemical pathologist since its inception. This block provides teaching to final-year medical students on appropriate selection and interpretation of laboratory tests in all pathology disciplines and includes lectures in radiology, nuclear medicine and evidence-based medicine. Student feedback regarding teaching has, for the most part, been positive.

3.2. Postgraduate

MMed Other Disciplines

The department participates in the teaching and assessment of MMed students in paediatrics, internal medicine, neurology, nuclear medicine and family medicine. Registrars in paediatrics and internal medicine attend a compulsory two-year pathology course, which requires that they present seminars on selected pathology topics. In the other disciplines, chemical pathologists present tutorials and set examinations, which have to be passed by registrars.

MMed Chemical Pathology and Clinical Pathology

Chemical pathology registrars play a key role in delivery of the diagnostic service and contribute to monitoring of internal quality control and turnaround times, evaluation of diagnostic methods and review of laboratory standard operating procedures. Formal assessments during the first year include examinations in physiology (primary) and clinical chemistry (at MBChB VI level). During the second year registrars attend an eight-month molecular pathology module. After 24 months in the training programme, registrars write intermediate examinations in chemical pathology that follow the Colleges of Medicine of South Africa (CMSA) format. For the research component of the MMed, they attend an applied research methodology module and complete a research project, the results of which are presented in a mini-dissertation and/or publication in a peer-reviewed scientific journal.

In accordance with CMSA regulations, all registrars have to compile a portfolio that details different aspects of training for the duration of the course. There are four formal contact sessions per week: Tuesday departmental seminar, Wednesday endocrine meeting, Thursday laboratory calculations/management tutorial and Friday Journal Club/Case discussion. From 2017, the university primary examination will be replaced by the new College of Pathologists FCPath (Chem) part I examination.

Clinical pathology registrars follow the same programme when they rotate through the department, initially for a six-month period, followed by two four-month rotations after successful completion of the primary examinations.

BSc (Hons) and MSc Chemical Pathology

The BSc (Hons) programme includes the following modules: a) Principles and Practice of Clinical Chemistry; b) Pathophysiology; c) Laboratory Management; d) Medical Biostatistics; e) Molecular Pathology; and f) Applied Research Methodology. The Medical Biostatistics module is presented over fourteen weeks by lecturers from the Department of Statistics at the University of Pretoria. Honours students are expected to complete the same Molecular Pathology module as registrars. It is comprised of weekly lectures, several practical and formal examinations. Theoretical knowledge of chemical pathology is assessed during seven written tests and a final year-end examination. Each student has to complete a research project under supervision and to present and write up their work in the form of a mini-dissertation. Skills taught during practical sessions and rotation through the diagnostic laboratory at SBAH, are honed by performing semi-independent laboratory work on the bench during the course of conducting the research project. On completing the BSc (Hons) degree, many graduates proceed to enrol for the MSc in chemical pathology or allied disciplines.

For 2015, two students enrolled for the BSc (Hons) in chemical pathology and two for 2016. Two students completed their MSc degrees and will be conferred their degrees at the end of April. Both these students have found positions in private pathology laboratories. Two MSc students, one whose study is a collaboration between Chemical Pathology and the Department of Forensic Science, will be handing in their dissertations for examination by the end of May 2016.

Technologists

The department provides in-service teaching and training to student medical technologists registered for chemical pathology and clinical pathology. The lectures presented for the BSc (Hons) programme, of which there are 26 per year, are attended by technologists/technicians as well as technologist interns for CPD purposes.
Current Staff Complement (32)

<table>
<thead>
<tr>
<th>Role</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOD</td>
<td>1</td>
</tr>
<tr>
<td>Pathologists</td>
<td>3</td>
</tr>
<tr>
<td>Secretary</td>
<td>1</td>
</tr>
<tr>
<td>Registrars</td>
<td>6</td>
</tr>
<tr>
<td>Manager Laboratory</td>
<td>1</td>
</tr>
<tr>
<td>Supervisor Laboratory</td>
<td>-</td>
</tr>
<tr>
<td>Medical Scientists</td>
<td>1</td>
</tr>
<tr>
<td>Intern Medical Scientists</td>
<td>-</td>
</tr>
<tr>
<td>Medical Technologists</td>
<td>9</td>
</tr>
<tr>
<td>Student Medical Technologists</td>
<td>5</td>
</tr>
<tr>
<td>Technicians</td>
<td>1</td>
</tr>
<tr>
<td>Student Medical Technicians</td>
<td>2</td>
</tr>
<tr>
<td>Technical Assistant</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>32</strong></td>
</tr>
</tbody>
</table>

Vacant posts exist for a laboratory supervisor, medical technologists and laboratory assistants. It is expected that the posts for the laboratory supervisor and laboratory assistant will be filled by 01 May 2016. With the current staff complement, it is difficult to achieve the required TAT.

Table 42: The effect of increased volumes

<table>
<thead>
<tr>
<th>Department</th>
<th>Trak-Care Volumes</th>
<th>Oracle Volumes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>December ’15</td>
<td>January ’16</td>
</tr>
<tr>
<td>Chemical Pathology</td>
<td>168 145</td>
<td>199 272</td>
</tr>
</tbody>
</table>

The table above demonstrates the variance of volumes between TrakCare and Oracle. TrakCare volumes show the actual volumes handled by staff within the laboratory, whereas Oracle only produces billable statistics.

Figure 2: Increase in volumes – month-to-month and year-to-year (TrakCare volumes have been used)

Professional Development

Postgraduate students enrolled: 11 – seven MMed, two MSc, two BSc (Hons)
Postgraduate students graduated: 3 – two MSc and one BSc (Hons)

Table 43: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>16</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
4. RESEARCH ACTIVITIES

4.1. Research Units

Staff in the department have active links with:

- Institute of Cellular and Molecular Medicine, directed by Prof. M Pepper
- Bioinformatics Unit, University of Pretoria, directed by Prof. F Joubert.

4.2. Research Projects

Completed Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Mutations in the androgen receptor gene and the fibrillin-3 gene in South African women with polycystic ovary syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Dr C van Niekerk, Dr NM Oosthuizen, Miss M Nöthling</td>
</tr>
<tr>
<td>Funding</td>
<td>NHLS Research Trust, University of Pretoria</td>
</tr>
<tr>
<td>Duration</td>
<td>2011–2014</td>
</tr>
<tr>
<td>Short Description</td>
<td>Polycystic ovary syndrome (PCOS) is the most prevalent endocrinological disorder in women worldwide, characterised by menstrual dysfunction, infertility, obesity and metabolic syndrome. This study investigates microsatellites and methylation differences in the androgen receptor and fibrillin-3 genes between cases.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Ms M Nothling successfully obtained her MSc degree for this project which will be conferred by the end of April 2016.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Identification of CYP21A2 mutations within South African patients suffering from congenital adrenal hyperplasia caused by 21-hydroxylase deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Dr C van Niekerk, Dr NM Oosthuizen, Mr J Lombard</td>
</tr>
<tr>
<td>Funding</td>
<td>NHLS Research Trust</td>
</tr>
<tr>
<td>Duration</td>
<td>2011–2015</td>
</tr>
<tr>
<td>Short Description</td>
<td>Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder caused in 90% of cases by mutations in the CYP21A2 gene. The main aim of the study is to identify and compare mutations in South African CAH patients with those documented in European populations by utilising HRM real-time PCR and sequencing.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Mr J Lombard is in the process of writing his MSc dissertation and will be submitting it for examination by the end of May 2016.</td>
</tr>
</tbody>
</table>

Existing Ongoing Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Genetic analysis of inherited forms of hypophosphataemic rickets in South African patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Dr C van Niekerk, Dr NM Oosthuizen, Ms E Pretorius</td>
</tr>
<tr>
<td>Collaborators</td>
<td>Prof. J Pettifor, Dr K Thandrayen, Department of Paediatrics, University of the Witwatersrand</td>
</tr>
<tr>
<td>Funding</td>
<td>NHLS Research Trust</td>
</tr>
<tr>
<td>Duration</td>
<td>2012–2017</td>
</tr>
<tr>
<td>Short Description</td>
<td>The aim of this study is to identify and characterise mutations prevalent in South African patients with hypophosphataemic rickets. Mutations in the PHEX, FGF-23, DMP-1 and SLC34A3 are responsible for X-linked, autosomal dominant, autosomal recessive and hypercalcicuric forms of inherited hypophosphataemic rickets respectively. Causative genes will be analysed by means of conventional PCR, HRM real-time PCR and DNA sequencing.</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Ms E Pretorius obtained her MSc degree for this project in 2015. Two journal articles are being prepared for submission. This is an ongoing project and will continue for the foreseeable future.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Quantifying and analysing three genes from foetal DNA extracted from maternal plasma to establish foetal sex and RhD blood grouping for routine testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Dr C van Niekerk, Ms N Matthee</td>
</tr>
<tr>
<td>Collaborators</td>
<td>Dr H Lombaard, Maternal and Foetal Medicine Unit, SBAH</td>
</tr>
<tr>
<td>Funding</td>
<td>NHLS Research Trust</td>
</tr>
<tr>
<td>Duration</td>
<td>2014–2015</td>
</tr>
</tbody>
</table>

Short Description: The aim of this study is to identify and compare mutations in South African CAH patients with those documented in European populations by utilising HRM real-time PCR and sequencing. Outcomes: Mr J Lombard is in the process of writing his MSc dissertation and will be submitting it for examination by the end of May 2016.
Short Description: The aim of this study is to quantify and analyse foetal DNA, extracted from maternal plasma, to establish routine tests for foetal sex determination and RhD blood grouping in the Department of Chemical Pathology. This will be done by employing restriction enzyme digestion, real-time PCR and multiplex PCR.

Outcomes: Ms N Matthee successfully obtained her MSc degree for this project which will be conferred by the end of April 2016. This is an ongoing project and will continue for the foreseeable future.

Project Title: Post-mortem genetic testing of Long QT syndrome in sudden infant death (SIDS) cases at the Pretoria Medico-Legal Laboratory

Researchers: Dr C van Niekerk, Dr L du Toit-Prinsloo, Mrs B van Deventer

Collaborators: The departments of Chemical Pathology and Forensics

Outcomes: Mrs B van Deventer is in the process of writing her dissertation and will be submitting it for examination by the end of May 2016. One journal article has been submitted for publication (awaiting the outcome).

Project Title: Molecular modelling of ligand-receptor interactions: Application to the oestrogen receptor, insulin receptor and HIV protease/integrate systems

Researchers: Prof. T Pillay, Dr M Islam

Duration: 2013–2016

Short Description: This project is funded by a University of Pretoria Vice-Chancellor's postdoctoral fellowship, awarded to Prof. T Pillay. Dr Islam is the incumbent of the fellowship and the project aims to characterise molecular interactions of the insulin receptor with its ligands including structural analogues and variants of native insulin, as well as mutant insulins found in humans. These studies will provide further insight into ligand-receptor interactions.

Outcomes: The work on the oestrogen receptor ligands, insulin receptor and HIV protease and integrate systems is described in several publications listed in the publication list.

New Projects

Project Title: Quantifying and analysing three genes from foetal DNA extracted from maternal plasma to establish foetal sex and RhD blood grouping for routine testing (R89 700)

Short Description: The aim of this study is to quantify and analyse foetal DNA, extracted from maternal plasma, to establish routine tests for foetal sex determination and RhD blood grouping in the Department of Chemical Pathology. This will be done by employing restriction enzyme digestion, real-time PCR and multiplex PCR.

This project has resulted in an MSc degree for Ms Nicolene Matthee, and the project will be ongoing.

Project Title: Plasma D-Lactate as a diagnostic tool in acute appendicitis, diverticulitis and blunt abdominal trauma.

Short Description: The aim of this project is to evaluate the potential use of plasma D-Lactate as a diagnostic tool in acute appendicitis, diverticulitis and blunt abdominal trauma in humans and compare the usefulness of D-lactate, in conjunction, with white blood cell count, CRP and serum amylase and to determine whether D-lactate will be a useful test to assist in clinical diagnosis and investigation of patients presenting with acute abdominal pain.

Project Title: Development and validation of a reverse phase high performance thin layer chromatography (RP-HPTLC) method for the separation of porphyrins in the investigation of suspected porphyrias

Short Description: The diagnosis of the porphyrias is based on the analysis of porphyrin levels in serum, urine and stool. The most common method for analysis involves extraction and analysis by chromatography. Whilst HPLC methods are ideal, they require expensive dedicated equipment and highly skilful expertise. In most diagnostic hospital laboratory settings thin layer chromatography is used but often this method cannot separate isocoproporphyrin as a distinct band. In this project, the utility of a novel reverse-phase HPTLC method will be evaluated for urine and faecal prophyrin separation, with the idea being to introduce this method nationally, if it proves to be robust.

4.3 Research Funding

The Department was awarded an NRF postdoctoral fellowship for Dr MA Islam to continue work on molecular modelling of ligand-receptor interactions.

Project Title: Molecular modelling of ligand-receptor interactions and application to communicable and non-communicable disease.
5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

National

**Oral presentations**


Pillay TS. Cost containment in the NHLS: How can we effectively manage the use of laboratory tests? Invited speaker at PathRed 2015, Emperor’s Palace, Kempton Park, 15–16 April 2015.

**Poster presentations**


**International**

**Oral presentations**


Pillay TS. Digital publication in academia: Recent advances. IFCC General Conference, Madrid, 18–22 March 2016.

**Poster presentations**


6. **ACADEMIC AND RESEARCH HONOURS AWARDS/RECOGNITION**

Prof. Pillay was elected to the membership of the Academy of Science of South Africa in recognition of his contributions. The academy recognises the country’s most outstanding and celebrated scholars by electing them to Membership of the Academy.

7. **ADDITIONAL INFORMATION**

- Prof. Pillay is Editor of the Journal of Clinical Pathology, a BMJ journal group based in London and a member of the International Committee of the Royal College of Pathologists and secretary and council member of the College of Pathologists, South Africa.
- Prof. Pillay was appointed as country advisor for South Africa by the Royal College of Pathologists, London and Chair of the Policy, Advocacy and Communications group of the Royal College of Pathologists International committee.
- Prof. Pillay published a second digital interactive textbook, Interactive mathematics for laboratory medicine, in September 2015 and this has been released in 52 countries.
- Prof. Pillay delivered a keynote address at the General Conference of the International Federation of Clinical Chemistry and Laboratory medicine (IFCC) in Madrid, Spain, 18–22 March 2016.
- Prof. Pillay was appointed to the Medical and Dental Board of the HPCSA by the Minister of Health in 2015. Prof. Pillay convened and organised the Scientific Workshop at the Pathology Research and Development (PathReD) Congress 2015, held from 15–16 April 2015 at Emperors Palace, Johannesburg, South Africa. The Congress was an inaugural event, organised by the NHLS and themed “Enriching Health through Research: Paving the Future.”
Haematology

Head: Prof. Roger Pool

1. ABOUT THE DEPARTMENT

The Department of Haematology renders tertiary laboratory and clinical services to the SBAH, Tshwane District Hospital, Kalafong Hospital and surrounding clinics. It also acts as a referral centre for Limpopo, Mpumalanga, North West and parts of Gauteng (Tembisa, Mamelodi).

Clinical services are organised under the umbrella of the departments of Internal Medicine and Paediatrics, while laboratory services fall within the ambit of the Tshwane Academic Division of the NHLS. Research interests include haemophilia, neutrophil extracellular traps, calreticulin in myeloproliferative disease, JAK-2 assay methods, point-of-care (POC) testing and immunophenotyping. The department obtained a 100% pass rate for postgraduate BSc (Hons), MSc, MMed and FCPath (Haem) Part II examinations. The department was given an award for a Faculty Day presentation and Dr J Potgieter received an award from the University of Pretoria for excellence in teaching.

Table 44: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist</th>
<th>Med Doctors</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6</td>
<td>7</td>
<td>2</td>
<td>10</td>
<td>2</td>
<td>26</td>
<td>27</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

Laboratory services are offered from two separate sites viz. the SBAH core laboratory and the Institute of Pathology, Prinshof Campus.

The bulk of diagnostic work in terms of test volumes is performed in the core laboratory. These tests are mainly the full blood count (FBC), erythrocyte sedimentation rate (ESR) and clotting profiles. More specialised, lower volume tests are performed on the Prinshof Campus including bone marrow aspirate and trephine biopsy examinations, HPLC, haemoglobin electrophoresis, platelet aggregometry, platelet function testing (PFA), blood grouping, special haematology, immunohaematology, flow cytometry and molecular haematology.

A total of 356,496 tests was performed in the period under review which represents a 12.4% increase since 2014/15. Registrars spend equal amounts of time at each site over the course of the four-year training period.

2.1. Flow Cytometry

Specimens are analysed at the Department of Immunology and are interpreted and reported on by pathologists in the Department of Haematology. This is done in conjunction with the clinical presentation of the patient, often in consultation with the referring physician.

The co-operation of hospital management has been enlisted through electronic gatekeeping (EGK) in an attempt to cut down the number of inappropriate referrals for immunophenotyping, thus reducing costs.

A large number of requests are received for the investigation of chronic lymphoproliferative disorders and, to this end, the panel used for these disorders has been expanded.

2.2. Clinical Haematology

The adult haematology clinic continues to provide a consultation service both to the SBAH and to the wider medical community of Pretoria and the surrounding areas. The clinic also serves as an important vehicle for the teaching of undergraduate medical students as well as haematology and internal medicine registrars. During the period under review, 574 patients were seen at the clinic. Members of the department also provided valuable input into the paediatric haematology clinic.

A clinical haematologist was appointed on a sessional basis with funds provided by a University of Pretoria Clinical Training Grant. Registrars meet regularly with this consultant both for tutorials and also for bedside teaching, using facilities provided by the Department of Internal Medicine. There is an urgent need for a full-time clinical haematologist and for a clinical haematology unit to be established at TAD with a view to training fellows in Clinical Haematology.

2.3. Haemophilia Care

A total of 300 visits were made to the clinic during the year with the majority of patients having severe Haemophilia A. Many patients from outside Gauteng Province attend this clinic and are provided with factor which places a strain on the finances of the SBAH. An arrangement has been entered into whereby patients will receive a prescription for the required factor replacement which they will take to their referring hospital to be dispensed. The success of this project is currently being monitored.
3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Formal Lectures

The department participates in one teaching block and two special activities for undergraduate students.

• BLOCK 280 (Homeostasis) for MBChB II – Feedback from students on the newly designed lecture series was generally favourable. The results of the last group of students were excellent, with the overwhelming majority being promoted after the first examination.

• SA12 (Haematological Malignancy) for MBChB III – Case studies for this course were revised and rotations were divided into laboratory, radiological and clinical modules. Assessment was also changed to include both a 600-word case report and a multiple choice, computer-based examination. Students spend time on haematology, immunology, histopathology, genetics, radiation oncology, as well as medical and paediatric oncology as part of their rotation in this block.

• SA13 (Laboratory Medicine) for MBChB VI – This is the last formal instruction to student interns on laboratory medicine. Topics covered include FBC, nutritional and haemolytic anaemias, bleeding disorders, hypercoagulable states and blood transfusion. In this block students are taught how to work up a patient with haematological disease, as well as cost-effective and rational use of laboratory resources. Lectures are given in one of the new 400-seat auditoria within the Tswelopelo Building which has just been completed and which is equipped with state-of-the-art audiovisual facilities. The new building is situated on the Prinshof South campus of the University.

Small Group Tutorials

Student interns spend two days in the Department of Haematology as part of the student intern rotation. During this period they have tutorials on a large number of haematological conditions, and are taught how to interpret the most commonly requested haematological tests. Most of these tutorials are led by registrars in the department. The second day of the rotation is spent in the haematology clinic where the students clerk patients and assist with drawing blood and arranging follow-up visits. Marks are allocated to students based on their participation in activities and their knowledge of haematology.

3.2. Postgraduate Teaching

MMed (Path)

A comprehensive practical and theoretical teaching programme has been put in place for registrars in haematology which seeks to cover the whole syllabus over a four-year period.

Registrars in haematology are expected to attend and pass courses in research methodology and molecular biology within the first 18 months of starting in a registrar post. An ongoing programme of registrar assessments has been put in place which includes formal examinations, evaluation of presentations and one-on-one interactions around the teaching microscope.

Formal written assessments take place four times a year and are tailored to the seniority of registrars. Once the assessments have been marked, feedback is given to each registrar on a one-to-one basis.

The HPCSA approved two additional registrar posts for the department with take effect from 2015. This brings the number of approved training posts to eight. Currently seven of these posts are funded.

PhD

Two pathologists are involved in PhD studies. One is studying the contribution of pneumolysin and hydrogen peroxide to the production of neutrophil extracellular traps (NETs) in response to Streptococcus pneumoniae while the other is looking at the effect of HIV infection on haematopoiesis, especially erythropoiesis. Initial data on haematological parameters in HIV infected patients is currently being collected.

MSc

The focus of the MSc programme is on the laboratory diagnosis of myeloproliferative disorders.

One student is developing an in-house JAK-2 assay method while the other is developing a method for detecting somatic mutations of calreticulin.

BSc (Hons)

The degree is based on course work, tutorials, oral presentations and a dissertation. Compulsory modules include applied research methods, medical biostatistics and molecular pathology. At the request of the university, the weighting of the research component has been increased to bring the course in line with overall academic policy.
Table 45: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>South African</td>
<td>12</td>
<td>5</td>
<td>5</td>
<td>100%</td>
</tr>
</tbody>
</table>

3.3. Other Training Information

Training of intern medical scientists with a view to completing their training portfolio continues in the department. A programme of haematology training for registrars in internal medicine and paediatrics has been established which takes place on a weekly basis throughout the year. Training is largely problem based. Presentations are prepared by registrars and discussions are moderated by consultants in the Department of Haematology.

4. RESEARCH ACTIVITIES

Research interests within the department include haemophilia comprehensive care, neutrophil extracellular traps, microRNA in chronic myeloid leukaemia, plasmablastic lymphoma, platelet activation, AML profiling using a micro-array platform and minimal residual disease detection by flow cytometry in childhood leukaemia.

The department is in the process of compiling a South African Haemophilia Registry which will eventually seek to list all haemophilia patients in the country with records of their treatment, hospital visits, surgery and other interventions. This list will be available to all Haemophilia Care Units to allow seamless follow-up of patients who move from one region to another. Such a register will also make gathering of statistical information much easier and allow for forward planning regarding the amount of factor which will be needed nationally.

One of the department’s consultants serves on the Global Alliance for Progress (GAP) initiative which seeks to bring the standards of haemophilia care between resource poor and resource rich nations closer to each other. The GAP in haemophilia is a ten-year healthcare development project, launched on World Haemophilia Day, April 2003. GAP’s primary goal is to greatly increase the diagnosis and treatment of people with haemophilia, and other bleeding disorders, in 20 targeted developing countries. The programme aims at closing the gap in treatment between developed and developing countries in three key areas: (i) the number of people born with haemophilia and those who reach adulthood; (ii) the estimated and actual number of people known with bleeding disorders; and (iii) the need versus the availability of treatment products.

The 20 countries selected for the first decade of GAP (2003–2012) include: Algeria, Armenia, Azerbaijan, Belarus, China, Ecuador, Egypt, Georgia, Jordan, Lebanon, Mexico, Moldova, Morocco, Peru, Philippines, Russia, Syria, Thailand, Tunisia, and South Africa.

The department is currently collaborating with the Department of Paediatric Oncology in a pilot project to follow up children with newly diagnosed leukaemia using a Beckmann Coulter Galios® flow cytometer and Euroflow® panels.

In compliance with directives from both the University of Pretoria and the NHLS to increase the number of qualified PhD staff, one pathologist is in the process of completing his PhD degree while another has started data collection for her PhD.

4.1. Research Projects

**Project Title:** The contribution of pneumolysin and hydrogen peroxide to the induction of neutrophil extracellular traps by *Streptococcus pneumoniae*

**Researcher:** Dr J Nel (PhD)

**Short Description:** The aim of this study is to evaluate the contribution of pneumolysin (ply) and hydrogen peroxide, individually or in combination, on the induction of neutrophil extracellular traps by *Streptococcus pneumoniae*. The study will seek to establish and optimise various assays to demonstrate and quantify NET formation, as well as to delineate the roles of hydrogen peroxide and pneumolysin in the induction of NETs. It will also ascertain the mechanisms which underpin NET formation in response to ply and hydrogen peroxide (i.e. induction of ROS and/or Ca$^{2+}$ influx) and investigate NET formation using intact wild-type and the corresponding gene knockout strains, in which the genes encoding ply or pyruvate oxidase have been selectively inactivated.

**Project Title:** Detection of the JAK2 V617F mutation using molecular methods

**Researcher:** Ms T Netshidzivhani (MSc)

**Short Description:** Janus kinase-2 (JAK-2) is a cytoplasmic tyrosine kinase with a role in signal transduction from multiple growth factors. JAK-2 is a key component of the JAK-signal transducer and activator of transcription (STAT) pathway. Janus kinase-signal transducer and activator of transcription signalling is crucial for definitive erythropoiesis, as well as the cytokine response by myeloid progenitors. A large number of different approaches for the detection of the V617F mutation have
been described. Two main criteria are important in the choice of an assay. Firstly it should be specific and secondly, the assay must be sensitive enough to be able to identify a JAK-2 V617F mutant allele with a burden as low as 1% to 3%. The aim of this study is to develop a real-time PCR assay for the detection of the JAK-2 V617F mutation.

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection of the somatic mutations of calreticulin in myeloproliferative disorders using molecular methods</td>
<td>Ms L du Toit (MSc)</td>
</tr>
<tr>
<td>Short Description</td>
<td>Calreticulin is a protein which binds calcium ions and is situated within the endoplasmic reticulum. It binds to misfiled proteins and prevents them from being exported from this site. In 2013, calreticulin mutations were detected in a large number of JAK-2 negative, MPL-negative patients with idiopathic myelofibrosis and essential thrombocythaemia. This mutation is now considered the second most common in myeloproliferative disorders. The presence or otherwise of this particular mutation is considered to have important prognostic implications for patients with myeloproliferative disorders. The student will research ways to develop an in-house method to detect somatic mutations of calreticulin.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet activation in patients with severe haemophilia A</td>
<td>Dr T Chetty (MMed)</td>
</tr>
<tr>
<td>Short Description</td>
<td>There have been conflicting reports in the literature as to the degree, if any, of platelet activation which is present in patients with severe haemophilia A. This study will use a flow cytometric method to identify platelets and use p-selectin expression as a marker for platelet activation to ascertain whether platelet activation is present in patients with severe haemophilia A.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Validation of the Mission Plus® haemoglobin testing system</td>
<td>Dr G George (MMed)</td>
</tr>
<tr>
<td>Short Description</td>
<td>This is a hand-held, POC instrument which is capable of producing a haemoglobin value within 15 seconds. The test is strip-based and requires 10µl of blood to produce a result. The aim of this study is to validate the instrument against standard haematology analysers viz. the Advia® 120 and 2120.</td>
</tr>
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<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>South African haemophilia database registry</td>
<td>Dr J Potgieter and Dr L Ntabeni</td>
</tr>
<tr>
<td>Short Description</td>
<td>A register of all haemophilia patients in South Africa will be compiled. This information will be available to all haemophilia comprehensive care units throughout the country and will assist in compiling statistics and estimating requirements for factor replacement on a provincial and national level.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method validation of the Alere INRatio PT/INR monitoring system</td>
<td>Dr T Njinga (MMed)</td>
</tr>
<tr>
<td>Short Description</td>
<td>A method validation on this POC instrument will be undertaken in which results will be compared with those obtained using the Sysmex 2010i which is the principal coagulation instrument used by the Department of Haematology.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer diagnoses made from bone marrow specimens from November 2012 to December 2015: A retrospective study</td>
<td>Ms N Swart (BSc (Hons))</td>
</tr>
<tr>
<td>Short Description</td>
<td>Examination of bone marrow is a very important aspect used to diagnose diseases especially those concerned with haematological abnormalities, even in the ever-developing fields of genetics and molecular techniques. Morphological evaluation of bone marrow provides information about the composition of the marrow as well as the identification of features that will allow for a successful diagnosis that would be missed if only peripheral blood were examined.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researcher</th>
</tr>
</thead>
<tbody>
<tr>
<td>A retrospective data analysis to compare the turnaround time of point-of-care haemoglobin tests to that of haemoglobin tests performed in the laboratory</td>
<td>Mr T Ya (BSc (Hons))</td>
</tr>
<tr>
<td>Short Description</td>
<td>The POC test is an evolution in diagnostic testing which has created a unique opportunity to increase the operational efficiency of clinical services and, in some cases, to improve patient outcomes. The purpose of this study is to compare the turnaround time of a single test (haemoglobin) when performed as a POC test versus a conventional test.</td>
</tr>
</tbody>
</table>
Project Title: Comparison of the AMLProfiler® with standard diagnostic procedures in patients with acute myeloid leukaemia
Researcher: Dr T Matlhako
Short Description: The AMLProfiler® is a diagnostic microarray chip for use with Affymetrix® microarray technology. The test incorporates seven molecular targets used to classify and establish prognosis in patients diagnosed with AML. These variables include translocations and mutations of genes that are involved in the pathogenesis of the disease. Identification of specific targets also plays an important role in the risk stratification of newly diagnosed patients. The aim of this study is to compare currently-employed diagnostic methods with the microarray chip in terms of labour, turnaround time and cost.

5. RESEARCH OUTPUT

5.1. Journal Publications

5.2. Conference Presentations

6. ADDITIONAL INFORMATION

6.1. Current Areas of Research Activity
• Clinical trials of recombinant FVIII in haemophilia
• Haemophilia care in developing countries
• The prognostic significance of CD34 expression in acute myeloblastic leukaemia
• JAK-2 assay
• Neutrophil extracellular traps
• MicroRNA in CML
• Plasmablastic lymphoma
• Point-of-care INR testing
• “Euroflow” 10 colour immunophenotyping in childhood leukaemia
• Molecular and cytogenetic analysis of AML using micro array technology
• Platelet activation in severe haemophilia A
• Thromboprophylaxis in orthopaedic surgery.
Immunology

Head: Prof. Riana Cockeran

1. ABOUT THE DEPARTMENT

The Department of Immunology was established in 1990 and is situated in the Tshwane Academic Division, and the University of Pretoria, Gauteng. The department conducts research and teaching/training at undergraduate and postgraduate levels. Students include medical technicians, technologists, scientists, undergraduate medical and paramedical students, as well as postgraduate students at the BSc (Hons), MSc and PhD levels.

Table 46: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>PhD Scientist</th>
<th>MSc Scientist</th>
<th>BSc (Hons) Scientist</th>
<th>Technologists</th>
<th>South African</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

The department provides a wide range of serodiagnostic tests (auto-immune, allergic, infectious diseases), flow cytometric determination of leukaemias and lymphomas (in partnership with the Department of Haematology), PLG CD4+ tests, as well as the diagnosis of primary and acquired immunodeficiency disorders, and HLA typing and HLA antibody detection (disease associations and organ transplantations).

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Teaching/training in basic/applied immunology is offered to student medical technicians/technologists/scientists, medical and paramedical students, as well as to students enrolled in various BSc (Hons) courses.

3.2. Postgraduate

Training is offered at BSc (Hons), MSc and PhD levels, while scientists and registrars/clinical assistants from medical microbiology, virology, haematology and clinical pathology rotate through the department’s research and diagnostic laboratories. In addition, lectures and tutorials are presented to clinical and pathology departments e.g. internal medicine, paediatrics, virology and microbiology. The department of immunology also provides access to equipment and supervision of researchers from other departments and academic institutions.

3.3. Professional Development

- Technicians: Five students qualified
- Technologist: One student qualified
- Postgraduate candidates graduated: One BSc (Hons), four MSc
- Postgraduate candidates registered in 2015: 29 (one BSc (Hons), 12 MSc, 16 PhD).

Table 47: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>36</td>
<td>9</td>
<td>8</td>
<td>89%</td>
</tr>
</tbody>
</table>

3.4. Other Training Information

The training figures presented are for the whole department, which includes UP-appointed staff members (Prof. R Anderson, Prof. MS Pepper, Dr A Allesandrini, Dr C Durandt, Dr HC Steel and Dr MC Cholo). Postgraduate students not registered within the department of immunology, but receiving training in the department are not included. In addition to the students mentioned above, several postgraduate students and registrars rotate through the department annually as part of their training.

4. RESEARCH ACTIVITIES

The research activities of the department, even though primarily laboratory-based, are in line with the national research strategies and priorities. The research that is undertaken has clear clinical/translational objectives into immunopathogenesis, diagnosis/prognosis, and...
immunopharmacotherapy of acute and chronic inflammatory disorders, of both infective (HIV/AIDS, TB, severe pneumococcal disease, severe sepsis) and non-infective (bronchial asthma, rheumatoid arthritis, toxicology of environmental and occupational substances) origin. Investigations into the effect of cigarette smoking as a major risk factor for the development of respiratory infection and resistance to antibiotics, effects of respiratory pathogens and their products on neutrophil extracellular trap formation, as well as pharmacogenetics, and stem cell harvesting and expansion with a view to future therapy options, are presently under way.

4.1. Research Units/Study Groups Linked to the Department

The Department of Immunology is associated with the Institute for Cellular and Molecular Medicine.

4.2. Research Projects

Infectious Diseases

Researchers: Prof. R Cockeran, Dr MC Colo, Prof. AJ Theron, Prof. R Anderson, Dr T Rossouw, Dr HC Steel, M Potjo, G van Dyk, A Osman, MT Mothiba, S Makubane, T Mboneni, M Madzime, M Boswell, Prof. C Feldman, Prof. TJ Mitchell

Short Description: Exposure to cigarette smoke condensate activates the production of biofilm by Streptococcus pneumoniae and causes the functional inactivation of the pro-inflammatory toxin, pneumolysin; which in turn can favour colonisation of the pneumococcus in the airways, and can underpin the susceptibility of smokers to severe pneumococcal infections. These effects can be attributed to the up-regulation of genes encoding the two component 11 system, as shown by the macrolide susceptible strain 172, and macrolide resistant strains 521 and 2507 (all serotype 23F). Presently investigations into the mutagenic properties of tobacco-related products, as well as the possible biofilm disruptive effects of components of the innate immune system are under way.

The major K+ transporter of Mycobacterium tuberculosis appears to be inactive in environments of neutral pH and high K+ concentrations. However, in mildly acidic environments, the genes related to these transporters are expressed at a markedly higher level, compatible with the role of K+ transporters in promoting intravascular and intragranuloma survival. More recent research focusses on the role of cigarette smoke on biofilm formation as well as on the potential of antimicrobial agents to target biofilm formation and non-replicating, biofilm-encased organisms; as well as the disruption of biofilms.

The recruitment of the ongoing study investigating the quantification and description of the development and persistence of HIV-1 resistance patterns in mothers and their infants in a longitudinal cohort at Kalafong has been completed. Investigations include the detection of a variety of biomarkers as a possible prognostic tool, and the identification of resistance patterns, is under way. In addition, investigations into immune activation are progressing well. Researchers in the department have been integral to the establishment of a South African drug-resistance database.

Inflammation

Researchers: Prof. R Anderson, Prof. AJ Theron, Dr JG Nel, Dr HC Steel, Dr MC Cholo, Prof. R Cockeran, M Makgobu, GA Makhubele, Prof. GR Tintinger, Dr PWA Meyer, Dr B Hodkinson, Prof. M Ally, E Musenga, Prof. M Tikly

Short Description: The major highlights of this research programme are investigations into the formation of neutrophil extracellular traps, as well factors that might influence their formation (including genetic and environmental factors) which are presently under way. Current research in the field of rheumatoid arthritis is focused on the identification of novel biomarkers, intra and extracellular, as predictors of response to therapy and outcome.

4.3. Grant Funding

- NRF: R1 260 000
- NHLS Research Trust: R90 000
- University of Pretoria: R1 100 000
- MRC: R1 400 000
- UP Equipment: R85 000.

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Book Chapters


5.3. Conference Presentations


6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

- Prof. Theresa Rossouw was awarded her associate professorship by UP.
- The manuscript: *Exposure of a 23F serotype strain of Streptococcus pneumoniae to cigarette smoke condensate is associated with selective upregulation of genes encoding the two-component system 11 (TSC11)* by Cockeran et al. was awarded best publication representing best group effort by the Faculty of Health Sciences, UP.
- The manuscript: *Optimisation of critical hairpin features allows miRNA-based gene knockdown upon single-copy transduction* by Myburg et al. was awarded best clinical publication by a young scientist (<35y) by the Faculty of Health Sciences, UP.
- The following Immunology students or post-doctorates received the following prizes for oral presentations at the Faculty Day of the Faculty of Health Sciences, UP:
  - First prize (basic sciences): van Rensburg J, presented: *Cystic fibrosis and rarefaction: unification through diversity.*
1. ABOUT THE DEPARTMENT

The Department of Medical Microbiology provides diagnostic services to three tertiary hospitals, viz. SBAH, Kalafong and Tembisa; regional and primary hospitals such as Tshwane District Hospital Pretoria West and Mamelodi Hospitals, as well as clinics in the Tshwane District. It is involved in Infection Prevention and Control Programmes for hospitals in the Tshwane region, as well as partnering with the Gauteng Department of Health in coordinating such activities in the province as well as at national level. The Medical Microbiology Laboratory continues to serve as an enhanced surveillance site for the National Institute of Communicable Diseases (NICO).

The Department of Medical Microbiology has an extensive teaching and training programme for both undergraduate students (MBChB, BCur, BPhys and BDiet) and postgraduate students (BSc (Hons), MMed, MSc, PhD and postdoctoral fellows). Clinical departments supported by the department are internal medicine, paediatrics, surgery, neurosurgery, cardiothoracic surgery, nephrology (incl. renal transplant unit) and the different ICUs. Five registrars are currently in training, one of whom will write final examinations in 2016. The academic personnel have joint appointments with the University of Pretoria.

There are four research themes in the department which are: tuberculosis, antibiotic resistance of clinically important pathogens, emerging and re-emerging pathogens, as well as sexually transmitted infections.

Table 48: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Med Doctors</th>
<th>PhD Scientist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>5</td>
<td>2</td>
<td>20</td>
<td>1</td>
<td>33</td>
<td>33</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

The department provides diagnostic laboratory services for Steve Biko Academic and Tshwane District Hospitals. It further provides referral diagnostic and clinical services for Kalafong, Mamelodi and Tembisa Hospitals as well as several Primary Health Care Clinics in the Tshwane District. It serves as one of the referral laboratories for hospitals in the Gauteng area of the NHLS structure as well as primary healthcare clinics served by the Tshwane district. The volume of tests performed during the review period was 498 928, which a 10% increase since the previous year. GeneXpert testing amounted to 58 573 tests which is an increase of 18% over the previous year.

Two new testing modalities were implemented: i) A molecular test for the detection of Pneumocystis jirovecii. The laboratory is currently the only NHLS laboratory performing this test. Test volumes have steadily increased since its introduction with the total number of tests for the first year being 575.

ii) Towards the end of the year the department implemented an algorithmic approach for the detection of Clostridium difficile which encompasses a rapid immunochromatographic test (C diff quick) as a first step, followed by a molecular test (GX P C diff). This approach is cost-saving, has increased sensitivity to the previous test method, and has an improved turnaround time. This department is the first in the NHLS to implement such a testing algorithm and the first to use the C diff quick.

The department continues to serve as an enhanced surveillance site for the National Institute of Communicable Diseases (NICD), actively participating in the GERMS SA surveillance programmes for enteric pathogens, mycology, parasitology and respiratory and meningeal pathogens, as well as the pneumococcal vaccine surveillance programme.

2.1 Clinical and consultative support

Clinical staff (pathologists and registrars) participate in several ward rounds at SBAH. These include adult ICU, surgery ICU, neurosurgery, cardiothoracic ICU, nephrology and renal transplant unit. In addition to structured ward rounds, ongoing clinical support is given to all other disciplines at SBAH as well as Tshwane District Hospital, and telephonic consultations are held with clinicians from Kalafong, Tembisa and Mamelodi hospitals.

The pathologists are actively involved in various committees at SBAH. These are the Pharmacy and Therapeutics Committee, Antibiotic Stewardship in collaboration with the Division of Infectious Diseases, Pathology Task Team and the Infection Control Committee. The department remains actively involved in the infection prevention and control programmes (e.g. assistance in management of outbreaks) for the hospitals served, and partners in national, provincial and district infection prevention and control initiatives.
3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Teaching and training are provided to medical technologists, undergraduate medical and dental students, as well as allied healthcare students in the disciplines of nursing, physiotherapy and dietetics. Interaction with medical undergraduates is over five years, with intensive teaching done during the second semester of the second year for medical and dental undergraduates. The dental undergraduates now receive intensive training during the first semester of the third year.

3.2. Postgraduate

Teaching and training programmes are offered for BSc (Hons), MSc and MMed, PhD and postdoctoral fellow training. Registrars are prepared for both the MMed and Federation of South African Societies of Pathology (FSASP) examinations through a structured training programme. Support is offered to rotating registrars by the internal medicine, paediatrics and neurology departments.

3.3. Other Training Information

- Intern medical technologists: Six
- Student technicians: None
- Intern Medical Scientists: Two

Table 49: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Qualification</th>
<th>Total Number of Trainees</th>
<th>Final Year Trainees</th>
<th>Successful Completion</th>
<th>Percentage of Successful Completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSc Hons</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>100%</td>
</tr>
<tr>
<td>MSc</td>
<td>28</td>
<td>18</td>
<td>9</td>
<td>50%</td>
</tr>
<tr>
<td>PhD</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>100%</td>
</tr>
<tr>
<td>Registrars</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>50%</td>
</tr>
<tr>
<td>Med Tech Students</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>100%</td>
</tr>
<tr>
<td>Intern Med Scientist</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Post doc</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>All</td>
<td>37</td>
<td>27</td>
<td>73%</td>
<td></td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

Research in the department is predominantly laboratory-based. There are four focus areas of research in the department.

Tuberculosis Research Programme

This programme focuses on the evaluation and optimisation of molecular-based assays for the rapid detection, identification, characterisation and epidemiology of *Mycobacterium* species obtained from clinical specimens. Included in this programme is the evaluation of conventional and molecular methods for the detection of resistance genes of *M. tuberculosis* strains, as well as the determination of the genetic relatedness of *Mycobacterium* species that are circulating in the Pretoria region. Other areas of activity include evaluating the immune response, drug and vaccine delivery systems as well the effect of biofilms on the activity of antimycobacterial agents on *Mycobacterium tuberculosis*. Several studies on operational research are also being done including the evaluation of molecular transport media and the optimisation of molecular assays in smear-negative HIV-positive patients, as well as innovative approaches to the use of NMT in resource constrained high burden settings.

Researchers:  
Mr S Omar (PhD student), Ms NE Maningi (PhD student), Mr EE Marubini (MSc student), Mr S Atanda (MSc student), Ms S Matukane (MSc student), Mr SSM Rasehlo (MSc student), Ms L Modipane (BSc (Hons) student), Dr K-A Strydom, Dr M Matabane and Dr Moncho (MMed students)

Supervisors:  
Prof. NM Mbelle, Prof. B Fourie, Prof. R Peters, Dr F Ismail, Dr BT Magazi and Dr NA Ismail

Collaborators:  
Prof. M van der Walt (MRC Pretoria); Dr AM Dyrrol-Riise and Prof. N Langeland (University of Bergen, Norway); Dr A Friedland, Dr L Erasmus (NTBRL), Prof. N Beyers (DTTC), Dr C Boehme (FIND), Dr J Fischer (LHVD) and Dr Pasipasodyna (Baylor University, USA)

Funding:  
NHLS Research Trust, DTTC/USAID/TREAT TB

Research Projects

Project Title:  
Spoligotyping of *Mycobacterium tuberculosis* complex with different drug susceptibility profiles from extra-pulmonary isolates in the Tshwane Region
Aim: This study is to perform spoligotyping of *M. tuberculosis* complex with different drug susceptibility profiles from extra-pulmonary isolates submitted to the NHLS Tshwane Academic Division TB Laboratory

Researchers: Mr B Sibandze – BSc (Hons) student

Supervisors: Prof. NM Mbelle, Dr BT Magazi

Project Title: Characterisation of nontuberculous mycobacteria in sputum culture submitted for tuberculosis investigation in Pretoria

Aim: The aim of this study is to identify and determine the frequency of nontuberculous mycobacteria (NTM) in sputum specimens submitted for tuberculosis investigations at the Tshwane Academic Division, National Health Laboratory Service (NHLS), TB Laboratory.

Researchers: Ms L Modipane (Hons) student

Supervisors: Prof. NM Mbelle, Dr BT Magazi

Project Title: Evaluation of *Mycobacterium tuberculosis* clinical isolates with discordant rifampicin phenotypic and genotypic results from Pretoria, South Africa

Aim: The aim of this study is to perform next-generation full gene sequencing to characterize *M. tuberculosis* mutations in clinical isolates with discordant rifampicin phenotypic and genotypic susceptibility test results and relate these to the level of resistance as determined by the minimum inhibitory concentration (MIC).

Researchers: Mr E Marubini (MSc) student

Supervisors: Prof. BF Fourie, Dr BT Magazi

Antibiotic Resistance Research Programme

The focus of research projects in this research programme is on the molecular identification and characterisation of emerging and re-emerging pathogens, with special emphasis on the detection of specific antimicrobial resistance and virulence genes. The programme further seeks to establish the clonal diversity of clinical (including from cystic fibrosis patients), environmental and zoonotic isolates. The potential health risk of these bacteria, as a source of antibiotic resistance genes and the identification of specific markers for antibiotic resistance and vaccine development is also investigated. The research focuses on Gram-negative bacteria belonging to the family *Enterobacteriaceae* and Gram-positive bacteria of the genera *Staphylococcus, Streptococcus* and *Enterococcus*.

Researchers: Mr N Schoonraad (MSc student), Ms W Strasheim (MSc student), Mr R dos Santos (MSc student), Mr JE Louw (MSc student), Ms M Lowings (MSc student), Ms T Goolum-Mahomed (MSc student), Ms M Potgieter (MSc student), Mr R Schwim (MSc student), Ms T Hamwe (MSc student), Ms L Maboko (MSc student), Mr J Steyn (BSc (Hons) student), Ms T Pelego (BSc (Hons) Student), Ms K Moloto (BSc (Hons) student), Dr C Kingsburgh (MMed), Dr V Tshisevhe (MMed), Ms T Schmidt (PhD student), Ms G Ngoepe (PhD student) and Dr J Antiabong (postdoctoral fellow)

Supervisors: Dr MM Kock, Prof. MM Ehlers, Dr F Ismail, Prof. Mbelle and Dr BT Magazi

Collaborators: Prof. J Pitout (University of Calgary, Canada), Prof. S Enany (Suez Canal University, Egypt and a scholar at the Division of Infectious Diseases, School of Medicine, University of California, San Diego, USA), Prof. S Essack (University of KwaZulu-Natal), Dr P Geertsma (GDARD), Prof. R Masekela (Department of Pediatrics, University of Pretoria – now at KZN), Dr J Wadula (University of the Witwatersrand) and Dr E Moshokoa (Department of Urology, University of Pretoria)

Funding: NHLS Research Trust; RESCOM; Prof. MM Ehlers, BMAZD IRT, UP; Genomics Research Institute, UP

Research Projects

Project Title: Detection and identification of clinically relevant *Enterococcus* and *Staphylococcus* species isolated from surface water in Gauteng

Aim: The aim of this study is to detect and identify clinically relevant *Enterococcus* and *Staphylococcus* species from surface water samples using culture-dependent and culture-independent methods.

Researchers: Mr J Steyn (Hons) student

Supervisors: Prof. MM Ehlers, Dr MM Kock, Dr J Antiabong

Project Title: Detection and identification of β-lactamase genes in *Stenotrophomonas maltophilia* isolated from different water sources in Gauteng
Aim: The aim of this study is to detect and identify β-lactamase genes in *Stenotrophomonas maltophilia* isolated from different water sources in Gauteng

Researchers: Ms K Moloto (Hons) student

Supervisors: Prof. MM Ehlers, Dr MM Kock

Project Title: ST131 *Escherichia coli* in patients undergoing transrectal-guided prostate biopsy at a tertiary academic hospital in Pretoria

Aim: To describe the ST131 *Escherichia coli* isolates from a sample acquired from rectal swabs taken in patients at SBAH following trans-rectal ultrasound guided prostate biopsy procedures

Researchers: Ms T Pelego (Hons) student

Supervisors: Prof. NM Mbelle, Dr MM Kock, Dr EM Moshokoa (Department of Urology)

Surveillance Research Programme

This programme focuses on the continuous monitoring and surveillance of clinical pathogens, such as carbapenemase producing *Enterobacteriaceae*, *Clostridium difficile* and methicillin resistant *Staphylococcus aureus* strains associated with outbreaks in ICU wards and the risk to public health. It explores the diversity and clonal relatedness of methicillin resistant *Staphylococcus aureus* and clinically significant *Enterococci*. The determination of the circulating *Streptococcus pneumoniae* serotypes, including susceptibility, forms part of a surveillance study in children presenting for routine immunisation. It will further establish the clonal diversity of circulating pneumococcal strains.

Researchers: Mrs T Adelowotan (PhD student), Ms R Naidoo (BSc (Hons) student), Ms C Koekemoer (BSc (Hons) student), Ms B Akee (BSc (Hons) student)

Supervisors: Prof. NM Mbelle, Prof. MM Ehlers, Dr MM Kock and Mr Y Dangor

Funding: RESCOM; Prof. MM Ehlers Incentive Funding for Rated Researchers, NRF; NHLS Research Trust

Research Projects

**Project Title**: Prevalence of antibiotic resistant genes in clinical methicillin-resistant *Staphylococcus aureus* isolates obtained from tertiary academic hospitals in Pretoria

Aim: The aim of this study is to determine the prevalence of selected antibiotic-resistant genes in clinical methicillin-resistant *Staphylococcus aureus* isolates obtained from Steve Biko Academic Hospital in the Pretoria region

Researchers: Ms C Koekemoer (BSc (Hons) student)

Supervisors: Prof. MM Ehlers, Dr MM Kock, Dr J Antiabong

**Project Title**: Identification of virulence genes in clinical methicillin-resistant *Staphylococcus aureus* isolates obtained from a tertiary academic hospital in Pretoria

Aim: The aim of this study is to determine the prevalence of selected virulence genes in clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates obtained from a tertiary academic hospital in the Pretoria area

Researchers: Ms R Naidoo (Hons student)

Supervisors: Prof. MM Ehlers, Dr MM Kock, Dr J Antiabong

**Project Title**: Determining vancomycin susceptibility in methicillin-resistant *Staphylococcus aureus* isolates from clinical specimens obtained at a tertiary academic hospital

Aim: To determine vancomycin susceptibility in methicillin-resistant *Staphylococcus aureus* isolates from clinical specimens, using the Standard E-test, the Macro E-test and the Vitek2 automated system, comparing the results with those previously obtained from a similar study, and characterising isolates with MICs above 1 µg/ml using the Pulsed field gel electrophoresis technique

Researchers: Ms B-A Shey (Hons student)

Supervisors: Dr BT Magazi, Dr F Ismail

Sexual Health Research Programme

Research in this area focuses on the detection, identification and characterisation of sexually transmitted pathogens with an emphasis on bacterial vaginosis, *Trichomonas vaginalis*, *Neisseria gonorrhoeae* and genital mycoplasmas using molecular and phenotypic tools.
Researchers: Ms S Majola (BSc (Hons) student), Ms N Pruis (BSc (Hons) student), Ms H-S Jung (MSc student), Mr JT Sethowa (MSc student), Mr TC Duba (MSc student), Mr BI Osizigbo (MSc student), Mr MJ Redelinghuys (PhD student), Dr RK Biswas (Postdoctoral fellow)

Supervisors: Dr MM Kock, Prof. MM Ehlers

Collaborators: Dr T Crucitti (Institute of Tropical Medicine and Hygiene, Antwerpen, Belgium), Prof. H Lombaard (Head: Obstetrics and Gynaecology, Rahima Moosa Mother and Child Hospital, University of Witwatersrand)

Funding: NHLS Research Trust; RESCOM grants, UP; MRC grant; NRF Thuthuka grant; Genomics Research Institute, UP

Research Projects

Project Title: Genital mycoplasmas and bacterial vaginosis in pregnant and infertile women
Aim: The aim of this study is to detect genital mycoplasmas and bacterial vaginosis in pregnant and infertile women using electron microscopy and flow cytometry
Researchers: Ms N Pruis (Hons student)
Supervisors: Dr MM Kock, Prof. MM Ehlers, Mr MJ Redelinghuys

Project Title: Comparison of rapid tests and gold standard methods to detect bacterial vaginosis and Trichomonas vaginalis in pregnant women
Aim: The aim of this study is to diagnose bacterial vaginosis and Trichomonas vaginalis in pregnant women using rapid diagnostic methods, and to compare these tests to the gold standard methods
Researchers: Ms S Majola (Hons student)
Supervisors: Dr MM Kock, Prof. MM Ehlers, Mr MJ Redelinghuys

Project Title: Prevalence of aetiological pathogens of vaginal discharge and male urethritis syndromes in the Tshwane region (Part of study has been completed – to be presented at ASM Microbe 2016)
Researchers: Mr B Osizigbo (MSc student)
Supervisors: Dr MM Kock, Prof. MM Ehlers

Project Title: Biofilm formation in bacterial vaginosis
Aim: The aim of this study is to characterise the biofilm formation in bacterial vaginosis, as well as to detect, identify and characterise Gardnerella vaginalis
Researchers: Ms H-S Jung (MSc student)
Supervisors: Dr MM Kock, Prof. MM Ehlers

4.1. Research Projects

Project Title: Trichomonas vaginalis and bacterial co-infections identified in reproductive age women
Researchers: Mr J Sethowa (MSc student)
Aim: The aim of this study is to determine the prevalence of T. vaginalis and bacterial co-infections in reproductive age women. The secondary aim is to determine the antimicrobial susceptibility profiles and the genetic relatedness of N. gonorrhoeae isolates.

Project Title: Detection and characterisation of selected antimicrobial resistance and virulence genes of Pseudomonas aeruginosa isolated from water sources in the Gauteng region
Researchers: Ms L Maboko (MSc student)
Aim: The aim of this study is to detect and characterise selected antimicrobial resistance and virulence genes in Pseudomonas aeruginosa isolated from water sources in the Gauteng region

Project Title: Genetic characteristics of methicillin-susceptible Staphylococcus aureus strains circulating in the Pretoria region
Researchers: Ms M Potgieter (MSc student)
Aim: The aim of the study is to detect the antibiotic resistance and virulence genes associated with S. aureus isolated from different clinical specimens from hospitals and clinics in the Pretoria region

Project Title: Prevalence of antimicrobial resistance genes and the genetic relatedness of clinical Acinetobacter baumannii isolates circulating in the Pretoria region
Researchers: Ms M Lowings (MSc student)
Aim: The aim of this study is to determine the prevalence of selected antimicrobial resistance genes and to determine the genetic relationship among clinical *A. baumannii* isolates collected from the Kalafong Hospital and the Steve Biko Academic Hospital in the Pretoria region.

Project Title: Characterisation of zoonotic Gram-positive bacteria prevalent in slaughtered pigs and abattoir workers in Gauteng, South Africa.
Researchers: Mr N Schoonraad (MSc student).

Aim: The aim of this study is to determine the prevalence and characterise clinically important zoonotic bacteria prevalent in pigs and abattoir workers in Gauteng, South Africa.

Project Title: Molecular characterisation of β-lactamase genes in *Klebsiella pneumoniae* and *Escherichia coli* from wastewater.
Researchers: Mr Ricardo Dos Santos (MSc student).

Aim: The aim of this study is to identify β-lactamase genes in *K. pneumoniae* and *E. coli* wastewater isolates as well as from wastewater using polymerase chain reaction (PCR) assays and to genetically characterise the isolates using pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST).

Project Title: Molecular characterisation of antimicrobial resistance and virulence factors of methicillin-resistant *Staphylococcus aureus* strains circulating in the Pretoria region.
Researchers: Mr R Schwim (MSc student).

Aim: The aim of this study is to determine the prevalence of antibiotic resistance and virulence genes of clinical MRSA isolates and to determine the most dominant clonal complexes circulating in the Pretoria region.

Project Title: Effect of cigarette smoke on the antimycobacterial activity of anti-TB drugs on *Mycobacterium tuberculosis* biofilm.
Researchers: Mr S Rasehlo (MSc student).

Aim: To determine the effects of cigarette smoke on the response of *Mycobacterium tuberculosis* biofilm cultures to anti-TB drugs.

Project Title: Phenotypic and genotypic susceptibility testing of *Mycobacterium tuberculosis* cultures from Tshwane Metropolitan.
Researchers: Mr S Atanda (MSc student).

Aim: To assess the ability of the GenoType MTBDR DNA Strip and the Bactec MGIT 960 assay to detect resistance to first line and second line drugs in multidrug resistant *Mycobacterium tuberculosis* (MDR-TB) when compared to the agar-proportion method.

Project Title: Identification and molecular characterisation of clinically significant bacteria isolated from cystic fibrosis patients attending a clinic at a tertiary academic hospital.
Researchers: Ms T Mahomed (MSc student).

Aim: The aim of this study is to identify and characterise the clinically significant bacterial pathogens (*P. aeruginosa*, *S. aureus* and *B. cepacia* complex) isolated from CF patients attending a CF clinic at a tertiary academic hospital.

Project Title: Detection and characterisation of mycoplasmas in women visiting an antenatal or reproductive biology clinic.
Researchers: Mr T Duba (MSc student).

Aim: The aim of this study is to detect and characterise the mycoplasmas in women visiting an antenatal or reproductive biology clinic, followed by the detection of co-infections in these women.

Project Title: Detection and characterisation of clinically relevant species of *Staphylococcus* and *Enterococcus* in water samples obtained from the Gauteng region.
Researchers: Ms T Hamiwe (MSc student).

Aim: The aim of this study is to determine species prevalence, antibiotic resistance patterns, virulence markers and clonality among strains of *S. aureus*, *E. faecalis* and *E. faecium* isolated from water samples obtained from the Gauteng region.

Project Title: Molecular characterisation of bacteria implicated in intravascular catheter-related bloodstream infections, from a tertiary academic hospital.
Researchers: Ms W Strasheim (MSc student).
Aim: The aim of this research study is to identify and molecularly characterise bacterial isolates implicated in catheter-related bloodstream infections

Project Title: Comparison of three commercial molecular assays for the detection of Rifampicin and Isoniazid resistance among *Mycobacterium tuberculosis* isolates in a high HIV prevalence setting

Researchers: Dr KA Strydom (MMed) (Path) Microbiology

Aim: Research completed. Manuscript submitted for publication

Project Title: Performance evaluation of three commercial molecular assays for the detection of *Mycobacterium tuberculosis* from clinical specimens in a high TB-HIV-burden setting

Researchers: Dr M Matabane

Aim: Research completed. Manuscript submitted for publication

Project Title: Rapid identification and characterisation of Group B Streptococcus among pregnant women at Kalafong Hospital

Researchers: Dr M Said (MMed) (Path) Microbiology

Aim: The purpose of this study is to evaluate a rapid diagnostic molecular assay as well as the characterisation of Group B Streptococcus in pregnant women between 26 and 37 weeks gestation at Kalafong Hospital

Project Title: Evaluation of GenoType MTBDRplus Version 2.0 and GeneXpert MTB/RIF for the detection of *Mycobacterium tuberculosis* in smear negative TB samples from a high TB/HIV endemic area

Researchers: Dr M Moncho (MMed) (Path) Microbiology

Aim: Research complete. Compiling research report and draft manuscript

Project Title: Characterisation of Inhibitor Resistant Temoniera (IRT) producing strains of *Escherichia coli* and *Klebsiella pneumoniae* in Pretoria, South Africa

Researchers: Dr C Kingsburg

Aim: Protocol still in development

Project Title: A review of blood culture isolates and their antimicrobial susceptibility patterns obtained from children admitted to a tertiary hospital in Gauteng from January 2014 to January 2015

Researchers: Dr M Maharaj (Department of Paediatrics)

Aim: This project aims to identify the bacterial isolates and antibiotic sensitivity patterns of both community- and hospital-acquired infections at KPTH and classify the isolates according to certain paediatric age groups. This study will further review the appropriateness of the current empirical choice of antibiotics in children

Project Title: Profiling the vaginal microbiome and metabolome of reproductive-age women attending a tertiary academic hospital

Researchers: Mr S Redelinghuys (PhD student)

Aim: The purpose of this study is to characterise the vaginal microbiome and metabolome of reproductive-age women

Project Title: Characterisation and genotyping of methicillin-resistant *Staphylococcus aureus* isolates from a tertiary healthcare centre in Ogun state Nigeria

Researchers: Mrs T Adelowotan (PhD student)

Aim: The aim of this study is to identify, characterise and genotype the MRSA isolates collected from the nostrils of hospital patients and healthcare professionals at a tertiary hospital in Ogun state, Nigeria and to determine the effects of the lifestyle and the exposure of each participant using a questionnaire

Project Title: Genetic relatedness of zoonotic staphylococci recovered from close human contacts and bovine intramammary infections and investigation of the potential human health risk

Researchers: Ms T Schmidt (PhD student)

Aim: The aim of this study is to characterise and investigate the molecular relatedness of *S. aureus* and other *Staphylococcus* spp. isolated from close human contacts and dairy cows with intramammary infections
Project Title: In vitro immunobiology of polymicrobial-host interaction associated with bacterial pathogens of cystic fibrosis
Researchers: Ms G Ngoepe (PhD student)
Aim: To investigate the in vitro immunobiology of the polymicrobial-host interaction of the three major pathogens associated with cystic fibrosis, these are B. cepacia, P. aeruginosa and S. aureus

Project Title: Identification of novel marker candidates from T. vaginalis resistant to metronidazole
Researchers: Dr R Biswas (Post-Doctoral Fellows)
Aim: The aim of this study is to identify novel pathway specific candidate genes involved in resistance to metronidazole in T. vaginalis.

Project Title: Methicillin resistance mechanism and the epidemiological genetics of multi-drug efflux genes in clinical methicillin-resistant Staphylococcus aureus isolates
Researchers: Dr J Antiabong (Post-Doctoral Fellows)
Aim: To investigate the methicillin resistance mechanism and the epidemiological genetics of multi-drug efflux genes in clinical methicillin-resistant Staphylococcus aureus isolates

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Book Chapters


5.3. Conference Presentations

**National**

**Oral Presentations**


Peters RP. Transitioning from child to adulthood in the context of HIV. Symposium entitled “Hope for children in the era of HIV: take action now!” Karibu Lodge, Mopani District, 9 September 2015.


**Poster Presentations**


International

Oral Presentations


Invited speaker: PB Fourie. Inhaled microparticles of clofazimine: Status and prospects. 3rd International Conference on Inhaled Therapies for Tuberculosis and Other Infectious Diseases, Parma, Italy, 14–16 October 2015.

Fourie PB and Nettey OS. Clinical, epidemiological and patient compliance factors affecting deployment of inhaled therapies for TB in the field. 46th Union Conference on Lung Health, Cape Town, 2–6 December 2015.


Poster Presentations


Said M, Dangor Y, Sihlabela A, Mbelle N and Ismail F. Prevalence and demographic characteristics of Group B Streptococcus (GBS) colonisation in pregnant women at Kalafong Hospital, Pretoria, South Africa. E-poster. 25th ECCMID Conference, Copenhagen, Denmark, 25–28 April 2015.


SV Omar, RPH Peters, NA Ismail, AW Dreyer and PB Fourie. Molecular detection of M. tuberculosis from sputum in a novel transport medium is not affected by laboratory delay and ambient temperature. 46th Union Conference on Lung Health, Cape Town, 2–6 December 2015.

Medical Virology

Head: Prof. Lynne M Webber (MBChB (Pret) M Med Path Virol DTH)

1. ABOUT THE DEPARTMENT

The Department of Medical Virology offers routine virology diagnostic testing services, which include molecular biology testing and extensive training and teaching programmes; and initiatives for medical technologists, technicians and students, clinical registrars, medical scientists, intern medical scientists, and undergraduate and postgraduate health-care students (including dentistry students and medical support service students). Registrars from other clinical departments such as Paediatrics and Internal Medicine also receive clinical virology and pathology exposure and training. The department achieved its annual SANAS audit with resounding success for 2015 which serves as an indication of the outstanding and ongoing team-work, spirit and discipline of all members and students involved.

Research programmes and projects are diverse and extensive and there are mutual benefits for NHLS staff members and the University of Pretoria academics, registrars and students. The department has a number of members jointly appointed by the NHLS and the University of Pretoria, hence the impressive research and publication outputs. There are six specific research focus areas, namely Enteric Virus and Environmental Research Group, Blood-borne Virus Research Group, Zoonotic Virus Research Group, Reproductive Health and Virus Research Group, Mumps Virus Research Group and the recently established HIV and Opportunistic Virus Research Group. Miscellaneous and other areas of research are ongoing and encouraged; such as mumps virus research and the clinical consequences thereof and mosquito-borne animal and human infections and the recently expanded diverse research programme involving many zoonotic viruses (animal and human infections).

Community outreach programmes are sustained and extend to areas around Nelspruit, Polokwane, Barberton; North-West and Limpopo provinces. Community activities occur in the Gauteng region and many health-care professionals travel from around Southern Africa to attend. This has resulted in very positive feedback and has opened further research opportunities, collaboration and funding. Numerous international research collaborations have been sustained and expanded and international clinical and scientific researchers have visited and contributed to the Department of Medical Virology.

Diagnostic laboratory staff members continue to receive a number of awards at national meetings and staff members were awarded professional qualifications as indicated by the number of student technologist and technician qualifications, and clinical pathology registrar awards. Students rotating highly recommend and commend the Department of Medical Virology and the staff commitment. Students from other tertiary academic institutions also rotate through this department at regular and sustainable intervals (examples include Pathology registrars from Wits and the University of Limpopo). The diagnostic laboratory is involved in research activities with a research HIV DNA case series that resulted in current publications and has extended its research scope to other blood-borne and sexually transmitted viruses.

Numerous policy documents have been amended and proposed by members of the Department of Medical Virology.

The department encourages teambuilding exercises, such as annually celebrating and enjoying culturally diverse dishes contributed by each staff member on Heritage Day and organising a Christmas charity event. Photographs memorialising these events are displayed in the Routine Diagnostic Laboratory. In 2015 a number of orphanages were supported through charity-driven events. Charity-associated events were extended to old-age homes, and in December 2015 food and clothing were donated to orphanages and homes dedicated to homeless and displaced people.

Table 50: Total number of staff per profession and highest qualifications

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>White</th>
<th>Other</th>
<th>South African*</th>
<th>Total</th>
</tr>
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<td>-</td>
<td>1</td>
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<td>5</td>
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<tr>
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<td>-</td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
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<tr>
<td>Support</td>
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<td>-</td>
<td></td>
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<tr>
<td>South African*</td>
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<td>6</td>
<td>1</td>
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<tr>
<td>All</td>
<td>15</td>
<td>6</td>
<td>1</td>
<td>22</td>
<td>22</td>
</tr>
</tbody>
</table>

Important highlights and achievements of the Department of Medical Virology and the research programmes are the following:

- Community-outreach programmes within the Gauteng Province which has now expanded throughout Southern Africa, including countries such as Namibia, Zimbabwe and Botswana
• Research recognition and awards for the department are annually received at the University of Pretoria’s Annual Gala Dinners
• Prof. Webber is a research grant approver for the NHLS Research Trust Committee
• Under the direction of Dr Sim Mayaphi the HIV and Opportunistic Infections Research Group has four prestigious publications in national and international journals
• Dr Mayaphi was successfully accepted for his PhD degree in 2015
• Referral testing to the department for clinical specimens from other tertiary institutions was instituted.

2. DIAGNOSTIC SERVICE

The diagnostic service is managed through the routine diagnostic virology laboratory and operates throughout the week and over weekends. It offers a full 24/7 service, always accompanied by a registrar virologist on call, supported at all times by a consultant virologist pathologist. There is a standard call roster for the technical and support laboratory staff as well as the registrar on call. There are currently four registrars in the department and four consultant pathologists to assist and provide permanent support and advice to these registrars. The laboratory services include manual serology, automated serology, immunofluorescence methods, rapid methods and molecular biology, such as PCR techniques and molecular genotyping testing.

3. RESEARCH AND DIAGNOSTIC UNITS

The established Zoonosis Research Unit undertakes extensive research activities and also assists with certain diagnostic testing for animals and humans. The Enteric Research Unit does diverse environmental and water surveillance testing for selected viruses, e.g. noroviruses. The Reproductive Health Research Unit is thriving and publishing frontier clinical data and Dr Karin Richter has attended a number of international congresses. The recently established HIV and Opportunistic Research Unit has published extensively in nationally and internationally accredited and peer-reviewed scientific and medical journals in 2015.

The Diagnostic Virology Laboratory contributes to research activities and was nominated for the Best Academic Laboratory; the Laboratory Supervisor, Ms Jana Havinga continued to support the NHLS in her technical advisory capacity. Ms Havinga has extended her academic achievements, and is now also involved in teaching and continuous professional activities and was nominated as a prestigious member at an international training course. The Laboratory Manager, Ms Wendy Lenyatsa, is excelling in her own personal and academic growth and providing valuable time to students and the community.

Staff members include one technician, five student technologists, two medical student technicians, one student laboratory assistant and four rotating, technical students that work, assist and are involved in research activities and train in the diagnostic and molecular biology laboratories. There is a ratio of 4 qualified personnel: 6 students in the diagnostic laboratory but this changes depending on prevailing circumstances and training needs.

Rotating registrars from the University of the Witwatersrand and the University of Limpopo acknowledged the Department of Medical Virology for their time, interest and enthusiasm for the training and pathology-gained experience.

The annual SANAS audit for the Department of Medical Virology took place in 2015 and focussed on the Quality Management. The Diagnostic Laboratory is actively involved in research activities including a research case series (HIV DNA PCR results and interpretation) that has been accepted for publication. Dr M Brauer has been appointed Clinical Virologist and Consultant Pathologist in the Department and joins the experienced and able team of Dr Sim Mayaphi and Dr Karin Richter. Dr Brauer is now actively involved in research publications.

Three junior registrars are preparing for their primary examinations and one registrar is preparing for her final examinations at the Colleges of Medicine of South Africa (CMSA) in Clinical Virology.

The Diagnostic Laboratory passed the SANAS audit with resounding success. Prof. Webber is an experienced Lead and Technical Assessor for SANAS and Prof. MB Taylor, Dr M Wolfaardt and Ms W Lenyatsa are registered as Technical Assessors with SANAS.

The Routine Diagnostic Virology Laboratory processes at least 26 000 specimens per month. The number of specimens being tested is steadily growing.

The Zoonosis Research Unit (ZRU) offers routine and diagnostic testing for a large range of zoonotic virus-associated diseases and infections.

The Mumps Research Unit assists with testing clinically complex cases, often presenting with neurological complications and/or sequelae and publications are in preparation.
4. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department is involved in teaching programmes for under-graduate, postgraduate, medical scientists, medical intern scientist and PhD students, as well as medical registrars from diverse clinical disciplines. Continuous Professional Development (CPD) lectures and workshops are also conducted for qualified and specialist health care professionals. Dr Karin Richter organises regular scientific and medical meetings for the SA HIV Clinicians Society. These attract a diverse audience of health-care professionals.

Prof. Webber presents national and international lectures and is an invited Editor for two international Journals, namely the Journal of Human Virology and Retrovirology and the EC Journal of Bacteriology and Infectious Diseases. She is also a reviewer for the NHLS Research Trust Foundation and regularly reviews and approves research applications. She is an active member for the South African Medical Association (SAMA) CPD Committee and publishes widely in national and international journals.

Dr Sim Mayaphi is extensively involved with hospital infection control programmes through three tertiary academic hospitals and primary-linked health-care-facilities in the Gauteng and Mpumalanga provinces. Dr Mayaphi has an extensive research area and projects that generally involve HIV and opportunistic infections. The current project involves the detection of primary/acute HIV infections in an HIV hyperendemic area (Pretoria). This was registered in 2015 for his PhD. The research is ongoing and is revealing encouraging results and research outcomes for the Department of Medical Virology.

Community outreach programmes are in place and the department supports activities within the South African Rotary Programmes. The department offers a CPD-accredited annual and sustainable tutorial programme that is intra- and inter-departmental and accessible to any other health care professionals in the community and private sector. Personnel are encouraged to attend national and international congress as part of their CPD activities and career advancement. Research and publication awards are regularly received at the annual University of Pretoria Gala Dinner and Awards event. Dr J Mans received a merit award at the Exceptional Achievers Dinner of the Faculty of Health Sciences, University of Pretoria.

Table 51: Total number of trainees per qualification category and rates of successful completion/pass rates

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<tr>
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<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
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5. RESEARCH UNIT OVERVIEW

5.1. Enteric Virus and Environmental Research Group

Highlights

- Dr J Mans received a merit certificate at the Exceptional Achievers dinner for academic and NRF-rated researchers of the University of Pretoria, for her NRF Y2-rating (young researcher with potential to establish herself) on 22 April 2015 University of Pretoria.
- Ms JCF Bengone-Abogourin was awarded the Degree BSc (Hons) in Medical Virology at the University of Pretoria Autumn Graduation Ceremony on 24 April 2015.
- Ms M Muilwijk was awarded the Degree BSc (Hons) in Medical Virology at the University of Pretoria Autumn Graduation Ceremony on 24 April 2015.
- Ms V Somers was awarded the degree BSc (Hons) in Medical Virology at the University of Pretoria Autumn Graduation Ceremony on 24 April 2015.
- Mr JC Botha was awarded the degree MSc in Medical Virology (with distinction) at the University of Pretoria Spring Graduation Ceremony on 4 September 2015.

5.2. Zoonoses Research Unit

Highlights

The ZRU is continuing research and surveillance on zoonotic arboviruses according to the One Health approach. Publications have been submitted and talks given at both local and international meetings about emerging zoonotic arboviruses in South Africa. Over the last year papers were published describing: the molecular epidemiology and pathology aspects of West Nile virus in mice and horses; Shuivirus as a cause of neurological disease in horses and the full genome and molecular analysis of strains identified in South Africa; the molecular epidemiology, pathogenesis and seroprevalence of mosquito and tick borne viruses including WNV, Crimean Congo haemorrhagic fever.
virus, Bunyamwera virus and Ngari virus in vectors and humans in Kenya; and of WNV and Shuni in South Africa. Finally data was published on the newly developed macroarray chip that can detect 29 causes of febrile and neurological disease in humans and validated it against known and unsolved human cases of encephalitis and haemorrhagic fever symptoms in humans. Vector studies have identified WNV, Shuni and Middelburg and Sindbis as well as several uncharacterised flaviviruses in mosquitoes collected at sites in Gauteng, Marakele and Lepalale.

The programme has reached a level of maturity where outbreaks can be detected of arbovirus disease across South Africa through sentinel surveillance in animals and policy decisions in both human and animal health can be informed. Prof. Venter has a joint appointment with the Global Disease Protection Centre of the US–CDC in South Africa and consulted to the Department of Health on One Health and International Emerging Infections. As part of this she helped update the policy document on Anthrax, and establish a One Health Forum in the DoH. She spent a month with WHO Afrot in the Congo as Ebola liaison. Three students continued their PhD studies in the programme for 2015. Two postdoctoral fellows were also in the programme over the last year.

International collaboration was established with the Robert Koch Institute and a 5-year grant was selected to support febrile disease surveillance in South Africa, Cote de Ivoir, Burkina Faso and the Democratic Republic of the Congo. The GDD is continuing to support the programme on neurological arboviruses.

Prof. Venter is still involved in several respiratory virus publications and organised the international Respiratory Syncytial Virus Conference in Cape Town during the review period. She is an advisor for the World Health Organization (WHO) on implementing surveillance for respiratory viruses into the Influenza network across Africa.

- MSc student graduating: June Williams (2011–2014)
- Postdoctoral fellows: the numbers have increased within the above-stated research programmes.

Prof. Robert Swanepoel’s contract came to an end the end of December 2014. He has transferred to the Veterinary Faculty in February to continue some projects there. We are still completing a number of papers together. This was finalised in 2015 and the papers were in preparation in 2015.

Grants

The ZRU, together with the following partners, has been awarded funding from the African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA) project:

- University Teaching Hospital, University of Bouake, Cote d’Ivoire
- National Laboratory of Agricultural Development/Central Laboratory of Animal Pathology, Cote d’Ivoire
- National Institute for Biomedical Research, Kinshasa, Democratic Republic of the Congo (DRC)
- Kinshasa University Hospital, University of Kinshasa, DRC
- National Institute of Communicable Diseases (NICD), Johannesburg, Republic of South Africa (SA)
- Robert Koch Institute, Berlin, Germany
- Institute of Tropical Medicine and International Health, Charite University Hospital, Berlin Germany
- PI Richter (UP), Venter (CDC)
- GDD-UP for Zoonoses CoAg – USD560 000 for first year. ZRU has received USD185 100 specifically.

Policy Documents

- Policy reports: participated in updating the notifiable disease policy report for the DOH, 2015.
- Guidelines: participated in the writing of the testing guidelines for dangerous and emerging viruses in Africa with the WHO AFRO. (January 2015).

Important Collaborations

National

- CDC-South Africa Ebola response team – Participated in biweekly CDC-South Africa Ebola team meetings
- Member of the Multi-sectorial National Ebola outbreak and response team. Supporting the South African government efforts of preparedness and response through consultation and technical support
• Policy development on clinical management and laboratory aspects; specialist consultation on Ebola to the government and supplying information where needed, including writing of the Director General of Health’s speech for the opening of the regional South African Development Community Countries training; facilitate dialogue between the Corporate Biological Engagement Program of the US and South African stakeholders to support the Ebola response in West Africa and locally.

**International**

• Support of training for SADC countries on Ebola preparedness for laboratories, Port Health and clinical stakeholders, ongoing into 2015.

• Facilitate negotiations between DTRA and NICD for support for the Ebola diagnostic laboratory in South Africa, Sierra Leone and training facility for pre-deployment in South Africa, ongoing into 2015.

• Prof. M Venter was deployed to Congo Brazzaville as CDC liaison for the World Health Organization Ebola preparedness of high risk uninfected countries and has continued consultations.

• Prof. Venter’s research unit was requested to create a questionnaire for African laboratories in the Influenza and Emerging and Dangerous pathogens networks to assess the capacity of countries to detect emerging zoonotic diseases and training needs in the face of the Ebola outbreak.

**Other Collaborations**

• Prof. Paulo Almeida, from the Institute for Hygiene and Tropical Medicine, Universidade Nova De Lisboa, has joined the ZRU as part of a Visiting Prof. Programme to spend a 6 month sabbatical working on mosquito vectors of arboviruses. Prof. Almeida used his own funding to visit us again in early January and was brought to UP again in March with funding from Prof. Braack to support the cross Africa field collection work and Prof. Venter to support ZRU activities. Prof. Almeida has been interviewed to take up a position in the program as full time entomologist in August already, outcome pending.

• Collaborations with Jeroen Kortekaas of the Central Veterinary Institute, Lelystad, the Netherlands on Shuni virus full genome sequencing and reverse genetics was started earlier this year and led to a publication on the Genome of Shuni virus. Results from the Shuni virus were analysed in 2015 and reported at the Departmental Journal Club meetings in 2015.

• Collaborations with Rosemary Sang from KEMRI in Kenya have led to several publications on arboviruses in Kenya. The collaboration continued on into 2015.

• A Collaboration Network was started around One Health across African laboratories involved with the CDC’s Cooperation programs (see details below)

• Prof. Venter has since August been working with the NICD, Department of Health, WHO and CDC efforts to support the efforts to support the Ebola outbreak.

**Quality and Audits**

The Zoonosis research laboratory unit has been accredited by the Department of Forestry and Fisheries (DAFF) in June 2014 for the following tests: West Nile Virus, Wesselsbron, Middelburg, Sindbis, Shuni virus and Equine encephalosis virus. The BSL3 laboratory has also been recertified by DAFF and registered with the Department of Trade and Industry. Services continued into 2015.

The diagnostic Medical Virology services were audited by SANAS and were recommended for continued services and received full and immediate accreditation.

Clear evidence of all work translated to policy or service:

• Prof. LM Webber is a technical assessor in clinical virology and molecular biology for SANAS, as well as a lead assessor

• Prof. M Taylor is a technical assessor for medical virology for SANAS;

• Dr M Wolfaardt is a technical assessor for medical virology for SANAS;

• Ms W Lenyatsa is a technical assessor for medical virology for SANAS;

• Prof. Webber, Dr Brauer, Dr Mayaphi, Dr Richter have contributed academic and technical data to the Block Four academic book for undergraduate medical students and have made contributions to other block books, as prescribed by the Faculty of Health Sciences, University of Pretoria;

• Prof. Webber is a committee member of the SAMA CPD Committee;

• The registrars provide seminars and lectures regularly to the laboratory staff and students for TAD NHLS and the University of Pretoria;

• Staff development is highly encouraged and supported and Master’s and PhD enrollment are supported throughout;

• National and international consultations are part of the Department’s routine duties and involve diverse virological and infectious disease subjects.
6. RESEARCH ACTIVITIES

The current research activities are diverse and include research on blood-borne viral pathogens such as HIV, hepatitis B virus and HTLV-1; enteric viruses; zoonotic viruses; human papillomaviruses; and neurotropic viruses, predominantly mumps virus. The expertise available is extensive including clinical virologists, PhD qualified staff, senior medical scientists, postdoctoral staff, diagnostic laboratory supervisors and the laboratory manager.

Research and financial grant awards were given to many staff members. The department has a recently established Zoonosis Research Unit, where research activities include the identification and characterisation of enteric and environmental viruses, identification and surveillance of zoonotic arboviruses, respiratory viral research, identification of primary HIV-1 infections in an HIV hyperendemic setting and early responders to HIV-therapy, the proportion of HIV-2 among patients testing HIV-1/HIV-2 ELISA positive at TAD NHLS, molecular characterisation of hepatitis B virus infections from hospital patients and human papillomavirus collaborative research. There is also ongoing research on blood-borne viruses in post-mortem specimens and publication outcomes in collaboration with the Department of Forensic Medicine.

Research activities have also been extended to include insect- and animal-borne infections relevant to human health issues and possible community health preventative measures within the Zoonosis Research Unit.

Excellence in norovirus research is recognised worldwide and numerous national and international presentations took place in 2015/16.

6.1. Research Projects

Current Blood-borne Virus Group Research Niches

Ongoing Projects

**Project Title:** Human immunodeficiency virus (HIV) resistance mutations  
**Duration:** February 2013–December 2015

HIV surveillance – initiated, including HIV-2 surveillance; HIV testing in post-mortem specimens older than 5–7 days; Opportunistic infections such as TB and cryptococcus species – diagnostic testing and surveillance testing; Post-mortem specimens, other than blood, for HIV and other blood-borne virus testing; Opportunistic virus research studies; and Hepatitis B virus research data and surveillance

Completed Projects

**Project Title:** Multi-site HPV vaccine acceptability study  
**Principal Investigator:** J Smith (University of Northern Carolina, USA)  
**Country Consultants:** South Africa: K Richter; Malaysia: K Morgan; South Korea: C Joo; Spain: S de Sanjose; Brazil: P Naud  
**Duration:** November 2012–June 2014, data analysis commenced in 2015  
**Funding:** GSK  
**Status:** This study is being prepared for national and international publication

**Project Title:** Prevalence of oral and oropharyngeal HPV in a selected South African male population: A pilot study  
**Principal Investigator:** C Davidson  
**Supervisor:** S Boy  
**Co-supervisor:** K Richter, Medical Virology, University of Pretoria/NHLS TAD  
**Duration:** May 2012–May 2014  
**Funding:** Department of Oral Pathology, University of Pretoria and SADA  
**Status:** Completed and published in 2015

Enteric Virus research studies

**Study Title:** Molecular epidemiology and characterisation of norovirus infection in HIV-seropositive patients in Gauteng, South Africa  
**Supervisor:** Prof. M Taylor  
**Co-supervisor:** Dr J Mans  
**Duration:** 2015–2016  
**Status:** Ongoing
Virus zoonoses research studies

**Study Title:** Multiple viral zoonoses research projects, nationally and internationally  
**Supervisor:** Prof. M Venter  
**Co-supervisors:** Prof. L Braack/Dr M Pretorius  
**Duration:** 2015–2016

Neurotropic virus research studies

**Supervisor:** Prof. L Webber  
**Duration:** 2014–2015  
**Status:** In preparation for publication

6.2. Grant Funding

- Development of serological diagnostic techniques for selected arthropod-borne virus infections. Institutional Research Theme (IRT) R80 000. Development of serological tests for antibodies to arboviruses – TIA/TAHC grant of R600 000 for one year, renewable for a further two years.
- Molecular epidemiology of arboviruses identified as causes of neurological disease in horses in South Africa: WNV, Shunivirus and Middelburgvirus. Surveillance of zoonotic vector-borne neurological diseases in humans and animals in South Africa – CDC-GDD grant of US$300 000 for one year renewable.
- Investigation of the role of zoonotic arboviruses in neurological disease in humans in South Africa – MRC of South Africa grant, R130 000 per annum.
- Numerous other grants have subsequently been applied for and have been awarded selectively.

7. RESEARCH OUTPUT

7.1. Journal Publications


Editorial, KL Richter. Cervical cancer prevention in South Africa: HPV vaccination and screening both essential to achieve and maintain a reduction in incidence. SAMU. 2015; 105(1).


7.2. Technical reports


7.4. Courses/Lectures/Workshops/Meetings
Drs J Mans and W van Zyl attended the TNM course for supervisors, 10 November 2015 in Pretoria. Dr W Van Zyl also attended a joint convening meeting of the University of Washington.

Prof MB Taylor:
- Hosted a successful Polio Surveillance and Diagnostic Tools: Convening & Training Workshop on 1–5 June 2015, in collaboration with members of the Enteric Virus and Environmental Research Group and sponsored by PATH
- Attended the Polio Stakeholders’ Symposium, 10–11 September 2015, Tsogo Sun Garden Court, OR Tambo Airport, Johannesburg.

Prof. L Webber:
- Attended the Roche Vaccine Symposium, 4 February 2015, Sandton Sun, Johannesburg
- Attended monthly meetings at the South African Medical Association as a serving member of the Continuing Professional Development for Healthcare Professionals in South Africa Committee
- Consults for POLMED, Qualsa Health and Metropolitan Health Company and attends monthly strategic planning meetings at the site office in Arcadia, Pretoria.
- Is an active member of the Afrikaanse Geneesheer Vereneging and regularly gives seminars and workshops for doctors nationally. She has been a member for the last 20 years.

Prof. M Venter:
- Attended the DoH Infectious Disease Cluster Chief Directors’ Strategic Planning Meeting, 5 March 2015
- Attended the Global Disease Detection Strategic Planning Retreat, 3 March 2015
- Attended the DoH Multisectorial National Outbreak Response Team Meeting, 11 March 2015
- Invited speaker at the National Zoological Gardens One Health Workshop, 24–26 February 2015
- Attended the DoH ‘One Health Stakeholders’ Meeting and presented the terms of reference for a one health advisory group for South Africa, 31 March 2015.

International
- Prof. Venter was deployed to Congo Brazzaville in January 2015 as CDC liaison for WHO Ebola preparedness of high risk uninfected countries.
- Prof Venter was an invited speaker at the Informal Consultation on RSV using the Global Influenza Response Networks Surveillance (GIRNS) platform, WHO, Geneva, Switzerland, 25–27 March 2015.
- Prof. Venter discussed Tools for the Improved Surveillance of Poliovirus at the University of Pretoria–KEMRI Collaborative Project, KEMRI, Nairobi, Kenya, 23 March 2015.
• Prof. S Meschke and Ms C Fagnant from the School of Public Health, University of Washington visited Prof. MB Taylor and the Enteric Virus and Environmental Research Group, 18–19 March 2015. They trained researchers on the recovery of viruses from large volumes of water using a field kit and Nanoceram filters.

• Dr C Burns from the Polio and Picornavirus Laboratory Branch, Division of Viral Diseases, CDC Atlanta, visited the Enteric Virus and Environmental Research Group on 28 October 2015 to discuss polio surveillance data and to make arrangements to supply the group with polio-specific typing reagents.

7.5. Conferences Presentations


Braack L. Research undertaken by the University of Pretoria Centre for Sustainable Malaria Control. SADC Annual Malaria Managers Meeting. Johannesburg, 26–28 August 2015.


Mabasa VV, Taylor MB, Mans J. Poster presentation. Surveillance of norovirus GII.4 in selected sewage samples from Gauteng and the Free State. Faculty Day, Faculty of Health Sciences, University of Pretoria, 18–19 August 2015.


Muilwijk M, Van Zyl WB, Taylor MB. Poster presentation. The detection and characterisation of enteroviruses in wastewater discharge and surface water in Gauteng, South Africa. 18th Symposium of Health-related Water Microbiology, Lisbon, Portugal, 13–18 September 2015.

Muilwijk M, Van Zyl WB, Taylor MB. Presentation The assessment of sewage treatment efficacy through the detection and characterisation of human enteroviruses. Faculty Day, Faculty of Health Sciences, University of Pretoria, 18–19 August 2015.


Rachida S, Matsapola P, Wolfäardt M, Taylor MB. Molecular identification of unique hepatitis A virus strains in South Africa. Presentation. Faculty Day, Faculty of Health Sciences, University of Pretoria, 18–19 August 2015.


Webber LM. Presentation. First meeting of the Senate Committee for Teaching and Learning for the Revised Policy on Curriculum Design and Development, Senate Hall, Main Campus, University of Pretoria, 4 November 2015.

7.6. Invited Lectures


7.7. External/Internal Examiner/External moderator/Reviewers

Prof. LM Webber:

- Internal examiner for the M Med Microbiology registrars and the Clinical Pathology registrars.
- External examiner for the medical virology registrars at the University of Limpopo and an external examiner, moderator and convenor for the College of Medicine (CMSA), Medical Virology.

Dr W van Zyl:

- External moderator for subject “Industrial Biotechnology (IBI401T)” at the Tshwane University of Technology – June 2015
- Mediating examiner for an MSc in Chemical Pathology, University of Pretoria, titled “Mutations in the androgen receptor and the fibrillin-3 genes in South African women with polycystic ovary syndrome” – October 2015
- External examiner for three BSc (Hons) projects in Medical Microbiology at the University of Pretoria – November 2015
- External moderator for subject “Microbiology: Biological III (MGB301)” at the Tshwane University of Technology – December 2015
- Reviewed two manuscript for Food and Environmental Virology.

Prof MB Taylor:

- Handling editor for a number of manuscripts submitted to the Journal of Applied Microbiology and Letters in Applied Microbiology for consideration for publication.
- Reviewed manuscript for Virology Journal – March 2015.
Dr J Mans:

- Reviewed Research grant proposals for the Poliomyelitis Research Foundation - April 2015.

Dr M Wolfaardt:

- Reviewed a manuscript for Food and Environmental Virology - April 2015.

7.8. Current Research

Enteric and environmental viruses; Blood-borne viruses; HIV; Hepatitis B virus; Neurotropic viruses; Zoonotic viruses; Human papillomaviruses; Noroviruses.

8. ADDITIONAL INFORMATION

- The Department offers a 24/7 diagnostic virology service, with a registrar on call supported by a clinical virologist and pathology specialist.
- There is an active academic programme that involves undergraduate health-care professional students, postgraduate health-care professional students and registrars, medical scientist students, medical technology and technician students.
- Team-building exercises occur regularly and are annually sustainable.
- Teaching, training and professional development are critical components of the Department's visions and missions and these include involvement with hospital infection control programmes at tertiary hospital facilities and primary care clinics and units.
- Research activities are diverse and intensive and include the following focus areas, namely: blood-borne viral pathogens and disease; environmental and enteric viruses, zoonotic viruses, human papillomaviruses and neurotropic viruses including mumps virus, other research on new and emerging viruses as indicated currently.
- The recently established Zoonosis Research Unit is research intensive and has a number of scientific publications in peer-reviewed journals.
- The Enteric Virus and Environmental Research Group has attracted a number of postgraduate students and the number of publications in peer-reviewed scientific journals is growing at an impressive rate. The Group operates under the mentorship of the Rand Water Chair in Public Health, Prof. MB Taylor.

Clear evidence of all work translated to policy or service:

- There are approximately 15 members of staff, including students, providing routine diagnostic services but the numbers do change according to rotating staff members nationally and internationally throughout the year.
- The diagnostic service staff also participate in research projects;
  1. Approximately 26 000 specimens are processed monthly but this number may increase according to work demand and volumes;
  2. According to the needs for NHLS and the University of Pretoria the Department may need to accommodate more specimens;
  3. Other NHLS institutions and Universities, such as the University of Limpopo as an example, refer diagnostic specimens in order to maintain the required turnaround times;
  4. Prof. Webber is a SANAS accredited lead and technical assessor;
  5. Prof. Taylor is a SANAS accredited technical assessor;
  6. Ms Wendy Lenyatsa is a SANAS accredited technical assessor;
  7. Dr M Wolfardt is an accredited SANAS technical assessor;
  8. Ms Jana Havinga has been providing training within the NHLS nationally;
  9. The registrars are all actively involved in community outreach programmes and continuous professional development programmes;
  10. The Department receives annually awards for research projects and publications at the Annual Gala Dinner of the Health Sciences Faculty, University of Pretoria;
  11. The Department has more than 28 national and international publications in peer-reviewed Journals in 2015 and recent articles have been submitted.
  12. Prof. Webber and Prof. Taylor are on the editorial boards of national and international Journals.
Anatomical Pathology

Head: Prof. JW Schneider

1. ABOUT THE DEPARTMENT

Among others, the division provides a comprehensive autopsy service, as well as diagnostic surgical and cytopathology service to Tygerberg Hospital (TBH) and the Western Cape public health sector. It also manages the AIDS Malignancy Consortium and AIDS and Cancer Specimen Resource Sub-Saharan Africa Regional Biospecimen Repository (SSA RBR), funded by the National Institutes of Health (USA) (NIH).

The division is involved in several national and international collaborative research projects, including the Department of Pathology and Developmental Biology and Pathology Centre at the Boston Children's Hospital, USA; Vreije University, Amsterdam, and Desmond Tutu TB Centre, Stellenbosch; and Lineberger Comprehensive Cancer Center, University of North Carolina, USA.

Staff members contributed 12 articles to professional journals and presented several papers or posters at national and international congresses. There are 34 approved, ongoing research projects under the auspices of the division.

The division offers several training and research programmes, including specialist training in Anatomical Pathology (MMed), BSc (Hons) (Pathology), M (Pathology), PhD (Anatomical Pathology), and MSc (Cytopathology). It also trains medical technologists from other African countries to develop their expertise and skills.

Table 52: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>12</td>
<td>1</td>
<td>29</td>
<td>17</td>
<td>59</td>
<td>59</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

The division provides a diagnostic service to TBH and approximately half of the Western Cape’s public health sector. Consultation services are offered to the private sector and NHLS laboratories in the Eastern Cape. Special services and expertise include electron microscopic support for service and research, a FNA clinic, rapid on-site cytology diagnostic services, and consultation services, especially in the fields of dermatopathology, electron microscopy, neuropathology, nephropathology, perinatal pathology and cytopathology, as well as the application of flow cytometry and cellblocks using material obtained from FNA of lymph nodes and other selected tissues.

The prion laboratory, the only one of its kind in Africa, offers specialised skills and infrastructure as a referral laboratory for specimens with suspected prion disease. The Electron Microscopy Unit provides a service to the public and private sectors and to researchers from other faculties at Stellenbosch University (SU) and other higher educational institutions, including the University of the Western Cape (UWC) and the Medical Research Council (MRC).

During the reporting period, the Surgical Pathology Laboratory processed 30 576 cases, a 1.5% increase on the previous year. The Electron Microscopy Laboratory processed 523 cases (22.59% increase), and the Immunohistochemistry Laboratory performed 23 798 immunohistochemical stains (24% increase) and 1 330 direct immunofluorescence stains (12% increase). Staff conducted 30 adult and 75 paediatric autopsies.

The Cytopathology Unit processed 65 982 gynaecological cases (7.2% decrease from previous year), 4 617 non-gynaecological cases (10 % increase) and 9 561 FNAs (6.2% increase), including the performance of 3 988 on-site FNAs on patients in the FNA clinic (0.8% increase) and on 369 patients in theatre (8.1% increase). The overall year-on-year workload for Cytology increased by 5%. Both the Cytopathology and Histopathology laboratories retained their SANAS accreditation.

The Pathology Research Facility enables the development and introduction of new diagnostic molecular pathology tests through national and international collaboration. In addition to supporting clinical geneticists, selected molecular tests are offered for the diagnosis, prognosis and therapeutic interventions of various haematological malignancies, colorectal carcinoma and carcinoma of the breast, including MammaPrint that can be performed on formalin-fixed and paraffin-embedded tissue samples. New tests introduced during the last year include MPL exon 10 (proto-oncogene thrombopoietin receptor on chromosome 1); CALR exon 9 (endoplasmic reticulum luminal Ca2+-binding chaperone protein which regulates homeostasis) for BCR-ABL negative myeloproliferative neoplasms (MPNs); and quantitative fluorescent PCR for Aneuploidy. The total number of tests performed in the Pathology Research Facility increased from 771 to 970 (25.8% increase from 2014). It trained two intern scientists in Molecular Biology, both successfully registered with the HPCSA.

The division expanded its ongoing support of diagnostic anatomical pathology services to the Eastern Cape through assistance with excessive routine workloads and diagnostic consultations from pathologists in Mthatha, Port Elizabeth and East London.
3. TEACHING AND TRAINING

3.1. Undergraduate
Staff service as consultant lecturers clinical modules in the first, second, third, fourth and fifth years of the MBChB programme, and also lecture students in Physiotherapy and Occupational Therapy.

The restructuring of phase II (middle clinical rotation) of the MBChB programme in 2015 led to the loss of contact time (laboratory visit, FNA tutorials and practical case examples) with students during years four and five. A pilot programme, implemented in January 2015, introduced a longitudinal clinical rotation to elucidate the role of pathology, radiation and imaging in the diagnosis and management of disease processes. Students received pathology-specific outcomes and instructions to compile a portfolio consisting of two case reports of patients managed by the student during their clinical rotation. Student participation and output confirmed that they were able to integrate theoretical knowledge into a practical presentation, which could be assessed. The student feedback in general was very positive. A portfolio workshop in August 2015 was integral to the finalisation of the Longitudinal Middle Clinical Rotation in Pathology, Radiation and Imaging, which was implemented in January 2016 and rolled out across all the clinical rotations.

Radiology, Nuclear Medicine and Clinical Oncology have integrated into the module to equip medical students with the necessary knowledge, skills and attitudes to comprehensively assess, investigate, diagnose and refer patients with cancer, as well as manage symptoms associated with cancer or cancer-related treatment. The module was set up on the SU’s SunLearn platform, which offers real-time online interaction with students. The new module remains a work in progress, with almost unlimited potential for learning and assessment in pathology.

During the past year, pathologists from the division served as external examiners for MBChB students at Walter Sisulu University (WSU) in Mthatha, as well as for BChD students at the UWC.

One pathologist attended a Professional Educational Development for Academics short course on teaching, learning and assessment within the context of current thoughts on university teaching.

3.2. Postgraduate
There are twelve Anatomical Pathology registrars in the division, and a further three junior and one senior registrar in Oral Pathology (UWC). In addition, two registrars in Forensic Medicine rotate for one year of training in Anatomical Pathology. Postgraduate students include two PhD, seven MSc (Cytopathology), three M (Pathology) and one BSc (Hons) student.

Other postgraduate teaching activities include lectures to BSc (Hons) (Reproductive Biology) students; teaching MMed students in family medicine on how to perform FNAB; and teaching Anatomical Pathology and Normal Histology to registrars from clinical disciplines to prepare them for the College of Medicine of SA (CMSA) examinations.

The HPCSA-registered MSc (Cytopathology) programme runs over a minimum of two years and has a modular design in keeping with the latest international trends. The programme is offered through distance education and includes a research component. Ongoing national and international moderation of the programme confirmed its high quality and standard, and the programme remains the only Cytopathology degree programme in Africa.

Pathologists from the division participated as examiners or moderators in CMSA examinations, and as external examiners for MMed research assignments.

The FNA and Gynaecological Cytology Tutorial (Sydney Tutorial) was jointly organised by Prof. Wright and Prof. Field from Sydney, Australia, at the Stellenbosch Institute for Advanced Study from 7–10 January 2016 under the auspices of the Royal College of Pathologists of Australasia Foundation, the Division of Anatomical Pathology at SU and NHLS Tygerberg. This is planned to be a biannual event.

The speakers included, amongst others, Associate Prof. Andrew Field, Notre Dame University, Sydney, Australia; Dr William Geddie, University Health Network, Toronto, Canada; Dr Matthew Zarka, Mayo Clinic, USA; Prof. Colleen Wright, NHLS Port Elizabeth and SU; Dr Pawel Schubert, Division of Anatomical Pathology, SU and NHLS Tygerberg; Prof. Komala Pillay, University of Cape Town (UCT), and Dr Luvo, NHLS. The workshop offered a comprehensive update on several topics related to cytopathology to more than 80 delegates, of whom more than 30 were from African countries. Donations made to the Royal College of Pathologists of Australasia Foundation offered financial support to delegates from African countries.

The short course in FNAB for Professional Nurses is run in collaboration with the Division of Nursing Sciences and Anatomical Pathology as a distance-mediated programme under the supervision of Prof. Wright. The theoretical component is offered via DVD and the theoretical assessment is undertaken at a local NHLS laboratory, followed by the performance of at least 100 FNABs under supervision at a NHLS FNA Clinic. The results are then sent to Prof. Wright for final assessment of competence.
Pathologists from the division continued to train clinicians in correct technique of FNAB. Prof. Wright trained clinicians in Port Elizabeth and East London in November as part of the MRC funded TB-Child Network Training in the Eastern Cape.

Medical Technologists and Technicians

- Two cytotechnologists completed their BTech degree in 2015 and three are enrolled part-time to complete their studies in 2016
- Two technologists enrolled for their Masters in Pathology in 2016
- One Histotechnologist (diploma) and one BHSc student in Histotechnology were trained. Two histotechnicians are undergoing training.

Table 53: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th>Qualification</th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMed</td>
<td>12</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MSc (Cytopathology)</td>
<td>7</td>
<td>-</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>MSc (Pathology)</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>PhD</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Technologist</td>
<td>1</td>
<td>-</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Technician</td>
<td>2</td>
<td>-</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>BHSc</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>BTech</td>
<td>5</td>
<td>-</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td><strong>33</strong></td>
<td><strong>10</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3.3. Other Training Information – Outreach Programmes

The division is involved with the training of medical staff and healthcare workers at regional hospitals and clinics to develop their skills and confidence to perform FNAB for cytology.

Academic support is offered to pathologists in the Eastern Cape in that the division provides specialised pathological tests and consultations on various tissue samples from the NHLS Anatomical Pathology Laboratories at Nelson Mandela Academic Hospital in Mthatha and Port Elizabeth. There is also close collaboration with pathologists at WSU to exchange teaching material and comment on diagnostically challenging cases.

Staff continued to teach FNAB technique to clinicians as part of the maintenance of competence initiative by the Western Cape Department of Health, and organised and participated in outreach projects in Worcester, Hermanus, Port Elizabeth and East London. The aim is to train clinicians and nursing sisters in the optimal FNAB technique to ensure that better quality specimens reach the Cytology Laboratories.

Pathologists, registrars and the nursing sister from the division offered a FNAB training session at the IXth International Childhood TB Training Course that was held at Goudini from 28 September–2 October 2015, as well as the 7th SA AIDS Conference that took place from 9–12 June 2015 at the Durban International Convention Centre.

As part of a collaborative project, funded by an Africa Collaboration Grant from SU to support a Comprehensive Cytopathology/Cytotechnology Training Programme for Uganda (CCCTPU), a cytotechnologist from the division visited Makere University in Kampala in October 2015 to assist with training in basic cytotechnology.

The division trained medical technologists from Ghana and Rwanda to acquire expert skills in special stains for surgical pathology. It also trained a DST/NRF-funded intern scientist in 2015. Staff participated in the HPCSA accreditation of postgraduate MMed training programmes.

Prof. Colleen Wright was invited to present a lecture entitled ‘FNA as a diagnostic tool in HIV/AIDS lymphoma’ at the AMC and AIDS Cancer Specimen Resource (ACSR) Symposium on HIV/AIDS Malignancies in Sub-Saharan Africa, held from 31 July to 1 August 2015 in Cape Town.

Prof. Kotze registered the 10th Applied Genetics Workshop, held in October 2015, as a short course at SU. She successfully applied for a UK-South Africa Researcher Links Grant from the NRF to the value of R200 000 to invite international speakers to this event. Part of this funding was used for the P5 Africa Congress on Personalised Medicine and Point of Care, which took place on 23–24 March 2016 in Cape Town.

Prof. JW Schneider organised the Confronting the Challenges Relevant to HIV/AIDS Malignancies in Sub-Saharan Africa Symposium, that was held under the auspices of the AMC and ACSR on 31 July to 1 August 2015, Cape Town, South Africa.
Professional Development

Postgraduate students graduated: one M (Pathology); one PhD (Anatomical Pathology).

Postgraduate students enrolled: two PhD, twelve MMed, seven MSc (Cytopathology), three M (Pathology), one BSc Hons.

HPCSA internship in Molecular Biology completed: two (Pathology Research Facility Laboratory).

4. RESEARCH ACTIVITIES

The major international collaborative research programme with pathologists and clinicians from the Department of Pathology and the Developmental Biology and Pathology Centre, Boston Children’s Hospital, USA, is entering the last year of recruitment. This is a ten-year study investigating the role of perinatal alcohol exposure in sudden infant death syndrome and stillbirth (PASS Research Network) in 1,200 maternal foetal deaths and is funded by NIHCD and NIAAA. Prof. Wright is a member of the steering committee for this study and she and the team closely collaborate with pathology colleagues at Harvard University in Boston to complete collaborative microscopic projects that are part of the project as a whole. She attended the face-to-face meeting in Washington in September 2015.

The division operates the National Cancer Institute–supported AIDS Malignancy Consortium and AIDS and Cancer Specimen Resource SSA RBR. The SSA RBR aims to collaborate closely with other South African and African institutions and researchers to establish a central biorepository site for sub-Saharan Africa that is fully integrated within the AIDS Cancer Specimen Repository (ACSR), and can proactively obtain relevant biospecimens and data for coordinated research on HIV-related malignancies. Biospecimens and data that have been obtained with informed consent and processes under best practices for biorepositories will be available at no cost to African researchers with approved research projects. Prof. JW Schneider, principal investigator for this project, attended the AMC Investigator’s Fall Meeting that was held in Bethesda, Maryland on 28–29 October 2015.

4.1. Research Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researchers</th>
<th>Funding</th>
<th>Short Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-associated renal biopsy disease in a South African centre</td>
<td>WD Bates</td>
<td>None</td>
<td>Histopathological analysis of 385 renal biopsies from TBH.</td>
</tr>
<tr>
<td>Hepatitis B-associated Glomerulonephritis</td>
<td>WD Bates, MR Moosa</td>
<td>None</td>
<td>A clinicopathological comparison of children and adults with HBV-associated membranous GN and an adult group with idiopathic MGN.</td>
</tr>
<tr>
<td>Percutaneous pericardioscopy in tuberculous pericarditis: Improving the diagnostic yield and gaining new insights into the pathogenesis of TB pericarditis</td>
<td>CG Kyriakakis, G Walzl, A Doubell, A Whitelaw, WD Bates, R Warren, K Hoek</td>
<td>Division of Cardiology</td>
<td>Improving the diagnostic yield and gaining new insights into the pathogenesis of TB pericarditis.</td>
</tr>
</tbody>
</table>
**Project Title:** A case series of renal amyloidosis at Tygerberg Academic Hospital, Cape Town  
**Researchers:** H Hassen, WD Bates, MR Moosa  
**Funding:** Division of Nephrology  
**Short Description:** A clinicopathological review of patients diagnosed with amyloidosis on renal biopsy in TBH over a 30-year period from 1985–2015.

**Project Title:** The clinical relevance of repeat renal biopsies in the management of lupus nephritis: The Tygerberg Hospital experience  
**Researchers:** EK Tannor, WD Bates, MR Moosa  
**Funding:** Division of Nephrology  
**Short Description:** A clinicopathological review of the role and value of repeat renal biopsies in TBH SLE patients over a 30-year period from 1985–2015.

**Project Title:** A review on the spectrum of paediatric lung pathology seen in surgical specimens in an academic centre, in a region with high tuberculosis and HIV prevalence  
**Researchers:** P Botha, P Goussard, R Gie, PT Schubert  
**Funding:** None  
**Short Description:** To describe the histopathological features of paediatric lung pathology surgical specimens with special reference to tuberculosis and HIV.

**Project Title:** Placental histopathology in congenital syphilis: A review of pathology seen in the Western Cape, and to investigate the impact of HIV on the morphology  
**Researchers:** C du Toit, CA Wright, JL van der Merwe, PT Schubert  
**Funding:** None  
**Short Description:** To describe the histopathological features of syphilis in the placenta in the Western Cape and to note if HIV changes the morphology.

**Project Title:** Analysis of the clinical utility of gene expression profiling in relation to conventional prognostic markers in South African patients with breast carcinoma  
**Researchers:** KA Grant, JP Apffelstaedt, CA Wright, MJ Kotze  
**Funding:** Cape Peninsula University of Technology (CPUT) Research Fund, CANSA, SHIP  
**Short Description:** In the rapidly developing area of breast cancer treatment, continuous monitoring of new technologies against current standards is advisable. Assessment of the clinical utility and analytical validation (quality assurance) of transcriptional profiling in South African breast cancer patients is envisaged to not only contribute to improved quality control and the optimisation of laboratory techniques used, but will also assist in the selection of a subgroup of breast cancer patients that will benefit most from transcriptional profiling. Accurate assessment of HER2 status is of particular interest.

**Project Title:** Bone health in postmenopausal patients with breast cancer treated with aromatase inhibitors: factors predicting the risk for osteoporosis  
**Researchers:** Dr K Baatjes, N van der Merwe, Prof. MJ Kotze, Prof. JP Apffelstaedt, Dr AV Peeters  
**Funding:** Medical Research Council (SHIP)  
**Short Description:** Postmenopausal women will receive a specific medication for breast cancer, called aromatase inhibitors, which may worsen the bone thickness in some but not all women. Clinical and pharmacogenetic studies will be performed to determine in which women the bone thickness will change and in whom it remains the same. Blood tests and bone thickness measurements will therefore be performed on all participating women before and during treatment.

**Project Title:** Development and application of a pathology-supported pharmacogenetic test for improved clinical management of South African patients with breast cancer and associated co-morbidities  
**Researchers:** N van der Merwe, MJ Kotze, J Bezuidenhout, R Pienaar, S Janse van Rensburg  
**Funding:** Medical Research Council (SHIP), CANSA  
**Short Description:** Breast cancer is a heterogeneous disease characterised by genetically distinct subtypes that differ in their response
to treatment. The purpose of the proposed study is to expand the cancer genetic testing service offered in South Africa to provide a pharmacogenomics algorithm applicable to all breast cancer subtypes. A pathology-supported genetic testing approach will be implemented as a screening step to select patients most likely to benefit from whole exome/genome sequencing as the next frontier in personalised medicine.

Project Title: Application of personalised medicine using an integrated service and research approach
Researchers: Prof. MJ Kotze, Dr H Luckhoff, Prof. S Janse van Rensburg, Dr D van Velden, DH Geiger, LR Fisher, KE Moremi
Funding: CANSA, NRF Winetech, THRIP
Short Description: Development of a novel pre-screen algorithm for cardio-metabolic risk management using a genomics database resource.

Project Title: Identification of biomarkers for HIV-related lymphoma in South African populations
Researchers: SC Rossouw, A Christoffels, BK Ndomba, A Abayomi, C Swanepoel, B van Rooyen, R Grewal, F Bassa, N Mohamed, JW Schneider
Funding: SARChI chair in Bioinformatics, NRF
Short Description: This study focuses on matrix-assisted laser desorption ionisation mass spectrometry imaging (MALDI MSI) to investigate protein profile signatures and to identify protein biomarkers in South African HIV-related lymphoma cases in the Western Cape.

Project Title: Villitis of unknown etiology: Review of 300 cases and correlation with pregnancy outcome
Researchers: V Pretorius, P Schubert, D Hall, CA Wright, D Mason
Funding: SU Research Assistant funding
Short Description: A retrospective, descriptive study of all placentas submitted for histopathological evaluation to the Division of Anatomical Pathology between 1 January 2010 and 31 December 2014 in which chronic villitis was diagnosed with clinical correlation.

Project Title: Construction of tissue microarrays for Kaposi’s sarcoma and other HIV/AIDS-related malignancies for research purposes. A retrospective study
Researchers: JW Schneider, Prof. CA Wright, L Banach
Funding: NCI
Short Description: Documentation of relevant clinicopathological information of patients with HIV/AIDS-related malignancies, preparation of tissue microarrays from submitted tissue samples, and access to this information and samples for researchers with approved research protocols.

Project Title: Development of the AIDS Malignancy Consortium (AMC) and ACSR Sub-Saharan Africa Regional Biorepository (SSA RBR).
Researchers: JW Schneider
Funding: NCI
Short Description: The SSA RBR aims to collaborate closely with other South African and African institutions and researchers to establish a central biorepository site for sub-Saharan Africa that is fully integrated within the ACSR, and can prospectively obtain high quality biospecimens and data with informed consent and according to best practices for biorepositories. The biospecimens and data are available at no cost to African researchers with approved research projects related to HIV-related malignancies. The SSA RBR furthermore supports AMC clinical trials in SSA and promotes and performs research and training pertaining to the science of biobanking.

Project Title: Origin and lineage in differentiation of Kaposi’s sarcoma
Researchers: JW Schneider, K Corcoran, D Dittmer
Funding: NIH
Short Description: Using tissue microarrays, standard and two-colour immunohistochemistry, and laser capture microscopy, this study will test the hypothesis that there exist different sub-types of KS tumour cells within a single KS lesion.

Project Title: The clinicopathological spectrum of sub-clinical acne keloidalis nuchae (AKN) with correlation to its dermoscopic features: A cross-sectional analytical study
<table>
<thead>
<tr>
<th><strong>Project Title</strong></th>
<th><strong>Researchers</strong></th>
<th><strong>Funding</strong></th>
<th><strong>Short Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>The clinicopathological spectrum of cutaneous granulomatous inflammation: A retrospective descriptive study</td>
<td>S Fakir, JW Schneider, WI Visser</td>
<td>Division of Dermatology, SU</td>
<td>This study focuses on the classification of granulomatous dermatitis, as defined by the aetiology and histomorphology of granulomas in skin biopsies, and the importance of clinical correlation and ancillary investigations to arrive at a specific diagnosis.</td>
</tr>
<tr>
<td>The clinicopathological spectrum of panniculitis: A retrospective descriptive study</td>
<td>C Mathobela, JW Schneider, HF Jordaan</td>
<td>Division of Dermatology, SU</td>
<td>This study focuses on the classification of panniculitis, as defined by the aetiology and histomorphology of panniculitis in skin biopsies, and the importance of clinical correlation and ancillary investigations to arrive at a specific diagnosis.</td>
</tr>
<tr>
<td>The retrospective value of skin biopsy in histologically confirmed cases of the perivascular dermatitis subgroup of the inflammatory dermatoses</td>
<td>B Tod, HF Jordaan, JW Schneider</td>
<td>None</td>
<td>This study examines 163 skin biopsies with a histological diagnosis of perivascular dermatitis (as defined by Ackerman's algorithm) to assess the value the skin biopsy added in the final diagnosis of each case. While previous studies have examined similar data within the field of inflammatory dermatoses, to our knowledge no study has focused specifically on the perivascular dermatitis group.</td>
</tr>
<tr>
<td>The spectrum of changes seen with placental intravascular organisms</td>
<td>PT Schubert, D Roberts, Z Sherif, D Mason</td>
<td>None</td>
<td>Bacterial testing using PCR methodology on Formalin Fixed Paraffin Embedded (FFPE) blocks to identify specific organisms associated with the spectrum of changes seen with placental intravascular organisms.</td>
</tr>
<tr>
<td>The utility of open lung biopsy in infants and children admitted in a paediatric intensive care unit (ICU)</td>
<td>A Gie, PT Schubert, P Goussard, J Morrison, R Gie</td>
<td>None</td>
<td>To determine if the histopathological result altered the treatment in infants and children in the ICU who underwent an open lung biopsy for severe or persistent lung illness.</td>
</tr>
<tr>
<td>The sensitivity and specificity of radiological features of Hirschsprung's disease in a cohort of South African children</td>
<td>SCS Vlok, SW Moore, RD Pitcher, PT Schubert</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>
Short Description: Assessment of the radiological features in Hirschsprung’s disease, as well as a comparison with literature and children who present with intestinal pseudo obstruction due to other causes.

Project Title: The value of auramine staining vs Papanicolaou-induced fluorescence and Ziehl Neelsen staining in fine needle samples from palpable lymph nodes in children with TB lymphadenitis

Researchers: MM Selepe, A van Wyk, CA Wright

Funding: None

Short Description: Comparative study and extension of the initial project to determine whether auramine staining is superior to Papanicolaou-induced fluorescence when analysing mycobacterial autofluorescence in fine needle samples from palpable lymph nodes in children.

Project Title: Fine needle aspiration biopsy in paediatric lymphadenopathy – changing clinical practise over a decade

Researchers: C Sher-Locketz, CA Wright, S Moore, PT Schubert

Funding: None

Short Description: Descriptive study of the range of diagnoses made on cytological and histological specimens in patients 15 years and younger between 2004 and 2014, and comparing these results to those of the previous decade.

Project Title: Genome-wide admixture mapping to identify prostate cancer risk loci in South African men

Researchers: P Fernandez, VM Hayes, A van der Merwe, WD Bates, AC van Wyk, D Petersen

Funding: Not applicable to histopathology part of project

Short Description: Differences in genetic background occurring in populations may be responsible for the observed ethnic differences in prostate cancer risk. Admixed populations arising from a mixture of two or more different ancestral populations (e.g. African, European or Asian) allow identifying chromosomal regions with a higher proportion of the genome inherited from the particular ancestral population in which the disease is most prevalent. Consequently, these differences have the power to determine the genetic risk variants responsible for the disease. This multi-national and multi-institutional study aims to perform a genome-wide admixture screen in a unique admixed South African population group to identify putative prostate cancer risk variants.

Project Title: Detection of metastatic breast cancer in sentinel lymph nodes

Researchers: A van Zyl, JW Schneider

Funding: NHLS

Short Description: The study aims to determine the most cost-effective histological and immunohistochemical examination of sentinel lymph nodes for the detection or exclusion of metastatic breast carcinoma.

Project Title: T cell cytokine response and bacterial burden in central nervous system granulomas in tuberculous meningitis patients

Researchers: P Versteegen, M van der Kuip, SL van Elsland, D Zaharie, AM van Furth

Funding: NRF

Short Description: To gain more knowledge about the difference in bacterial burden in the three different CNS granulomas in humans, in correlation with the T cell cytokine response (in particular IL-2, IL-17 and IL-10).

Project Title: Evaluation of the FluoroType MTB assay for detection of Mycobacterium tuberculosis complex DNA in fine needle aspiration biopsy (FNAB) specimens

Researchers: C Hayes, A de Kock, RM Warren, S Govender, CA and Wright

Funding: NRF, NHLSRT

Short Description: The FluoroType MTB assay (FT MTB) is a new semi-automated HyBeacon-based PCR assay for the detection of Mycobacterium tuberculosis complex (MTBC) in respiratory and non-respiratory clinical specimens. The aim of the study was to evaluate the FT MTB assay for the detection of MTBC in FNAB specimens and to compare these results to culture, cytology an Xpert® MTB/RIF assay.

Project Title: The role of Placental Histology in adverse pregnancy outcome at a referral hospital in the Eastern Cape

Researchers: MS Mabenge, CA Wright
Funding: NHLS Trust
Short Description: Adverse pregnancy outcome continue to pose a challenge and contributes significantly towards litigation in obstetrics globally, but the Eastern Cape province, where poverty is rife, is noted internationally for its perinatal mortality rate. Dora Nginza Hospital, the only high-risk obstetric referral unit in Port Elizabeth, Eastern Cape, serves the western half of the Eastern Cape region. In order to try to determine the underlying factors leading to these figures, the Obstetrics Department in Dora Nginza Hospital have been submitting placentas for histopathology in cases of unexpected poor birth outcomes (i.e. 5 minute Apgar of below 7, fresh still birth) since March 2012.

Project Title: Perinatal And Neonatal Mortality Rates In Bishop Lavis Over Seven Years
Researchers: HJ Odendaal, CA Wright, PT Schubert, CA Groenewald, LT Brink, E Geldenhuys, D Mason
Funding: PASS Study
Short Description: The Safe Passage Study (SPS) is a prospective study to determine the effects of alcohol consumption and smoking during pregnancy on stillbirths and infant deaths during the first year of life. A total of 7 060 participants were recruited from the antenatal clinics in Bishop Lavis and Belhar over a seven-year period. All infants were followed up for one year to determine stillbirth, early and late neonatal, perinatal and infant mortality rates in a well-defined community where the outcomes of all pregnancies were recorded.

5. RESEARCH OUTPUT

5.1. Publications


5.2. Conference Presentations

**Oral Presentations**


Mohamed N, Wright CA. Fine needle biopsy aspiration biopsy in paediatric mycobacterial lymphadenitis. IXth International Childhood Training TB Training Course, October 2015, Goudini.

Mabenge MS, Wright CA. The role of Placental Histology in adverse pregnancy outcome at a referral hospital in the Eastern Cape. 35th Priorities in Perinatal Care Conference, 8–11 March 2016, Bela-Bela, South Africa.


Odendaal HJ, Wright CA, Schubert PT, Groenewald CA, Brink LT, Geldenhuys E, Mason D. Perinatal and neonatal mortality rates in Bishop Lavis over 7 years. 35th Priorities in Perinatal Care Conference, 8–11 March 2016, Bela-Bela, South Africa.


Rigby J. Gastrointestinal Seminar, IAP Congress, 24 September 2015, University of the Witwatersrand (Wits), Johannesburg.


Schneider JW. The role of the pathologist in HIV/AIDS-related cancer diagnosis: challenges and opportunities in a limited resource setting. AMC/ACSR Symposium: Confronting the Challenges Relevant to HIV/AIDS Malignancies in Sub-Saharan Africa, 31 July–1 August 2015, Cape Town, South Africa.


Wright CA. FNA as a diagnostic tool in HIV/AIDS lymphoma. AMC/ACSR Symposium: Confronting the Challenges Relevant to HIV/AIDS Malignancies in Sub-Saharan Africa, 31 July–1 August 2015, Cape Town, South Africa.

Wright CA, Schubert PT. FNA and Gynaecological Cytology Tutorial. Infectious Diseases – Case Based Tutorial, 7–10 January 2016.
Poster Presentation


6. ACADEMIC AND RESEARCH RECOGNITION/AWARDS

The division was closely involved in the successful application for the establishment of an AIDS Malignancy Clinical Trial site at TBH and SU. In addition its staff received the following recognition:

- Prof. Maritha Kotze:
  - UK-SA Researcher Links Grant awarded by the NRF
  - Appointed as committee member of the Cape Breast Forum
  - Registered the 10th Applied Genetics Workshop as a short course at SU
  - Co-organiser of the P5 Africa Congress, 23–24 March 2016
  - Arranged Familial Hypercholesterolaemia Workshop supported by the Lipid and Atherosclerosis Society of South Africa on 24 March 2016
  - Reviewed several Masters and PhD theses, both internal and external.

- Dr N Mohamed won the first prize for a diagnostic brain smear interpretation competition at the 30th Euro-CNS Course: Tumors of the Central Nervous System hosted by European Confederation of Neuropathological Societies

- Prof. JW Schneider was appointed as a member of the ACSR Executive Committee

- Dr D Zaharie was appointed as reviewer for International Journal of Neuroscience and South African Journal of Radiology.

6.1 Other Attendance

- Dr P Schubert: International Paediatric Pathology Association Advanced Course in Paediatric Pathology, 12–19 September 2015, Fontainebleau, France.
- Dr D Zaharie: 31st Euro-CNS Course: Developmental Neuropathology, 21–23 October 2015, Amsterdam, the Netherlands, hosted by European Confederation of Neuropathological Societies.
- Prof. JW Schneider: 15th International Conference on Malignancies in AIDS and other acquired immunodeiciencies, Lister Hill Center Auditorium, NIH campus, Bethesda, Maryland.
Chemical Pathology

Head: Prof. RT Erasmus

1. ABOUT THE DEPARTMENT

The Chemical Pathology Division is SANAS-accredited and provides a 24-hour service to TBH and some of the clinics and secondary hospitals in the Western Cape. This service was expanded in April 2011 to include Eerste River Hospital and more peripheral clinics.

It is involved in numerous research projects, ranging from diabetes to multiple sclerosis and HIV, and collaborates with other pathology divisions as well as other institutions. It also actively fosters international collaborations.

The division is involved in undergraduate and postgraduate training of medical students, registrars, BSc graduates, masters, doctoral students and technologists, and regularly organises training programmes in laboratory management.

Table 54: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist (incl. HoD)</th>
<th>PhD Scientist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African*</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
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<td>2</td>
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<td>9</td>
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<td>12</td>
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</tr>
<tr>
<td>South African*</td>
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<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>2</td>
<td>13</td>
<td>1</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

As mentioned above, the division provides a comprehensive 24-hour service to TBH and some of the clinics and secondary hospitals in the Western Cape region, as well as Eerste River Hospital and more peripheral clinics. It is one of the referral centres for samples from the Eastern Cape, particularly the Nelson Mandela, Livingstone and East London hospitals. Work from the Northern Cape is being referred to the division since 2014, while KwaZulu-Natal commenced with referrals from Albert Luthuli, King Edward and Mahatma Gandhi hospitals in January 2015. At present, the Tygerberg Business Unit services clients from more than 800 locations. The diagnostic service provides a testing platform for various trials which are incorporated into the daily routine service.

In 2015 the division retained its SANAS accreditation status with the addition of Urine Chemistry. It also had a successful Health and Safety audit and satisfactory EQA results.

All vacant technologist and scientist posts were filled. Four technologists received their BHSc (Bachelor of Health Science) degrees, one received her Masters’ Degree in Pathology from SU and one registrar passed her college exams.

The appointment of a supervisor for the automation area has improved accreditation processes and work continuity. Collaborations and communications with the Virology, Immunology, Haematology and Microbiology laboratories continued and assisted in improving workflow in order to improve laboratory performance. This has also been demonstrated with regards to the TBH Pharmacology Department.

2.1 Challenges

Ongoing deterioration of major analysers had a major impact on routine work and turnaround time (TAT). The tender for new equipment was delayed as a change in work environment necessitated it to be resubmitted to include a consolidated platform and automated pre-analytical system. Breakdown procedures had to be modified as a result of the delays, compounded by the fact that parts were not available in the country.

Ongoing problems were experienced with referral samples as these were incorrectly captured at referral sites and cannot be modified upon receipt.

Hospital air conditioning and water supply were major problems between December 2015 and January 2016. The major challenges faced therefore were to maintain TAT due to equipment and infrastructure problems.
Vacant registrar and pathologists posts were not filled. Implementation of the new LIS TrakCare in August 2015 negatively impacted TAT as it is a cumbersome system presenting ongoing challenges.

3. TEACHING AND TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Teaching and training of undergraduate medical students continues to be a priority. The Basis of Disease Module is chaired by Dr Rensburg, with Dr Hoffman as secundus. This module is presented to MBChB I students and forms the basis of Pathology teaching. Prof. Zemlin is involved in MBChB II lectures (Respiratory and Cardiovascular modules). In recent years, the division introduced case-based learning in which smaller groups are involved.

The MBChB IV and V students visit the laboratory as part of their middle clinical rotation. This rotation involves a more intimate teaching environment and exposes the students to the laboratory as well as haematology case studies. The registrars in the division actively participate in this programme which runs throughout the academic year.

3.2. Postgraduate

The division is involved in co-ordinating two postgraduate modules – the Laboratory Management Postgraduate Module (Prof. Zemlin) and Molecular Diagnostics (Dr Hoffman). The division continues to take part in organising the Diagnosis and Screening Module of the Masters Degree in Clinical Epidemiology organised by the Centre for Evidence-based Health Research (Prof. Erasmus and Dr Rensburg).

The division was involved in supervising two masters, five MMed (including two clinical pathologists) and five doctoral and postdoctoral students/fellows. Prof. Janse van Rensburg lectured honours students in Medical Biochemistry.

Prof. Erasmus and Prof. Zemlin, together with the programme committee, were involved in the revision of the Laboratory Management Module. The division continues to attract senior technologists and pathologists from across the continent to its training programme on Laboratory Management, which forms part of the LabSkills Africa Programme, supported by the Royal College of Pathologists, UK. A technologist from Zimbabwe, a scientist from the UK, a pathologist from Nigeria, two technologists from Zambia, and two consultants from Nigeria attended the three-month integrated Laboratory Management Programme which was held from May–July 2015. Two publications resulted from this rotation – one was accepted in a peer-reviewed journal and another is in the process of being prepared for submission.

Division staff continued to expand the research focus groups on POC testing and Personalised Medicine established in 2014. Members of the division continue to serve on several national (NHLS Expert Committee) and international committees (International Federation of Clinical Chemistry). Prof. Janse van Rensburg served on the SA National Committee for the International Brain Research Organisation (IBRO).

Specialists, postgraduate students, and medical technologists from the division attended several courses during 2015 as part of continuous professional and skills development.

Table 55: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th>Qualification</th>
<th>Total Number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>#BSc Honours</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>#MSc</td>
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<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Registrars</td>
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<td>100%</td>
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<tr>
<td>PhD</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>Post-Doctoral</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>South African</td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>100%</td>
</tr>
<tr>
<td>All</td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>100%</td>
</tr>
</tbody>
</table>

3.3. Other Training Information

Outreach and Community Interaction

The division continued to provide outreach services to Karl Bremer and Paarl hospitals.

Professional Development

Members of the division were involved as external examiners at the University of Zimbabwe, WSU, North West University, University of KwaZulu-Natal (UKZN) and University of Limpopo. One was an internal examiner for two doctoral studies. Over 20 manuscripts were reviewed.

Members of the division are actively involved in the SAACB, the International Federation of Clinical Chemistry and Laboratory Medicine, Federation of South African Societies of Pathology, College of Pathologists of East, Central and Southern Africa, IBRO, the SANS and the Multiple Sclerosis Care Trust.

4. RESEARCH ACTIVITIES

The division has developed various research themes which have evolved over the past four years:

- The clinical audit and laboratory management team is led by Prof. Zemlin, who is also involved in a study on HbA1c and risk factors of cardiovascular disease in a local community (her PhD study) and markers of inflammation in treatment-naïve HIV individuals. The latter study is being performed by two masters students, an MMed candidate and a MSc candidate, both of whom graduated cum laude at the end of 2015. The MMed work was published in a peer-reviewed journal. Prof. Zemlin completed her PhD thesis which has been accepted with minor changes.

- Senior laboratory professionals from Nigeria and Zimbabwe attended an abbreviated laboratory management module at the division and performed pre-analytical audits. One has been accepted for publication in a peer-reviewed journal and another is being prepared for publication. The division’s expertise in laboratory management led to Professors Erasmus and Zemlin being invited:
  - To part of the programme and faculty committee of the Association of Public Health Laboratories (USA) and George Washington University
  - To organise a public health management course in Cape Town (9–20 Feb 2015)
  - As speakers at Kenya Association of Clinical Pathologists, Diani Beach, Mombasa
  - To present a workshop on scientific writing.

- Dr Hoffman leads the team on Reference Range Values, which is a collaborative study with a private pathology laboratory, Nigeria, Kenya and Japan. Dr Hoffmann is also performing research on acanthosis nigricans and diabetes mellitus which is her PhD study. Two manuscripts from this group have been submitted for publication in Clinica Chimica Acta.

- Dr Rensburg is involved in establishing a research group on POC testing. This group advises nationally and is involved in community-based studies with Family Medicine.

- Dr Ali is studying the pathophysiology of fat accumulation in various disease states in collaboration with the Department of Biochemistry.

- Prof. Janse van Rensburg leads the group on multiple sclerosis and schizophrenia. Prof. Erasmus continues to be involved with many of these groups, but is also extensively involved in a study on diabetes and associated cardiovascular risk factors in the mixed ancestry population of the Western Cape. The latter is a research project in collaboration with CPUT (Prof T Matsha) and MRC (Prof. A Kengne). Many of these research groups have external collaborators.

4.1. Research Units/Study Groups Linked to the Department

- Reference Range Project: Prof. Erasmus and Dr Hoffmann, in collaboration with Prof. Ichihara from Japan and Pathcare
- Bellville South Study: Professors Erasmus, Zemlin and others in collaboration CPUT (Prof. Matsha) and MRC (Prof. Kengne)
- The HIV Activation and Inflammation Group (HAIG). Professors Zemlin and Erasmus, in collaboration with the divisions of Haematology and Virology
- Point of Care Group: Prof. Erasmus and Dr Rensburg, in collaboration with Prof. Mash of Family Medicine
- The Audit and Laboratory Management Group: Professors Zemlin and Erasmus, in collaboration with other divisions and African countries (Nigeria, Kenya and Zimbabwe)
- Multiple Sclerosis and Schizophrenia Group: Professors Janse van Rensburg and Erasmus, in collaboration with Prof. Kotze, Geneticist, Division of Anatomical Pathology, and Dr Van Toorn, Department of Paediatrics and Child Health
- Personalised Medicine Group: Professors Kotze, Erasmus, Schneider and Janse van Rensburg and the MRC (Dr T Bunn).

4.2. Research Projects

| Project Title | HIV activation and inflammation Study (HAIG) – ADMA levels |
| Researchers | H Ipp, AE Zemlin, CA Hudson |
| Funding | NHLS, Harry Crossley, the Poliomyelitis Research Foundation (PRF), MRC |
**Project Title:** Cinnamon in the life of patients with type 2 diabetes  
**Researchers:** A Ali, B Baker, R Peterson  
**Status:** First part of the project, which included cellular studies, completed. Results was presented as talk in an international conference on obesity in 2015.

**Project Title:** The effect of TB on fat accumulation and adipocyte gene expression  
**Researchers:** A Ali, RT Erasmus, P van Helden, B Baker, R Peterson  
**Project Title:** Derivation and validation of an HbA1c optimal cut-off for diagnosing prediabetes in a South African mixed ancestry population with a high risk of diabetes mellitus  
**Researchers:** AE Zemlin, TE Matsha, AP Kengne, RT Erasmus  
**Funding:** NHLS, CPUT  
**Project Title:** Correlation of E-selectin levels with carotid intima media thickness and cardio-metabolic profile of mixed ancestry South Africans: A cross-sectional study  
**Researchers:** AE Zemlin, TE Matsha, AP Kengne, RT Erasmus  
**Funding:** NHLS, CPUT  
**Project Title:** High molecular weight adiponectin levels are neither influenced by adiponectin polymorphisms, nor associated with insulin resistance in mixed-ancestry hyperglycaemic subjects from South Africa  
**Researchers:** AE Zemlin, TE Matsha, AP Kengne, RT Erasmus  
**Funding:** NHLS, CPUT  

**Completed Projects**

**Project Title:** Predictors of cardiovascular risk and glucose tolerance in a mixed ancestry population  
**Researchers:** T Matsha, RT Erasmus, S Hassan, D Soita  
**Funding:** CPUT  
**Project Title:** Free light chains in treatment-naive HIV subjects  
**Researchers:** AE Zemlin, H Ipp, MA Rensburg, S Maleka, RT Erasmus  
**Funding:** NHLS, K-funding  

**Ongoing**

**Project Title:** Establishing reference values for common biochemical analytes in African countries  
**Researchers:** RT Erasmus, M Hoffman, J Wassung, T Matsha, K Ichihara  
**Funding:** NHLS, Beckman Coulter, Pathcare  
**Project Title:** Molecular investigation of genetic factors that are associated with insulin resistance and obesity in a South African population  
**Researchers:** RT Erasmus, T Matsha, S Hassan, Z Vergotine  
**Funding:** MRC, CPUT, SU  
**Project Title:** HbA1c as a screening tool for diabetes mellitus and pre-diabetic conditions and the investigation of traditional and future biochemical predictors of cardiovascular risk in a local urban community of Cape Town  
**Researchers:** AE Zemlin, RT Erasmus, TE Matsha  
**Funding:** CPUT and NHLS  
**Project Title:** Mechanism of Lipodystrophy in patients with HIV  
**Researchers:** A Ali, RT Erasmus, P van Helden, B Baker, R Peterson  
**Funding:** SU and NHLS
<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researchers</th>
<th>Funding</th>
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<tbody>
<tr>
<td>Hormonal regulation of Vaspin</td>
<td>A Ali</td>
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<tr>
<td>Hypogonadism in patients with Type 2 diabetes</td>
<td>A Ali, T Matsha, RT Erasmus</td>
<td>CPUT</td>
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<tr>
<td>The effect of Vit. D on fat accumulation and insulin resistance</td>
<td>A Ali, T Matsha, RT Erasmus</td>
<td>SU/CPUT</td>
</tr>
<tr>
<td>The development of a comprehensive gene-based, pathology supported intervention programme for improved quality of life in patients diagnosed with multiple sclerosis (MS)</td>
<td>S Janse van Rensburg, MJ Kotze, D Geiger, W Davis, K Moremi, M Rensburg, F Cronje, MMJ de Klerk, RT Erasmus</td>
<td>NHLS K-funding, NHLS Development Grant, Winetech Grant</td>
</tr>
<tr>
<td>Dietary supplementation with eicosapentaenoic acid in patients with schizophrenia: Clinical efficacy and changes in cell membrane fatty acids</td>
<td>S Janse van Rensburg, MJ Kotze, D Geiger, H Lückhoff, RT Erasmus</td>
<td>NHLS K-funding, Harry Crossley</td>
</tr>
<tr>
<td>Point of Care Testing (POCT) evaluations</td>
<td>MA Rensburg, RT Erasmus</td>
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<tr>
<td>The prevalence and clinical significance of acanthosis nigricans in diabetic and non-diabetic women of mixed ancestry</td>
<td>M Hoffmann, FS Hough, W Visser, W Ferris</td>
<td>Harry Crossley, K-funding</td>
</tr>
<tr>
<td>E-selectin levels in treatment-naive HIV subjects</td>
<td>AE Zemlin, H Ipp, M Hoffman, RT Erasmus</td>
<td>Harry Crossley, PRF, NHLS</td>
</tr>
<tr>
<td>Levels of procalcitonin in treatment-naive HIV subjects</td>
<td>AE Zemlin, H Ipp, D Phatlhane</td>
<td>Harry Crossley, PRF, NHLS</td>
</tr>
<tr>
<td>Evaluating point of care testing for glycated haemoglobin in primary care facilities of the Western Cape</td>
<td>R Mash, RT Erasmus, M Rensburg, C Vos, A Ugoagwu</td>
<td>Harry Crossley</td>
</tr>
<tr>
<td>Lipodystrophy study – KIDCRU</td>
<td>M Rensburg, S Innes</td>
<td>KIDCRU</td>
</tr>
<tr>
<td>Influence of storage time and temperature on stability of serum and urine osmolality</td>
<td>MR Davids, M Rensburg, K Bezuidenhout</td>
<td>K-funding</td>
</tr>
</tbody>
</table>
Project Title: Radio opaque contrast medium interference in capillary zone electrophoresis of serum in the clinical laboratory
Researchers: M Hoffmann, E Hitchcock, WP Meyer
Funding: Harry Crossley, NHLS

Ongoing (New)
Project Title: Screening and diagnosis of pre-diabetes and diabetes using a point of care instrument for glycated haemoglobin (Hba1c) in a community at high risk of developing diabetes
Researchers: J Esser, MA Rensburg, RT Erasmus, AE Zemlin
Project Title: Glycated haemoglobin (HbA1c) method performance and utilisation at NHLS laboratories in South Africa
Researchers: J Esser, RT Erasmus, AE Zemlin
Project Title: Development and validation of a screening tool for antibody deficiency in South Africa
Researchers: MA Rensburg, M Esser, J Peter
Funding: Harry Crossley
Project Title: Characterisation of the phenotype and genotype in a family with symptomatic hypokalaemia
Researchers: D van der Merwe, MA Rensburg, MR Davids

4.3. Grant Funding
• MRC Flagship Grant – R2.0 million: Prof. Erasmus. Study of cardiovascular risk factors in mixed ancestry population, Co-principal investigator
• NRF-rated Researcher Incentive Fund – R40 000 per annum for seven years (R280 000): Prof. Erasmus
• NRF Invited Speaker Fund – R30 000: Prof. Erasmus
• NHLS Development Grant 004_94337 – R90 000: Prof. Janse van Rensburg. The development of a rapid polymerase chain reaction-based assay for improved clinical management of patients with metabolic syndrome and non-alcoholic fatty liver disease
• NHLS Development Grant: Determination of CKD in mixed-ancestry population using a POCT
• NRF Incentive Funding – R280 000: Prof. Zemlin
• MRC Newton Grant – R1 million: Collaborator (Principal Investigator: T Matsha, CPUT)
• Scientific Travel Grant – R15 000: Prof. Erasmus
• SU Staff Exchange Grant – R15 000: Prof. Erasmus
• NRF-rated Researcher Incentive Fund – R40 000 per annum for seven years (R280 000): Prof. Zemlin
• K-funding (KNC 158) 2015 R17 636: Prof. Zemlin and Dr Phatlhane. The value of procalcitonin compared to other known inflammatory markers and stage of disease in asymptomatic HIV-infected ART-naive patients
• NHLS Development Grant (004_94435) – R 90 000: Prof. Zemlin/Dr Phatlhane. The value of procalcitonin compared to other known inflammatory markers and stage of disease in asymptomatic HIV-infected ART-naive patients
• Harry Crossley 2015 – R 15 397: Prof. Zemlin/Dr Hoffman. E-selectin, other cell adhesion molecules and markers of inflammation in treatment-naive individuals living with HIV
• K-funding (KNC 166) – R16 205: Prof. Zemlin/Dr Hoffman. E-selectin, other cell adhesion molecules and markers of inflammation in treatment-naive individuals living with HIV
• Scientific Travel and Publication Fund– R9 300: Prof. Zemlin/Dr Hoffman.

Invited Grant Review
Prof. Zemlin (2)
Prof. Janse van Rensburg (2)
Prof. Erasmus (3)
Dr Hoffman (2)
5. RESEARCH OUTPUT

5.1. Journal Publications


**Journal Articles (Non-subsidised)**


**5.2. Conference Presentations**

**National Conferences**

**Oral Presentations**


Phatlhane DV, Zemlin AE, Erasmus RT. The usefulness of repeat polyethylene glycol (PEG) precipitation of macroprolactin extraction in hyperprolactinaemia. PathReD, April 2015, Johannesburg.

**Poster Presentations**


Phatlhane DV, Zemlin AE, Erasmus RT. The usefulness of repeat polyethylene glycol (PEG) precipitation of macroprolactin extraction in hyperprolactinaemia. PathReD, April 2015, Johannesburg.

**International Conferences**

**Poster Presentations**


Van Sensie N, Janse van Rensburg S, Geiger D, Lückhoff H, Kotze MJ. Investigating the role of polymorphic variants in the catechol-O-methyltransferase (COMT) gene rs4680 (472G>A) and methylenetetrahydrofolate reductase (MTHFR) gene rs1801131 (1298A>C) and rs1801133 (677C>T) as modifiers of disability in patients with multiple sclerosis. 12th International Conference of the Society of Neuroscientists of Africa, 26–30 March 2015, Durban.


Conference Organised
PS Medicine in Africa Conference, 23–24 March 2016 – International Conference with 30 national and international speakers

Invited Speaker
- Zemlin AE, Hoffman M, Erasmus RT. E- Selectin and markers of inflammation in treatment-naïve individuals living with HIV. KACP, November 2015, Diani Beach, Mombasa, Kenya
- Zemlin AE. Writing a Research Budget and Project Management. KACP, November 2015, Diani Beach, Mombasa, Kenya
- Erasmus RT. POCT evaluations. Society of Medical Laboratory Technologists of South Africa, May 2015, Port Elizabeth
- Erasmus RT. POCT evaluations. Great Minds Meeting, 3 Nov 2015, Berlin, Germany
- Erasmus RT. Roche Forum– Panel on POCT, Johannesburg
- Erasmus RT. POCT evaluations. South African Medical Device Industry Association, 23 August 2015, Johannesburg
- Erasmus RT. Quality Management. COLABIOCLI, 23–25 September 2015, Quito, Ecuador
- Erasmus RT. POCT evaluations. Association of Clinical Biochemists of India, 2015, Chandigarh, India.

International Workshops/Conferences
- Workshop on Method Validation and POCT Curriculum – Dr Phatlane, Dr M Rensburg and Prof. Erasmus
- Scientific Writing Workshop, KACP– Professors Zemlin and Erasmus.
Research Translated to Diagnostic Technology

- Nova StatStrip is a precise and accurate point-of-care instrument for the measurement of glucose
- HbA1c not useful for detecting pre-diabetes in local communities.

Academic and Research Honours Awards

- Prof. Zemlin – C2 NRF Rating
- M Hoffman – MPath (cum laude)
- R Erasmus – Appointed Visiting Professor at the Era Medical School, Lucknow, India.

Student Supervision

- One MMed (Professors Zemlin and Erasmus)
- One MSc (Professors Zemlin and Erasmus)
- Two MTech (CPUT) (Professors Erasmus and Janse Van Rensburg)
- Five doctoral (Professors Erasmus and Janse Van Rensburg).

Students Graduated

Doctoral
Vergotine Z. Molecular investigation of genetic factors that are associated with insulin resistance and obesity in a South African population. PhD, 2015. 100 pp.

Masters
Hoffman M. E-Selectin in treatment-naive HIV. MSc, 2015. 10 pp.

MMed
Dr D Phatlane

Thesis Examined

- Masters, WSU – Prof. Zemlin
- Four BSc (Hons), University of Limpopo – Prof. Erasmus
- PhD, University of Limpopo – Prof. Erasmus
Haematological Pathology

Head: Prof. Akin Abayomi

1. DIAGNOSTIC SERVICE

The Haematological Pathology Division is SANAS-accredited and provides a 24-hour service to TBH and some of the clinics and secondary hospitals in the Western Cape. This service was expanded in April 2011 to include Eerste River Hospital and more peripheral clinics. It is also one of the referral centres for samples from the Eastern Cape, particularly from Nelson Mandela Hospital. An antenatal blood group typing service is provided to the hospital and large regions in the Western Cape, in association with Groote Schuur Hospital.

The division, in conjunction with the Pathology Research Facility, implemented the following molecular based tests in 2015:

- Acute myeloid leukaemia (AML): Screening for NPM1 (exon 12) mutations in patients with normal karyotype AML
- Chronic myeloid leukaemia: The validation of GeneXpert for detection of p210 BCR-ABL transcript in patients with chronic myeloid leukaemia was completed and implemented
- Myeloproliferative neoplasms: MPL exons 10 and CalR exon 9 mutation assay were implemented in 2015.

2. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

2.1. Undergraduate

Teaching and training of undergraduate medical students continues to be an important part of the division’s goals and priorities, and Dr Manjati serves as its undergraduate representative. It is involved with teaching and training of various undergraduate students, including MBChB I, III, IV and V, and encompasses the important basics of haematological disease. The division also involved in lectures and tutorials as part of the Essentials of Disease Processes Module which is presented to MBChB I students. Dr Manjati served on in the SU Academic Committee that conceptualised, drafted and implemented the new MBChB middle clinical rotation (MBChB 4 and 5) module.

2.2. Postgraduate

Dr R Grewal represents the division and manages the curriculum for all pathology-related postgraduate training. During the past year, the division recruited three Haematopathology registrars and one Supernumerary registrar in haematopathology. It also contributed towards the training a Clinical Pathology registrar every year, and remains involved in the training of Clinical Haematology registrars (a subspecialist degree), as well as Internal Medicine registrars rotating in Clinical Haematology every three months.

Our Pathology registrars are exposed to various modules, including Laboratory Medicine, Blood Bank, Clinical Haematology and Molecular Medicine.

We also have 11 MMED registrars under the supervision/co-supervision of Drs Grewal, Manjati, Swanepoel and Bassa from Clinical Haematology, Professors Hofmann and Zemlin from Chemical Pathology and Dr Mohammed from Anatomical Pathology.

Dr Swanepoel represents and manages the curriculum of all post-graduate science students. In 2015 the division’s third PhD student was awarded his doctoral degree under the supervision of Dr Ipp. The division currently has three MSc students under the supervision/co-supervision of Dr Grewal, Dr Swanepoel and Prof. Abayomi.

Dr Swanepoel acted as supervisor and co-supervisor for the following scientist interns as part of the Haematology and Molecular Biology Discipline Programme:

- Mr T Reid (Haematology) – Supervisor: Successfully submitted portfolio end of March 2015
- Dr B van Rooyen (Molecular Biology) – Supervisor: Submitted portfolio end of March 2015
- Dr M Sanderson (Molecular Biology) – Co-Supervisor: Submitted portfolio end of March 2015
- Dr B Nkambule – Supervisor: Submitted portfolio end of September 2015
- Dr L Paul (Molecular Biology) – Co-Supervisor: Submitted portfolio end of September 2015.
The following students graduated:

- Ms N Goqoza (Supervisor: Dr T Manjati): MTech – An audit of pre-analytical variables that affect coagulation test results in TBH
- Mr T Reid (Co-supervisor: Dr H Ipp): MSc – B cell activation in chronic HIV: novel surrogate markers and immunomodulation
- B Nkambule (Supervisor: Dr H Ipp): PhD – Platelet flow cytometry and coagulation tests as markers of immune activation in asymptomatic HIV
- Dr T Manjati (Supervisor: Dr H Ipp): MMed (Haematology) – Immune activation is associated with decreased thymic function in untreated HIV positive patients.

Specialists, postgraduate students, and medical technologists from the division attended several training courses/conferences/congresses during the year as part of continuous professional and skills development.

Laboratory staff members are also involved in the training of laboratory technologists at Karl Bremmer Hospital to assess common hematologic conditions, as well as the training of all supernumeraries who come from various countries in Africa.

<table>
<thead>
<tr>
<th>Table 56: Number of postgraduate students</th>
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<tr>
<td>MMed (Haem Path) current:</td>
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<tr>
<td>FCHAem Part 1:</td>
</tr>
<tr>
<td>FCHAem Part 2:</td>
</tr>
<tr>
<td>BSc (Hons) graduates in haematology:</td>
</tr>
<tr>
<td>MSc current:</td>
</tr>
<tr>
<td>PhD (current):</td>
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<tr>
<td>PhD graduated:</td>
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<tr>
<td>Intern scientist:</td>
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<tr>
<td>MSc graduated:</td>
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<tr>
<td>Clinical pathology:</td>
</tr>
<tr>
<td>MMED Graduate</td>
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<tr>
<td>Clinical Haematology current:</td>
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3. RESEARCH INITIATIVES AND PROJECTS

The division continued its involvement in several research initiatives. At present, there are five active research groups, namely:

- HIV Activation and Inflammation Group (HAIG)
- Tygerberg Lymphoma Study Group (TLSG)
- TB Cytokine Group
- FISHflow Research Group
- Biobanking Research Group (NSB).

There are also a number of active research projects among the division's honours, masters, PhD and MMED students. These projects are ongoing or were completed during the year.

The division is involved in several biobanking-related initiatives with the aim of making the Faculty of Medical Health and Sciences (FMHS) a centre of excellence for biobanking-related research and promoting greater understanding of biobanking technology and the ethical, legal, and social issues associated with it. Biobanking-related achievements included:

- Tygerberg NHLS/SU Biorepository (NSB) was awarded an Aids Malignancy Consortium/AIDS Cancer Specimen Resource Biorepository Grant. The NSB falls under the direction of Prof. Abayomi and Dr Swanepoel (Operational Manager) and is registered at the SU as a fully operational biobank. It is a collaboration between SU, NHLS, South African National Bioinformatics Institute (SANBI, located at the UWC), Rutgers University Cell & DNA Repository (RUCDR), Scripps Research Institute for Regenerative Medicine, and various divisions under the Pathology Department.
- The division is involved in a partnership between SANBI, the European Union and other African institutions in a multi-million rand grant to fund global research infrastructure for biobanking and bioinformatics. The European Commission, in association with the Horizon 2020 Work Programme, provisioned a budget of approximately R30 million over a period of three years for the B3Africa Initiative. B3Africa has the following strategic aims:
- Create a harmonised, ethical and legal framework between European and African partner institutions, which is essential to an acceptable informatics platform that allows sharing bio-resources and data and consolidate the Africa-EU biobank co-operation.
- Provide an ‘out-of-the-box’ informatics solution that facilitates data management, processing and sharing that can be used under challenging networking conditions in Africa and Europe.

3.1. Research Projects

The Tygerberg Lymphoma Study Group

**Project Title:** Malignant lymphoma incidence and HIV-related lymphoma subtypes in the Western Cape of South Africa

**Researchers:** EA Abayomi, R Grewal, C Swanepoel, T Reid, F Bassa, N Mohamed, S Isaacs, F Masaigwa, C Roussouw (UWC)

**Funding:** NIH, through the Sub-Sahara Africa Lymphoma Study and ACSR, CANCA-SA

**Short Description:** A multidisciplinary approach to improve the understanding of how HIV is transforming the incidence, pattern and prognosis of malignant lymphoma and define a cost-effective policy model and strategic approach to management in the Western Cape, as well as the sub-continent.

**Sub-studies for degree purposes that forms part of the TLSG**

**Project Title:** Development of a cost-effective ten-colour flow cytometry panel which will aid in the characterisation of HIV-related lymphoma’s (HRL) in the TBH catchments area of South Africa

**Researchers:** F Masaigwa (MSc student), C Swanepoel, R Grewal, B Nkambule, EA Abayomi

**Funding:** D43 Scholarship, NHLS Development Grant, Harry Crossley South to South Research Bursary

**Short Description:** This study aims to evaluate the use of an expanded immunophenotypic panel (Euroflow) in improving the understanding of how HIV is transforming the lymphoma incidence, pattern and prognosis in the TBH catchments area. The objectives are to determine the suitability of using the optimised Euroflow panels for correctly diagnosing lymphoma and leukaemia and whether optimised Euroflow panels provide a differential in the diagnosis of early HRL using the Infinicyt™ software by establishing and comparing South African population profiles to the European profiles. The study also aims to set up Infinicyt™ software APS (COMPASS) for TBH lymphoma and leukaemia cases.

**Project Title:** The incidence of Hodgkin lymphoma over a ten-year period at Tygerberg Hospital

**Researchers:** N Naidoo, N Mohamed, F Bassa, EA Abayomi, R Grewal

**Project Title:** A look at Castleman’s disease over a ten-year period at Tygerberg Hospital

**Researchers:** E Mahroug, F Bassa, EA Abayomi, R Grewal

**Project Title:** The incidence of DLBCL over a ten-year period at Tygerberg Hospital

**Researchers:** L Mazwi, N Mohamed, F Bassa, EA Abayomi, R Grewal

**Project Title:** The incidence of Burkitt Lymphoma over a ten-year period at Tygerberg Hospital

**Researchers:** E Musekwa, N Mohamed, F Bassa, EA Abayomi, R Grewal

**Project Title:** Identification of biomarkers for HIV-related lymphoma in South African populations

**Researchers:** C Rossouw, A Christoffels, EA Abayomi, J Schneider, N Mohammed, C Swanepoel, R Grewal, F Bassa

**Short Description:** A collaborative study between the TLSG and SANBI. It proposes to identify and compare protein profile signatures in HIV-related lymphoma tissues from a South African population using Matrix-assisted Laser Desorption Ionisation Mass Spectrometry Imaging (MALDI MSI). These signatures will be used to search for protein biomarkers that identify tumour tissues and tumour grade.

**Project Title:** Management of lymphoma in a centre with high HIV and TB prevalence

**Researcher:** F Bassa (PhD)

**Project Title:** A retrospective review of Hodgkin lymphoma at TBH with reference to the impact of HIV

**Researcher:** M Cass (MPhil)
Project Title: Retrospective study of the clinical features of patients with plasmablastic lymphoma at Tygerberg Hospital
Researcher: Z Solomons (MPhil)

Project Title: Mathematical modelling of early initiation of HAART to Forestall AIDS-related non-Hodgkin lymphoma in the Western Cape, South Africa: a cost-effectiveness analysis
Researcher: I Kyomugisha (MSc)
Funding: CANCA
Short Description: This is a collaborative study between the TLSG and the SU Mathematics Department.

**HIV Activation and Inflammation Group (HAIG)**

The HAIG group came to an end with the departure of Dr Ipp. It, however, still has active students and numerous outputs in the form of publications. Two subprojects are still active as collaborations between the divisions of Haematology and Virology, the Desmond Tutu HIV Centre and IDM Institute of Infectious Disease and Molecular Medicine at the UCT, and the Division of Chemical Pathology, NHLS Tygerberg.

Project Title: Development of an affordable panel of biomarkers of immune activation and inflammation in asymptomatic HIV-infection in order to identify patients at risk of accelerated disease or other complications in resource-limited settings
Researchers: H Ipp, R Glashoff, L Bekker, A Zemlin, T Reed, S Loots, S Mburu, B Nkambule
Funding: SHARP/PRF Funding
Short Description: This project aims to delineate affordable and easily measurable markers of the activation and inflammatory status of the immune system in asymptomatic HIV-infection to identify patients who may be at greater risk of progressive disease or adverse events. This would lead to the design of a panel of tests for application in resource-limited settings that have direct impact on the management of patients in the chronic stage of HIV-infection. The implementation of this approach would facilitate earlier access to treatment, ultimately assisting in delaying the onset of AIDS. A secondary objective is the identification of points of potential therapeutic interventions in the inflammatory signalling cascade and antioxidant metabolic pathways.

Project Title: Haemostasis and platelet activation in HIV
Researchers: B Nkambule (PhD student), G Davison, H Ipp
Funding: K-funding; NHLS grants
Short Description: To investigate the extent of activation of platelets in patients with HIV, together with the measurement of the blood concentrations of fibrinogen and D-dimer. The aim is to compare platelet activation in HIV patients with uninfected controls. This project includes collaboration between the Division of Haematology and CPUT’s Biomedical Science Unit. This student was awarded his doctoral degree in March 2015 on this project.

Project Title: Immune activation is association with decreased thymic function in untreated HIV positive patients
Researchers: T Manjati, B Nkambule, H Ipp
Funding: NHLS grant
Short Description: A study of untreated HIV infected and uninfected African people in Cape Town. The study questions whether thymic function would be increased or decreased in the HIV-infected group, compared to the controls; and whether there was any correlation with immune activation levels. The team developed a flow cytometry method to investigate thymic function simultaneously with levels of immune activation. To the best of their knowledge, this is the first study of this type in Africa.

**TB Cytokine Group**

Project Title: Rapid, blood and bone marrow-based TB diagnostic test which characterises and distinguishes between BCG, latent and active TB using flow cytometry by measuring intracellular cytokines released by CD4 T helper cells
Researchers: C Snyder (MSc student) R Grewal, L Mutema, EA Abayomi, C Swanepoel, F Bassa, T Reid
Funding: NHLS grants, Harry Crossley
Short Description: This project is a collaboration between the divisions of Haematology and Clinical Haematology.
**Biobanking**

**Project Title:** Development of Africa H3 Biorepositories to facilitate studies on biodiversity, disease and pharmacogenomics of African populations

**Principal Investigator:** EA Abayomi

**Co-investigators:** C Swanepoel, E Fakunle, B van Rooyen, R Grewal, A Christoffels, C Rossouw, M Sheldon, A Brooks

**Short Description:** This project is a collaboration between the division and SANBI, the Department of Chemical Physiology (UWC), Centre for Regenerative Medicine (UWJC), Scripps Research Institute (USA) and RUCDR (USA). The biorepository team set up governance, operations and test biorepository protocols for human tissue, such as nucleic acids and blood. This was achieved through the assessment of its current practices to identify strengths and weaknesses, upgrade repository practice and infrastructure and conduct validation and quality control tests for specific biospecimens. In June 2014 the biorepository became a fully functioning biorepository capable of receiving and distributing samples from and to national, African and international clients using international standards. Services include DNA extraction, sample logistic management, PBMC isolations, cell viability assays, mycoplasma PCR and storage in liquid nitrogen as well as at -80°C. The biorepository took part in an international proficiency assessment of certain assays and achieved its external quality assurance (EQA) on this level. Although the biobank is no longer funded by the NIH H3Africa project, it has just secured a new grant from B3Africa European Union as a collaborator to promote and develop a Laboratory Information Management System specific for biobanking.

**Project Title:** Evaluation and validation of room temperature biospecimen transportation and storage technologies as an alternative, cost-effective solution to cold chain logistics and storage within biobanking and/or diagnostics

**Researchers:** F Albufathi (MSc student), T Reid, S Isaacs, R Grewal, EA Abayomi, C Swanepoel

**Funding:** NIH H3Africa, EU B3Africa

**Short Description:** This is a sub-study that forms part of the biobank initiative. Room temperature technologies are being investigated as a greener, cost-effective alternative in comparison to cold chain logistics. Various room temperature storage stabilisers are being investigated over different temperature conditions and time periods to determine whether genomic integrity of samples are being maintained in the presence or absence of stabilisers.

**FISHFlow Research Group**

**Project Title:** A new paradigm using established multiplex flow cytometry for cost-effective viral load monitoring and the identification of sanctuary sites with support evolving strategies aimed at eradicating HIV infection and its multiple associated viral infectious agents, namely HPV and HCV

**Researchers:** EA Abayomi, R Grewal, T Manjati, C Swanepoel, G Jacobs, F Abulfathi (MSc student), T Reid, H Botha (IncellDx), B Patterson (IncellDx)

**Short Description:** New approaches for the monitoring and treatment of HIV are needed, specifically tests that identify the cellular location and active state of HIV, which are critical to adapting current therapies and developing new therapies for the purpose of eradication. Current plasma viral load tests are too expensive and cannot identify the source of virus or predict feeder sanctuary cellular compartments. This proposal is designed to implement technology that identifies cell-associated transcriptional activity of HIV along with cell surface markers of HIV pathogenesis to facilitate the development of new and significantly more effective, targeted treatment options. This technology, known as Simultaneous Ultrasensitive Subpopulation Staining/ Hybridization In Situ (SUSHI), was invented by Prof. Bruce Patterson from Stanford University and developed by IncellDx into an established modality for high resolution monitoring of cellular integrated viral nucleic acids. SUSHI techniques are simple and cheap and used to immunophenotype intact cells (lineage and maturity) in peripheral blood mononuclear cells (i.e. lymphocytes, monocytes, macrophages, NK cells) and other tissue-derived cells with transcriptionally active HIV. Increased levels of cellular unspliced HIV-1 mRNA are predictive of viral breakthrough well before plasma viral load or increased cell-associated HIV DNA is detectable. Identifying the cell source of actively replicating HIV allows for targeted therapy (immunologic and pharmacologic) and eradication, unattainable by current plasma viral load or CD4 counts assays. SUSHI is a single platform assay and is superior to and more economic than conventional fragmented monitoring tests of CD4 and plasma viral load using expensive real-time PCR, which rely on different and independent reaction and often different cumbersome platforms. SUSHI, and variations on this technology, is developed for HIV, HCV, HPV/cervical carcinoma, and can be adapted for MTB, as well as additional STDs as a single, centrally located cost-effective and more informative modality for diagnosis and monitoring for effective treatment options. This approach also has implications for supporting vaccine research and development (R&D). This proposal will develop local capacity in support of implementation, as well as training, research and development for clinical application in urban, suburban, peripheral and rural outposts to support effective
treatment throughout the country, irrespective of existing infrastructure. This project is a collaboration between the Division of Haematology, Department of Obstetrics and Gynaecology, and Division of Virology and IncellDx.

**Project Title**: Climate change and environmental health  
**Researchers**: EA Abayomi  
**Short Description**: Prof. Abayomi was the lead author on the health chapter in the second *South African National Communication on Climate Change* in keeping with the requirements of the United Nations Intergovernmental Panel on Climate Change. This is in collaboration with the South African National Biodiversity Institute and the Department of Environment and Water Affairs. It is a follow-up study of the long-term mitigation scenarios on climate change. Prof. Abayomi has subsequently been a collaborator on a new Africa Development Bank grant to assess the impact of climate change in three low-lying megacities in Africa – Cape Town, Lagos and Cairo, with specific responsibility for the health implications.

**Clinical Audit Projects**

**Project Title**: Vitamin B12 and folate testing in patients with normocytic anaemia or isolated macrocytosis at Tygerberg NHLS  
**Researchers**: N Davids  
**Co-supervisor**: TS Manjati

**Project Title**: An audit of pre-analytical variables that affect coagulation test results in TBH  
**Researchers**: N Goqoza (completed ethics and graduated)  
**Co-supervisor**: TS Manjati

**Project Title**: An audit on the assessment of bone marrow turnaround time  
**Researchers**: W Serfontein  
**Co-supervisor**: R Grewal, TS Manjati

**Project Title**: An audit on bone marrow aspiration and biopsy for pancytopenia  
**Researchers**: B Cochraine  
**Co-supervisor**: R Grewal, TS Manjati

**Project Title**: Post-analytical audit of flow cytometry reporting at a tertiary level hospital in Cape Town  
**Researchers**: S Irusen  
**Co-supervisor**: R Grewal, TS Manjati

**Project Title**: A five-year retrospective audit of electrophoresis test prevalence, requesting patterns, yield and related bone marrow biopsy findings at a South African tertiary hospital, 2010–2015  
**Researchers**: N Naidoo, RT Erasmus, R Grewal, AE Zemlin

4. **RESEARCH OUTPUT**

4.1. **Journal Publications**


4.2. Conference Presentations

**International (Invited Speaker)**


Abayomi AE. Biobanking and biosafety containment in the midst of a highly contagious dangerous BSL4 Category pathogen outbreak. ISBER 2015 Annual Meeting, 5–9 May 2015, Phoenix, Arizona, USA.


Abayomi AE. Attended the VI International Eurasian Haematology Congress, 14–18 October 2015, Mardan Palace Hotel, Antalya, Turkey.


Abayomi AE. Facilitator, chair of plenary session and invited speaker: Introduction by GET and WATER overview of WHO biobanking meetings Consultative Forum to Define a Biobanking and Biosecurity Agenda and Roadmap for Guinea, 8–11 March 2016, Guinea.


Abayomi AE. Biobanking governance, community engagement and ethics in Africa. Consultative Forum to Define a Biobanking and Biosecurity Agenda and Roadmap for Guinea, 8–11 March 2016, Guinea.

Abayomi AE. Governance: Round table Discussion and Recommendation [breakaway session]. Consultative Forum to Define a Biobanking and Biosecurity Agenda and Roadmap for Guinea, 8–11 March 2016, Guinea.


**Proceedings: Invited Speaker (National)**


Abayomi AE. Framework for Best Practice in Genomics and Biobanking, 23 March 2016, Spier, Cape Town.

**International Poster Presentations**

Manjati T, Nkambule B, Ipp H. Immune activation is associated with decreased thymic function in untreated HIV positive patients. Indian Ocean Rim Laboratory Haematology Congress 2015.

Medical Microbiology and Immunology

Head: Prof. A Whitelaw

1. ABOUT THE DEPARTMENT

The SANAS-accredited Division of Medical Microbiology and Immunology offers a diagnostic service in microbiology, immunology and serology to TBH, as well as surrounding regional, district and primary level healthcare facilities which refer patients to TBH.

The division is involved in teaching undergraduate students at SU and offers postgraduate degrees (BSc (Hons), MSc, PhD), as well as training of registrars in Clinical Microbiology, Clinical Pathology, Adult and Paediatric Infectious Diseases. Registrars from a number of clinical and laboratory disciplines rotate through the Immunology Division, which is headed by Prof. Esser. Student technologists and intern scientists in both Immunology and Microbiology are also trained in the division.

The team is involved in a variety of research projects, both self-initiated and as collaborators with other departments in the university, and national and international partners. There are ongoing initiatives to improve its 'footprint' in other African countries through collaborative projects, as well as through the Programme for Health Professions Training, an EU-funded African mobility scheme.

Table 57: Total number of staff per profession and highest qualification (as of 31 March 2016)

<table>
<thead>
<tr>
<th>Pathologist (incl. HoD)</th>
<th>Med Doctors</th>
<th>PhD Scientist</th>
<th>BSc Honours</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>4</td>
<td>5</td>
<td>-</td>
<td>23</td>
<td>-</td>
<td>-</td>
<td>32</td>
</tr>
</tbody>
</table>

Only includes NHLS staff, i.e. pathologists, registrars, NHLS scientists and technologists

2. DIAGNOSTIC SERVICE

Consultants and registrars offer a comprehensive consultative service, including 24-hour on-call availability, ward rounds in ICUs, clinical meetings and antibiotic stewardship ward rounds. The division’s ability to expand these services was limited due to staff constraints. Dr Maloba was a welcome addition to the team in January 2015. However a second vacant pathologist post remained unfilled until March 2016, when the division was pleased to welcome Dr Pienaar. The prolonged vacancy, combined with the conversion of one fulltime post to 5/8 in January 2016 presented ongoing challenges. This was exacerbated by the resignation of the scientist in December 2015, although the post has subsequently been filled. Despite these challenges, the division was able to recommence on-site clinical rounds at Khayelitsha District and Worcester hospitals.

The Immunology consultant provides a clinical service in immunology, in collaboration with the Paediatric and Adult Infectious Diseases Services at TBH. A further weekly clinical service is provided at the Paediatric and Adolescent Rheumatology Clinic at TBH. Both these services include a weekly outreach clinic, extensive telephone and e-consulting to advise on further investigations, as well as participation at ward rounds and presentations at academic functions.

Members of the division continue to be involved in antibiotic stewardship governance committees at hospital, provincial and national levels, as well as other provincial and national bodies. These include the Microbiology, Immunology and Clinical Pathology expert committees and subcommittees, the SA Society of Clinical Microbiology, the NHLS Microbiology Advisory Committee, the Provincial Antimicrobial Stewardship Committee and visiting team, the Infection Control Society of Southern Africa, and the Federation of Infectious Disease Societies of Southern Africa. The Immunology Unit is also represented on the South African Immunology Society’s Education Committee, the Primary Immunodeficiency Working Group of ALLSA, The Board of the African Society for Primary Immunodeficiencies, and the Board of the HIV Outreach Programme and Education (HOPE) NGO.

The shortage of technologists, due to both resignations and illness, was felt acutely in 2015. Fortunately all vacant technologist posts had been filled by the middle of March 2016. The laboratory was re-accredited by SANAS in August 2015, and two molecular tests were successfully added to the accreditation schedule.

Specimen volumes in the routine laboratory were similar to the previous year (approximately 2% increase). TB culture volumes were also similar. However, the volumes of GeneXpert tests increased markedly (41% increase), which may be due to increased use of the assay for extrapulmonary and paediatric TB, as well as collaboration with diagnostic research projects.
The new laboratory information system, TrakCare, was rolled out to TBH and the rest of the province in 2015. There were a number of challenges related to adjusting workflows and becoming familiar with the new system. While many of these challenges have been overcome, this is an ongoing process.

In conjunction with the NHLS Groote Schuur, a provincial policy regarding acceptance and rejection criteria for pus swabs was developed and circulated in 2015. This has been implemented, and its impact on volumes and specimen quality will be monitored.

### 3. TEACHING AND TRAINING AND PROFESSIONAL DEVELOPMENT

#### 3.1. Undergraduate

The division is involved in undergraduate student training, including lectures for MBChB students and BSc dietetics students. Additional tutorials are offered to students based at the Rural Clinical School in Worcester and final year students at TBH. These tutorials are focused on antibiotic stewardship and appropriate laboratory use, and are held in collaboration with the Infectious Disease Division and Department of Pharmacology. Dr Hoffmann represents the Department of Pathology on the Undergraduate Programme Committee.

#### 3.2. Postgraduate

The division was re-accredited for specialist training by the HPCSA in August 2015. It is also accredited with the HPCSA to train intern medical scientists in both Microbiology and Immunology specialities; however no intern scientists were employed in 2015.

The division has five registrars specialising in Clinical Microbiology, one of whom successfully completed the MMed part I in 2015. One candidate attempted the final CMSA examination in 2015, but was unfortunately unsuccessful. Clinical Pathology and Infectious Disease registrars rotate through the division. The division also contributed to the Postgraduate Diploma in Infection Control offered by the Unit for Infection Prevention and Control at SU.

Pathology registrars from other divisions, such as Adult and Paediatric Infectious Diseases fellows and trainees from UCT and Red Cross Children’s Hospital, as well as experiential students from the UWC rotate through the Immunology Unit.

Members of the division are involved in supervising BSc (Hons), MSc and PhD students, and contribute to the lecture and tutorial programme offered to the BSc (Hons) students, as well as one of the modules of the Masters in Clinical Epidemiology, offered by the Centre for Evidence-based Healthcare. In February 2016, the division admitted its first MSc student from Ghana under the Programmes for Health Professions Training in Africa Scheme, funded by the Education, Audio-visual and Culture Executive Agency of the EU.

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>13</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

Includes registrars, BSc Hons, MSc, PhD as at 31 March 2016

### 4. RESEARCH ACTIVITIES

The division continued to build on a number of well-defined research themes, developing both capacity and expertise, and ensuring that the research objectives meet national priorities. These themes were:

- Laboratory diagnosis of infectious disease, including TB
- The epidemiology and pathogenesis of staphylococcal infections
- Diagnosis, epidemiology and impact of antimicrobial resistance
- Detection and management of primary immunodeficiencies.

#### 4.1. Research Units/Study Groups Linked to the Department

**Project Title:** The Primary Immunodeficiency Registry of South Africa  
**Investigator:** M Esser  
**Short Description:** The registry continues to promote the networking for laboratory diagnosis and treatment of patients with primary immunodeficiencies. This ongoing study is starting to reflect individual patterns of immune deficit specific to South African, with a high prevalence background of infectious diseases.
**Project Title**: Global antibiotic resistance prescribing in children (GARPEC)
**Local Investigators**: A Whitelaw, A Dramowski, H Finlayson, H Rabie
**Principal Investigator**: M Sharland, St George's University, London
**Short Description**: This study aims to establish a network of paediatric centres globally who will be able to collect data on bloodstream infections (BSI) in children, as well as antibiotic prescribing practices, in order to understand the burden of BSI in this population, and to formulate recommendations to guide local practices.

**Project Title**: Burden of antibiotic resistance in neonates from developing societies (BARNARDS)
**Local Investigators**: L Paterson, A Whitelaw, K Hoek, S Mehtar, A Bulabula
**Principal Investigator**: T Walsh, University of Cardiff
**Short Description**: This multi-country study will describe the role of maternal transmission of Gram-negative bacilli to neonates, with a focus on the epidemiology and transmission dynamics of multi-resistant organisms.

**Project Title**: The AFROStrep Study: A surveillance system for group A streptococcal infection in South Africa
**Investigators**: B Mayosi (Principal Investigator), M Engel, D Barth, A Whitelaw, M Nchabeleng
**Short Description**: This group is developing surveillance systems for both streptococcal pharyngitis and invasive streptococcal infection. This will allow for a better understanding of the burden of disease, facilitate studies evaluating the impact of new diagnostic tests, and allow for a description of the epidemiology of circulating strains which may inform current and future vaccine development.

### 4.2. Research Projects

**Ongoing projects**

**Project Title**: Characterisation of a novel staphylococcal cassette chromosome mec element (SCCmec) identified at Tygerberg Hospital
**Supervisors**: K Hoek, A Whitelaw
**Student**: K Nel (MSc)

**Project Title**: Are we bottling it up in ‘vein’? An audit of blood culture practices at a district hospital in Cape Town
**Investigators**: MS Abrahams, H Orth

**Project Title**: Evaluation of real-time PCR assays to diagnose *Pneumocystis jirovecii* pneumonia and analysis of the molecular epidemiology
**Supervisor**: A Whitelaw, K Hoek
**Student**: D Banda (MSc)

**Project Title**: Birth cohort study to focus on the immune and environmental risk parameters of HIV-exposed infants
**Investigators**: M Esser, M Cotton (KIDCRU)
**Funding**: Peter Wall Institute of Advanced Studies from and in collaboration with the University of British Colombia.

**Project Title**: A model of care – the role of the HOPE Cape Town Community Health Worker (HCHW) in preventing and reducing HIV treatment failure in children in the Delft Community, Western Cape
**Investigator**: M Esser, J Cunningham

**Project Title**: Rheumatoid factor-negative polyarticular-onset juvenile idiopathic arthritis in a mixed racial South African cohort
**Supervisor**: M Esser
**Status**: Study in conjunction with Department of Paediatrics and Child Health, completed in December 2013, thesis in preparation for MMed.

**Project Title**: A genomic and bioinformatics analysis of candidate genes underlying early onset SLE in a South African family
**Co-investigator**: M Esser (Study in conjunction with Nephrology Department, UCT)
Project Title: Identification of novel candidate genes for susceptibility to tuberculosis by identifying disease causing mutations in individuals with primary immunodeficiencies
Principal Co-Investigators: M Esser, G Kinnear (Department of Molecular Medicine and Genetics)
Other Investigators: E Hoal, M Moller, M Schoeman, M Urban, M Esser
Short Description: Study in conjunction with Nephrology Department, UCT. This interdepartmental study investigates patients with suspected genetic immunodeficiencies for mutations relevant to susceptibility to tuberculosis in a TB-endemic region.

Project Title: Stool samples for the rapid diagnosis of tuberculosis in children
Supervisor: K Hoek, E Walters, R Warren
Student: C Bosch (MSc)

Project Title: Investigation of the oral and gut microbiome of patients with metabolic syndrome
Supervisor: K Hoek, A Whitelaw
Student: J Pekeur (MSc)

Project Title: The role of AGR type and AGR functionality in bacterial physiology and clinical disease in Staphylococcus aureus
Investigators: M Newton-Foot, A Whitelaw, K Hoek, J Taljaard, H Rabie, R Warren, K Nel van Zyl

Project Title: Population structure and biofilm formation of Pseudomonas aeruginosa isolated from patients with severe burn wounds and cystic fibrosis at Tygerberg Hospital
Supervisors: K Hoek, M Newton-Foot, A Whitelaw
Student: B van Biljon (MSc)

New Research Projects

Project Title: The epidemiology of ESBL-production in Enterobacteriaceae with chromosomal beta-lactamases
Supervisors: K Hoek, A Whitelaw
Student: L Paterson (BSc Hons)
Funding: NHLS Research Trust Development Grant
Short Description: This study described the prevalence of ESBLs in a collection of isolates with chromosomal beta lactamases, and includes a preliminary evaluation of the reliability of different phenotypic methods for detecting these enzymes. It described the molecular epidemiology of the ESBLs.

Project Title: The Contribution of outer membrane porin expression to ertapenem resistance in Enterobacter isolates from Tygerberg Hospital
Supervisors: K Hoek, A Whitelaw
Student: J Sieberhagen (BSc Hons)
Funding: TBC
Short Description: A collection of ertapenem non-susceptible Enterobacter isolates were studied to describe the mechanism of carbapenem resistance.

Project Title: B-lactam resistance mechanisms in Enterobacter spp. isolates from Tygerberg Hospital
Supervisors: M Newton-Foot; A Whitelaw
Student: Ms D Okyere (MSc)
Funding: TBC
Short Description: This study will build on the provisional results of the two above studies, and in particular will take the description of the mechanisms of ertapenem resistance forward.

Project Title: A point-prevalence study of adult in-patients to determine colonisation with carbapenemase-producing Enterobacteriaceae in TBH
Supervisors: R Hoffmann, K Hoek
Student: P Nel (MMed)
Funding: NHLS Research Trust Development Grant
Short Description: This point-prevalence survey of all adult in-patients at TBH will describe the prevalence of faecal carriage of carbapenem-resistant Enterobacteriaceae.

Project Title: The epidemiology and clinical impact of Gram-negative bacteraemia at Tygerberg Hospital
Funding: NHLS Research Trust Development Grant
Supervisors: A Whitelaw, M Newton-Foot
Student: L Paterson (MSc)
Short Description: This study will characterise all bacteraemic isolates of Klebsiella pneumoniae and Escherichia coli, describe the underlying beta-lactam resistance mechanisms (if present), and describe the clinical presentations and outcomes of the patients.

Project Title: Percutaneous pericardioscopy in TB pericarditis: Improving the diagnostic yield and gaining new insights into the pathogenesis of TB pericarditis
Investigators: C Kyriakakis (PhD student), G Doubell, A Whitelaw, M Newton-Foot, C Rautenbach
Short Description: This study, housed in the Cardiology Department, will evaluate a range of diagnostic approaches for TB pericarditis among patients presenting with pericardial effusions.

Project Title: An epidemiological study of acute respiratory tract infections in Harare, Zimbabwe
Supervisors: A Whitelaw, P Miles (University of Nottingham)
Student: R Mapondera (MSc Clinical Epidemiology)
Short Description: This study, based in Harare, Zimbabwe, used routine laboratory data to identify patients with suspected respiratory infections and then described the clinical, microbiological and epidemiological features of the patients.

Project Title: Multiplex real time polymerase chain reaction for organism detection in community acquired pneumonia in adults in Tygerberg Hospital
Investigators: S Brett (MMed), A Whitelaw, M Newton-Foot, B Allwood, H Kreuger (BSc Hons)
Funding: TBC
Short Description: This study aims to describe the clinical characteristics and outcomes of a cohort of adult patients admitted to TBH with acute community-acquired pneumonia, and will describe the aetiological agents detected using both culture and a multiplex real-time PCR assay.

Project Title: Molecular epidemiology of S. aureus in Northern, Central and Southern Africa
Investigators: A Whitelaw, G Revathi, A AbouElfetouh, M Newton-Foot, K Nel van Zyl, G Omuse, M Al-Seqely
Funding: NRF
Short Description: This study aims to describe the molecular characteristics (based on MLST, spa-typing and SCC-mec typing) of clinical S. aureus isolates from Nairobi, Kenya and Alexandria, Egypt, and compare these results to what is known about the molecular characteristics of isolates from South Africa.

Project Title: Evaluation of two molecular methods to rapidly identify Staphylococcus aureus and methicillin resistance from positive blood cultures
Investigators: K Reddy (MMed student), A Whitelaw, M Newton-Foot, Dr K Hoek
Funding: NHLS Research Trust Development Grant
Short Description: This study is evaluating the performance of the GeneXpert SA/MRSA assay to rapidly identify and differentiate between methicillin susceptible and resistant S. aureus from positive blood cultures. Clinical data are being collected to describe clinical practice in relation to a positive blood culture, and possibly predict the likely clinical benefit of this technology.

4.3. Grant Funding

New awards in 2015/2016:

NHLS Research Trust Development Grant x 3; NRF x 1 (SA-Egypt collaboration)
5. RESEARCH OUTPUT

5.1. Journal Publications (Subsidised)


Journal Articles (Non-subsidised)


5.2 Masters Completed


Wilcox SV. Molecular diagnostic approach to determine the degree of photo-aging of the skin. *MSc GeneeskWet* 2015; p 127

5.3. Conference Presentations

Oral Presentations

*International*

- 3rd Workshop on Diagnostics of Immunodeficiencies 2015 22–24 June 2015, Kirchzarten, Germany
- International Primary Immunodeficiencies Congress (IPIC) 2015, 5–6 November 2015, Budapest, Hungary

*National*

- 6th FIDSSA Congress, 5–8 November 2015, Drakensberg
- PS Africa Congress 2016, 23–24 March 2016, Cape Town
- FMHS 59th Annual Academic Day 2015, 13 August 2015
- UCT Division of Family Medicine Conference for General Practitioners, 18–22 January 2016.

Poster Presentations

*International*


*National*

- NHLS PathReD, 15–16 April 2015, Johannesburg
- 6th FIDSSA Congress, 5–8 November 2015, Drakensberg
- FMHS 59th Annual Academic Day 2015, 13 August 2015.

6. ADDITIONAL INFORMATION

6.1. Outreach and Visitors

The division hosted an exchange student from McMaster University in Canada, as well as a student from Alexandria, Egypt as part of the NRF-funded exchange programme.

Prof. Esser was promoted *ad-hominem* to Associate Professor in June 2015. She is one of the founder members of the NGO, HOPE Cape Town (founded in 2001), which strives to improve the quality of life and full potential of children and families affected by HIV/AIDS and related illnesses through its work in the Western Cape.
HOPE Cape Town operates exclusively in the Western Cape, specifically in primary healthcare facilities in 18 low-income communities in the northern part of the Cape Town metropole, with an office in the children wards at TBH. The organisation’s beneficiaries includes people of all age groups who are infected with or affected by HIV/AIDS, as well as their families and fellow community members, but the main focus is on children who are infected or affected by HIV/AIDS. HOPE Cape Town attaches great importance to partnerships and co-operation with the Health Departments of the City of Cape Town and the Western Cape, as well as with local NGOs and Community-based organisations that work in the same field. The HCHW’s at TBH are now trained breastfeeding counsellors and promoters and are regularly involved in giving breastfeeding education. HOPE staff hosted a GO-Box project at Tygerberg Children’s Hospital and at community level. This is an early childhood development programme working with HIV positive children, and HOPE Cape Town has contracted a project-specific, registered occupational therapist. The NGO also offers counselling and therapeutic group work services by a registered social worker to HIV positive children at TBH and in the communities, and provides supplementary food for caregivers in TBH wards as well as food parcels for those in need when they are discharged.

The popular HOPE Elective Student Programme introduces international medical students to the reality of paediatric medicine in Cape Town, both at TBH and in the surrounding communities. This is done in partnership with KIDCRU.

In one of the 16 communities where HOPE Cape Town is operational with a total of 23 community health workers, it is specifically involved with innovative approaches to developing sustainable projects in the crime-riddled, marginalised community of Blikkiesdorp. Here HOPE Cape Town doctors, along with an outreach doctor from TBH are involved in running the Paediatric ARV Clinic at the Delft Community Health Centre.

To address the new challenges of successful and uninterrupted chronic HIV care, the HOPE TO HOME project was launched at TBH in July 2015 to bridge the gap between in-patient and out-patient community care of children who are discharged.
1. ABOUT THE DIVISION

The Medical Virology Division delivers a comprehensive diagnostic virology service, including virus isolation and an extensive repertoire of serological and molecular assays, with a special focus on antiretroviral drug resistance testing. Staff, postdoctoral fellows and postgraduate students are successfully conducting research on several themes, often with national and international collaborators. While HIV accounts for a major portion of routine diagnostic tests and is the focus of several research areas, a number of additional research activities are being pursued.

The division was awarded a grant by the MRC as the TBH-MRC Collaborating Centre for HIV Laboratory Research (TygHIVLab). Within the collaborating centre, three specific research projects are being pursued:

- Evaluation of novel monitoring approaches for ART success
- Study of HIV persistence in patients on long-term antiretroviral therapy
- Characterisation and pathogenesis of HIV-1 in neurocognitive disorder (HAND) in South Africa.

Following the success of the first meeting of the Point-of-Care Testing Research Network Africa, organised by several senior members of the Pathology Department in February 2015, it was decided to organise follow-up conferences, albeit with a wider scope. The PS Africa Congress 2016 (http://www.psafrika.org) was held on 23–24 March 2016, again in Cape Town, under the motto ‘Leveraging Point of Care Testing and Personalised Medicine to Advance Healthcare’; P4 Medicine stands for ‘predictive’, ‘preventative’, ‘personalised’ and ‘participatory’; this represents a systems approach to medicine, based on the co-ordinated use of technological developments, including genetic testing, molecular analyses, computational tools, etc. While P4 medicine is likely to revolutionise healthcare, the question is in how far it will also benefit those outside well-resourced settings. We therefore complemented the four P’s with a fifth, for ‘Point-of-Care testing’ (PoCT). While PoCT is experiencing rapid development with more and more tests becoming available clinically, much remains to be discussed regarding its integration into the healthcare system. The PS Africa Congress 2016 attracted over 150 delegates from around the world for a highly interesting scientific programme complemented by an industry exhibition that received much interest. Further such meetings will surely follow.

TBH Virologist, Dr Jean Maritz, was invited to participate in the HIV Early Infant Diagnosis (EID) Consortium organised by the African Society for Laboratory Medicine (ASLM) and the London School of Hygiene and Tropical Medicine (LSHTM), while his colleague Prof. Gert van Zyl continues to serve on the Western Cape’s Third-Line Antiretroviral Treatment Committee and the NHLS’s HIV Drug resistance Testing Subcommittee.

Our ongoing investigation into HIV-1 diversity indicates that the HIV-1 subtype C epidemic is slowly changing, with the increased detection of unique recombinant forms (URFs), as well as a possible new complex circulating recombinant form (CRF) to the different provinces. Further investigations with Cameroonian collaborators expanded the characterisation of HIV-1 to include Group O sequences. The team thus has access to a wide variety of HIV-1 subtypes from at least two of the groups, M and O. Investigating sequences obtained from the start of the epidemic in the early 1980s allowed the research team, together with its collaborators in KwaZulu-Natal, to date the origin of the HIV-1 subtype C epidemic in southern Africa and specifically South Africa to around 1960, while dynamic reconstruction revealed strong growth during the 1970s and 80s.

With collaborators from TBH, the division investigated HIV-1 positive women co-infected with human papillomavirus (HPV). This study, initiated by Dr Zeier, showed that antiretroviral therapy (ART) reduces cervical HPV infection in a time-dependent and immunologically mediated manner. Reducing cervical HPV infection in women living with HIV infection should be seen as one of the many benefits of initiating ART.

The BSL3 Laboratory received provisional accreditation from the Department of Agriculture, Forestry and Fisheries (DAFF) during 2015 and is being managed as such already. The laboratory will be fully operational as a biosafety level 3 laboratory (pending the final outstanding validation document).

Table 59: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3</td>
<td>2</td>
<td>9</td>
<td>4</td>
<td>18</td>
</tr>
</tbody>
</table>

Table 59: Total number of staff per profession and highest qualification
2. DIAGNOSTIC SERVICES

The Diagnostic Section’s workload decreased slightly in comparison with the previous year, to a total of 273,862 tests. This is mostly due to the fact that the herpes simplex virus antibody testing is now complete for the first stage of the PopART trial. The section tested 7,560 serum specimens from the Western Cape as part of the annual HIV Antenatal Survey for HIV and syphilis.

The Diagnostic Section was once again highly profitable. A number of new assays have been accredited, namely Epstein Barr virus (EBV) viral load; hepatitis B virus (HBV) PCR, viral load and genotyping; hepatitis E virus (HEV) PCR as well as IgG and IgM antibody testing; and qualitative PCR assays for parvovirus B19, a panel of 16 respiratory viruses, and polyomaviruses JC and BK.

The excellent quality of the work done by the Diagnostic Section was once again confirmed during the annual SANAS accreditation visit and is reflected in the good results obtained in various external quality assurance programmes. Turnaround times were affected negatively by various issues, including being severely short-staffed and the implementation of TrakCare.

As the only NHLS laboratory in the coastal region performing routine cell culture and virus isolation, TBH continues to provide training for registrars and student medical technologists from Groote Schuur, as well as infectious diseases sub-specialist trainees. TBH is also the only laboratory in the whole country still performing Coxsackie virus neutralisation assays and one of only a few NHLS laboratories to perform HIV drug resistance testing for routine diagnostic purposes. Prof. Van Zyl serves on a sub-committee of the NHLS Virology Expert Committee to help develop additional capacity for HIV drug resistance testing in the NHLS.

One medical technologist, one laboratory assistant and one registrar resigned and one laboratory clerk retired. New staff members include one medical technologist, transferred from Immunology, and one from Groote Schuur, one registrar and one laboratory clerk. The division struggled to fill technologist posts as the salary does not seem attractive for most applicants.

3. TEACHING AND TRAINING

3.1. Undergraduate

The division’s medical staff have significant teaching commitments in various modules of the faculty’s MBChB and Allied Health Sciences programmes, and one of the virological pathologists acts as chairperson for the MBChB IV Infectious Diseases and Immunology Module.

3.2. Postgraduate

The postgraduate platform comprises registrars in Medical Virology, Medical Microbiology and Clinical Pathology, plus Infectious Diseases (ID) sub-specialty trainees. The diagnostic platform provides training specifically on the assays only performed at TBH for Virology registrars, student medical technologists and ID sub-specialty trainees from Groote Schuur.

The Virology registrar who joined the division in January 2015 resigned after her first year, finding Virology too academic, and was replaced with another candidate. An intern scientist was appointed in April 2015. Two intern medical technologists were in training in 2015/16, of whom one resigned as he wanted to pursue another career. The other wrote his examination March 2016 with results pending. Another intern medical technologist was appointed in February 2016.

A total of 11 PhD students, 13 MSc students, six BSc Honours students and four MMed Medical Virology candidates (registrars) were enrolled during the reporting period. Many of them received bursaries from the Poliomyelitis Research Foundation, the NRF, the MRC and other funding bodies. In addition, a number of postgraduate students, registered in other divisions, departments and faculties, were co-supervised. Four BSc Honours students, five MSc students and two PhD students graduated during the reporting period.

The BSc Honours course was extensively revised and updated, sharing some parts, such as Molecular Biology, with the Medical Microbiology one.

Additional teaching and training activities comprise the South-to-South Partnership for Comprehensive Paediatric HIV Care and Treatment, the Postgraduate Diploma in Infection Control, the Immunology Interactive Forum, which includes both basic and advanced aspects of immunology, the HIV Management Diploma course, the BSc (Physiology) course at SU main campus and the Diploma in Tropical Medicine and Hygiene course at the London School of Hygiene and Tropical Medicine.

The division again hosted several foreign students, including some through the German Academic Exchange Service (DAAD) RISE Internship Programme for undergraduate students. These foreign elective students spent between six weeks and three months experiencing a very active laboratory work programme with all its aspects, mostly working on existing research projects. While this provides exciting opportunities for these students to experience laboratory research in action, it also allows the division to pursue small projects that would not fit easily into postgraduate projects, due to being too small, too exploratory or too applied.
Table 60: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>37</td>
<td>11</td>
<td>11</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Professional Development**

- Four BSc Honours, five MSc, Two PhD
- Four BSc Honours, three MMed, ten MSc, 12 PhD, two Postdoctoral Fellows
- Two NRF internships completed.

## 4. RESEARCH ACTIVITIES

The division’s research areas encompass a number of relevant themes, with special emphasis on HIV as a major health problem in South Africa and the region.

### 4.1. Research Projects

**Project Title:** Molecular characterisation and diversity of HIV

**Researchers:** S Engelbrecht, RH Glashoff, E Vardas, GB Jacobs (NRF Early Career Advancement Award), S Moyo, D Njenda, V Ruhanya (PhD students), S Kiewietz, AEA Obasa, SG Mikasi and JO Gichana (MSc students)

**Collaborators:** S Seedat (Department of Psychiatry, TBH), T de Oliveira and E Wilkinson (Africa Centre for Health and Population Studies, UKZN), J Joska (Department of Psychiatry, UCT), R Paul (Department of Psychology, University of Missouri, St. Louis, USA), A Sönnerborg and U Neogi (Karolinska Institute, Sweden), G Ikomey (Center for the Study and Control of Communicable Diseases, Faculty of Medicine and Biomedical Science, University of Yaoundé I, Cameroon)

**Funding:** PRF, SU, NHLS Research Trust, NIH, MRC, NRF, HIV Trust (UK)

**Short Description:** One of the features of HIV-1 is its extreme genetic diversity, which impacts on diagnostic assays, antiretroviral treatment, prevention and vaccine development. Although HIV-1 subtype C strains predominate in South Africa, it is essential to study HIV-1 on an ongoing basis to gain a better understanding of the viruses in circulation. There is a need for more near-full-length genome sequences, as partial HIV-1 sequences may underrepresent viral recombinant forms. We are currently investigating more than 100 unique (URF) and also one possible circulating recombinant form (CRF) using both Sanger and next-generation sequencing techniques. It is still unclear what role these unique strains will play in terms of antiretroviral treatment in the long term and what challenges they will pose to vaccine development. It therefore remains vitally important to monitor HIV-1 diversity in South Africa and worldwide as the face of the epidemic is continually changing. Although South Africa is the country with the highest number of HIV-1 infections, there is limited knowledge on the origin of the subtype C epidemic in the country. Having access to samples dating from 1984 to date, we could investigate the origin and history of HIV-1 subtype C in southern Africa. During this study we identified the first transmission clusters of HIV-1 in South Africa. The results from this study are unique in that they show that HIV-1 subtype C was circulating in the Cape Metropolitan area prior to the first documented cases of heterosexual acquired HIV-1 subtype C in the late 1980s. The origin of the HIV-1 subtype C epidemic in southern Africa and South Africa was placed around 1960 (95% HPD 1956–64), while dynamic reconstruction revealed strong growth during the 1970s and 80s (Wilkinson et al., 2015).

**Project Title:** Immunological aspects of HIV-1 infection: cellular role players and biomarkers of immune activation and impact of co-infections on acquisition risk and pathogenesis

**Researchers:** R Glashoff, S Engelbrecht, E Vardas (Medical Virology TBH/Lancet Laboratories, Johannesburg), H Ipp (PhD student), D de Swardt (PhD student, to graduate 2016), K Poovan (PhD student, graduated MSc 2015), S Naidoo (PhD student), E Teer (PhD student, registered in Physiology)

**Collaborators:** M Cotton (KidCru, Department of Paediatrics, SU and TBH), A Zemlin (Division of Chemical Pathology, NHLS Tygerberg), L Bekker (Desmond Tutu HIV Foundation/UCT)

**Funding:** PRF, NHLS Research Trust, NIH

**Short Description:** Several projects are currently studying immune activation and inflammation in chronic HIV infection and its impact on immune cell numbers, phenotypes and function. The impact of immune activation on both B and T cell subsets and function are being evaluated. An important component of the research is assessment of innate immune role players; particularly monocytes and dendritic cells (DC) and their cellular products. More recently, the immune status of HIV-infected infants treated early and the relationship of immune biomarkers to viral reservoirs are being studied.
Recent work has shown that dendritic cell (DC) depletion (both pDC and mDC) in chronic HIV-1 infection is exacerbated by active pulmonary TB disease. The TNF-α receptor 2 (TNFR2) has been highlighted as an important DC-specific marker that is upregulated in chronic HIV-1 infection. DC function, as measured by Toll-like receptor (TLR) stimulation by cognate ligands, appears not adversely affected in HIV infection. Increased migration from peripheral blood and/or increased death due to apoptosis is likely the primary cause of the depletion. The relationship of increased TNF-α in TNFR2 upregulation is currently under investigation.

The inflammatory CD14+16+ monocyte subset is increased in chronic HIV-1 infection. We have shown that the inflammatory monocyte subset is potently phagocytic for red cells. The expanded CD14+16+ subset has also been shown to display increased markers of gut translocation. This subset also shows increased IL-10 production following stimulation, implicating it in attempted dampening of inflammation and HIV control (publication in preparation).

Markers of immune exhaustion/dysfunction in T cells have been investigated in the context of chronic HIV-1 infection and TB-HIV co-infection. We have shown significant TB-associated increases in Tim-3 and PD-1 on CD8+ T cells, and immune activation directly implicated in driving this expression. We are currently investigating Tim-3 in more detail with regard to functional responsiveness of CD8+ T cells. In addition, other negative regulators of T cell function, i.e. Lag-3 and 2B4, are being investigated in both CD4+ and CD8+ lymphocytes in chronic HIV-1 infection with and without TB co-infection. 2B4 appears a promising marker – significantly upregulated in chronic infection – an independently regulated from PD-1 and Tim-3.

Early ARV treatment of children is important for controlling the HIV reservoir. Collaborative research using the CHER cohort (KIDCRU) is examining the relationship of immune status (cell numbers, phenotypes and serum biomarkers) to latent viral reservoir (as measured by cell-associated DNA (CAD) and viral outgrowth. A PhD student is working on this and will receive advanced training at Pittsburgh during 2016.

A major thrust of all this research is to define novel, cost-effective surrogate markers of immune activation for use in the South African setting, and to investigate potential therapeutic agents or intervention strategies to minimise activation-associated immune dysregulation. Aligning biomarker research to latent reservoir readouts is important for implementation of ‘cure’ approaches in future.

Project Title: Investigation of viral respiratory pathogens in cases of sudden unexpected death in infants (SUDI) in the Cape Town metropole
Researchers: C de Beer, H la Grange (MSc student, graduated), D Matshazi (MSc student), D Cupido (NRF Intern)
Collaborator: J Dempers (Department of Forensic Pathology/Western Cape Forensic Services, TBH)
Funding: PRF, NHLS Research Trust, NHLS K-funding, Harry Crossley Foundation, MRC SIR
Short Description: The majority of SUDI cases occur in infants between one and six months of age. Inflammatory changes in the upper and lower respiratory tract are a frequent finding and respiratory tract infection in the days preceding death have been documented repeatedly. Furthermore, viral respiratory infections have commonly been found in autopsy samples.

So far, a total of 148 cases have been investigated. A high percentage showed evidence of bacterial and/or viral pathogens. Histological findings suggest infection in a high percentage of the SUDI cases. In addition, the highest number of SUDI cases in this study appeared in the colder months, which is consistent with the literature. The study was able to confirm the presence of bacterial and viral pathogens in SUDI cases, but the extent to which these contribute to death needs to be elucidated.

An extension of this study investigates lung tissue for viral pathogens using Luminex assays, as well as immunological biomarkers of infection.

Project Title: Human Papillomavirus
Researchers: RH Glashoff, S Engelbrecht, GB Jacobs (NRF Career Advancement Fellow), S Isaacs
Collaborators: M Zeier (Infectious Diseases Clinic, TBH), H Botha, (Gynaecological Oncology Unit, TBH) A Giuliano (Moffitt Cancer Research Institute, Tampa, USA)
Short Description: The role of sexually transmitted infections (STI) and human papillomavirus (HPV) in HIV-1 acquisition is being investigated in a collaborative clinical study. This study serves as a precursor to investigating HPV vaccination in young women as a preventative strategy for preventing HIV-1 acquisition (EVRI study). A phase III trial is planned for 2015/16. The current research is focusing on HPV detection and genotyping to assess prevalence and subtype distribution in a cohort of young sexually active women in the Western Cape.

The most important finding so far is the extremely high prevalence of both HPV and STIs in young females in the Western Cape. The prevalence of STIs such as syphilis, gonorrhoea, chlamydia and HSV-2 was also determined. STI prevalence was high, with 6.2%, 10.9%, and 32.8% testing positive for syphilis, gonorrhoea, and chlamydia respectively, and 46.5% positive for HSV-2 antibodies. Prevalence of at least one of 37 HPV types was 86%, with 64% harbouring >2 concurrent HPV types. Future work will target investigation of immune status and inflammation in the female genital tract.
We demonstrated the feasibility of conducting randomised placebo controlled trials of HPV vaccines among South African women at high risk for HIV infection. However, given the high burden of STIs, phase III HIV prevention trials need to intervene at young ages and must screen and treat multiple STIs concurrently to have a measurable impact on HIV acquisition.

HIV-infected women have an increased risk for the development of invasive cancer and the lack of consensus on the effect of cART on cervical HPV infection provided us with an opportunity to conduct a large prospective cohort study. Using advanced and more robust statistical techniques, we compared the effect of cART on each individual HPV genotype to the effect that cART has on HPV-16. We found that cART reduced cervical HPV infection in a time-dependent and immunology-driven manner. Reducing cervical HPV co-infection in women living with HIV infection should be seen as one of the many benefits of initiating ART (Zeier et al., 2015). In an international collaboration, we also assessed the feasibility of conducting a phase III HIV prevention trial using a multivalent human papillomavirus (HPV) vaccine. Literature suggests that similar to HSV-2 and bacterial STIs, HPV infection may increase susceptibility to HIV-1. Results from this study demonstrated the feasibility of conducting future HPV vaccine trials to reduce HIV acquisition in high-risk populations and highlighted the need to intervene at an early age and concurrently screen and treat multiple STIs (Guiliano et al., 2015).

**Project Title:** The role of cytokines and impact of HIV on the severity and pathogenesis of necrotising enterocolitis

**Researchers:** C de Beer

**Collaborators:** S Moore and M Arnold (Paediatric Surgery, TBH and SU)

**Funding:** PRF, NHLS Research Trust

**Short Description:** Necrotising enterocolitis (NEC) pathogenesis remains elusive, although the cytokine inflammatory cascade remains important in its pathophysiology. Maternal HIV infection has been identified as an independent risk factor, associated with increased mortality. This may relate to the enhanced endothelial activation and inflammation in HIV infection. Pro-inflammatory interleukin (IL)-12 and IL-18 have been implicated in NEC pathogenesis. IL-10 is a marker of severe NEC, while the anti-inflammatory IL-10 is protective against NEC. These inflammatory and counter-inflammatory proteins are similarly implicated in HIV-related immune modulation. This study aims to evaluate how HIV exposure (as compared to HIV non-exposure) impacts on NEC disease pathogenesis, prevalence and severity. Clinical markers of disease severity and mortality, as well as serum levels of cytokine inflammatory responses, are evaluated in infants with severe NEC referred for surgical evaluation.

**Project Title:** Very early diagnosis of HIV infection in infants and HIV persistence in early treated children

**Researchers:** J Maritz, GU van Zyl, W Preiser, MG Katusiime (PhD student)

**Collaborators:** M Cotton, H Rabie, S Holgate and L Frigati (Department of Paediatrics, TBH), GB Theron (Department of Obstetrics and Gynaecology, TBH), JW Mellors (University of Pittsburgh), M Kearney (National Cancer Institute, Frederick, Maryland), JB Nachega (Centre for Infectious Diseases, SU), VA Cox, AK Nelson (MSF Khayelitsha), G van Cutsem (MSF South Africa).

**Funding:** NHLS Research Trust, industry sponsor

**Short Description:** This project aims to investigate various aspects relating to the early diagnosis of HIV infection in infants in order to improve care. HIV-1 infection remains a major cause of morbidity and mortality in infants globally, despite considerable advances in the prevention of mother-to-child transmission of this infection. HIV-1 can be transmitted transplacentally, during delivery or through breastfeeding. In infants infected with HIV, early initiation of ART and therefore very early diagnosis of the infection in the first few weeks of life significantly reduces HIV-associated morbidity and mortality compared to deferred initiation.

Specific aspects being investigated include the optimal age of diagnosis for the prevention of morbidity, maternal factors constituting a high risk for transmission of the virus to infants, and the impact of a point-of-care (POC) diagnostic approach on patient treatment and retention.

Linked to this project is a new collaborative one to study HIV persistence and HIV diversity and integration sites, aiming to quantify and characterise mechanisms of HIV persistence in children from the CHER cohort.

To date, approximately 1 300 patients have been recruited from two study sites and a third site may be established in the near future. Preliminary follow-up results of HIV-infected babies have been encouraging, and data from the project have been presented at three international and one national conferences.

**Project Title:** Pooled testing as a bridging technology until point-of-care testing becomes available

**Researchers:** W Preiser, J Maritz, GU van Zyl

**Collaborators:** A Welte, C van Schalkwyk (DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis, US)

**Funding:** NHLS Research Trust, PRF, SA MRC
### Project Title
The Tygerberg evaluation site for point-of-care assays for CD4, viral load and early infant diagnostic testing

### Researchers
- W Preiser, GU van Zyl, J Maritz, T Stander
- M Esser (Immunology, NHLS Tygerberg), VA Cox (MSF Khayelitsha)

### Collaborators
- Unitaid via LSHTM

### Short Description
The goal of this project is to conduct high quality evaluations for POC tests for HIV-related markers, namely CD4, HIV viral load and EID. During the period under review, we planned validations of the Iquum LIAT HIV PCR analyser and the LYNX p24 POC test for early infant diagnosis of HIV infection, which is due to start soon.

### Project Title
Antiretroviral drug resistance: epidemiological, clinical and diagnostic aspects

### Researchers
- GU van Zyl, W Preiser, S Engelbrecht, GB Jacobs, R Fisher (PhD student), M Claassen (medical technologist), SG Mikasi (MSc student)
- R Shafer (Stanford University), U Neogi and A Sönnerborg (Karolinska Instituted, Stockholm, Sweden), C Scheller (University of Würzburg, Germany)

### Collaborators
- PRF, NHLS Research Trust, Gilead Germany, MRC

### Short Description
An audit of antiretroviral drug resistance in diagnostic samples received at TBH Virology, in collaboration with Stanford University, with the purpose of keeping abreast of any changes in the incidence of such mutations as the ART Programme comes of age, has been published. We continue to monitor drug resistance patterns. As part of the collaboration with Karolinska Instituted, viral diversity and HIV protease inhibitor-associated mutations are investigated.

The use of nevirapine (NVP) for PMTCT poses a risk of inducing resistance in the infant should he/she become infected. However, viral variants harbouring these resistance mutations may wane over time and are therefore often undetectable by standard resistance testing using bulk sequencing, by the time patients require therapy. As part of a PhD project, we are performing deep sequencing of HIV in such PMTCT-exposed yet infected children. However, deep sequencing methods used to detect minor resistant variants may not reliably quantify these variants due to PCR or sequencing error. The results from this study are currently being analysed.

### Project Title
Potentially emerging zoonotic viral diseases

### Researchers
- W Preiser, M Andersson, NL Ithete and T Suliman (postdoctoral fellows), N Sampson, K Poovan and K Malan (PhD students), B Kleinhans (MSc student), T Lopes (MSc student, graduated)
- S Matthee (Department Conservation Ecology and Entomology, SU), D Krüger (Institute for Virology, Charité, Humboldt University, Berlin, Germany), JF Drexler and C Drosten (Institute for Virology, Universitätsklinikum Bonn, Germany), C Matthee (Evolutionary Genomics Group, Department of Botany and Zoology, SU), MC Schoeman (School of Life Sciences, UKZN), RI Cable (Western Province Blood Transfusion Service, Cape Town), S Korsman (NHLS Groote Schuur/UCT)
Funding: Deutsche Forschungsgemeinschaft (Africa Infectiology Programme), PRF, NHLS Research Trust, Harry Crossley Foundation

Short Description: An ongoing project aimed at identifying and characterising novel viruses occurring in small mammals, i.e. rodents, shrews and bats, that potentially may be transmitted zoonotically and cause human disease. Animal samples are screened for the presence of viral genome. This project has identified and is in the process of characterising several novel astro-, arena- and coronavirus sequences in rodents, shrews and bats. This work is done in close collaboration with bat and rodent specialists who not only contribute animal samples for testing, but also valuable zoological and ecological data that are needed to better understand the relationship between these viruses and their wildlife hosts as the key to determining the magnitude of the risk to humans. Of the multitude of viruses present in wild animals, relatively few have so far crossed the ‘species barrier’ and caused human infections. The question is why this happens, whether it is predictable in any way, and how one could quantify the risk?

The most intriguing discovery to date is a novel beta-coronavirus which turned out to be a close relative of the recently emerged Middle East Respiratory Syndrome (MERS) coronavirus. This work has resulted in two widely read and much-cited papers, seeing that it provides important clues to bats as a possible original source of this ongoing outbreak.

Having detected infection with hepatitis E virus (HEV) in several patients in Cape Town, another line of study aims to elucidate the prevalence of past and active HEV infection in blood donors and to determine risk factors for HEV infection in this population, in co-operation with colleagues from the Western Province Blood Transfusion Service; and to search for serological and molecular evidence of HEV infection in pigs slaughtered locally in co-operation with colleagues from Groote Schuur/UCT and the provincial Veterinary Services in Elsenburg.

Project Title: The Global HIV Vaccine Research Consortium (GHRC): Virological and immunological characterisation of cryopreserved blood and virus samples
Researchers: C de Beer, W Preiser, I Mentoor, M Golden, T Meyer (BSc Hons students, graduated)
Collaborators: H von Briesen (Fraunhofer-Institut für Biomedizinische Technik, Germany)
Funding: Bill and Melinda Gates Foundation
Short Description: The division was a primary site for the GHRC, which established a fully functional cryolaboratory at TBH that collects samples from recently infected HIV patients. PBMC isolation was done according to specifically developed protocols on the ChameleonLab system. Plasma and serum were stored at -80°C, and PBMCs were stored in the cryolaboratory in liquid nitrogen, using an Askion workbench with computer-controlled cooling rates and an access tower with computerised access and a temperature controlled environment. This access tower facilitates the placement of samples in liquid nitrogen tanks and captures all the information from the microchips in an electronic database. These original samples were used by global collaborators involved in vaccine and neutralisation assay development and optimisation. Excess PBMC, plasma and serum samples are still being used for postgraduate research projects.

Project Title: AIDS and Cancer Specimen Resource (ACSR) and AIDS Malignancy Consortium (AMC) Sub-Saharan Africa Biorepository
Collaborating researcher: W Preiser
Principal Investigator: JW Schneider (Anatomical Pathology, NHLS Tygerberg)
Funding: NIH ACSR
Short Description: This major project aims to establish a central biorepository site for sub-Saharan Africa that can proactively obtain and make available relevant biospecimens and data for co-ordinated research and studies on HIV-related malignancies.

Project Title: Hepatitis B virus (HBV): HIV co-infection, immune activation and hepatocellular carcinoma
Researchers: M Andersson, R Glashoff, W Preiser, T Maponga (PhD student), N Chotun (PhD student), C Tamandjou (MSc student)
Collaborators: S Ijaz and RS Tedder (Public Health England, London, UK), E Nel (Department of Paediatics, TBH), L Fourie (Department of Oncology, TBH), Dieter Glebe (Universität Giessen, Germany), B Robertson, W Spearman and M Kew (UCT), P Ruff (Wits), P Veersamy and V Fredlund (UKZN), A Neugut, R Santella and J Jacobson (Columbia University, New York)
Funding: PRF, NHLS Research Trust, Gilead Germany

Short Description: Investigations of the prevalence and character of chronic HBV infection in HIV-infected and -uninfected pregnant women and in their infants have been published and further studies are ongoing. The prevalence of HBV infection in infants born to HIV-positive mothers is being studied through a retrospective cohort study using banked samples from an International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT) trial. We are also evaluating testing pregnant women with an HBsAg rapid test to identify those at risk of transmitting HBV to their babies.

A multi-site study aims to assess prevalence, presentation, survival and risk factors of HIV-associated hepatocellular carcinoma. This study will describe the demographics, HIV status, risk factors, including HBV status with characterisation of HBV, aflatoxin adduct testing and patient survival time post diagnosis.

A PhD project (submission 2016) is investigating the impact of HIV co-infection on fibrosis and markers of immune activation or inhibition in patients with chronic HBV infection. In particular, it aims to determine whether gastro-intestinal tract (GIT) leakage in HIV infection impacts on markers of immune status in HBV infection. Data appears to indicate that gut translocation is associated with either HIV or HBV viral load. Due to study cohorts being on therapy, immune activation is not directly associated with gut translocation markers. An important aspect of this research is an examination of liver fibrosis and how it relates to other immune factors, and why co-infection exacerbates fibrosis in HBV infection.

5. RESEARCH OUTPUT

5.1. Publications


Oral and Maxillofacial Pathology

Head: Prof. JJ Hille

1. ABOUT THE DEPARTMENT

The Department of Oral and Maxillofacial Pathology of the University of the Western Cape is a relatively small department, located in the NHLS Laboratories on the 10th floor at Tygerberg Hospital. It is the only diagnostically active pathology department within the university, and shares laboratory facilities and the diagnostic platform with the Division of Anatomical Pathology, University of Stellenbosch, in a unique and rational way. This enables the department to provide comprehensive oral and maxillofacial/head and neck clinico-pathological consultation services to the University of the Western Cape (UWC’s) oral health centres located at Tygerberg, Mitchell’s Plain and Groote Schuur Hospitals, and the Ear Nose and Throat, Oncology and Dermatology divisions of Tygerberg Hospital and large regional hospitals in the Eastern Cape.

The department participates in the activities of the Anatomical Pathology Expert Committee of the NHLS and represents the university on the National Academic Pathology Committee (NAPC).

The department continues to conduct ground breaking research in liquid-based cytology diagnostics of (pre) cancers of the mucosal surfaces of the upper aero-digestive tract, and the epidemiology of oral/head and neck cancers in Africa, as part of the terms of reference of the WHO Collaboration Centre in Oral Health for sub-Saharan Africa, affiliated to the Faculty of Dentistry of the UWC. Furthermore it conducts research in dental abnormalities in intellectually disabled children in the Western Cape and runs various projects in forensic odontology.

The department has access to the joint NHLS/University of Stellenbosch Pathology Research Facility, which offers various diagnostic molecular pathology tests through national and international collaboration.

With only two full-time NHLS consultants, one full-time UWC consultant, one part-time UWC consultant (Forensic odontology) and three registrars, the department bore a heavy undergraduate and postgraduate teaching load at the University of the Western Cape’s Faculty of Dentistry.

Table 61: Total number of staff per profession and highest qualification

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<thead>
<tr>
<th>Pathologist</th>
<th>South African</th>
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2. DIAGNOSTIC SERVICES

Through the joint NHLS platform, approximately half of the Western Cape public health sector is reached. Consultation services are offered to the NHLS laboratories in the Eastern Cape to increase registrars’ teaching exposure. Second opinions are available to the private sector. Furthermore the shared diagnostic platform empowers the department to offer special services and expertise, including electron microscopic support for service and research, and fine needle aspiration and upper aero-digestive tract brushings with rapid on-site cytology diagnostic services. The various adjunct specialised services and case numbers during the reporting period are described in the Division of Anatomical Pathology of the University of Stellenbosch report. The overall year-on-year workload for both biopsy/surgical pathology and cytology again increased substantially, mainly due to the overflow from the Eastern Cape laboratories.

The department continued and extended its oral/head and neck diagnostic support services to pathologists in the Eastern Cape through assistance with excessive routine workloads and diagnostic consultations, including the occasional telepathology service to pathologists in Mthata.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

The undergraduate dental student classes are large (± 90 students). The following modules are offered: BCHD II – Basis of Disease Processes; BCHD II – System’s Based Pathology; BCHD IV – Oral Pathology. Modules in Basic Pathology and Oral Diseases are offered to Oral Hygiene Students (classes of ± 40 students). Furthermore there is significant involvement in the continuous development of the BCHD and BOH programmes, and the general Teaching and Learning Programme of the Faculty of Dentistry.

3.2. Postgraduate Programmes

The department has three registrars (one externally funded from Ghana) who are undergoing specialist training in Oral and Maxillofacial Pathology (MChD). A new externally funded registrar from Kenya has been appointed for 2016. The FCPath (SA) Part I of the training is achieved by functioning and receiving training as registrars in Anatomical Pathology on the joint NHLS diagnostic and training platform.
with the Division of Anatomical Pathology of the University of Stellenbosch. Part II of the training takes place on the clinico-pathological training platform of the oral health centres of the UWC and the NHLS diagnostic platform in Tygerberg and the Western Cape. There were two full-time MSc students registered with the department.

Important postgraduate teaching activities further include:

- An intensive course in Diagnostic Oral Pathology on intermediate level offered to three MChD students in Oral Medicine and Periodontics
- A course in generic Oral Pathology was offered to seven MSc students from other clinical departments
- Courses in performing fine needle aspiration biopsies (FNABs) and oral exfoliative cytology are offered to oral health staff and postgraduate students
- Participation in, and co-ordination of various examinations of the College of Pathologists and Maxillofacial and Oral Surgeons are routine activities.

**Specialised courses attended**

- Dr Afrogheh completed his one-year research fellowship in Head and Neck Pathology at Massachusetts General Hospital/Harvard University in July 2015.
- Dr Afrogheh also attended the biennial Harvard Head and Neck Pathology course: Current Concepts in Head and Neck and Endocrine Pathology. Fairmont Copley Plaza, Boston, MA, USA June 3–6 2015.
- Prof. Hille attended the satellite and evening Specialty Conferences in Head and Neck, Endocrine Pathology, Bone and Soft Tissue Pathology, Head and Neck Lesions at the Interface of Benign and Malignant, and Bone Pathology. USCAP Meeting, Boston, 21–27 March 2015.
- Prof. Hille also attended the AIDS malignancy symposium: Confronting the Challenges Relevant to HIV/AIDS Malignancies in sub-Saharan Africa. Cape Town 31 July–01 August 2015.

**Medical technologists and technicians**

See report for the Division of Anatomical Pathology, University of Stellenbosch.

**Table 62: Total number of trainees per qualification category and rates of successful completion/pass rates**

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
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<td>All</td>
<td>3</td>
<td>1</td>
<td>No candidates</td>
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**3.3. Other Training Information**

**Outreach Programmes**

The department worked in close collaboration with pathologists at Walter Sisulu University (occasionally utilising telepathology) and Port Elizabeth, to exchange teaching material and to offer comments on diagnostically challenging oral/head and neck cases. Academic support is offered to pathologists in the Eastern Cape through the joint UWC-University of Stellenbosch diagnostic platform to provide specialised pathological tests and consultations on various tissue samples from the NHLS Anatomical Pathology Laboratories at Nelson Mandela Academic Hospital in Mthatha, Frere Hospital in East London and Port Elizabeth Provincial Hospital.

Oral Pathology staff participates in outreach projects organised by the Division of Anatomical Pathology of the University of Stellenbosch, teaching the FNAB technique to clinicians as part of the maintenance of competence initiative of the Western Cape Department of Health, as well as other specialised courses.

**4. RESEARCH ACTIVITIES**

**4.1. Research Units/Study Groups linked to the Department**

The Department of Oral and Maxillofacial Pathology is linked to the Oral Cytology Global Network (OCGN) and the African Oral Cytology Network (AOCN), which are exemplary models of international team science.

The newly established African Ameloblastoma Research Network (AARN) is a co-operation programme between the USA, Nigeria and the NHLS/UWC Department of Oral and Maxillofacial Pathology.
Dr Afrogheh established an international research link with Head and Neck Pathology, Harvard Medical School and Ophthalmic Pathology, Mass Eye and Ear Infirmary (MEEI), Harvard Medical School, mainly on HPV cancer-related and thyroid pathology research. Funding has been granted through Massachusetts General Hospital (MGH) and possibly by the NHLS Research Trust.

4.2. Research Projects

**Project Title:** The epidemiology of oral cancer in Africa  
**Researcher:** Prof J Hille  
**Research Activity:** Gauge the burden of incidence and mortality of oral cancer in Africa using IARC – GLOBOCAN data

**Project Title:** Validation of a novel grading system for oral liquid-based cytology  
**Researchers:** Prof J Hille, Dr AH Afrogheh. Ongoing evaluation – see 2014/15 report

**Project Title:** Educational models for clinical- and laboratory skills transfer for the diagnosis of early oral cancer using oral liquid-based cytology  
**Researchers:** Prof J Hille, Dr AH Afrogheh, ongoing – see 2014/15 report  
**Funding:** NHLS Research Trust

**Project Title:** MYB and Notch-1 overexpression in adenoid cystic carcinoma  
**Principal Investigator:** Dr J Aster (Consultant Hematopathologist, Brigham and Women’s Hospital and Director of the Aster Laboratory, Harvard Medical School)  
**Co-investigator:** Dr A Afrogheh  
**Research Activity:** To create a clinical database of all patients treated for adenoid cystic carcinoma at MGH between 2000 and 2014, and to correlate the clinical findings (e.g. outcome, recurrence) with immunohistochemical expression of Notch-1  
**Funding:** MGH

**Project Title:** Evaluation for high-risk HPV in squamous cell carcinomas and precursor lesions arising in the conjunctiva and lacrimal sac  
**Principal Investigator:** Dr AH Afrogheh  
**Supervisors:** Dr WC Faquin, Director of Head and Neck Pathology, Harvard Medical School; and Prof. FA Jakobiec, Director of the David G Cogan Laboratory of Ophthalmic Pathology, Massachusetts Eye and Ear Infirmary (MEEI), Harvard Medical School  
**Funding:** MGH and possibly NHLS Research Trust

**Project Title:** Impact of reclassifying non-invasive follicular variant of papillary thyroid carcinoma on the risk of malignancy in the Bethesda System for Reporting Thyroid Cytopathology  
**Principal Investigator:** Dr WC Faquin  
**Co-investigator:** AH Afrogheh  
**Research Activity:** Record the demographic information, cytology diagnoses, and surgical pathology follow-up of all thyroid FNABs performed between 1 January 2013 and 30 June 2014 at MGH. Calculate the risk of malignancy (ROM) with and without NI-FVPTC  
**Funding:** MGH

**Project Title:** Molecular characterisation of papillary thyroid carcinoma developing in a pre-existing follicular adenoma.  
**Principal Investigator:** Dr AH Afrogheh  
**Supervisor:** Dr WC Faquin, Director of Head and Neck Pathology, Harvard Medical School.

**Ongoing Project.**

**Project Title:** Genomic characterisation of Hurthle cell tumors of the thyroid gland  
**Principal Investigator:** Dr S Parangi, Director of MGH Endocrine Surgery Fellowship and Director of MGH Thyroid Cancer Research Laboratory
Co-investigator: Dr AH Afrogheh
Research Activity: Review H & E sections from all Hurthle cell tumors diagnosed at MGH between 2000 and 2014. Identify representative tumor and normal thyroid tissue for whole exome sequencing at Broad institute. Ongoing project.

Project Title: Molecular characterisation of an endometrial endometrioid adenocarcinoma metastatic to a Thyroid Hürthle cell adenoma with cancensis of follicles.
Principal Investigator: Dr AH. Afrogheh
Supervisor: Dr WC Faquin, Director of Head and Neck Pathology, Harvard Medical School

Project Title: Role of apoptosis in oral lichen planus
Principal Investigator: Prof. JJ Hille.
Postgraduate Student Project Leader: Dr M Zwet
Collaborators: Dr H Adeola, Dr A Afrogheh
Research Activity: Oral lichen planus (OLP) is a frequently occurring oral disease that remains inscrutable in respect of its pathogenetic mechanisms and effective therapy. Even though its incidence is relatively lower in sub-Saharan Africa, OLP is frequently diagnosed in South Africa, particularly in the Western Cape, probably due to demographic reasons. OLP presents in a variety of clinical forms, histologically characterised by basal keratinocyte destruction and interface lymphohistiocytic infiltration. Apoptosis is possibly involved in the resolution of the inflammatory process and cells. Hence this project seeks to elucidate the molecular role of apoptosis in OLP and suggest therapeutic options for its management.

Project Title: Application of liquid-based cytology in screening oral mucosal changes among Khat chewers in Kenya
Principal Investigator: Prof. JJ Hille
Postgraduate Student Project Leader: Dr M Ndonga
Collaborators: Dr A Afrogheh, Oral and Maxillofacial Pathology, UWC/NHLS Tygerberg; Dr H Adeola, Oral and Maxillofacial Pathology, UWC; Dr P Schubert, Anatomical Pathology, US/NHLS Tygerberg
Research Activity: Khat as a psycho-active stimulant drug with social and cultural importance in various communities, particularly in Eastern Africa and the Arabian Peninsula, with increasing global consumption as a result of migration and improved transportation. In Kenya, the drug is commonly known as Miraa and is chewed in various communities for social, cultural and occupational reasons. Adverse systemic and oral effects of khat consumption have been documented. However, its role and pathogenesis in oral, potentially malignant, lesions and oral cancer remains unclear. Several in vitro studies on animals and human cells have been conducted and have illuminated various ways in which this substance alters normal cell function, particularly when its use is combined with other carcinogens such as alcohol and tobacco. Despite the wide distribution of khat chewing, the majority of the studies on this drug and its effects have been conducted in Yemen with few studies in other parts of the world and even fewer in Kenya. The project aims to describe the social and demographic characteristics of khat chewers in Kenya; the habits associated with khat chewing; clinical features of oral mucosal changes occurring in Kenyan khat chewers; cytological changes seen in cells exfoliated in oral mucosallesions from khat application site found in Kenyan khat chewers; and to compare cytological changes in cells from exfoliated, other apparently unaffected, oral mucosal sites to those obtained from oral mucosal lesions of Kenyan khat chewers.

Project Title: Dental implications of intellectual disability in South African children
Researchers: Dr T Roberts, Prof. L Stephen (UWC) and Prof. P Beighton (UCT)

Research in Forensic Odontostomatology (at press/to be published)

Project: Bite mark analysis of patients who have had orthodontic treatment. Mohamed N and Phillips VM. SADA Journal

Project: Deriving an appropriate adult dental age estimation table for a Western Cape population sample. Phillips VM and Chandler S. Part of a PhD study

Project: Gustafson’s method of adult dental age estimation revisited. Chandler S and Phillips VM. PhD study
**Project:** The incidence of taurodontism in a Western Cape sample. To be published in SADA Journal. 4th-year student project.

**Project:** The incidence of supernumerary teeth in a Western Cape sample. To be published in SADA Journal. 4th-year student project.

### 4.3. Grant Funding

**Project:** Application of liquid-based cytology in screening oral mucosal changes among khat chewers in Kenya

**Researchers:** Prof. JJ Hille (Principal Investigator) and M Ndonga

**Grant:** NHLS Research Trust – R78 000

### 5. RESEARCH OUTPUT

#### 5.1. Journal Publications


#### 5.2. Abstracts


5.3. Conference Presentations and Invited Lectures

**International Oral Presentations**


**National Oral Presentations**


5.4. Plenary Talks

**International**

Hille J. Workshop presenter: Oral cancer recognition, oral cytology and FNAB (Fine Needle Aspiration) Workshop. Dental School, University of Nairobi, Nairobi, Kenya.

Hille J. Novel liquid-based oral cytology for early diagnosis of oral cancer. (Guest lecture) Dental School of the University of Ibadan, Nigeria, 7 September 2015.

Adeola H. Molecular pathology of human papilloma virus (HPV) infection and oral/oro-pharyngeal carcinomas. (Refresher course) National Postgraduate Medical College of Nigeria, 8 September 2015.

**National**

Hille J. Translational research into the practical and laboratory evaluation of suspicious oro-pharyngeal and laryngeal mucosal lesions. Pathology Research Day, NHLS Tygerberg, 4 June 2015.

Hille, J. Pathology reporting for HNSCC – What we report and why. Department of Clinical Oncology, Tygerberg Hospital, 29 June 2015.


6. RESEARCH TRANSLATED TO DIAGNOSTIC TECHNOLOGY, POLICY OR SERVICE

7. ADDITIONAL INFORMATION

- Dr A Afrogheh completed, with distinction, a one-year Fellowship in Head and Neck Pathology at Harvard University in Boston, USA in July 2015. He received the Clinical Research Fellowship Plaque for 2015.
- Prof. J Hille represented the University of the Western Cape on the National Academic Pathology Committee (NAPC) and served as nominated trustee on the NHLS Research Trust.
- Prof. J Hille was appointed as a member of a panel of experts to review the Diploma in Dental Therapy at the National Health Training College of Lesotho, June 2015.
- Prof. J Hille was convener and co-ordinator of FCPath (SA) (Oral Pathology) Part II examinations of the CMSA College of Pathologists, May 2015.
- Prof. J Hille was examiner of primary examination in Pathology for FC Dent and FC MFOS, CMSA, April 2015.

7.1. Conferences and courses attended

Prof. J Hille:

- 94th General Session of the International Association of Dental Research (IADR), Boston, USA, 11–14 March 2015
- North American Society of Head and Neck Pathology, Boston, USA, 22 March 2015
- United States and Canadian Academy of Pathology (USCAP)/International Association of Pathology Annual Meeting, Boston, USA, 21–27 March 2015
- AIDS Malignancy Symposium: Confronting the challenges relevant to HIV/AIDS malignancies in sub-Saharan Africa, Cape Town 31 July–01 August 2015
- First International Association of Oral Pathology (IAOP) Conference in Lagos, Nigeria, 9–11 September 2015
- South African Society of Clinical Cytology (SASCC) Academic Day, Tygerberg, 29 August 2015
- 50th Congress of the South African ENT Society (ENT/SAAA/SASLHA), Cape Town, South Africa, 18–21 October 2014
- The 1st Global Oral Cancer Forum Meeting. Henry Schein Foundation, New York, USA, 4–5 March 2016

Dr Afrogheh:

- Biennial Harvard Head and Neck Pathology Course, Boston, USA, June 2015
- South African Society of Clinical Cytology (SASCC) Academic Day, Tygerberg, 29 August 2015

Dr H Adeola:

- First International Association of Oral Pathology (IAOP) Conference, Lagos, Nigeria, 9–11 September 2015

Dr JH Opperman:

- 1st Forensic Odontology Conference, Khartoum, Sudan, 8–10 August 2015
UNIVERSITY OF THE WITWATERSRAND (WITS)
Anatomical Pathology

Head: Prof. Martin Hale

1. ABOUT THE DEPARTMENT

The Anatomic Pathology Department at Wits provides all the pathology requirements inclusive of histology, cytology and autopsy pathology for patients admitted to the academic hospitals in the Johannesburg region, namely Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Chris Hani Baragwanath, Helen Joseph and Raheema Moosa hospitals. In addition, the department is responsible for offering similar care to all provincial hospitals in Gauteng and North West Province. It also offers a referral consultation service to the SADC countries including Namibia, Botswana, Zimbabwe, Lesotho, Kenya and Swaziland and private sector pathology practices.

The Anatomical Pathology laboratory at CMJAH remains an accredited laboratory. The audit was successfully completed in October 2015. The laboratory at Chris Hani Baragwanath Hospital is also a SANAS-accredited laboratory with the audit successfully completed in March of 2016. The Cytology laboratory, a SANAS-accredited laboratory will be re-accredited in April 2016.

Table 63: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Medical Doctors</th>
<th>Registrars</th>
<th>MSc Scientist</th>
<th>Technologists</th>
<th>Student Technologists</th>
<th>Technicians</th>
<th>Student Technicians</th>
<th>Support</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>23</td>
<td>2</td>
<td>20</td>
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<td>34</td>
<td>8</td>
<td>13</td>
<td>5</td>
<td>44</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

During the period 1 April 2015 to 31 March 2016, the department based at CMJAH saw a total of 46581 routine cases including neuropathology, renal pathology, oral pathology and bone marrow trephines. A total of 310 specimens required electron microscopy and an average of 2993 immunohistochemistry tests were performed each month. A total of 770 polymerase chain reaction (PCR) tests was performed including 206 B-cell rearrangement studies and 199 T cell rearrangement studies, 247 mycobacterial DNA studies, 21 Bartonella studies, 20 HHV8 (herpesvirus 8) studies, 16 microsatellite instability studies, 22 parvovirus studies and 39 rt-PCR studies (synovial sarcomas). A total of 2231 bone marrow trephines were processed and 119 frozen sections were done.

Consultations and reviews were received internationally from Namibia and Kenya and nationally from Pietersburg, Cape Town, East London, Port Elizabeth and Bloemfontein. These also included consultations from private practice laboratories in Johannesburg, Pretoria, Durban, Port Elizabeth and Cape Town. Sixty five (65) post-mortems were performed from CMJAH and Helen Joseph Hospital.

The histopathology unit sited at Chris Hani-Baragwanath was responsible for a further 15642 routine histology specimens, including neuropathology cases and renal biopsies. Twenty-six post-mortems were performed and 6564 immunohistochemistry tests were done. Sixteen frozen sections were done.

The cytology unit reported 128856 pap smears, 11485 non-gynaecological exfoliative cases and 9020 FNAs, including palpable masses, radiologic-guided FNAs and intraoperative FNAs.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

Consultants and registrars within the department contribute extensively to lectures and practical theme sessions to the graduate entry medical programme (GEMP) 1 and 2 and all registrars participate as facilitators in GEMP small-group, problem-based learning. In addition, students undergoing their surgical rotations in GEMP 3 and 4 receive weekly clinicopathological teaching at both Charlotte Maxeke Academic and Chris Hani Baragwanath Hospitals.

Consultants and registrars in the department co-ordinate and deliver the anatomical pathology curricula for the BPharm, BSc (Physiotherapy and Occupational Therapy) and BDS degrees.

3.2. Postgraduate

Lectures are given over four blocks during the academic year to MSc students in physiotherapy and occupational therapy. The department is also involved in the teaching of pathology for the Diploma in Tropical Medicine and Hygiene offered by Wits.
All registrars in the Department of Anatomical Pathology are registered for the degree of MMed (Anatomical Pathology) with Wits. In addition to their surgical pathology training, registrars in anatomical pathology follow a formal academic programme drawn up annually by the department. Two pathologists are registered for their PhD degrees.

The department is in the process of initiating an intern scientist programme. The application has been sent to the HPCSA and a site visit from the HPCSA is imminent. Furthermore the department has embarked on introducing a Bachelor of Health Sciences Honours programme in the field of Anatomical Pathology.

The cytology unit trains registrars in anatomical pathology, medical officers, technologists, technicians, and laboratory assistants.

Table 64: Record of pass rates in FCPath (Anat) exams 2015/16

<table>
<thead>
<tr>
<th>Year 2015</th>
<th>Dr E McAlpine</th>
<th>Dr T Pitjadi</th>
<th>Dr Y Reddy</th>
<th>Dr R Maritz</th>
<th>Dr K Fearnhead</th>
<th>Dr R Maritz</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCPath (Anat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>MMED</td>
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</tr>
</tbody>
</table>

A further six members of staff have completed their MMed research projects and are awaiting graduation. Of these six, four are registrars who will graduate once they have passed their FCPath Part II examination.

3.3. Other Training Information

Technologist Training

Medical technologists and technicians are given theoretical and on-the-bench training. Laboratory supervisors give a one-hour lecture per week, and also give students assignments/tasks to complete. The students are trained on the bench by supervisors and senior technologists. From Tuesdays to Thursdays of every week, students are given an hour and a half each day for studying, completion of assignments or other matters related to their training. During this time they are not involved in any routine work.

International Outreach

Prof. Hale is involved in an initiative called African Strategies for the Advancement of Pathology (ASAP). This is an international working group trying to improve the practice of pathology and the training of pathology in Africa. Prof. Hale is involved in pathology training and has recently been appointed as the Chair of the ASAP Board, a “not for profit” organisation registered in Denver, Colorado. Prof. Hale was also appointed as the Chair of the Finance Committee of the International Academy of Pathology and is the Vice President for Southern Africa for the International Academy of Pathology.

4. RESEARCH ACTIVITIES

- Prof. Martin Hale hosted and co-ordinated the IAP 2015 Congress which was held at the Wits Medical School, Parktown, Johannesburg from 24–25 September 2015. Delegates included pathologists and registrars from Cote d’Ivoire, Nigeria, Rwanda, Tanzania, Uganda, Botswana, Zimbabwe and South Africa.
- Prof. Hale hosted and co-ordinated the ASAP workshop which took place on 26 September 2015 at St. John’s College in Parktown.
- Dr Agata Czajkowski, Dr Peter Swart and Dr Reubina Wadee attended the International Paediatric Pathology Association course which was held in France from 13–19 September 2015.
- Dr Pulane Mosiane attended a three-week Renal Pathology fellowship at Vanderbilt University, hosted by Dr Agnes Fogo, from 20 July–7 August 2015.
- Prof. Wayne Grayson hosted the 12th Annual Johannesburg Dermatopathology Symposium at the Faculty of Health Sciences, University of the Witwatersrand, on 23 January 2016.

Visitors to the Department

Dr Ann Nelson from the Joint Pathology Center, Armed Forces Institute for Pathology, presented a lecture to the department on 8 October 2015, entitled: The approach to the diagnosis of the infectious disease. This was followed by a slide presentation.

Other visitors to the department included Prof. Druclilla Roberts from Harvard University and Prof. Mary Sheppard from the University of London whose fields of expertise include neonatal and placental pathology, and cardiovascular pathology respectively.
4.1. Research Projects

**Project Title:** Prevalence of anal dysplasia using anal cytology testing and associated risk factors.
**Investigators:** E Jong and C Finhaber (Right to Care – Helen Joseph Hospital), P Michelow (Cytology Unit, Department of Anatomical Pathology, NHLS, Wits)
**Funding:** Centers for AIDS Research (CFAR) (grant of US$20 000).

**Project Title:** Evaluation and impact of screening and treatment approaches for the prevention of cervical neoplasia in HIV+ women in Burkina Faso and South Africa (HARP).
**Sponsor:** London School of Hygiene and Tropical Medicine (LSHTM), London, UK
**Investigators:** Reproductive Health Research Unit at Wits, Dr P Michelow, Cytology Unit and Department of Anatomical Pathology at Wits and NHLS, National Institute for Communicable Diseases, LSHTM, University of Ouagadougou, Montpellier University.
**Funding:** European Commission/ FP7-HEALTH. 2010.2.4.1–4.

**Project Title:** Molecular profiling of colorectal cancer in a cohort of South African patients.
**Principal Investigator:** M McCabe, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Supervisor:** Dr Y Perner, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Collaborator:** Dr L Cronje, Division of Microbiology, School of Pathology, Wits

**Project Title:** ACTG A5282 trial.
**Investigator:** Dr P Michelow, Cytology Division, Anatomical Pathology Department

**Project Title:** Laboratory Diagnosis of Epstein-Barr virus in diffuse large B-cell lymphomas.
**Principal Investigator:** Dr Y Perner, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Project Leader:** S Naidoo, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Funding:** NHLS Research Trust Grant

**Project Title:** Her2 over-expression in gastric carcinoma: A study of the prevalence in the South African population and the concordance between FISH and BDISH.
**Researcher:** Dr T Pitjadi, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Supervisor:** Dr P Swart, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Funding:** NHLS Research Trust

**Project Title:** The accurate classification of hydatidiform moles using p57 immunohistochemistry and molecular genotyping: A study of 50 recent cases at Chris Hani Baragwanath Hospital.
**Researcher:** Dr M Kaaka, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Supervisor:** Prof. M Hale, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Funding:** NHLS Research Trust

**Project Title:** Does human immunodeficiency viral (HIV) infection affect the integration of the human papillomavirus (HPV) by using p16 as a marker: A retrospective study.
**Researcher:** Dr D Fassom, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Supervisor:** Prof. M Hale, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
**Funding:** NHLS Research Trust

**Project Title:** Prevalence of TB and other treatable diseases at autopsy in South Africa.
**Researchers:** A collaborative study between Dr T Omar of the Department of Anatomical Pathology, NHLS, Wits and the Aurum Institute, and Prof. A Grant of LSHTM
**Funding:** Bill and Melinda Gates Foundation
4.2 New Research

Project Title: A comparison of immunohistochemistry and PCR in the assessment of BRAF V600E mutation in papillary thyroid carcinomas.
Researcher: Dr Y Smith, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Dr Peter Swart, School of Pathology, Division of Anatomical Pathology, NHLS and Wits

Project Title: Evaluation of the performance of an automated slide profiler in the detection of cytological abnormalities in the screening of cervical smears.
Researcher: Dr N Ntshwanti, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Dr T Omar, School of Pathology, Division of Anatomical Pathology, NHLS and Wits

Project Title: KRAS expression in pancreatic adenocarcinoma.
Researcher: Dr S Ngwenya, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Dr S Pather, School of Pathology, Division of Anatomical Pathology, NHLS and Wits

Project Title: Utility of breast fine needle aspiration in children and adolescent cancers.
Researcher: Dr Y Reddy, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Dr P Michelow, School of Pathology, Division of Cytology in Anatomical Pathology, NHLS and Wits

Project Title: The role of histopathology in the diagnosis of BK virus associated nephropathy in post-transplant biopsies.
Researcher: Dr N Mbatha, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisors: Dr P Mosiane, School of Pathology, Division of Anatomical Pathology, NHLS and Wits and Prof. M Altini, School of Pathology, Division of Anatomical Pathology, Wits

Project Title: High risk pathological features in retinoblastoma.
Researcher: Dr L Ngobese, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisors: Dr Eunice van den Berg, School of Pathology, Division of Anatomical Pathology, NHLS and Wits and Prof. M. Altini, School of Pathology, Division of Anatomical Pathology, Wits.

Project Title: Discordances in biological markers ER, PR, HER2 and Ki-67 after neoadjuvant chemotherapy in breast cancer.
Researcher: Dr M Bromfield, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Dr R Mohanlal, School of Pathology, Division of Anatomical Pathology, NHLS and Wits

Project Title: HPV genotypes in carcinoma of the cervix in HIV positive women in Zimbabwe.
Researcher: Dr W Mudini, supernumerary registrar in the School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisors: Prof. M Hale, School of Pathology, Division of Anatomical Pathology, NHLS and Wits and Prof. M Altini, School of Pathology, Division of Anatomical Pathology, Wits

Project Title: Molecular epidemiology of Azole-resistant Candida species in South Africa, (for PhD).
Researcher: R Magobo, School of Pathology, Division of Anatomical Pathology, Wits
Supervisor: Dr N Govender, NICD, NHLS

Project Title: Endometrial carcinoma: Microsatellite instability and suspected Lynch Syndrome in the greater Johannesburg area (2009–2015), (for PhD).
Researcher: Dr R Wadee assisted by Ms S Naidoo, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Prof. W Grayson, School of Pathology, Division of Anatomical Pathology, Wits.

Project Title: Prognostic influence of MYC aberrations and other clinicopathological factors of high grade B-cell non-Hodgkin lymphomas in adult and paediatric patients, (for PhD).
Researcher: Dr S Pather, School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Prof. M Hale, School of Pathology, Division of Anatomical Pathology, NHLS and Wits and Prof. M Patel, Division of Haematology, Baragwanath Hospital

Project Title: Molecular studies in oral plasmablastic lymphomas, (for PhD in Anatomical Pathology).
Researcher: Dr S Meer, School of Oral Health Sciences, Division of Oral Pathology, Wits
Supervisor: Dr P Willem, School of Pathology, Division of Cytogenetics, NHLS and Wits

Project Title: Prognostic significance of PHH3, Ki-67 and BCL-2 in prostate cancer.
Researcher: Dr A Phillips, supernumerary registrar in the School of Pathology, Division of Anatomical Pathology, NHLS and Wits
Supervisor: Prof. M Hale, School of Pathology, Division of Anatomical Pathology, NHLS and Wits

Project Title: Minimally invasive autopsy study.
Collaborators: Prof. M Hale, Dr S Pather, Dr E van den Berg and Dr R Wadee, School of Pathology, Division of Anatomical Pathology, NHLS and Wits; Prof. S Madhi, Respiratory Meningeal Pathogens Research Unit, NICD; and Dr S Zaki, CDC, Atlanta

Project Title: Syndromic surveillance for non-cryptococcal invasive fungal infections.
Principal Investigator: Dr N Govender, NICD, NHLS
Collaborators: NICD, South Africa: Dr N Govender, Dr S Iyaloo, Ms T Maphanga, Ms R Mpembe and Chris Hani Baragwanath Hospital; Prof. A Karstaedt, Dr F Shaid, Prof. C Menezes, Dr M Tsitsi, Dr K Roberg, Dr J Nkhalil, Dr A Motau, Dr J Wadula, Dr S Seetharam, Dr E van den Berg (Anatomical Pathology)
Funding: NICD. NHLS Research Trust

4.3. Grant Funding
- NHLS Research Trust; CFAR; Departmental funds; Bill and Melinda Gates Foundation
- European Commission FP7-HEALTH, NICD.
4.4. National and international collaborative research:

Dr P Michelow
Right to Care
ACTG - AIDS Clinical Trials Group

L Fatman
University of Pennsylvania (with CHBara Endocrinology Unit)

Dr E van den Berg
Martin Luther University, Germany
International Agency for Research on Cancer

Dr T Omar
Aurum Institute and London School of Hygiene and Tropical Medicine
Perinatal HIV Research Unit
National Institute of Communicable Diseases
Johns Hopkins University
Unitat de Tuberculosi Experimental, Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Barcelona

Prof. M Hale
Dr Sherif Zaki, Centre for Disease Control and Prevention,
Atlanta.

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2 Book Chapter


5.3. Conference Presentations

International


Local Poster Presentations


6. ACADEMIC AND RESEARCH RECOGNITION/AWARDS

Prof. Hale was appointed section editor for the American Journal of Clinical Pathology.

6.1. Postgraduate students

- At the end of March 2016 there were 23 (including three supernumerary) registrars enrolled for the MMed degree
- Dr Y Perner, Dr T Omar, Dr T Pitjadi and Dr S Ngwenya, consultants in the department, are also registered for the MMed at Wits
- Dr P Michelow is registered for a postgraduate diploma in Health Science Education at Wits
- Dr R Wadee, Dr S Pather and Dr S Meer are registered for their PhD degrees in Anatomical Pathology.

6.2 Postgraduate students that qualified

- Four FCPath (Anat) – Dr E McAlpine, Dr Y Reddy, Dr T Pitjadi and Dr R Maritz
- Two MMed – Dr K Fearnhead and Dr R Maritz.

7. ADDITIONAL INFORMATION

7.1. Quality Assurance Programmes

The department subscribes to the following RCPA Quality Assurance Programmes:

General Diagnostic; Breast Diagnostic; Specialist Diagnostic Dermatopathology; Specialist Diagnostic Gynaecological; Specialist Diagnostic Neuropathology; Specialist Diagnostic Paediatric; Specialist Diagnostic Urology; Specialist Diagnostic Oral Pathology; Specialist Gastrointestinal Pathology Module; Electron Microscopy Programme Diagnostic and Technical Module; Technical Module; Immunohistochemistry Technical Module; Immunohistochemistry Breast Markers Module; Immunohistochemistry Lymphoma Markers Module.

The Department also subscribes to the following UK NEQAS Quality Assurance Programmes: IgH/TCR Clonality; Molecular Detection of Mycobacterium.
Chemical Pathology

Head: JA George

1. ABOUT THE DEPARTMENT

The Department of Chemical Pathology runs two large diagnostic laboratories, one at Charlotte Maxeke and the other at Chris Hani Baragwanath (CBH). Staff supports the undergraduate MBBCH programme from years one to six through lectures, tutorials and examinations. A number of staff are involved in supervision of postgraduates, from honours students to doctoral candidates.

The Chemical Pathology laboratories provide clinical chemistry results to patients and consultative services to doctors regarding appropriate, cost-efficient use of the laboratory. As a very extensive repertoire of tests is performed in the academic complex, this unit serves as a reference laboratory to other NHLS laboratories. The automated laboratories at both Charlotte Maxeke and CBH are high volume, 24-hour/ seven days a week laboratories. The laboratories experience a high turnover of technologists. With the average time to train a technologist to be competent in all areas of the auto-laboratories being 12–18 months, this has given rise to many challenges. In addition, continued financial constraints within the NHLS have hindered the process of appointments. Despite the challenges, both laboratories maintained SANAS accreditation. Together, the laboratories run over 300 000 tests per month.

Table 65: Total number of staff per profession and highest qualification

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<tr>
<th></th>
<th>Black</th>
<th>Coloured</th>
<th>Indian</th>
<th>White</th>
<th>Other</th>
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<td>Pathologist</td>
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<td><strong>All</strong></td>
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<td><strong>5</strong></td>
<td><strong>7</strong></td>
<td><strong>-</strong></td>
<td><strong>-</strong></td>
<td><strong>38</strong></td>
<td><strong>41</strong></td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

Senior staff serve on several NHLS and other committees such as the Expert Committee, Point-of-Care working group, Standardisation Committee and HPCSA. The pathologists are further involved in serving on university committees and teaching at the undergraduate and postgraduate levels.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department offers a BSc (Hons) degree for Chemical Pathology students. In the reporting period, two students attained the qualification and four new students enrolled for the degree. The department has also established an MMed programme and the first Part 1 examinations will be written in October this year.

Table 66: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th></th>
<th>Black</th>
<th>Coloured</th>
<th>Indian</th>
<th>White</th>
<th>Other</th>
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<tr>
<td>Intern Scientists</td>
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<td>PhD</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>South African</td>
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<td>-</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>12</td>
<td>12</td>
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<td><strong>-</strong></td>
<td><strong>-</strong></td>
<td><strong>9</strong></td>
<td><strong>10</strong></td>
</tr>
</tbody>
</table>
4. RESEARCH ACTIVITIES

Research focuses on obesity and cardiovascular disease, including adipocyte biology and development and the role of adipocytes in different diseases. Current projects include an investigation of the role of alkaline phosphatase on preadipocyte maturation; the association between body fat mass and the immunological response to anti-retroviral therapy; the genetics of obesity in various African populations; differences in the immune pathophysiology of type 1 diabetes in black African and white populations; changes in body fat distribution and CVD risk factor levels during the menopause transition in African females; and the association of vitamin D serum levels with pregnancy and foetal outcomes.

The Department also houses a chromatography unit with access to LC-MS/MS and HPLC instruments. This unit undertakes research related to toxicology and projects currently being developed include iohexol measurement for assessment of estimated GFR; novel diagnostic techniques for TB; measurement of testosterone levels in post-menopausal African females; measurement of drugs of abuse in human samples; and the measurement of anti-retroviral agents in human serum.

Post graduate students are nested within research projects related to those described above. Many students are staff members but the department also co-supervises students from other departments e.g. physiology, internal medicine, human genetics, public health and sports science, among others.

4.1. Grant Funding Research Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Grant Holder</th>
<th>Collaborators</th>
<th>Funding Agency</th>
</tr>
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<tbody>
<tr>
<td>Branched chain amino acids and the metabolic syndrome in Africans and Asians</td>
<td>J George</td>
<td>T Snyman and L Khambule</td>
<td>FRC Individual Agent – Amount: R50 000</td>
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<tr>
<td>Determining the role of miR-9 on lipid accumulation in the preadipocytes in 3T3L-1</td>
<td>E Cave</td>
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<td>FRC Individual Grant – Amount: R16 000</td>
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<td>The role of vitamin D in the pathogenesis of type 1 diabetes in the South African black population</td>
<td>S Bhola</td>
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<td>FRC Individual Grant – Amount: R5 000</td>
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<tr>
<td>Vitamin D, parathyroid hormone and pregnancy outcomes</td>
<td>J George</td>
<td>N Crowther, S Norris</td>
<td>MRC self-initiated grant – Amount: R199 390</td>
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<tr>
<td>Serum circulating miRNA profiling for identification of potential markers of diabetic nephropathy in black type 2 diabetic South Africans</td>
<td>C Padoa</td>
<td></td>
<td>MRC SIR – Amount: R199 888</td>
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<tr>
<td>The prevalence of lectin like low density lipoprotein receptor 1 (LOX1 k167N polymorphism in hyperlipidaemic patients in the South African population</td>
<td>N Naran</td>
<td></td>
<td>NHLS (K-funding) – Amount: R20 590</td>
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<tr>
<td>The pharmacokinetics of Abacavir and its active metabolite, carbovir-5 triphosphate, in children on concomitant TB treatment at the Rahima Moosa Mother and Child Hospital</td>
<td>J George</td>
<td>T Snyman, K Technau and G Sherman</td>
<td>NHLS large grant – Amount: R497 851</td>
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<tr>
<td>Project Title</td>
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<td>Funding Agency</td>
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<tr>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------</td>
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<tr>
<td>Assessment of kidney function in African subjects</td>
<td>J George</td>
<td>NHLS Research Trust – Amount: R90 000</td>
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<tr>
<td>Vitamin D levels in pregnant women</td>
<td>J George</td>
<td>NHLS Research Trust – Amount: R1 000 000</td>
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</tr>
<tr>
<td>The role of vitamin D in the pathogenesis of type 1 diabetes in the South African black population</td>
<td>C Padoa</td>
<td>NHLS Research Trust – Amount: R88 120 (2 years)</td>
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</tr>
<tr>
<td>Metabolomic profiling of endogenous serum steroids</td>
<td>G Mezoh</td>
<td>NHLS Research Trust – Amount: R100 000</td>
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<tr>
<td>Serum circulating miRNA profiling for identification of potential markers of diabetic nephropathy in black type 2 diabetic South Africans</td>
<td>C Padoa</td>
<td>NHLS Research Award – Amount: R496 445 (3 years)</td>
<td></td>
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<tr>
<td>Determining the in vitro level of foam cell formation in different South African populations: A potential role for tissue non-specific alkaline phosphates</td>
<td>N Crowther</td>
<td>NRF – Amount: R540 000</td>
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<tr>
<td>Validation of Antiretroviral (ARV) drug on liquid chromatography mass spectrometry (UPLC-MS/MS)</td>
<td>D Legg-E’Silva</td>
<td>Start-up Funds – Amount: R12 025 (1 year)</td>
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<td>Determining the role of miR-9 on lipid accumulation in the preadipocyte cell in 3T3-L1</td>
<td>E Cave</td>
<td>Start-up Funds – Amount: R27 000 (2 years)</td>
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<td>Elucidating the mechanism through which tissue non-specific alkaline phosphatase mediates intracellular lipid accumulation</td>
<td>E Cave</td>
<td>Thuthuka NRF</td>
<td></td>
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<tr>
<td>Chronic kidney disease and risk factors</td>
<td>J Fabian, S Naicker</td>
<td>MRC Newton – Amount: R10 000 000 (3 years)</td>
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<tr>
<td>Validation of eGFR equations in South Africans</td>
<td>J Fabian, J George</td>
<td>International Society for Nephrology – Amount: $20 000</td>
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</table>
4.2. Awards/Prizes

**Project Title:** Investigation into the effect of HIV viral proteins on endothelial function in the HIV infected population  
**Researcher:** G Mezoh  
**Funding Agency:** OWSD and SIDA

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

**International**

- George J. Chronic kidney disease in Africa. AFCC.
- Padoa CJ, Rheeder P, Cave E and Crowther NJ. The role of Genes and Autoimmunity on ethnic differences. International Diabetes Federation.
- Cave E, Crowther N. Inhibition of the pyrophosphate transporter (ANK) enhances intra-cellular lipid accumulation in murine 3T3-L1 preadipocytes. UK Congress on Obesity.

**Local**

- Mphayi M, Bello B and George J. Modalities of PSA testing in Gauteng. PathRed.
- Padoa CJ, Rheeder P, Cave E. The role of genes and autoimmunity on ethnic differences. PathRed.
- Cave E and Crowther N. TNF receptor associated factor 2mRNA is down regulated during intracellular lipid accumulation in the 3T3-L1 mouse preadipocytes cell line. PathRed.
- Cave E and Crowther N. Inhibition of the pyrophosphate transporter (ANK) enhances intra-cellular lipid accumulation in murine 3T3-L1. PathRed.
• Letswalo K and Naran N. The prevalence of lectin like low density lipoprotein receptor 1 (LOX-1 k167N polymorphism in hyperlipidaemic patients in the South African population. PathRed.


• Letswalo K and Naran N. The prevalence of lectin like low density lipoprotein receptor 1 (LOX-1 k167N polymorphism in hyperlipidaemic patients in the South African population. SEMDSA

6. ACADEMIC AWARDS

• Eleanor Cave received the SEMDSA Travel Award
• Dr Jaya George was promoted to Adjunct Professor
• Associate Professor Nigel Crowther was promoted to Professor.
Clinical Microbiology and Infectious Diseases

Head: Prof. AG Duse

1. ABOUT THE DEPARTMENT

The department supports the NHLS/Wits academic complex that includes four academic/tertiary hospitals, as well as the referral mycobacteriology and immunology laboratories located on the Braamfontein NHLS campus. All sites, with the exception of the Helen Joseph NHLS Laboratory, are fully accredited by SANAS. Clinical Microbiology and Infectious Diseases (CMID) has a state-of-the-art molecular laboratory; a BSL-3 facility for research on special pathogens and specialised infection control; public health; and oral microbiology laboratories. It also provides microbiology consultative and diagnostic services to the Donald Gordon Medical Centre (DGMC) as a joint partnership between Contract Laboratory Services (Wits Health Consortium), the Faculty of Health Sciences of the University of the Witwatersrand and the Mediclinic Hospital Group. The division’s influence extends to promoting high-quality microbiology and infection control and prevention services throughout South Africa.

Maximising healthcare delivery to the nation is of the highest priority to the division, as well as playing a leading role in confronting the problems of infectious diseases in Southern Africa through education and training of all categories of healthcare students and professionals; research into preventive and control strategies; and the provision of services to affected patients and their families. CMID provides microbiology diagnostic and clinical consultative services, as well as specialised infection prevention and control, outbreak response and public health laboratory services. Outbreak response activities are not confined to South Africa but, under the auspices of organisations such as the World Health Organisation (WHO) and International SOS, extend to viral haemorrhagic fever outbreak containment activities in other African countries. CMID was actively involved in the 2014 and ongoing West African Ebola Viral Disease (EVD) outbreak. Furthermore, in South Africa, CMID plays a key role in development of policies and procedures, facility assessments and training for management and infection prevention and control of viral haemorrhagic fevers such as EVD.

The mission of the division is to strengthen the disciplines of microbiology and infectious diseases, and positively impact on the diagnosis, treatment and control of infectious and communicable diseases. Infection prevention and control (IPC) has been identified as a key priority on the Department of Health’s healthcare delivery agenda.

The Michael A Emmerson South African Healthcare Infection Surveillance Centre (SA-HISC), situated at the NHLS Infection Control Laboratory (Wits Medical School), is actively involved, in collaboration with the Department of Health and Social Services in Belfast, Northern Ireland, in healthcare-associated infection (HAI) surveillance. Following a HAI prevalence pilot study conducted in Gauteng Province in 2005, and a multicentre HAI survey in 2011, the centre has trained healthcare workers in collecting surveillance data from many healthcare facilities countrywide and has measured HAIs in ten hospitals, six of which are designated National Health Insurance (NHI) pilot sites. These hospitals are distributed among the following provinces: two Gauteng, two North West, two Eastern Cape and four Free State. The HAI prevalence by infection category and associated risk factor findings are aimed at strengthening infection prevention and control (IPC) programmes and influencing IPC policy at both provincial and national levels.

The department has an excellent track record in basic science, clinical, and contract research, and encourages active collaboration with other centres locally, nationally and internationally. CMID works in collaboration with the National Institute of Communicable Diseases (NICD) and several staff members of the NICD hold joint appointments in the division in the School of Pathology.

Additionally CMID, through strategic partnerships with the NHLS, CDC/PEPFAR and the Department of Health (DoH), is involved in IPC health system strengthening in long-term hospitalisation TB healthcare facilities (dedicated hospitals for the management of MDR and XDR-TB cases). In collaboration with the Department of Molecular Medicine and Haematology, Right to Care and the Global Fund, CMID is spearheading the infection prevention and control component of a “Towards Zero TB Transmission” programme in key management areas of the Department of Justice and Correctional Services.

CMID units and NHLS laboratories:

- Infection Control
- Charlotte Maxeke Johannesburg Academic Hospital
- Mycobacteriology Referral Laboratory, Braamfontein Campus
- Immunology (Acting Custodianship), Braamfontein Campus
- Helen Joseph/Rahima Moosa
- Chris Hani Baragwanath.
The department is extensively involved in undergraduate and postgraduate training of health sciences students, biotechnologists, medical microbiology technicians and technologists, scientists, microbiology pathology registrars and other postgraduate students.

CMID personnel continue to face challenges but have remained highly dedicated to ensure that the departmental outputs are of best possible quality.

2. **DIAGNOSTIC SERVICES**

2.1. **Infection Control Laboratory**

The Infection Control Services Laboratory hosts a diverse range of functions. These include clinical microbiology, enhanced antibiotic testing including phenotypic characterisation of antimicrobial resistance patterns, environmental microbiology (legionella, air samples, etc.), public health (water, milk and food), and molecular diagnostics for bacteria and viruses.

The Antibiotic Laboratory is involved in the comparative analysis of various generic antibiotics to their innovator product and thus assists new drug development companies in testing these new agents. In food poisoning outbreaks, this laboratory is responsible for processing the relevant samples. Environmental samples deemed necessary after a hospital outbreak are also processed by this laboratory. The legionella section of the Infection Control Laboratory is involved in a number of activities including the testing of water samples from various industries for legionella contamination.

The Legionella Action Group is chaired by Rob Stewart. This group meets twice-yearly and is made up of various interested parties from laboratory, industry and water treatment companies. The group has adapted the British Standard document (The Control of Legionella in Water Systems) for South African conditions under project number SABS: SC147B Legionella G_SANS 893-1 & 2. (Document published in 2013).

A comprehensive IPC support service is offered to the CMJAH and all surrounding hospitals, including an outbreak response service for nosocomial infections. This is supplemented by molecular testing including strain typing. The pathologist in this laboratory heads up the CMJAH IPC committee, which oversees all infection prevention and control services for the hospital.

2.2. **Mycobacteriology Referral Centre**

The laboratory is a biological safety level (BSL) III facility and processes clinical specimens for mycobacteriology culture. It operates on a high-throughput basis and receives specimens from the greater Gauteng area (Ekurhuleni District [Gauteng East], West Rand District [Gauteng West], Sedibeng District [Gauteng South], and Centre of Johannesburg Metropole District), selected referring sites from Limpopo, Mpumalanga and the North West provinces, as well as referrals from private mining hospitals.

The scope of testing includes: (i) direct smear microscopy on specimens, (ii) microscopy performed on decontaminated and concentrated specimens, (iii) culturing of mycobacteria using WHO-recommended automated liquid culturing system (MGIT), (iv) molecular identification of mycobacterium species from positive cultures, (v) molecular drug susceptibility testing from specimens or from positive cultures for isoniazid and rifampicin, (vi) culture-based drug susceptibility testing for first and second-line anti-mycobacterial agents, (vii) molecular drug susceptibility testing from positive cultures for the fluoroquinolone and injectable agents, and (viii) Xpert MTB/RIF testing on pulmonary and extra-pulmonary specimens.

The laboratory works closely with district tuberculosis (TB) co-ordinators, provincial Department of Health, and NGOs involved in the management of patients with TB. The collaboration involves communication of all TB-resistant isolates to the respective management teams. The referral laboratory accepts specimens for processing from laboratories unable to process their current workloads either for operational, staffing, or stock availability reasons.

As TB is a national priority, an extensive advisory service is offered by laboratory staff. Clinicians and healthcare workers consult directly with staff or via e-mail. In collaboration with the DoH, twice monthly outreach activities are carried out by the pathologist at healthcare centres throughout Gauteng, guiding clinicians and nursing staff on management issues. Periodically, the DoH arranges TB symposia to discuss TB management trends and the pathologist participates from a TB diagnostic perspective.

2.3. **Charlotte Maxeke Hospital**

The laboratory serves as a routine diagnostic microbiology laboratory that receives clinical specimens from the following hospitals and referral laboratories: CMJAH, Tembisa Hospital, Edenvale Hospital, Far East Rand Hospital, Yusuf Dadoo Hospital and DGMC. The laboratory processes clinical specimens for bacterial and fungal culture, identification and antimicrobial susceptibility. Selected serological testing, and bacterial, fungal and viral antigen detection assays are also offered.

Pathologists and registrars actively participate in clinical ward rounds and clinical consultations on a daily basis, including paediatric, adult and cardiothoracic ICU ward rounds, as well as adult and paediatric infectious diseases ward rounds.
2.4. Chris Hani Baragwanath Hospital
The CHBH laboratory continues to provide a basic laboratory service to the hospital and 53 clinics in surrounding areas and retained SANAS accreditation to ISO 15189 in 2015.

Pathologists and registrars interact daily with the clinicians, offering consultative services, and participate in ward/unit clinical rounds such as adult infectious diseases and medicine, surgical, neonatal, gynaecology/obstetrics, paediatric infectious disease, and burns. The unit also services the new Zola Jabulani Hospital.

2.5. Helen Joseph Hospital
Helen Joseph Hospital is serviced by a clinical pathology laboratory comprising several disciplines i.e. microbiology, haematology and chemical pathology. The microbiology laboratory has several functions. One of its missions is to provide cost-effective and professional microbiology diagnostic services to the public health catchment area, which comprises several district hospitals, primary healthcare clinics and other state institutions (e.g. prisons). This includes transportation of specimens, on-site diagnostic services, referral of tests to reference laboratories, and timely delivery of quality results together with the accurate interpretation of those results. The microbiology laboratory provides services to a number of surrounding public healthcare centres including district hospitals, step-down facilities, as well as primary healthcare clinics.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT
The division plays an active role in the medical undergraduate syllabus at the University of the Witwatersrand. This includes lectures, tutorials and practicals for nursing students, dental, pharmacy and medical students in the graduate entry medical programme (GEMP). The staff engages students as facilitators in problem-based learning (PBL) sessions. Diagnostic and clinical immunology was also taught to groups including registrars and general practitioners.

The department offers postgraduate programmes to Diploma in Tropical Medicine and Hygiene (DTM&H) students, infection prevention and control practitioners, intern medical scientist, and Masters and PhD candidates. An MSc (Med) with particular emphasis on infection prevention and control on a course-work and research report basis, has been initiated.

The microbiology registrars and laboratory managers of Chris Hani undertook to give training and lectures to external hospitals (such as Kopanong and Sebokeng) and laboratories on topics such as MRSA, quality assurance, antibiotic stewardship, and approach to processing CSF and blood culture specimens. Most of the other laboratories conduct their own in-house training on a regular basis and all staff members are motivated to attend all workshops offered (TB microscopy, risk assessment, health and safety).

Members of the laboratory staff are also responsible for teaching in the form of lectures to postgraduate students and groups, including registrars in various clinical departments at teaching hospitals.

3.1. Undergraduate
All registrars, consultants and scientists from all the laboratories are involved with undergraduate teaching and training, as well as facilitating, which includes modular or full-time courses to the following categories of university students: second-year molecular medicine students, second-year fundamentals of health and disease students, medical students in their first, second and third years of the GEMP study, and third-year dental, pharmacy and nursing students.

Training modules are offered for intern medical technicians, technologists and biotechnologists. The Oral Microbiology Department offers lectures to dental students from first to third year and to oral hygiene students from first year. All receive lectures and hands-on practicals. Ongoing training of intensive care hospital staff at the CMJAH and the DGMCH was conducted and encompassed surveillance of hospital-associated infections. Training of infection and prevention control practitioners is offered as part of a course by the department.

During the two-year internship HPCSA intern scientists are trained in the molecular diagnostic laboratory and rotate to other sections of the microbiology laboratory. Each candidate is expected to independently perform three small research projects and submit research reports.

3.2. Postgraduate
The department has provided facilities and supervision to MSc, MMed, DTech and PhD students. Students receive immunological training throughout the year and tutorials are offered on a regular basis. Students’ work, dissertations and theses are closely supervised.

The department is involved in programmes for, IPC practitioners, intern medical scientist, DTM&H students and Masters and PhD candidates. An MSc (Med) with particular emphasis on infection prevention and control on a course-work and research report basis has been initiated.
The microbiology registrars and laboratory managers of Chris Hani undertook to give training and lectures to external hospitals and laboratories on topics such as MRSA, quality assurance, antibiotic stewardship, and approach to processing cerebrospinal fluid (CSF) and blood culture specimens. Most of the other laboratories conduct their own in-house training on a regular basis and all staff members are motivated to attend all workshops offered, i.e. TB microscopy, risk assessment, health and safety.

3.3. Academic Input at Various Levels

- Microbiology registrar training in the laboratory: includes bench diagnostics, interpretation of results, and rational use of antibiotics in the treatment of infectious diseases. Registrars rotate on a three-monthly basis.
- Infectious diseases (ID) sub-specialist training (ID Fellows at the hospital [adult ID] and Rahima Moosa Hospital [paediatric ID]). CHBH, CMJAH and the mycobacteriology referral unit undergo training in clinical microbiology over a consecutive two-month period. This is an official component of their super-specialist training, as stipulated by the Colleges of Medicine, South Africa.
- Introduction to the clinical microbiology laboratory for medical registrars attached to the infectious diseases unit at all units. Weekly laboratory didactics given.
- Weekly didactics to the microbiology laboratory staff: Introduction of new diagnostics, review of latest susceptibility guidelines, review of identification of micro-organisms, review of internal and external quality control procedures, training for accreditation.
- Attendance and contributions at various departmental academic activities/meetings every Tuesday and Friday.
- GEMP: Facilitation of themed sessions and invigilation of Objective Structured Clinical Examinations.
- Teaching: Lectures in clinical microbiology and infectious diseases to dental, nursing, pharmacy and medical students. Setting examination questions for lectures covered. Lectures to newly rotating interns, medical officers, registrars, as well as IPC nurses, on nosocomial infections and hospital infection control.
- Research: Laboratory-based research on clinical isolates.

3.4. External Teaching/Training

- An update on current NHLS TB diagnostics
- Appropriate use of antimicrobial agents.

3.5. Continuing Education Unit Courses in the NHLS

- Internal Quality Control Workshop NHLS Braamfontein
- NHLS CEU Antimicrobial Susceptibility Testing Workshop.

4. Research Activities

4.1. Research Projects

| Project Title | Protocol development and optimisation for diagnosis of paediatric tuberculosis using stool specimens |
| Researchers  | L Scott, W Stevens, G Reubenson, MP da Silva, A Coovadia, N Gous, S Khan |
| Collaborators | D Alland (New Jersey Medical School Rutgers, the State University of New Jersey, Newark, USA), P Nabeta (Medical Officer, FIND, Switzerland) |
| Status       | Diagnostic testing ongoing |

| Project Title | Wild-type minimum inhibitory concentration distributions of second-line drugs in *Mycobacterium tuberculosis* clinical isolates in relation to recommended concentrations in Limpopo Province, South Africa |
| Researcher    | NM Seloma (MSc in the Medical Sciences, School of Health Sciences, University of Limpopo) |
| Supervisor   | NTC Maguga-Phasha (University of Limpopo) |
| Co-Supervisors | MP da Silva, ME Makgatho (University of Limpopo), EF Mbajiorgu (University of Limpopo) |
| Status       | Testing complete and dissertation write-up in progress |

| Project Title | Clinical outcomes of patients with rifampicin resistance by gene Xpert MTB/RIF delayed hybridisation discordant with confirmatory testing in Gauteng, South Africa (COUGH) |
| Principal Investigator | R Berhanu (Right to Care) |
| Co-Investigators | MP da Silva, K Schnippel, R Kularatne, L Scott, W Stevens, C Firmhaber, CL Lippincott |
| Collaborators | National Priority Programme, Right to Care |

Project Title: Characterisation of *M. tuberculosis* complex isolates with discordant rifampicin susceptibility test results
Principal Investigator: M Nicol (University of Cape Town)
Co-Investigators: N Beylis, J Wojno, V Allen, Y Ghebrekristos, MP da Silva
Collaborators: NHLS Greenpoint, NHLS Groote Schuur, NHLS Braamfontein, University of Cape Town
Status: Ongoing.

Project Title: Validation of HainMTBDR plus Version 2.0 (V2.0) performed directly on clinical specimens and positive cultures
Rationale: V2.0 has a less-labour-intensive DNA extraction protocol. Sensitivity for detection has also been improved in relation to the version one platform. V2.0 is also more cost-effective as the extraction consumables need not be purchased separately (as with version 1.0) and are included with the testing kit
Researcher: MP da Silva
Status: Validation completed August/September 2014. Version 2.0 has been rolled out in the current diagnostic testing algorithms.

Project Title: Validation of HainMTBDRsl Version 2.0 performed on positive cultures
Rationale: Culture-based drug susceptibility testing for second-line anti-TB drugs cannot be performed on contaminated cultures. Thus, patients with pre-XDR or XDR-TB are not diagnosed. For contaminated cultures, testing by MTBDRsl (for the fluoroquinolones and injectable agents) is a useful screen for pre-XDR- and XDR- TB strains.
Researcher: MP da Silva
Status: Validation completed December 2014. MTBDRsl has been rolled out in the current referral laboratory diagnostic testing algorithms. National roll-out of the platform is imminent.

Project Title: Validation of HainMTBDRsl Version 2.0 performed directly on smear-positive specimens
Collaboration: MP da Silva, AW Dreyer (CTB, NICD), N Ismail (CTB, NICD)
Status: Validation in the planning stages.

Project Title: Validation of culture-based drug susceptibility testing (DST) for moxifloxacin, amikacin, and capreomycin (National NHLS validation)
Rationale: Standardisation of DST for second-line drugs across the NHLS TB culture laboratories
Researcher: MP da Silva for the Braamfontein laboratory – this is a national validation involving several TB culture laboratories
Status: Validation is ongoing.

Project Title: Validation of the Hain MPT64 antigen platform for detection of *Mycobacterium tuberculosis* complex off positive cultures
Rationale: The referral laboratory currently uses two manufacturers to supply MPT64 antigen platforms. The validation will take the form of an inter-manufacturer comparison with the aim of streamlining and using the platform from a single supplier
Researcher: MP da Silva
Status: Comparative evaluation in the planning phase.

Project Title: *Clostridium difficile* infection at CH Baragwanath Academic Hospital: A retrospective review
Researchers: C Menezes, A Karstaedt, S Seetharam, F Sahid, M Tsitsi, K Roberg, J Wadula, LL Winchow
Status: Ongoing.

Project Title: Evaluation of XpertCarba-R on the GenXpert System (HTA Project)
Researchers: S Seetharam, J Wadula, L Monwabisi
Status: Ongoing.
<table>
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<tr>
<th>Project Title</th>
<th>Status</th>
<th>Principal Investigator</th>
<th>Supervisor</th>
<th>Researchers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidemiology of candidemia at Chris Hani Baragwanath Hospital, 2009–2010</td>
<td>Ongoing.</td>
<td>S Seetharam</td>
<td>NP Govender</td>
<td></td>
</tr>
<tr>
<td>HIV and HBV prevalence in the Gauteng Southern Cluster Forensic Pathology Service Medico-legal Mortuary Facilities</td>
<td>Testing complete and dissertation write-up in progress.</td>
<td></td>
<td></td>
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<tr>
<td>DNA sequencing of moulds and thermally-dimorphic fungi causing invasive disease</td>
<td></td>
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<tr>
<td>Unit-specific and site-specific cumulative antibiograms, over a seven-year period (January 2007–December 2013), looking at the susceptibility trends of commonly isolated gram-negative and gram-positive organisms, specifically the “ESKAPE” organisms, causing infections at the Charlotte Maxeke Johannesburg Academic Hospital</td>
<td>MSc completed 2014.</td>
<td>N Bosman</td>
<td>W Lowman</td>
<td></td>
</tr>
<tr>
<td>Enhanced surveillance for hospital versus community-associated infections by methicillin-resistant Staphylococcus aureus</td>
<td></td>
<td>O Perovic</td>
<td></td>
<td>A Singh-Moodley, V Quan, R Kularatne, T Nana, K Baba</td>
</tr>
<tr>
<td>Punica granatum Linn (pomegranate) peel extract and oral pathogens</td>
<td>PhD, current.</td>
<td>Z Gulube (postgraduate completed 2014)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A comparison of pathogenic characteristics of Candida albicans isolated from the saliva of healthy subjects, patients with denture-related stomatitis and cancer patients wearing oral prostheses</td>
<td>MSc, current.</td>
<td>V Mothibe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of putative gliotoxin gene cluster in Candida albicans strains and other toxigenic compounds with particular reference to cytotoxicity and gene expression</td>
<td>PhD, current at University of Johannesburg.</td>
<td>N Tshabalala</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The effect of Punica granatum (pomegranate) peel and seed extracts on the virulence factors of Candida albicans</td>
<td>MSc completed 2015.</td>
<td>Treasure Mbatha</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Project Title:** Phytochemical analysis of *Dodonaeaviscosa var. angustifolia* and their beneficial effects against *Streptococcus mutans*

**Principal Investigator:** T Ngabaza

**Status:** MSc, current.

**Project Title:** Identification of *Mycobacterium tuberculosis* strains by mycobacterial interspersed repetitive units – Variable number of tandem repeats (MIRU-VNTR) typing

**Principal Investigator:** K Baird

**Status:** PhD, current.

**Project Title:** *In vitro* study of effectivity of bacteriophages in the prevention and degradation of biofilms formed by uropathogenic *E.coli* in urinary catheters

**Principal Investigator:** MM Wilson

**Status:** MSc, current.

**Project Title:** Invasive pneumococcal diseases study: Case control study to determine the effectiveness of two or more doses of PCV against all IPD and vaccine-type IPD in HIV-infected and uninfected children in South Africa

**Researchers:** GERMS-SA, NICD

**Collaborators:** Rahima Moosa Mother and Child Hospital and the Respiratory and Meningeal Pathogens Unit, NICD.

**Project Title:** Pertussis surveillance study

**Researchers:** GERMS-SA, NICD

**Collaborators:** Outbreak Response Unit, NICD

**Short Description:** A prospective, paediatric hospital-based sentinel surveillance programme for pertussis will be undertaken to provide a better understanding of pertussis epidemiology, clinical spectrum of disease, microbiological aspects (including antimicrobial susceptibility patterns, molecular epidemiology) and factors contributing to infection within the South African context. Rahima Moosa Hospital will be one of the paediatric sentinel sites. Analysis of such data will be used to inform South African pertussis management and control guidelines and policies, and assist with decisions regarding national pertussis vaccination policies. Such information will also be of benefit to neighbouring Southern African countries, none of which have active pertussis surveillance programmes and where the potential burden of the disease is also unknown.

**Project Title:** Laboratory-based antimicrobial resistance surveillance

**Researchers:** GERMS-SA, NICD

**Collaborators:** Antimicrobial Resistance Reference Unit, NICD

**Short Description:** A limited number of nosocomial bacterial pathogens such as invasive *Staphylococcus aureus*, *Klebsiella* species, have been identified to monitor trends in resistance. The aim is to establish a functional, integrated, antimicrobial resistance surveillance system for common, nosocomial, bacterial pathogens, in order to constantly assess the need for enhanced laboratory testing and to ensure the inclusion of appropriate empiric therapy in treatment guidelines. *Pseudomonas aeruginosa* was included as a surveillance organism in 2013. Isolates from blood cultures are being submitted for antimicrobial resistance analysis.

**Project Title:** Candidaemia surveillance study

**Researchers:** GERMS-SA, NICD

**Collaborators:** Mycology Reference Unit, NICD

**Short Description:** Emergence of resistance among invasive *Candida* spp. remains a significant concern, particularly as the availability and use of antifungal agents have increased in South Africa in recent years, especially in the private healthcare sector. Whether shifts in species distribution toward those less susceptible to theazole antifungals, such as *C. glabrata* and *C. krusei*, or possibly toward those less susceptible to echinocandins, such as *C. parapsilosis*, have occurred in South Africa amongst bloodstream isolates in recent years, is not clear. This study will serve to inform clinicians, managing candidaemia in daily clinical practice, of the epidemiology of this disease at sentinel sites in South Africa and will assist such clinicians with making appropriate choices of antifungal therapy with knowledge of species distribution and antifungal susceptibility data. Ultimately, the goal of the study is to optimise management and outcome for patients with bloodstream candida infections.
**Project Title:** Surveillance for nosocomial respiratory infections in South Africa

**Researchers:** GERMS-SA, NICD

**Collaborators:** Centre for Respiratory Diseases and Meningitis, NICD

**Short Description:** An active, prospective, hospital-based surveillance system is proposed to assist with characterising the epidemiology of nosocomial respiratory infections in South Africa. Surveillance officers will evaluate patients admitted to adult and pediatric medical wards and intensive care units to assess if they developed new signs and symptoms consistent with a respiratory infection after ≥ 48 hours of hospitalisation. Laboratory specimens will be collected from enrolled patients to assess for bacterial and viral pathogens that are associated with nosocomial respiratory infections. This system will enable the establishment of sentinel surveillance for nosocomial respiratory infections in South African hospitals and allow for the description of the epidemiology and clinical characteristics of patients with these infections. Defining the epidemiology of nosocomial respiratory infections in South African hospitals could provide valuable insight into understanding the burden of these conditions and assist with designing appropriate interventions to limit their spread.

5. **RESEARCH OUTPUT**

5.1. **Journal Publications**


5.2. **Conference Presentations**

Prof. Duse attended the following:
- Ethics and Formidable Infectious Diseases. Paediatric Ethics & Legal Topics Seminar. Wits Medical School, 28 March 2015
- Panel discussion and presentation: Ebola and precautions to prevent the spread of the disease. Symantec Corporation local and African teams. Midrand, 26 March 2015
- The 2014/15 West African Ebola haemorrhagic fever outbreak (Keynote address). Ebola Panel Discussion, Research and Innovation Day of the College of Agriculture and Environmental Sciences, UNISA, Florida, 3 March 2015
- Superbug: Ebola West Africa. Second Innings Membership, Sandringham, 1 March 2015

Other staff in the division, including Teena Thomas, Antoinette Moorman, Lizette du Toit, Desmond Schnugh and Ranmini Kularatne presented at the 6th FIDSSA Congress.

**Poster Presentations**

Oral Presentations


5.3. Academic and Research Honours Awards/Recognition

Prof. S Madhi:

- At the request of Precious Matsoso, Director General of Health, Republic of South Africa, Prof. S Madhi was tasked, on behalf of the NICD, to operationalise an Emergency Operations Centre (EOC) in preparation for the possibility of Ebola cases being imported into the country, and more broadly with regard to communicable disease outbreaks. Dec 2014–June 2015.

Prof. Adriano G Duse:

- Together with Dr Louise Claassens Director: Quality Assurance, Office of the Chief Operating Officer, Department of Health undertook country-wide EVD preparedness audits of designated hospitals.
- Was seconded as the lead in the Case Management and Infection Prevention and Control stream in the Emergency Operations Centre (EOC). Was deployed to Liberia in April 2014 and subsequently to Sierra Leone and Nigeria to assist with the containment of the Ebola virus outbreak in his capacity as VHF infection prevention and control expert by SOS International.

Dr N Bosman:

- Attended a parasite course at the London School of Hygiene and Tropical Medicine in July 2015.

Conference Sponsorship

- MP da Silva was sponsored to attend the 45th Union World TB Conference, Barcelona, Spain. Funding was allocated from the ongoing EXIT-RIF Study research funds.
- N Bosman, V Muthambi, M Riba, P Reddy and L Mothibi were sponsored by Pfizer to attend the IDEAL Meeting, Mount Grace Country House, 6–8 March 2015.

6. TRANSLATION TO POLICY

In addition to the activities translating to policy (mentioned in the introduction and overview), further unit-specific evidence includes:

- The Cryptococcal antigen lateral flow assay (LFA), which was evaluated in comparison to the Cryptococcal latex agglutination test (Meridian Bioscience Inc.) to determine its suitability for use as a routine diagnostic test in this laboratory, has now been implemented as a routine test for the diagnosis of invasive Cryptococcal disease and detection of asymptomatic Cryptococcal antigenaemia nationally within the NHLS.
- MICROSCAN™ (Siemens), VITEK II™ (BioMerieux) and BD Phoenix Comparative Evaluation study. The evaluation was performed and completed by CMJAH Microbiology Laboratory and the report was submitted to the HTA and Microbiology Expert Committee at the end of 2013. The results of this study were used as part of the tender process that resulted in the NHLS national roll-out of the VITEK II™ (BioMerieux) Microbiology Automated ID and AST testing instruments that commenced in mid-2014.
- Comparative Evaluation between the Meridian ImmunoCard™ Toxins A and B assay and the C.diffQuik Check Complete Immunoassay. The results of this study were published through Wits as a MMed project. The study results were also submitted to the HTA and the test approved for use nationally within the NHLS laboratories.
- Extra-pulmonary tuberculosis (EPTB) specimen testing by Xpert MTB/RIF was initially conducted at the Braamfontein Laboratory, funded by and in collaboration with the NHLS National Priority Programme. Data from the 1 175 specimens tested was published in 2014 (J Clin Micro 2014: 52 (6): 1818–1823). This data was included in the WHO meta-analysis on EPTB sample testing by Xpert MTB/ RIF. The WHO subsequently made recommendations, based on the meta-analysis, which were adopted by the DoH. Xpert MTB/RIF testing on EPTB was rolled-out by the NHLS in August 2014.
DST/NRF Centre of Excellence for Biomedical TB Research

Head: Prof. Bavesh Kana

1. ABOUT THE DEPARTMENT

The Wits node of the DST/NRF Centre of Excellence for Biomedical TB Research (CBTBR) is part of a flagship programme established by the National Research Foundation (NRF) to facilitate biomedical research on tuberculosis (TB) at three distinct nodes, Wits, Stellenbosch University (SU) and the University of Cape Town (UCT). A key feature of the Wits node is that it is co-hosted with the National Health Laboratory Service (NHLS). Under the leadership of Prof. Bavesh Kana, the research portfolio of the Wits node can be divided into the following broad thematic areas.

The first involves identification and validation of new drug targets for TB with a major focus on remodelling of the mycobacterial cell wall during growth and pathogenesis. This entails an extensive analysis of enzymes that hydrolyse different bonds in the peptidoglycan using an integrated computational biology, bacterial genetics and microbial physiology approach. In addition to this, mycobacterial energy metabolism has gained recent prominence due to the number of potential new (and existing) TB drugs that target this area of bacterial metabolism and the focus of work ongoing at the Wits node lies in further studying the respiratory chain in mycobacteria to uncover new points of vulnerability. DNA repair is also another area of substantive activity where the focus is on identifying the molecular determinants for the emergence of drug resistant strains.

The second prominent area of research involves the identification and characterisation of differentially culturable tubercle bacteria in the sputum of patients with active TB disease. In this regard, three prospective observational cohorts have been established to characterise bacterial populations when individuals present with active disease before, during and after treatment. Collaborators include various clinical research units and international experts. A fourth observation aimed at studying differentially culturable bacteria in drug resistant patients is also being undertaken.

The third area of research encompasses the development of novel models for use in counter-screening for tuberculosis drug development. These endeavours are aimed at generating various forms of non-replicating, drug tolerant organisms to use for screening against potential novel anti-tubercular agents, generated from partners at the H3D-Drug Discovery platform at the University of Cape Town.

Finally, the development of novel diagnostic validation reagents is the fourth significant area of activity at the Wits node. In this project, a new generation of reagents that now serve as industry standards for the validation and quality assurance for GeneXpert, a molecular diagnostic that has been rolled out in South Africa and over 30 other countries, have been developed.

Table 67: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Medical Doctors (PhD)</th>
<th>MSc Scientist</th>
<th>Technicians</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>7</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>15</td>
<td>16</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICE

Project Title: Establishment of an external quality assurance assay for GeneXpert

Researchers: Prof. Bavesh Kana

Collaborators: Prof. Lesley Scott and Wendy Stevens

Background: The rollout of GeneXpert in South Africa and globally required the establishment of verification and quality assurance systems. The Wits node of the CBTBR has been intimately involved in this process since 2010 through the development of a reliable and robust mechanism for bulk scale manufacture of inactivated tubercle bacteria. In 2015, the Wits node successfully provided for the entire global demand for verification material. In addition, they undertook a new project to develop a second generation of industry standards that are easier to produce and can be provided at lower cost to developing countries. They were successful in these endeavours and a new set of standards is currently being field tested. If successful, these reagents will revolutionise the global use of molecular diagnostics to detect TB infection.
3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

3.1. Undergraduate

- Dr Bhavna Gordhan from the Wits node of the CBTBR delivered a lecture to the second-year bioengineering students at Wits
- Dr Gordhan delivered lectures on the evolution of drug resistance to the third year BHSc class in 2015
- Prof. Kana delivered lectures on Mycobacteriology to the third year BHSc class in 2015.

3.2. Postgraduate

**Postdoctoral and Postgraduate Student Training**

**Postdoctoral Fellows**

*In progress:*
Dr Christopher S Ealand; Dr Melissa D Chengalroyen; Dr Julian Peters, Dr Herbert Longwe.

**PhD Students**

*In progress:*
Ms Amanda McIvor (Registered January 2014); Ms Nicole Collette Narrandes (Registered June 2013); Mr Sibusiso Senzani (Registered June 2013); Ms Andrea Papadopoulos (Registered February 2015)

**MSc Students**

*In progress:*
Mr Ditshego Ralefeta (Registered January 2014); Mr Gadisi Nthambeleni (Registered January 2014); Ms Zaahida Sheik Ismail (Registered April 2013); Mr Moagi Shaku (Registered January 2015); Ms Masethabela Maphatsoe (Registered January 2015); Mr Moeketsi Moseki (Registered January 2015); Ms Tebogo Rantsi (Registered January 2015).

*Graduated:*
Ms Sidhika Hariparsad (University of Pretoria, supervised by Prof. D Meyer and co-supervised by Prof. Kana); Ms Rukaya Asmal (Registered January 2012).

3.3. Teaching

Members of the Wits node of the CBTBR carried out the following teaching activities in 2015:

- Dr Gordhan taught molecular diagnostics and basic bacteriology to the second-year Bioengineering degree students at Wits
- Prof. Kana delivered a lecture on recombinant DNA and proteins to the registrars in 2015 (ANAP7000)
- Dr Gordhan delivered a lecture on gene manipulation to the registrars in 2015 (ANAP7000)
- Prof. Kana delivered a two-week lecture series on mycobacteria to the Honours students in the Molecular Medicine and Haematology Department.

Table 68: Total number of trainees per qualification category and rates of successful completion/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>13</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

3.4. Other Training Information

**Training visits and workshops attended by members of the Wits node**

- Ms Nicole Narrandes, PhD student undertook a 5 month working visit to the Nanyang Technological University, Singapore to work in the laboratory of Dr Kevin Pethe on the development of new TB drugs that target energy metabolism in the tubercle bacillus.

4. RESEARCH ACTIVITIES

4.1. Research Projects

**Project Title:** Characterisation of N-Acetylmuramoyl-L-alanine amidases in mycobacteria

**Researchers:** Mr S Senzani, Dr E Machowski, Prof. B Kana

**Collaborators:** Dr N Dhar, Dr D Li, Dr E Betzig
Background: N-Acetylmuramoyl-L-alanine amidases (amidases) are a group of peptidoglycan degrading enzymes that have been implicated in the final stages of daughter cell separation during cell division. In addition, these enzymes are involved in remodelling of the cell wall during stress conditions in other organisms. Their role in mycobacteria has remaining largely unexplored. Previously two amidase homologues in M. smegmatis were studied. A single, essential amidase (MSMEG_6935 – Ami2) which could serve as a novel drug target was identified.

Research Highlights: Research highlights include the discovery of a novel class of druggable peptidoglycan remodelling amidases, which are now being pursued further. In addition, a novel role for these enzymes in co-ordinating the correct spatial and temporal placement of other cell division proteins has been described. Consistent with this, the CBTBR demonstrated that the inability of amidase-defective cells to hydrolyse septal cell wall results in destabilisation of the FtsZ ring and in some cases rotation of the primary axis of the ring to allow for separation of abnormal buds. In addition, a mutant of M. tuberculosis, that is deleted for ami1-encoded amidase, was constructed and time-lapse analysis of division indicated that it is defective for cell division and forms mini cells.

Project Title: Characterisation of DD-Carboxypeptidases in mycobacteria
Researchers: Dr C Ealand, Ms R Asmal, Dr E Machowski, Ms Z Sheik Ismail, Mr D Ralefeta, Prof. B Kana
Collaborators: Dr C Bertozzi, Dr S Siegrist

Background: DD-Carboxypeptidases (DD-CPases) are low molecular weight penicillin binding proteins that play an important role in regulating biosynthesis of cross-linked peptidoglycan in bacterial cells and through their activity, they can modulate cell growth. Work at the CBTBR entails characterisation of these enzymes as potential drug targets.

Research Highlights: Wits node researchers identified a novel essential, LMW PBP, which is required for cell elongation during bacterial growth and remodelling of division scars after daughter cells separate. Deletion of multiple LMW PBPs results in cells that bend at tips and display increased sensitivity to antibiotics that target the cell wall.

Project Title: Characterisation of resuscitation promoting factors in mycobacteria
Researchers: Mr G Beukes, Dr E Machowski, Mr D Ralefeta, Dr C Ealand, Prof. B Kana
Collaborators: Dr N Dhar

Background: Resuscitation promoting factors are a group of peptidoglycan degrading enzymes that have been implicated in stimulating the growth of dormant bacteria. They are of particular interest as they have been postulated to modulate growth of M. tuberculosis, thereby promoting reactivation of infection in individuals that harbour latent tuberculosis infection. These researchers previously demonstrated that deletion of multiple rpf-like genes in M. smegmatis leads to defective entry into a non-culturable state.

Research Highlights: In 2015, the CBTBR demonstrated that rpf deletion mutants displayed defective biofilm formation, with altered spatial organisation of individual cells within the biofilm matrix. This defect is reversed upon provision of culture filtrate from wild type M. smegmatis, but not from rpf deletion mutants, confirming the requirement for continuous production of RpfPs for biofilm maturation in M. smegmatis. Mutants lacking two or three rpf genes displayed increased susceptibility to detergent, vancomycin and cephalosporins. Cellular localisation studies revealed that both RpfA and RpfB localise predominantly to the septum whilst RpfE localises to a region between mid-cell and the cell pole, suggestive of specialist function. Single cell time-lapse microscopy revealed stochastic rpf gene expression, in bursts, within a single colony that is suggestive of cellular scouts, which sense the environment. These effects are currently being studied further.

Project Title: Characterisation of m23-domain-containing peptidases in mycobacteria
Researchers: Mr M Shaku, Ms A Papadopoulos, Prof. B Kana

Background: Bacterial M23 metallopeptidases form part of a highly diverse group of enzymes characterised by their endopeptidase activity in hydrolysing peptide bonds found in peptidoglycan and elastin. The diversity of the published crystal structures of these peptidases has resulted in confusion regarding their involvement in bacterial cellular processes.

Research Highlights: The CBTBR has undertaken to characterise the functional diversity of these M23 peptidases in mycobacteria and study the relationship between their structure and substrate specificity. In addition, catalytically inert or degenerate Lysostaphin-like metallopeptidases (dlYtMs) have drawn much attention as these have proven to directly regulate the muralytic activity of LytC type amidases described above. Recent findings from the CBTBR outline a role for these proteins in facilitating the final steps of cell division and daughter cell separation.

Project Title: Characterisation of the respiratory chain in mycobacteria
Researchers: Ms N Narrandes, Mr M Moseki, Prof. B Kana
Collaborators: Prof. K Pethe

Background: The respiratory chain in M. tuberculosis is the target of a recently licensed new TB drug and several existing groups of promising small molecules. The effect of these drugs on cellular metabolism requires further study to elucidate any adaptive consequences of inhibiting the respiratory chain and to highlight possible new vulnerabilities.

Research Highlights: Work at the CBTBR involved an analysis of mutants that lack different components of the mycobacterial respiratory chain. Using existing mutants of M. smegmatis and M. tuberculosis, defective for the cytochrome bd oxidase (CbdO), it has been demonstrated that whilst not essential for growth under carbon-rich conditions, the CbdO is required for optimal ATP production in both M. smegmatis and M. tuberculosis. It has been further shown that nitrate reductase deficient strains of M. smegmatis still retain the ability to assimilate nitrate, possibility through the function of a novel nitrate reductase that has not been characterised. In addition, loss of CbdO or nitrate reductase results in increased sensitivity to oxidative stress in M. smegmatis and M. tuberculosis.

Project Title: Characterisation of DNA repair pathways in mycobacteria

Researchers: Mr G Nthambeleni, Prof. B Kana, Dr B Gordhan

Background: The maintenance of genomic integrity during infection is critical for controlling mutation rates and the emergence of drug resistance variants in M. tuberculosis. Consequently, DNA repair pathways are predicted to be central in controlling mutation avoidance in mycobacteria. Research at the Wits node is aimed at further understanding the base excision repair (BER) pathway in M. smegmatis and M. tuberculosis.

Research Highlights: In 2015, the Wits node published the results of an investigation into the combined role of MutY and the Formamidopyrimidine (Fpg/MutM) DNA glycosylases. It demonstrated that deletion of mutY resulted in enhanced sensitivity to oxidative stress, an effect which was exacerbated in a Δfpg1 Δfpg2 double mutant. Furthermore, combinatorial loss of the mutY, fpg1 and fpg2 genes resulted in a significant increase in mutation rates, suggesting interplay between these enzymes in mycobacteria.

Project Title: Identification and characterisation of dormant bacterial populations in the sputum of patients with active TB disease

Researchers: Dr M Chengalroyen, Mr G Beukes, Ms A Papadopoulos, Dr B Gordhan, Dr J Peters, Ms A McIvor, Ms T Masangana

Collaborators: Dr N Martinson, Ms M Letuli, Dr L Lebina, Dr Z Waja, Ms F Shahim, Dr W Mac Kenzie, Dr R Hafner, Prof. G Churchyard, Prof. M Barer, Dr G Mukamolova, Prof. R Warren, Dr L Streicher

Background: The Wits node initiated a project in 2012 that was aimed at identification of differentially culturable tubercle bacteria (DCTB) in the sputum of patients with active TB disease through supplementation of sputum cultures with culture filtrate, from M. tuberculosis. This project has been under way for two years and recruitment was intensified over the last 18 months.

Research Highlights: From the 110 individuals assessed in the first study, researchers at the CBTBR observed that the majority of individuals (54%) had mixed populations of Rpf dependent/independent DCTB whilst 16% had no differentially culturable organisms. Moreover, HIV-1 seronegative individuals compared to HIV-1-infected individuals displayed a higher proportion of DCTB. In a separate longitudinal cohort, the CBTBR undertook to detect, quantify and characterise DCTB subpopulations in tuberculous sputum during treatment of drug sensitive tuberculosis. The primary aims were to (i) describe the behaviour of DCTB during treatment with the understanding that these organisms reflect persisters that are tolerant to antibiotic killing, (ii) assess the presence of DCTB at the end of treatment and, (iii) determine if the quantum or rates of decline in DCTB during treatment is predictive of cure and/or relapse. Thus far, 175 patients have been recruited to the study, with 61 patients successfully completing 6-months treatment. Through the analysis, a description has been provided for the first time, of the rates of decline of DCTB during treatment, which are significantly slower than conventionally detectable organisms. The data also suggest the presence of a residual viable population of DCTB at the end of treatment; however this result requires further microbiological confirmation. Collectively, the work from the Wits node in this regard has provided novel insight into an important area of TB biology and identified possible new endpoints for assessment of new drugs, novel regimens and host-directed therapies.

5. RESEARCH OUTPUT

5.1. Journal Publications


5.2. Conference Presentations

Conferences and Meetings

*International invited/plenary/keynote addresses/conference talks*


*National Invited/Plenary/Keynote Addresses/Conference Talks*


- Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease. The Institute for Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa, 26 November 2015.

- Kana BD. Peptidoglycan remodelling during mycobacterial cell division and tuberculosis disease. The Perinatal HIV Research Unit, Soweto, Johannesburg, South Africa, 1 October 2015.


- Gordhan B. The contribution of Nth and Nei DNA glycosylases to mutagenesis in *Mycobacterium smegmatis*. Oral Presentation. NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa, 15–16 April.


• Ealand C and Kana B. DacB: An essential enzyme for mycobacterial growth. Poster and short talk. NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa, 15–16 April.

• Ealand C and Kana B. An essential DD-carboxypeptidase determines localisation of peptidoglycan synthesis in mycobacteria. Oral, Health Sciences – Symposium for Postdoctoral and Carnegie Fellows, Johannesburg, South Africa

International Poster Presentations


National Poster Presentations


• Narrandes N and Kana B. Characterisation of the electron transport chain in mycobacteria. NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa, 15–16 April.

• McIvor A, Gordhan B, Martinson N, Waja Z and Kana B. Detection of differentially culturable tubercle bacilli by exogenous cyclic-AMP in drug-susceptible patients at baseline. NHLS Pathology and Research Development Congress (PathRed), Johannesburg, South Africa, 15–16 April.


• Rantsi TC, Kana B and Gordhan B. Molecular basis of the interplay between the Nth and the Nei DNA glycosylases in the base excision repair pathway in Mycobacterium smegmatis. Molecular Biosciences Research Thrust (MBRT) Symposium, Wits, Johannesburg, South Africa, 3 December 2015.


6. ACADEMIC AND RESEARCH/RECOGNITION AWARDS

In 2015/16, members of the Wits node of the CBTBR received the following awards and recognition:

• Prof. B Kana was selected to represent Wits at the Higher Education Leadership and Management Programme, hosted by Higher Education South Africa (HESA) – now Universities South Africa (USA). The programme involved three workshops that ran from 25–27 February, 22–24 April and 24–25 June 2015, in Johannesburg.
• Prof. B Kana was selected as the ‘Titan’ for South Africa, the SADC region and the African continent in the Medical and Veterinary category. CEO Global hosts an annual selection of Titans, selected through a rigorous nomination and judging process that was audited by KPMG in 2015. The Titans – Building Nations programme recognises influential men who embody the spirit of excellence and have made meaningful contributions to their organisations, society and the African continent. These individuals shift the African landscape for the purpose of sustainable growth and display an unwavering commitment to the development of their nations. For more information please visit: www.titans-building-nations.co.za
• Prof. B Kana was admitted to the Academy of Science of South Africa.
• Prof. B Kana was awarded a B3 rating by the National Research Foundation.
• Dr M Chengalroyen was awarded third prize for a poster presentation at the Molecular Biosciences Thrust Symposium, held on 3 December 2015.
• Ms Z Sheik Ismail won the prize for best poster presentation in the Communicable and Non-Communicable Diseases track at the inaugural NHLS Pathology Research and Development Congress (PathReD).
• Dr C Ealand was awarded the MRC Career Development Award.
• Ms A Papadopoulos was selected by the MRC as a National Health Scholar.

7. ADDITIONAL INFORMATION

7.1. Communication and Outreach Activities 2014

• Members of the Wits node participated in the University open and exhibition days. They created and manned an exhibit to profile the work done at the CBTBR.
• In March 2015, Prof. Kana served as a judge for the 2014 (to be awarded in 2015) edition of the Discovery Health Journalism Awards. He reviewed health related journalism in different categories, including television, radio, print media and trade publications. He provided feedback to journalists regarding reporting style and made recommendations to improve health reporting in these sectors. Prof. Kana was invited to attend the awards function on 27 May 2015, where presentations were made to the journalists with winning entries.
• Prof. Kana participated in the following interview/profile pieces: Television: South African Broadcast Services – SABC1 (30 min profile show for the youth); MNET: Mela (45 min profile show); Radio: South African Broadcast Services (Panel interview on TB on World TB Day).
• Members of the Wits node, together with members from other nodes participated in radio interviews, broadcast in the nine official languages of South Africa. These interviews profiled the work done in the CBTBR and were also targeted at attracting school children to careers in science.
• Prof. Kana participated in a press conference with Section 27 and TAC where it was announced that Johnny Clegg would be partnering with TAC to raise money for TB awareness. His address to the press highlighted the role that civil society can play in the implementation of the post-2015 WHO strategy. Clegg handed over a cheque for R100 000 to TAC to kick-start TB awareness and urged the commercial sector to follow suit.
• Prof. Kana delivered a 30 min public lecture entitled ‘Differential bacterial growth states in active TB disease’ at the National Institute for Communicable Diseases. The theme was ‘The new post-2015 global TB strategy? The end game’.

7.2. Review Work and Committee and Expert Panel Membership

Thesis Examination

• Prof. Kana served as an external examiner for a PhD dissertation submitted to the University of KwaZulu-Natal
• Dr Gordhan served as an external examiner an MSc dissertation submitted to the University of Stellenbosch.
Journal Editing and Reviews


Expert Panel or Committee Membership

Prof. Kana participated in the mid-term review of the SA-Swiss Joint Bilateral Grant Programme in Basel, Switzerland, and served as a member of the Global Alliance for TB Drug Development Working Group on New TB Drugs. In addition he served on:

- The Scientific Advisory Committee of the Cape-Town HVTN Immunology Laboratory
- The Board of the Sydney Brenner Institute for Molecular Biosciences
- The Board of the Microscopy and Microanalysis Unit, Wits
- The University Research Council (URC), Wits
- The FRC Budget Task Group, Faculty of Health Sciences, Wits
- The Advisory Board for the Faculty of Health Sciences, Wits
- The Executive Committee of the School of Pathology, Faculty of Health Sciences, Wits
- The Research Entity Forum, Faculty of Health Sciences, Wits
- The Faculty of Health Sciences Research Equipment Review Committee, Wits
- The URC major and minor Equipment Review Committees, Wits
- The Faculty of Health Sciences Imaging Committee, Wits.

Prof. Kana and Dr Gordhan

- Served on the Faculty Research Council (FRC), Faculty of Health Sciences, Wits.

Dr Gordhan served on:

- The Research Entity Review Task Group, Faculty of Health Sciences, Wits
- The NRF Postdoctoral Review Committee.

Research Funding Reviews

Members of the CBTBR Wits node reviewed for the NHLS Research Trust, Biotechnology and Biological Sciences Research Council (BBSRC, UK), South African Medical Research Council (Newton Fund, SIR and various other programmes) and the National Research Foundation (Rating and Evaluation Programme and Competitive Grants).

Conference Organisation

- Prof. Kana served as Chair of the Scientific Organising Committee for the inaugural National Health Laboratory Service (NHLS) Pathology Research and Development Congress (PathReD) 2015.
1. ABOUT THE DIVISION

The Division of Human Genetics, NHLS and University of the Witwatersrand (Wits), has shown some positive changes over the last year. A number of medical scientist posts, which had been vacant for some time, were filled. This has resulted in improved laboratory service, reduction of backlogs and the initiation of new research and development projects. In the Clinical Genetics Section, the Registrar Training Programme has been re-instated as has the MSc in Genetic Counselling. Trainees have been enrolled in both these courses.

The laboratories continue to offer a high level of service, although new equipment is urgently needed in order to continue to develop and offer state-of-the-art testing.

The division continues to provide medical genetic laboratory and clinical services and its staff continue to train and teach at undergraduate and postgraduate level. The division continued to produce significant numbers of research outputs. Staff members are the driving force behind the functioning and success of the division.

Table 69: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>PhD Scientist</th>
<th>MSc Scientists and Counsellors</th>
<th>BSc (Hons)</th>
<th>Technologists</th>
<th>Support</th>
<th>South African</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>6</td>
<td>3</td>
<td>13</td>
<td>9</td>
<td>5</td>
<td>7</td>
<td>41</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC SERVICES

Diagnostic services are divided into laboratory services and clinical genetic services. There are four sections in the laboratory: Molecular Genetics; Cytogenetics; Applied Polymorphisms and Biochemistry; and Clinical Genetic Services.

2.1. Services Undertaken

Table 70: Tests/Patient Appraisals

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>2014/15</th>
<th>2015/16</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Genetics</td>
<td>5 693</td>
<td>6047</td>
<td>+6.22</td>
</tr>
<tr>
<td>Cytogenetics</td>
<td>2 428</td>
<td>2200</td>
<td>-9.34</td>
</tr>
<tr>
<td>Applied Polymorphisms &amp; Biochemistry</td>
<td>~7233</td>
<td>~9908</td>
<td>+37</td>
</tr>
<tr>
<td>Clinical Genetic Services</td>
<td>1 439</td>
<td>1762</td>
<td>+22.45</td>
</tr>
</tbody>
</table>

Molecular Genetics

The Molecular Diagnostic Laboratory remains the largest diagnostic laboratory in the country, performing specialised testing for more than 40 genetic disorders, including almost 80% of tests offered nationally. It receives a large number of referrals from the public sector as well as a proportion from the private sector, with services also rendered to patients outside of South Africa. The laboratory participated for the first time in 2015 (Spring) in the European Molecular Genetics Quality Network external quality assessment scheme and performed well. The laboratory is currently training two intern medical scientists. The staff complement has increased and this has allowed for improved turnaround times and active participation in research and development of new tests. The laboratory successfully implemented a new testing procedure for Charcot-Marie-Tooth disease and Hereditary Neuropathy with Liability to Pressure Palsies. The laboratory is actively involved in supervising postgraduate Honours degree research projects.

Cytogenetics

The Cytogenetics Laboratory continues to provide a pre- and post-natal laboratory service nationally for five provinces (Gauteng, Eastern Cape, Limpopo, North West and Mpumalanga) and internationally (Namibia, Zambia, Zimbabwe and Botswana). For Fluorescent in situ Hybridisation (FISH) studies, services are also provided for KwaZulu-Natal and some private laboratories. New staff members have been appointed and the large backlog has been cleared. Turnaround times have been reduced drastically and will be in line with acceptable standards within a few months. The laboratory continues to obtain good results from the proficiency testing through the College of American Pathologists (CAP).
**Applied Polymorphisms and Biochemistry**

Main activities include parentage testing, QF-PCR for the detection of chromosomal aneuploidies and tests for inherited biochemical abnormalities. Test numbers have increased by approximately 37% overall since 2014/15. This is largely due to the NHLS providing services to the Department of Home Affairs for identity testing. This section remains short-staffed primarily due to the volume increase and this has had an adverse impact on turnaround times and progress towards accreditation. Proficiency testing was done for Paternity Testing and QF-PCR through CAP and Cytogenetic External Quality Assessment Services (CEQAS) respectively and excellent results were obtained.

**Clinical Genetic Services**

The medical geneticists and genetic counsellors of the section continue to see patients in both the state and private hospital sector. Genetic clinics are run at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH), Chris Hani Baragwanath Hospital (CBH), Rahima Moosa Mother and Child Hospital, Helen Joseph Hospital and the Donald Gordon Medical Centre (DGMC). Patients and their families with a wide variety of genetic conditions are seen through these clinics. In addition to patient care and management, other important roles of the staff members of the Clinical Section include teaching, supervising and training students and interns.

The staffing situation in the Clinical Genetics Section continues to improve. A genetic counsellor from the UK has been appointed to a full-time genetic counselling post. The section was given provisional re-accreditation by the HPCSA and three Medical Genetics registrars were appointed in training posts. More staff members will assist with the heavy clinical load on the section. More posts for genetic counsellors and medical geneticists are needed in order to improve public access to genetic services. The position of Head of the Clinical Section has been advertised and the selection and appointment of a candidate is awaited. The Clinical Section took on four new MSc (Med) Genetic Counselling students at the beginning of 2016 and teaching and training is well under way.

**2.2. Human Genomic Diversity and Disease Research Laboratory**

**Genetic Ancestry Testing**

The laboratory offers genetic ancestry testing to all individuals interested in their genetic ancestry lineages. During the period of this report 185 genetic ancestry tests were conducted that generated an income of R177 300. This activity contributes to the public understanding and education of science.

**3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT**

- The Division of Human Genetics contributes to both undergraduate and postgraduate teaching in the Faculty of Health Sciences, Wits
- Prof. JGR Kromberg continues to assist on a voluntary basis with research supervision and mentoring of staff who have limited research experience. She has recently been appointed as an Honorary Associate Professor in the division
- Members of the Clinical Section of the division serve on the Committee of the College of Medical Genetics of South Africa, with Prof. Amanda Krause serving as President of the College of Medical Genetics
- Prof. Amanda Krause has also served as chair of the Genetics Expert Committee of the NHLS since July 2015.

**3.1. Undergraduate**

In the MBBCh course, undergraduate teaching is provided to medical students in molecular medicine in the second year and in medical genetics in GEMP 1, 2 and 3. The division is also involved in teaching Molecular Medicine III, a subject now being offered to BHSc students as a major option. Teaching of biomedical engineers (second year), a course within the Faculty of Engineering, is also undertaken. The division gives human and medical genetics lectures to undergraduates in physiotherapy, speech therapy, pharmacy and occupational therapy.

**3.2. Postgraduate**

The division continues to offer the BHSc (Hons) Human Genetics degree and currently has nine students – the highest number for many years. It also offers MSc (Med) by research, MSc (Med) Genetic Counselling and PhD degrees. The MSc (Med) Genetic Counselling degree was reinstated in 2016 after three years in abeyance. The degree is now offered as a two year part-time degree and four new students were accepted to start on 1 February 2016. The division also received HPCSA reinstatement as an accredited training unit for registrars in Medical Genetics during 2015 – three candidates have subsequently been enrolled. Members of the division are involved in teaching in several other postgraduate courses at Wits.
Table 71: Total number of trainees per qualification category and rates of successful completions/pass rates

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Students and interns</td>
<td>(42 students + 8 interns)</td>
<td>(15 BHSc (Hons), 1 MSc, 1 intern)</td>
<td>7</td>
</tr>
</tbody>
</table>

### 3.3. Professional Development

Postgraduate candidates enrolled in the Division of Human Genetics (1 April 2015–31 March 2016): 42; 15 BHSc (Honours) (six in 2015 and nine in 2016), ten MSc (Med) Human Genetics, four MSc (Med) Genetic Counselling, three MMed Medical Genetics, nine PhD, and one postdoctoral fellow.

Postgraduate candidates who graduated during the year (1 April 2015–31 March 2016): seven; six BHSc (Honours), and one MSc (Med) Human Genetics.

### 4. RESEARCH ACTIVITIES

The research undertaken in the division reflects the wide interests of its senior staff. Research and development on medical genetic tests for locally relevant medical genetic disorders continues as before. BSc (Hons), MSc and PhD students and a Claude Leon Postdoctoral Fellow continue to do research within the division. Some MSc and PhD students of the division are doing genomic research while based at the Sydney Brenner Institute for Molecular Bioscience, one of the six 21st Century Wits Institutes, a joint Faculty initiative (Science and Health Sciences).

#### 4.1. Research Projects

**Project Title:** Lactase persistence alleles reveal partial East African ancestry of southern African Khoe pastoralists  
**Researchers:** Prof. H Soodyall  
**Collaborators:** Dr CM Schlebusch and Prof. M Jakobsson (Uppsala University, Sweden) Prof. M Lombard (University of Johannesburg, South Africa)  
**Funding:** MRC, NHLS  
**Short Description:** The ability to digest milk into adulthood, lactase persistence (LP), as well as specific genetic variants associated with LP, is heterogeneously distributed in global populations. These variants were most likely targets of selection when some populations converted from hunter-gatherer to pastoralist or farming lifestyles. Specific LP polymorphisms are associated with particular geographic regions and populations; however, they have not been extensively studied in southern Africa. The LP-regulatory region was investigated in 267 individuals from 13 southern African populations (including descendants of hunter-gatherers, pastoralists, and agropastoralists), providing the first comprehensive study of the LP-regulatory region in a large group of southern Africans. The “East African” LP single-nucleotide polymorphism (SNP) (14010G>C) was found at high frequency (>20%) in a strict pastoralist Khoe population, the Nama of Namibia, suggesting a connection to East Africa, whereas the “European” LP SNP (13910C>T) was found in populations of mixed ancestry. Using genome-wide data from various African populations, admixture (13%) was identified in the Nama, from an Afro-Asiatic group dating to >1 300 years ago, with the remaining fraction of their genomes being from San hunter-gatherers. Evidence was also found of selection around the LCT gene among Khoe-speaking groups, and the substantial frequency of the 14010C variant among the Nama is best explained by adaptation to digesting milk. These genome-local and genome-wide results support a model in which an East African group brought pastoralist practices to southern Africa and admixed with local hunter-gatherers to form the ancestors of Khoe people.

**Project Title:** Natural selection for the Duffy-null allele in the recently admixed people of Madagascar  
**Researcher:** Prof. H Soodyall  
**Collaborators:** Prof. M Shriver (Penn State University, USA)  
**Funding:** MRC, NHLS  
**Short Description:** While gene flow between distantly related populations is increasingly recognised as a potentially important source of adaptive genetic variation for humans, fully characterised examples are rare. In addition, the role that natural selection for resistance to Vivax malaria may have played in the extreme distribution of the protective Duffy-null allele, which is nearly completely fixed in mainland sub-Saharan Africa and absent elsewhere, is controversial. Both these issues were addressed by investigating the evolution of the Duffy-null allele in the Malagasy, a recently admixed population with major ancestry components from both East Asia and mainland sub-Saharan Africa. Genome-wide genetic data and extensive computer simulations were used to show that the high frequency
of the Duffy-null allele in Madagascar can only be explained in the absence of positive natural selection under extreme demographic scenarios involving high genetic drift. However, the observed genomic single nucleotide polymorphism diversity in the Malagasy is incompatible with such extreme demographic scenarios, indicating that positive selection for the Duffy-null allele best explains the high frequency of the allele in Madagascar. The selection coefficient was estimated to be 0.066. Because Vivax malaria is endemic to Madagascar, this result supports the hypothesis that malaria resistance drove fixation of the Duffy-null allele in mainland sub-Saharan Africa.

**Project Title:** A genomic portrait of haplotype diversity and signatures of selection in indigenous southern African populations

**Researchers:** Prof. H Soodyall

**Collaborator:** Prof. R Ramesar (University of Cape Town, South Africa)

**Funding:** MRC and other sources (NRF & NHLS for field work) to Prof. H Soodyall

**Short Description:** A study was conducted that made use of genome-wide, dense SNP (about 900K) and copy number polymorphism data of indigenous southern Africans. The genetic contribution to southern and eastern African populations was demonstrated, which involved admixture between indigenous San, Niger-Congo-speaking and populations of Eurasian ancestry. This finding illustrated the need to account for stratification in genome-wide association studies, and that admixture mapping would likely be a successful approach in these populations. A strategy was developed to detect the signature of selection prior to and following putative admixture events. Several genomic regions show an unusual excess of Niger-Kordofanian, and unusual deficiency of both San and Eurasian ancestry, which were considered the footprints of selection after population admixture. Several SNPs with strong allelle frequency differences were observed predominantly between the admixed indigenous southern African populations, and their ancestral Eurasian populations. Interestingly, many candidate genes, which were identified within the genomic regions showing signals for selection, were associated with southern African-specific high-risk, mostly communicable diseases, such as malaria, influenza, tuberculosis, and human immunodeficiency virus/AIDS. This observation suggests a potentially important role that these genes might have played in adapting to the environment. Additionally, analyses of haplotype structure, linkage disequilibrium, recombination, copy number variation and genome-wide admixture, highlight and support the unique position of San relative to both African and non-African populations. This study contributes to a better understanding of population ancestry and selection in south-eastern African populations; and the data and results obtained will support research into the genetic contributions to infectious as well as non-communicable diseases in the region.

**Project Title:** The identification of genetic markers of obesity risk and body composition in a South African black population

**Researchers:** Ms V Pillay, Dr Z Lombard, Prof. N Crowther, Prof. H Soodyall

**Collaborators:** Prof. M Ramsay, Prof. S Norris (MRC/Wits Developmental Pathways for Health Research Unit)

**Funding:** NRF Thuthuka, NIH (H3Africa Collaborative Centre), University of the Witwatersrand – Faculty Research Trust

**Short Description:** Heritability studies of body mass index (BMI) suggest that there is a significant genetic component (40–70%) contributing to this complex trait. Currently almost a 100 obesity risk loci have been identified through recent genome-wide association meta-analyses, however there is very little African-centric research in this area. The overall aim of this study is to assess whether risk loci previously associated with obesity show a similar trend overall aim of this study is to assess whether risk loci previously associated with obesity show a similar trend in a South African black population. The Metabochip is a genotyping array designed for replication and fine mapping loci linked to cardiometabolic and atherosclerotic traits. This study focuses on the Bt20 cohort, which is the largest and longest running birth cohort study in Africa. Bt20 cohort participants (median age 17.9 years) and their female caregivers (median age 40 years) (n=2282) were genotyped using the MetaboChip. The association between each SNP and BMI, waist circumference, waist-to-hip ratio, total fat mass, total lean mass and percentage body fat with adjustment for covariates were estimated using linear regression. Statistical analyses were performed using PLINK (software vs. 1.9). Following genotype and phenotype quality control measures, the final dataset comprised 972 samples containing 140649 SNPs and 954 samples containing 127764 SNPs in the caregivers and cohort participants, respectively. Significant association signals were observed with different body composition measures. Most notably were associations with total body fat and variants on chromosome 1, with rs6425446 near SEC16B showing the strongest association (P=4.09 x 10-7) signal. Variants in SEC16B have previously been associated with increased risk for obesity in both European, African American and Asian populations, therefore confirming the global role of this locus with body composition. This study highlights genetic risk factors for obesity in black South Africans living in an urban environment where the prevalence of obesity is rising. This study generated novel data supporting universal risk alleles for obesity across many populations, but also highlights significant differences in this African population. The extensive data will also be used by other scientists to examine associations with cardiometabolic risk factors (e.g. blood pressure).
<table>
<thead>
<tr>
<th>Project Title</th>
<th>The Wnt signalling pathway in systemic sclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Ms J Frost, Prof. M Ramsay</td>
</tr>
<tr>
<td>Collaborators</td>
<td>Prof. M Tikly (Division of Rheumatology, University of the Witwatersrand, Dr X Estivill (CRG, Barcelona, Spain)</td>
</tr>
<tr>
<td>Funding</td>
<td>Connective Tissue Diseases Research Fund (University of the Witwatersrand Medical School), Scientist Exchange Programme (Novartis, Switzerland)</td>
</tr>
<tr>
<td>Short Description</td>
<td>Systemic sclerosis (SSc) is a complex autoimmune disease involving the immune system, vasculature and extracellular matrix. Dysregulation of the Wnt pathway has been implicated in the development of fibrosis in SSc and is proposed to contribute to a failure to maintain tissue homeostasis and appropriate immune response. The objective of this research study was to explore the role of altered Wnt pathway gene regulation in the development of fibrosis in black South African SSc patients with early, diffuse disease (dcSSc). The first aim was to examine differential gene expression in the Wnt pathway and the second aim to examine differential expression of microRNAs that potentially target Wnt pathway genes. Skin biopsies from eight black South African patients with dcSSc, samples from both the forearm (affected skin) and the back (unaffected skin), and eight ethnically matched healthy control skin samples were examined. The Wnt pathway RT2 Profiler qPCR Array (84 Wnt pathway genes) was used to assess differential gene expression, single gene TaqMan assays for validation and small RNA-sequencing for microRNA analysis. Data analysis was done using HTqPCR, NormqPCR and DESeq2 software. Gene expression patterns revealed five distinct differentially expressed gene clusters. Two clusters displayed genes that were upregulated in both affected and unaffected SSc skin compared to controls (one showing a more heterogeneous pattern than the other). Another showed consistently decreased gene expression and two revealed more complex patterns responsible delineating the patients into two groups. The gene expression was validated for five genes. The sRNA-seq data showed differential expression of 31 miRNAs that target the Wnt pathway genes, including miR-335 and miR204 that are important regulators of normal tissue development. Other dysregulated miRNAs have been linked to fibrotic and autoimmune diseases. In this group of dcSSc patients, there is differential gene expression of several Wnt pathway genes that delineate the patients into two distinct groups. This could point to differences in disease aetiology leading to distinct clinical outcomes, such as inflammation. Together with the differentially expressed microRNAs, the findings indicate a substantial contribution of epigenetic changes to the pathogenesis, progression and diverse clinical features of dcSSc.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>FC Gamma Receptor III polymorphisms and copy number variation as risk factors for Systemic Lupus Erythematosus in black South African patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Ms N Bloch, Ms J Frost</td>
</tr>
<tr>
<td>Collaborators</td>
<td>Dr N Govind (Division of Rheumatology, University of the Witwatersrand)</td>
</tr>
<tr>
<td>Funding</td>
<td>Connective Tissue Diseases Research Fund (University of the Witwatersrand, Medical School)</td>
</tr>
<tr>
<td>Short Description</td>
<td>Systemic Lupus Erythematosus (SLE) is a multi-systemic autoimmune disease with varied symptoms and clinical presentations caused by genetic and environmental factors. The genes, Fc gamma receptors IIIA and IIIB, code for the Fc gamma receptors which are cell surface glycoproteins that are involved in the interaction and removal of antigen-antibody complexes from the body into cells. These genes have been shown to be associated with SLE susceptibility and disease in previous studies. The project objective is to determine if single nucleotide polymorphisms (SNPs), allotypes and copy number variation present within the Fc gamma receptor genes IIIA and IIIB contribute to the susceptibility of SLE within the black South African population. DNA from 145 black South African patients who have been diagnosed with SLE will be investigated using TaqMan Genotyping assays to determine SNP differences and an ARMS-PCR will be used to determine the allotype differences. Copy number variation will be investigated through the use of real-time PCR. The FCGRIIIA 66L/R/H (rs10127939) and 176V (rs3969991) SNPs have been shown to have strong associations with SLE pathogenesis when present together, in African Americans, and therefore it would be expected to be strongly associated within the South African black population. Two allotypes exist on FCGRIII, FCGRIII-NA1 and FCGRIII-NA2. The NA2 allotype is most strongly associated with SLE among Chinese patients and therefore one would not expect this allotype to be present within the South African black population. Low copy number variation with the FCGRIII gene has been shown to be associated with SLE. Therefore one would expect to see low copy number of FCGRIII within our population.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Systemic Lupus Erythematosis in a black South African population – Screening for candidate susceptibility loci</th>
</tr>
</thead>
<tbody>
<tr>
<td>Researchers</td>
<td>Ms M Cagnazzo, Ms N Bloch, Ms J Frost</td>
</tr>
<tr>
<td>Collaborators</td>
<td>Dr W Tulleken (Division of Rheumatology, University of the Witwatersrand)</td>
</tr>
<tr>
<td>Funding</td>
<td>Faculty Research Committee Funding (University of the Witwatersrand, Medical School)</td>
</tr>
</tbody>
</table>
| Short Description          | Systemic lupus erythematosis (SLE) is an autoimmune disorder of uncertain etiology, characterised by a
Huntington disease (HD) is an inherited, progressive neurodegenerative disease. It is caused by a trinucleotide repeat expansion in the HTT gene. An HD phenocopy (HDL2) has been described in patients with African ancestry. HDL2, due to a trinucleotide expansion in the JPH3 gene, appears to account for one third of confirmed HD diagnoses in South Africa. The clinical phenotype of HDL2 is broadly similar to HD but some differences have been observed. This study aims to systematically characterise the clinical phenotype of HDL2 from a neurological, neuropsychological and radiological perspective; and to compare it to HD. The study cohort will consist of at least 30 patients with HDL2 and an equal number with HD. This study is ideally placed to provide novel insights into a disease which, to date has been poorly characterised, and which has important significance for diagnosis and management of HD patients in South Africa and elsewhere. Twenty-seven participants have been enrolled into the study and been through the complete examination process. This includes 6 patients with HDL2, 9 patients with HD and 12 controls. Each enrolled patient has been examined completely by an experienced neurologist. He

**Project Title:** The clinical and genetic profile of Huntington disease-Like 2 (HDL2) in South Africa  
**Researchers:** Dr DG Anderson, Ms A Ferreira-Correia, Dr F Baine, Prof. A Krause  
**Collaborators:** Dr R Margolis, Johns Hopkins University, Baltimore, USA; Prof. J Carr, Stellenbosch University  
**Funding:** MRC Self-initiated Grant  
**Short Description:** Huntington disease (HD) is an inherited, progressive neurodegenerative disease. It is caused by a trinucleotide repeat expansion in the HTT gene. An HD phenocopy (HDL2) has been described in patients with African ancestry. HDL2, due to a trinucleotide expansion in the JPH3 gene, appears to account for one third of confirmed HD diagnoses in South Africa. The clinical phenotype of HDL2 is broadly similar to HD but some differences have been observed. This study aims to systematically characterise the clinical phenotype of HDL2 from a neurological, neuropsychological and radiological perspective; and to compare it to HD. The study cohort will consist of at least 30 patients with HDL2 and an equal number with HD. This study is ideally placed to provide novel insights into a disease which, to date has been poorly characterised, and which has important significance for diagnosis and management of HD patients in South Africa and elsewhere. Twenty-seven participants have been enrolled into the study and been through the complete examination process. This includes 6 patients with HDL2, 9 patients with HD and 12 controls. Each enrolled patient has been examined completely by an experienced neurologist.
has performed a standard neurological examination, the UHDRS and SARA (Scale for the assessment and rating of ataxia) (28). This has been videoed for record purposes, further assessment and so that a second neurologist can verify the observed features. Each enrolled patient has also been examined cognitively by a neuropsychologist. The UHDRS has been used, which uses the Verbal Fluency Test, Symbol Digit Modalities test (SDMT) and Stroop interference test. Additional tests of multiple cognitive functions have been included. MRIs have been performed on all except two enrolled patients, who were unable to tolerate the procedure. A number of parameters are being recorded, particularly with respect to the size of basal ganglia structures, presence of brain atrophy, cortical thickness. All participants in the study have had blood smears investigated by a haematologist for acanthocytes. Molecular genetic testing to confirm the gene mutation and repeat length has been confirmed for all subjects if not available.

Project Title: An investigation into the spectrum of Huntington disease phenocopies in the South African population
Researchers: Dr F Baine, Prof A Krause
Funding: NHLS Research Trust Grant
Short Description: Huntington disease (HD) is an inherited neurodegenerative disorder caused by an unstable expanded trinucleotide (CAG) repeat in the huntingtin (HTT) gene. The condition is debilitating and progressive, characteristically presenting with a triad of symptoms: behavioural problems, movement disorder and cognitive decline. From available records at the NHLS, a significant proportion (30–40%) of patients diagnosed with HD and referred for testing do not carry an expansion in the HTT gene and may have an HD phenocopy. The project aims to screen for known phenocopy mutations and has the potential to identify novel genes and/or mutations associated with the HD phenotype. No expansions have been identified thus far in the SCA7, SCA17 and DRPLA genes. One expansion has been identified in the SCA2 gene. Screening for additional known mutations is ongoing.

Project Title: Investigating known cancer susceptibility genes in a cohort of black South African breast cancer individuals
Researchers: Ms R Pitere, Dr F Baine, Dr R Kerr, Ms T Wainstein, Prof A Krause
Funding: Wits Seed Funding; AstraZeneca Pharmaceuticals (PTY) Ltd
Short Description: Previous research in the Division of Human Genetics has shown that 10% of black South African women with breast cancer can attribute their disease to germline pathogenic mutations in the BRCA genes. There is further indication that other inherited cancer susceptibility genes are contributing to the burden of inherited cancers in this population. These investigations have also revealed the presence of two potential founder mutations in the BRCA2 gene. The aim of the current study is therefore to explore the contribution of known inherited cancer susceptibility genes to IBC in this population. The study further aims to confirm whether the two BRCA2 mutations are indeed founders. A targeted gene panel will be used to achieve the first aim and haplotyping analysis the second. The founder mutation analysis is largely complete, having only detected one additional patient with the BRCA2 mutation in question. The targeted gene panel is in the process of being set up and these results are expected by the end of the year. It is hoped that the results of this study will contribute further to the understanding of IBC in this population and guide the implementation of improved genetic counselling and testing for these patients.

Project Title: A retrospective file review on Afrikaner individuals with a personal or family history of cancer
Researchers: Ms H Seymour, Ms T Wainstein, Ms S Macaulay, Ms T Haw, Prof A Krause
Funding: None
Short Description: In the Afrikaner population of South Africa, three founder mutations (c.1374delC and c.2641G>T in the BRCA1 gene and c.7934delG in the BRCA2 gene) have been identified which lead to Hereditary Breast and Ovarian Cancer Syndrome (HBOCS). The aim of the study was to determine the frequency of the three founder as well as other BRCA mutations in the study population. A retrospective file review on individuals of self-reported Afrikaner ancestry, with a personal or family history of breast and/or ovarian cancer, was carried out. Of 86 unrelated counselees whose files were reviewed, 54 (62.8%) underwent BRCA genetic testing; 18 (33.3%) tested positive for a mutation, and 14 of these (77.8%) for an Afrikaner founder mutation. Twelve counselees had the BRCA2 c.7934delG mutation. Four non-founder mutations were identified. BOADICEA scores were significantly higher in counselees who tested positive for a mutation than in those who tested negative. Founder mutation testing should be performed as a first-line option. BOADICEA is very useful in identifying counselees at high risk for a BRCA mutation and also assists with the decision to pursue further testing following a negative founder mutation result. These findings assist in guiding an informed genetic counselling service for at-risk individuals with an Afrikaner background. This work was published in the South African Medical Journal in March 2016.
**Project Title:** Determining the molecular basis of spinal muscular atrophy in the South African black population  
**Researchers:** Mrs E Vorster, Ms F Essop, Prof. A Krause  
**Funding:** NHLS Research Trust Grant, University of the Witwatersrand – Faculty Research Trust and MRC Holland  
**Short Description:** Spinal muscular atrophy (SMA) is a common neuromuscular disorder, characterised by muscle atrophy and impaired mobility. Homozygous deletions of the SMN1 gene, exon 7 are the main cause of SMA in ~95% of patients worldwide but only account for 51% of black South African SMA patients. The aim of this project is to further investigate the SMA disease mechanism in the black South African population. MLPA testing was performed on 197 unrelated black patients referred for SMA testing and 122 black negative controls. For comparison, 38 white SMA patients and 30 white negative controls were tested. Furthermore, 25 black SMN1 homozygous deletion families and 61 negative black families were tested to investigate CNV inheritance. This study confirms the presence of large CNVs of the SMN region in the black population. More than two copies of the SMN1 gene were observed in 51% of black negative controls in comparison to 3% of white negative controls, supporting the hypothesis of large rearrangements being present in the SMN region in the black South African population. The CNV pattern of patients who previously tested negative for the common SMN1 gene, exon 7 deletion and who are clinically suggestive of SMA did not differ significantly from negative controls, suggesting that MLPA might not be an appropriate technique to identify the elusive pathogenic rearrangement in black South African SMA patients.

**Project Title:** The mutation spectrum of Rett Syndrome in South Africa  
**Researchers:** Mrs E Vorster, Ms F Essop, Prof. A Krause  
**Funding:** NHLS Research Trust Grant  
**Short Description:** Rett syndrome (RTT) is a progressive, neuro-developmental disorder primarily affecting females, caused by mutations within the MECP2 gene. This study audited patients, referred with a suspected clinical diagnosis of RTT for testing to the NHLS, Johannesburg, Division of Human Genetics, from March 2002–October 2014. A total of 393 unrelated patients (366 females and 27 males) were referred for diagnostic testing, five asymptomatic mothers for carrier testing and two families for prenatal testing. Eighty-one females (81/366, 22.1%) tested positive for a pathogenic mutation. Overall, 35 different pathogenic mutations were identified of which eight were novel (six black, one mixed ancestry, one white). The average positive pickup rate of current RTT diagnostic testing is 20.6%. Recurrent mutations account for 69% (56/81) and novel mutations for 10% (8/81) of all mutations. Carrier and prenatal tests were all negative. Deletions have been reported to account for 32% of the mutations in classic RTT patients who test negative on sequencing analysis. MLPA analysis (using the P015C MLPA kit) is currently being performed on all patients who previously tested negative on sequencing analysis (n = 312) to identify potential deletions and duplication of genes involved in RTT. At the time of this update, 3.75% (3/80) of negative patients were found to have deletions/duplications. This is the first report on the mutation spectrum of RTT in Southern Africa and it is the largest molecular study thus far performed on African RTT patients.

**Project Title:** A six-year review (2009–2014) of MLPA testing performed in patients with developmental delay at the Division of Human Genetics, NHLS, Johannesburg  
**Researchers:** Mr Q Goodyear, Ms F Essop, Prof. A Krause  
**Short Description:** Developmental delay (DD) is characterised by a delay in at least two functional domains; speech/language, gross/fine motor, cognitive, social/personal and/or daily life activities. More than half of patients with DD are due to genetic factors. Chromosomal abnormalities are one such factor. The standard method for detecting chromosomal abnormalities/rearrangements is conventional karyotyping, but this has limitations, some of which can be overcome by use of the multiplex ligation-dependant probe amplification (MLPA) technique. MLPA can be used to screen for microdeletions/duplications (P245) and/or subtelomeric deletions/duplications (P036 and/or P070) using a set of probes specific to these regions. This is a six-year review of the use of MLPA in detecting chromosomal abnormalities in patients with DD. The review focuses on the detection rate of the technique in the South African setting as an alternative to CGH-array testing. In addition it reports on all the abnormalities identified in the patients.

**Project Title:** The identification and characterisation of the causative gene mutation for keratolytic winter erythema (KWE) in South African families  
**Researchers:** Ms T Ngcungcu and Prof. M Ramsay  
**Collaborators:** Dr B Linghu, Dr F Yang, Dr E Oakeley, Dr F Staedtler, Dr R Bruccoleri, Dr N Nirmala, Dr S Buechmann-Moller, Dr M Sultan, Dr J Szustakowski  
**Funders:** Novartis Institutes for BioMedical Research (NIBR)
Keratolytic winter erythema (KWE) is a rare skin disorder of unknown aetiology that results in skin peeling of the palms and soles in cold and dry conditions. KWE shows an autosomal dominant mode of inheritance and the causal mutation was localised to chromosome 8p22-p23 (KWE critical region). The aim of this study was to identify and characterise the causative mutation for KWE in South African families using targeted resequencing (8p22-23) and exome sequencing. A 7.67 kb tandem duplication within the KWE critical region was identified that encompasses an enhancer such that affected individuals have two copies. This tandem duplication was validated in all affected individuals, but the mechanism of action leading to the disease phenotypes remains unclear. Further functional analyses are required.

Gestational diabetes mellitus (GDM) is diagnosed when pregnant women exhibit high blood glucose levels for the first time during pregnancy. It is associated with short- and long-term morbidity in both the mother (increased diabetes, obesity and cardiovascular disease risk) and the offspring and is predictive for poor pregnancy outcomes. Adaptions of a foetus exposed to an adverse intrauterine environment are thought to act through epigenetic modifications which alter gene expression. These epigenetic changes are established early on in life and control the expression of certain genes during development. This study is nested in the Soweto Baby Growth study which is recruiting over 4 000 black South African women during the first trimester of pregnancy. At 24–26 weeks gestation, each participant has an oral glucose tolerance test (OGTT) to assess their glucose tolerance levels during pregnancy. Six mothers with GDM and six healthy controls were recruited, all of whom have had female babies. Study samples include venous blood from the mothers (at 29–33 weeks of gestation) and placental tissue biopsies (tissue of fetal origin). This novel study will provide new insights into the effect of GDM on black South African women and on the developing foetus. This study aims to identify genes that display significant differential expression in the blood and placenta of women with GDM compared to healthy controls and to understand their potential role in future risk for diabetes, obesity and cardiovascular disease in both the mother and her offspring.

Cancer is a non-communicable disease (NCD) and a critical health burden in Africa. Due to an increase in lifespan and adverse lifestyles and exposures, cancer is expected to increase on the continent. Urgent attention is necessary to create awareness of potential adverse drug effects and appropriate treatments and doses in African patients. Chemotherapy treatments are severe and expensive, with many unwanted side effects, placing strain and a large financial burden on the patients and their families. Some patients have a poor treatment outcome which may be attributed to mutations in genes that encode proteins involved in the metabolism, transport or excretion of the drug. These mutations vary in frequency among ethnic groups and highlight the need to study African populations. Many cancer drugs are flagged by the American Food and Drug Administration (FDA) for adverse drug reaction warnings associated with ethnicity. The mutations to which these warnings apply have been best characterised in populations of European, Asian and African-American ancestry, with very little research in African populations. This study will characterise the profile of pharmacogenomically relevant genetic variants in African populations, specifically within the genes that encode the metabolic targets of cancer drugs such as dihydropyrimidine dehydrogenase (DPD), thymidylate synthase (TYMS) and the cytochrome P450 gene family. Whole genome sequence data from African populations will be mined to identify single nucleotide polymorphisms, indels and copy number variants in key genes that have been implicated in adverse reactions or altered efficacy of cancer drugs. Allele frequencies and potential functional impact will be investigated. This approach could lead to the discovery of novel functional genetic variants in African populations and allele frequencies that would highlight the potential public health impact of using specific drugs. A pharmacogenomic approach tailored to African populations could help alleviate the cost of treatment and improve outcomes in African cancer patients.

The H19/IGF2 imprinted gene cluster and its role in birth weight variance in a black, South African cohort

Researchers: Ms L Jacobs, Dr Z Lombard, Ms S Macaulay

Collaborators: Prof. SA Norris (MRC/WITS Developmental Pathways for Health Research Unit)

Funding: NRF Thuthuka

Short Description: Weight at birth is one of the strongest predictors of perinatal morbidity and mortality, second only to preterm...
delivery, and a significant indicator of adult chronic disease development. New-borns of very low (<2 000g) and very high (>4 000g) birth weight, exhibit the highest risk of adverse birth outcomes. In a developing country like South Africa, there continues to be a prevailing problem of malnutrition in a large proportion of the population. Pregnant women and in turn their growing babies are among those most affected by under-nutrition and high calorie diets with little nutritional value. The proposed study will investigate genetic and epigenetic mutations within the human imprinting control region 1 (ICR1) and its associated imprinted genes H19 and insulin-like growth factor 2 (IGF2), which have been previously linked to fetal growth. The ICR1 is a differentially methylated region (DMR) located on chromosome 11p15.5. It controls the mono-allelic expression of functionally antagonistic genes, H19 and IGF2, which are expressed exclusively from the maternal and paternal alleles respectively. To date, the H19/IGF2/ICR1 gene cluster has been thoroughly interrogated for associations with birth outcomes in European cohorts, with little research conducted on African populations. This research project will attempt to fill the gap in the understanding of how maternal and paternal genotypes and epigenotypes modify foetal growth and development in a black South African cohort. A study of this nature is of particular importance in a population where more than 6 300 small for gestational age babies are stillborn annually.

**Project Title:** Glucose metabolism and pregnancy in South African women  
**Researchers:** Ms S Macaulay  
**Collaborators:** Prof. SA Norris (MRC/WITS Developmental Pathways for Health Research Unit) and Prof. D Dunger (Cambridge University)  
**Funding:** MRC and World Diabetes Foundation  
**Short Description:** Poor glycaemic control during pregnancy can have adverse effects on the mother and the developing foetus. Gestational diabetes mellitus (GDM) is defined as diabetes diagnosed for the first time in a woman during pregnancy and encompasses blood glucose levels within the diabetic and pre-diabetic range. The effects of exposure to hyperglycaemia on the foetus can present at birth and later in life. Offspring born to mothers diagnosed with GDM are often large (≥4 kg) which pose risk for delivery. In addition, these children are at risk of developing obesity and type 2 diabetes as they get older. Women diagnosed with GDM are also at risk of developing type 2 diabetes in their later years. The aims of the project are to determine the prevalence of GDM amongst pregnant women living in Soweto and to determine the effects of maternal glucose metabolism during pregnancy on fetal growth and neonatal anthropometric outcomes. The methodology involved in achieving the aims involves the recruitment of pregnant women from the Soweto region who undergo a series of questions and anthropometric measurements at five time points during their pregnancy. The women also undergo a 2 hour 75g oral glucose tolerance test (OGTT) at 24–28 weeks gestation in order to test for GDM. In addition, fetal ultrasound examinations are performed at each visit in order to monitor fetal growth, and finally, at delivery the length, weight and head circumference of the neonate is measured and a body composition assessment using the PeaPod is performed. The results obtained from this research will contribute towards the national health agenda regarding maternal and child health. As there is minimal information on glucose metabolism during pregnancy and the effects thereof on mother and child, the data that will be generated is much needed.

### 4.2 Grant Funding

Table 72: Grant funding

<table>
<thead>
<tr>
<th>Name of grant holder</th>
<th>Title of research project</th>
<th>Awarded by</th>
<th>Period</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ms Fahmida Essop</td>
<td>Screening patients with mental retardation (MR) for deletions, duplications, and copy number variants (CNVs) using the Affymetrix CytoScan™ HD Array</td>
<td>NHLS Research Trust – Extension</td>
<td>2013–2016</td>
<td>R90 000</td>
</tr>
<tr>
<td>Prof. Amanda Krause</td>
<td>The clinical and genetic profile of Huntington disease like 2 (HDL2) in South Africa</td>
<td>Medical Research Council Self-initiated Research Grant</td>
<td>2015 – 2018</td>
<td>R191 300 pa</td>
</tr>
<tr>
<td>Prof. Amanda Krause</td>
<td>An investigation into the spectrum of HD phenocopies in South Africa</td>
<td>NHLS Research Trust</td>
<td>2015 – 2016</td>
<td>R100 000</td>
</tr>
<tr>
<td>Dr Zané Lombard</td>
<td>Genetic and epigenetic risk factors for cardiometabolic disease in South Africans</td>
<td>NRF Thuthuka Development Grant</td>
<td>2015–2017</td>
<td>R354 000 pa</td>
</tr>
<tr>
<td>Ms Thandiswa Ngcungcu</td>
<td>The identification and characterisation of the causative gene mutation for keratolytic winter erythema (KWE) in South African families</td>
<td>MMUF Travel and Research Grant</td>
<td>2015 – 2016</td>
<td>R50 000</td>
</tr>
<tr>
<td>Mrs Elana Vorster</td>
<td>Determining the molecular basis of spinal muscular atrophy (SMA) in the South African black population</td>
<td>NHLS Research Trust – Extension</td>
<td>2014 – 2017</td>
<td>R180 000</td>
</tr>
</tbody>
</table>
5. RESEARCH OUTPUT

5.1. Journal Articles


5.2. Book Chapters

5.3. Conference Presentations
Table 73: Number of conference presentations

<table>
<thead>
<tr>
<th>Number of presentations made by Human Genetics staff and students</th>
<th>International congresses</th>
<th>National congresses</th>
<th>Local congresses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15</td>
<td>27</td>
<td>5</td>
</tr>
</tbody>
</table>
Molecular Medicine and Haematology

Head: Prof. Wendy Stevens

1. ABOUT THE DEPARTMENT

The department continues to play a critical role in delivering quality diagnostic services to patients in South Africa, both in the public and private sectors. It is one of the largest training facilities, with a high publication rate and relevant research output, including novel research and the (R&D) of new diagnostic techniques and their national implementation. Staff members have taken strategic positions in both international and national planning committees reporting to NHLS, the DoH and other organisations as national experts. This places high prevalence diseases like tuberculosis and HIV at the top of the agenda in national health planning, and focuses on high-risk populations. As a result, the department enjoys a close relationship with the DoH and with non-governmental organisations (NGOs), regionally and nationally. This has resulted in the accession to significant funding from internationally recognised bodies including the Global Fund, the CDC and the Bill and Melinda Gates Foundation, amongst others. In addition, several high profile grants have been awarded via the Medical Research Council (MRC) in South Africa, the National Research Foundation (NRF) and the Department of Science and Technology (DST). The department also assists and works closely with the National Priority Programmes (NPP) that has submitted a separate annual report on its activities.

2. DIAGNOSTIC SERVICE

Test volumes continue to increase year-on-year, and the test repertoire offered increases to accommodate the growing needs of the pathology service. The department contains a number of diagnostic units spread between Charlotte Maxeke Johannesburg Academic Hospital, Chris Hani Baragwanath Hospital and Helen Joseph Hospital, some of which are the referral or lead units in their specialised fields of pathology. The diagnostic units include:

- Automated Haematology
- Chris Hani Baragwanath, Haematology
- Clinical Haematology
- Flow Cytometry and CD4
- Haemostasis and Thrombosis
- Helen Joseph, Haematology
- HIV and Molecular Diagnostics Unit
- Immunohaematology
- Morphology
- Somatic Cell Genetics Unit
- Special Haematology.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

Each unit in the department plays a key role in teaching and training of both staff and students.

3.1. Undergraduate Education

The department has is involved in extensive undergraduate teaching in a number of courses in the Faculty of Health Sciences as well as the Molecular Medicine half course in the Biomedical Engineering (BEngSc (BME)) (28 students in 2015). In the Faculty of Health Science, the department is involved in teaching the Molecular Medicine II course for MBCh and BHSc students and the haematology block in the MBCh programme, as well as the Molecular Medicine III course for BHSc students. An average pass rate of 92.86% for undergraduate courses was achieved in 2015 (Table 74). The number of students enrolled in 2016 is indicated in the table below.
Table 74: Summary of undergraduate studies 2015/16

<table>
<thead>
<tr>
<th>Unit Code</th>
<th>Level Description</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAEM2000 – Molecular Medicine 2 MBCh</td>
<td>Level 2</td>
<td>Enrolled</td>
<td>284</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>267</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>94</td>
</tr>
<tr>
<td>HAEM2001 – Molecular Medicine 2 BHSc</td>
<td>Level 2</td>
<td>Enrolled</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>82</td>
</tr>
<tr>
<td>HAEM3002 – Molecular Medicine 3 BHSc</td>
<td>Level 3</td>
<td>Enrolled</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>90</td>
</tr>
</tbody>
</table>

Enrolled 322 387
Passed 299
Failed 23
Unit Pass % 93

3.2. Postgraduate Training
The department facilitates training for a number of postgraduate students (BSc Honours, MMed, MSc, PhD, and postdoctoral fellows). Most students obtain their degrees successfully. A number of the postgraduate degrees span over a number of years, and the pass rate indicated below is dependent on how many students graduate per year, and not how many complete their studies overall (Table 75).

Table 75: Summary of postgraduate studies 2015/16

<table>
<thead>
<tr>
<th>Unit Code</th>
<th>Level Description</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAEM4007 – Molecular Medicine Honours Coursework</td>
<td>Level 4</td>
<td>Enrolled</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>88</td>
</tr>
<tr>
<td>HAEM4008 – Molecular Medicine Honours Research Essay</td>
<td>Level 4</td>
<td>Enrolled</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>100</td>
</tr>
<tr>
<td>HAEM7001 – MMed Haematology</td>
<td>Level 7</td>
<td>Enrolled</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>25</td>
</tr>
<tr>
<td>HAEM7010 – MMed Research Report – Awaiting examiners</td>
<td>Level 7</td>
<td>Enrolled</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>100</td>
</tr>
<tr>
<td>HAEM7011 – MMed</td>
<td>Level 7</td>
<td>Enrolled</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>-</td>
</tr>
<tr>
<td>HAEM8000 – MSc</td>
<td>Level 8</td>
<td>Enrolled</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Passed</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failed</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Unit Pass %</td>
<td>9</td>
</tr>
</tbody>
</table>
### Unit Code and Level Description

<table>
<thead>
<tr>
<th>Unit Code</th>
<th>Level Description</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAEM8001 – MSc research</td>
<td>Level 8 Enrolled 10 5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAEM8004 – MSc/ MSc (Med) Dissertation: Awaiting examiner</td>
<td>Level 8 Enrolled 5 3 Passed 5 Failed 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAEM8006 – MSc Med Dissertation: Awaiting examiners</td>
<td>Level 8 Enrolled 1 4 Passed 1 Failed 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAEM9000 – PhD Thesis</td>
<td>Level 9 Enrolled 25 19 Passed 1 Failed 0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>HAEM9002 – PhD Thesis</td>
<td>Level 9 Enrolled 3 1 Passed 1 Failed 0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HAEM9003 – PhD Thesis: Awaiting examiners</td>
<td>Level 9 Enrolled 1 3 Passed 1 1 Failed 0</td>
<td>100</td>
<td>33</td>
</tr>
</tbody>
</table>

### Enrolled

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>99</td>
<td>90</td>
</tr>
<tr>
<td>Passed</td>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>Failed</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

### Unit Pass %

<table>
<thead>
<tr>
<th></th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit Pass %</td>
<td>30</td>
<td>1</td>
</tr>
</tbody>
</table>

### 3.3. Staff Development

A number of staff are trained in the department including Haematology and Clinical Pathology registrars, intern scientists, intern technologists and technicians. A summary of training outcomes is shown in Table 76 below.

### Table 76: Summary of staff training 2015/2016

<table>
<thead>
<tr>
<th>Trainees</th>
<th>Examination</th>
<th>Pass</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Intern haematology medical technologists</td>
<td>Board 18 March 2016</td>
<td>Awaiting result</td>
</tr>
<tr>
<td>2 Intern clinical pathology medical technologists</td>
<td>Board 18 March 2016</td>
<td>Awaiting result</td>
</tr>
<tr>
<td>5 Interns passed the Board examination</td>
<td>Board March 2015</td>
<td>May 2015</td>
</tr>
<tr>
<td>4 Registrars Oct 2015</td>
<td>FCPath</td>
<td>100% pass</td>
</tr>
<tr>
<td>1 Intern scientist (Molecular Biology)</td>
<td>HPCSA portfolio</td>
<td>Passed December 2015</td>
</tr>
</tbody>
</table>

A number of staff members attended various training courses including:

- Supervisor's skill development
- Approach to auditing
- Morphology course
- Biorad QC course
- First Aid training
- Fire Warden training
- TrakCare refresher
- Advanced Excel
- QC training on TrakCare
- WPS training
- SAFRI Fellowship in medical education (Drs Keene and Whalley)
- Health Science Educators course.

### 3.4 Other

- The Immunohaematology unit trained a number of clinicians, registrars and scientists in the Basic and Advanced Immunology Course.
- Dr Kuben Naidoo visited the European Synchrotron Radiation Facility (ESRF) and Institut Laue Langevin (ILL) in Grenoble, France to gain experience in structural biology techniques.
- Dr Dewaldt Engelbrecht visited the laboratory of Dr Mark Kennedy at Penn State University, USA and the laboratory of Dr Alvaro Molina-Cruz at NIH, USA to develop skills in infecting mosquitoes with malaria parasites.
- A number of postdoctoral fellows are being supervised in the department.
- Two Belgian students did their practical and passed their degrees.
- One Kenyan fellow completed fellowship in February 2016.
- One fellow from Ghana completed fellowship in March 2016.
- One Kenyan fellow started in March 2016.

## 4. Research Activities

By building on existing strengths of high quality research and diagnostic service provision to respond to societal needs, the department aims to seize new opportunities for collaboration and innovation. The department is staffed by a number of excellent researchers who supervise a number of research projects. Staff and students are encouraged to apply for grant funding, to publish their results in high quality journals and to present their research at both national and international conferences. The research outputs are summarised in the sections below.

### 4.1. Research Projects

<table>
<thead>
<tr>
<th>Project Title</th>
<th>Researchers</th>
<th>Funding</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicellularity genomics</td>
<td>Dr P Durand, Prof. RE Michod, Prof. B Olson, Prof. H Nozaki</td>
<td>NASA</td>
<td>4 years</td>
</tr>
<tr>
<td>Organellar genomes of the volvocines</td>
<td>Dr P Durand, D Smith</td>
<td>NASA</td>
<td>4 years</td>
</tr>
<tr>
<td>Protein Systems Biology of an evolutionary transition in individuality</td>
<td>Dr P Durand, F Dehne</td>
<td></td>
<td>1 year</td>
</tr>
<tr>
<td>Group formation in Chlamydomonas</td>
<td>Dr P Durand, Dr S Sathe</td>
<td>Wits</td>
<td>1 year</td>
</tr>
<tr>
<td>Benign ethnic neutropenia in children with malignancies</td>
<td>Dr J Vaughan, Dr G Naidu, Ms S Loonat, Ms M Mohubuke and Mr T Motsewakhumo</td>
<td>Wits FRC</td>
<td>2 years</td>
</tr>
<tr>
<td>Project Title</td>
<td>Researchers</td>
<td>Funding</td>
<td>Duration</td>
</tr>
<tr>
<td>-----------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td>------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Prevalence of cytopenias in HIV positive patients</td>
<td>Dr J Vaughan, Dr K Hodkinson</td>
<td>None</td>
<td>1 year</td>
</tr>
<tr>
<td>Validation of haematology slide review rules at various tiers of diagnostic</td>
<td>Drs N Bouwer, E Shaipkatz, J Vaughan and Prof. JN Mahlangu</td>
<td>None</td>
<td>2 years</td>
</tr>
<tr>
<td>The diagnostic utility and sensitivity of the GeneXpert® MTB/RIF in the</td>
<td>Drs N Subramony, J Vaughan and Prof. L Scott</td>
<td>Wits FRC</td>
<td>18 months</td>
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<tr>
<td>The effect of blood storage on red cell indices and haemoglobin sub-</td>
<td>Dr J Bailey, Ms P Khoza and Dr N Alli</td>
<td>None</td>
<td>1 year</td>
</tr>
<tr>
<td>The positive predictive value of various described formulae utilising red</td>
<td>Ms S Loonat, Dr J Vaughan and Dr N Alli</td>
<td>None</td>
<td>1 year</td>
</tr>
<tr>
<td>A five-year review of external quality assurance experience at a University</td>
<td>Ms B Moyake, Dr E Schapkaitz</td>
<td></td>
<td>3 months</td>
</tr>
<tr>
<td>Evaluation of the accuracy of instrument generated flags for automated</td>
<td>Ms S Rabu, Dr E Schapkaitz</td>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>Evaluation of the International Council for Standardization in Haematology</td>
<td>Ms M Mezgebe, Dr E Schapkaitz</td>
<td></td>
<td>6 months</td>
</tr>
<tr>
<td>The clinical utility of the automated fragmented red cell count for</td>
<td>Dr E Schapkaitz, Ms M Mezgebe, Prof. JN Mahlangu</td>
<td></td>
<td>12 months</td>
</tr>
<tr>
<td>Hereditary Elliptocytosis in a dizygotic twin – a case report</td>
<td>Drs L Swart, E Schapkaitz, K Naidoo, Prof. T Coetzer, Prof. J Poole</td>
<td></td>
<td>2 months</td>
</tr>
<tr>
<td>The spectrum of Myeloproliferative Neoplasms homozygous for the JAK2V167F</td>
<td>Drs T Glatt, E Schapkaitz</td>
<td></td>
<td>24 months</td>
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<td>Project Title</td>
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<tr>
<td>Evaluation of total laboratory automation for haematology at the Charlotte</td>
<td>Ms B Xhakaza, Dr E Schapkaitz</td>
<td>The Global Fund phase II</td>
<td>April 2013–March 2016</td>
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<td>Maxeke Johannesburg Academic Hospital</td>
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<tr>
<td>HIV drug resistance surveillance and HIV drug resistance testing capacitation</td>
<td>Dr S Carmona, Prof. W Stevens, Dr K Steegen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>carcinoma</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>The coding genome of HIV associated lymphomas in South Africa</td>
<td>Drs P Willem, Prof. L Pasqualucci, Prof. R Rabadan</td>
<td>NIH_R21 (Pl. P Willem)</td>
<td>May 2015–31 April 2017</td>
</tr>
<tr>
<td>Investigation of the role of miRNA in primary resistance to Imatinib or</td>
<td>Ms A de Klerk, Dr P Willem</td>
<td>Novartis Oncology</td>
<td>May 2014–Dec 2017</td>
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<tr>
<td>Nilotinib in chronic myeloid leukemia (CML) patients</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Identifying the genome-wide changes occurring in HIV-associated cervical</td>
<td>Ms G Cook, Dr P Willem</td>
<td>DE Wells and NHLS Trust</td>
<td>Dec 2014–Dec 2017</td>
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<tr>
<td>cancer</td>
<td></td>
<td></td>
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<tr>
<td>Gene defects in hereditary red cell membrane disorders</td>
<td>Dr K Naidoo</td>
<td>NHLS</td>
<td>2015</td>
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<tr>
<td>Malaria transmission-blocking drug discovery</td>
<td>Drs S Lauterbach, A Churchyard</td>
<td>MRC SHIP</td>
<td>2014–2015</td>
</tr>
<tr>
<td>Infection of Anopheles mosquitoes with <em>P. falciparum</em></td>
<td>Drs D Engelbrecht, S Shunmugam</td>
<td>MRC SHIP</td>
<td>2014–2016</td>
</tr>
<tr>
<td>Trafficking of malaria parasite proteins</td>
<td>Dr A Churchyard</td>
<td>Wits, NRF</td>
<td>2013–2016</td>
</tr>
</tbody>
</table>
Project Title: Programmed cell death in malaria parasites  
Researchers: Drs D Engelbrecht, W Viera, D Liebenberg  
Funding: Wits, NRF  
Duration: 2012–2016

Project Title: Glycerol kinase in malaria parasites  
Researchers: Dr K Naidoo  
Funding: Wits  
Duration: 2015

Project Title: Point-of-Care CoaguCheck INR analyser validation  
Researchers: Dr E Benade, Prof. B Jacobson, Dr S Louw  
Funding: Sanofi  
Duration: Completed

Project Title: Rivaroxaban activity testing and establishing a reference range  
Researchers: Dr S Louw and Prof. B Jacobson  
Funding: SASTH  
Duration: Completed and awaiting publication in SAMJ

Project Title: The utility of fibrinogen in DIC diagnosis  
Researchers: Drs S Louw and E Mayne  
Funding: No cost  
Duration: Ongoing

Project Title: The pathogenesis of HIV-related TTP  
Researchers: Drs S Louw and R Gouden  
Funding: No cost (record review)  
Duration: Ongoing

Project Title: Biological B-cell stimulatory markers in B-cell Non-Hodgkin lymphoma  
Researchers: L Cruywagen, C Worsley and Dr E Mayne  
Funding: NHLS Research Trust  
Duration: 2015–2017

Project Title: HIV-associated endothelial dysfunction in adults  
Researchers: Dr E Mayne  
Funding: Thuthuka NRF Fund  
Duration: 2013–2017

Project Title: Comparison to international observed full blood count and lymphocyte subset values of a cohort of clinically healthy South African children  
Researchers: Prof. D Glencross, Dr D Lawrie  
Funding: Welcome Trust  
Duration: Ongoing

Project Title: Understanding CD4 workflow across 60 NHLS CD4 laboratories: An analysis of national CD4 test volumes and turnaround times (TAT) in the context of specific HIV anti-retroviral treatment  
Researchers: Prof. D Glencross, Dr L Coetzee and Mr N Cassim  
Funding: NHLS/NRF
Duration: Ongoing

Project Title: Implementation of reflexed cryptococcal antigen screening in CD4 across South Africa: Understanding unit test costs, clinical cost effectiveness, pilot site evaluation and strategies for best practice implementation

Researchers: Prof. D Glencross, Dr L Coetzee and Mr N Cassim

Funding: NHLS/CDC

Duration: Ongoing

Project Title: Evaluation and validation of new and existing cryptococcal antigen screening technologies: Comparison of manual lateral flow assay and ELISA-based automated systems

Researchers: Prof. D Glencross, Dr L Coetzee and Mr N Cassim

Funding: NHLS/NRF

Duration: Ongoing

Project Title: Evaluation and validation of new and existing CD4 technologies: Comparison to predicate methods in laboratory and field studies

Researchers: Prof. D Glencross and Mr N Cassim

Funding: NHLS/NRF

Duration: Ongoing

Project Title: Assessing the impact of using a modification of Cohen’s method of standard setting on pass rates and pass marks for the Molecular Medicine course

Researchers: P Keene, S Schoeman, N Whalley, S Moch, G Mubuuke

Funding: Nil

Duration: 2 years

Project Title: Effects of the Academic Development Programme (ADP) tutorials on the quality of learning in second-year molecular medicine students

Researchers: N Whalley, Dr A Louw

Funding: Nil

Duration: 2 years

4.2. Grant Funding

Projects in the department are funded by various sources:

- AffreVac
- Bayer Health USA
- Bill and Melinda Gates Foundation
- Biogen Idec USA
- BMSIC – Bristol-Myers Squibb Inc Corp
- CANSA
- Carnegie Foundation
- CDC – Centres for Disease Control
- Cepheid
- CSL Behring, Germany
- Daiichi Sankyo Pharma Development
- DE Wells Research Grant
- Department of Health, South Africa
- Deutsche Forschungsgemeinschaft (DFG) and National Research Foundation (NRF) partnership
- DST – Department of Science and Technology
- Eisai Limited
Faculty Research Council (FRC)
FIND – Foundation of Innovative New Diagnostics
Fondazione Angelo Bianch Bonomi
Global Fund
Grand Challenges Canada
Griffins
IAVI – International AIDS Vaccine Initiative
Inspiration Biopharmaceuticals Inc
Institute of Global Health and Development
Johnson & Johnson Innovation
Medical Research Council (MRC)
NASA
National Institute of Allergy and Infectious Diseases
National Institute of Health (NIH), USA
NCA
Netherlands AIDS Fund
NHL Research Trust – National Health Laboratory Service Research Trust
NIH – National Institute of Health
NIH_R21
NNHF – Novo Nordisk Haemophilia Foundation
Nordisk Denmark
NRF – National Research Foundation
NRF Competitive Funding for rated researchers
Octapharma USA
PEPFAR
Quintiles-Clindepharm (Pty) Ltd
Right to Care
Roche Pharmaceutical USA
SAMi – South African Malaria Initiative
UNICEF – United Nations Children’s Fund
University of the Witwatersrand
USAID – United States Agency for International Development
World Federation of Haemophilia.

5. RESEARCH OUTPUT

The department increased its research output in the year under review (Table 77). Many of the research outputs are also reported in the NPP Annual Report.

Table 77: Research output of the Department of Molecular Medicine and Haematology

<table>
<thead>
<tr>
<th></th>
<th>2014/15</th>
<th>2015/16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal publications</td>
<td>80</td>
<td>82</td>
</tr>
<tr>
<td>Books/book chapters</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Conference presentations</td>
<td>70</td>
<td>91</td>
</tr>
</tbody>
</table>
5.1. Journal Publications


Ely A, Arbuthnot P. Differing prospects for the future of using gene therapy to treat infections with Hepatitis B virus and Hepatitis C virus. 

Ely A, Moyo B, Arbuthnot, P. Progress with developing use of gene editing to cure chronic infection with hepatitis B virus. 
*Mol. Ther.* (in press).

Engelbrecht D, Coetzer TL. Sunlight inhibits growth and induces markers of programmed cell death in 
*Plasmodium falciparum* in vitro. 


Kilfoil KM, Grant ML, Cerutti NM, Capovilla A, Papaathanasopoulos MA. Env-2DCD4 S60C complexes act as super immunogens and elicit potent, broadly neutralising antibodies against clinically relevant human immunodeficiency virus type 1 (HIV-1). 

*Clinical Infectious Diseases.* Published online 18 Feb 2015. DOI: 10.1093/cid/civ109. PMID: 25694653.


Sedick Q, Vaughan J, Tebogo P, Alli NA. Bone marrow aspirate microscopy v. bone marrow trephine microscopy for detection of *Mycobacterium Tuberculosis* infection.


5.2. Book Chapters

5.3. Conference Presentations

Oral Presentations


- Coetzee TL. In search of the Achilles heel of the malaria parasite. PathRed NHLS conference, Johannesburg, 14–16 April 2015.


- Dhar N. Ribozyme plasticity and molecular trade-offs enhance network stability at the origin of life. Oral. Wits Health Sciences Faculty Research Day.


- Durand P. Programmed cell death in phytoplankton blooms. Invited address at Biocomplexity Conference, University of Paris (Sorbonne), France.

- Featherston J. Draft genome of *Tetraebaena socialis*. Oral. 2nd Volvox Conference.


- Keene P, Schoeman S, Moch S, Whalley N, Mubuuke G. The impact of a modified Cohen method of standard setting on pass marks and pass rates in the Molecular Medicine II course. Faculty Teaching and Learning Symposium: From Molecules to the Workplace. Wits Faculty of Health Sciences, 2 September 2015.

• Liebenberg D, Coetzee TL. Novel binding partners for a P. falciparum Inhibitor of Apoptosis (IAP) Protein. MRC Malaria Research Meeting, Durban, 3–5 August 2015.


• Mahlangu J. Novel therapies in haemophilia. Orchid Medical Education Symposium, Sydney, Australia, 15–17 August 2015.


• Mayne E. Biorepositories in South Africa. H3 Africa Consortium meeting, October 2015.

• Naidoo K, Van Jaarsveld I, Coetzee TL. The reduced growth of glycerol kinase knockout Plasmodium falciparum parasites is associated with the down-regulation of lipid synthesis and membrane proteins involved in parasite invasion. MRC Malaria Research Meeting, Durban, 3–5 August 2015.


• Sathe S. Group Formation in Chlamydomonas is chimaeric and depends of morphological traits like size and swimming speed. Institute for Systems Biology Research Day.


• Stevens W. Viral load suppression and the role of viral load testing in the context of improved adherence. 7th HIV Clinicians Society meeting, Durban, South Africa, June 2015.


• Whalley NA and Keene P. Student perceptions and effects of ADP tutorials in the MBBCHIII and BHScM Molecular Medicine Course. Faculty of Health Sciences, Teaching and Learning Symposium: From Molecules to the Workplace, University of the Witwatersrand Health Sciences Faculty, 2 September 2015.


Poster Presentations

• Baker GL, Walton AH and Willem P. Kit mutations in core-binding factor acute myeloid leukaemia. 17th National Congress of South African Society of Medical Oncology (SASMO) and South African Society of Clinical & Radiation Oncology (SASCRo), CTICC, Cape Town, South Africa, 7–9 August 2015.


• Mahlangu JN. Masterclass: The future of hemophilia care in South Africa


• Oldenburg J, Srivastava A, Mahlangu J, Blanchette V, Kulkarni R, Li S, Tsoa E, Jain N. Modified haemophilia joint health scores (MHJHS) outcomes with recombinant factor VIII FC fusion protein (rFVIII-Fc) prophylaxis in subjects with severe haemophilia A. European Association for Haemophilia and Allied Disorders, Malmo, Sweden, 3–5 February 2016.
A number of staff members contributed towards national and international policies, and the development and implementation of new technologies and services. Again, many of these activities overlap with those of the NPP.

- Stevens W and NHLS Microbiology Expert Committee members. Department of Health. Urine LAM policy brief. Author/reviewer
- Glencross D, Cassim N, Coetzee L and colleagues. Cryptococcal antigen policy and implementation
- Cassim N. The ideal clinic
- Stevens W. The role of the gamma interferon assay in the diagnosis of latent TB. Policy Brief. 2015/ 2016 review
• Stevens W, Scott L. 2015 October, invited participant to ‘Models for Accelerating Treatment Initiation Technical Consultation’, Cape Town, organised by Bill and Melinda Gates Foundation, funded HE2RO project to present on ‘Point of Care Laboratory for ART Initiation’ together with Prof. Wendy Stevens. This is now being incorporated into a meeting report and a manuscript (Rosen S, et al.): Accelerating the uptake and timing of antiretroviral therapy initiation in sub-Saharan Africa: An operations research agenda.

• Stevens W, Scott L. 2015 April. Invited to co-present with Dr Alaine Nyaruhirira on ‘Advancements on GeneXpert remote connectivity and quality management’ at the Joint Partners Forum for Strengthening and Aligning TB Diagnosis and Treatment, WHO Executive Board Room, Geneva.

• Scott L. January 2015, April 2015, Consultant to WHO for evaluations of diagnostics applied to resource limited settings for HIV viral load and CD4 testing (ERPD- Expert Review Panel for Diagnostics, panel member)

• Mayne E. Africa Biorepository:
  - H3A Biospecimen Transport and Shipping SOP
  - Biospecimen Deposit Guidelines
  - H3africa Biospecimen Deposit MTA
  - Biospecimen release policy and Procedure
  - H3africa Data and Biospecimen Access Committee Guidelines.

6. ACADEMIC AND RESEARCH HONOURS AWARDS/RECOGNITION

• PM Durand appointed to the editorial board of Journal of Phycology.

• PM Durand appointed as Chairman of the South African National Phycology Culture Collection (SANPCC).

• Prof. Mahlangu was appointed Co-Chair of the Scientific Committee of the International Society of Haemostasis and Thrombosis.

• The Bleeding disorders Unit was designated as the International Haemophilia Training Centre (IHTC) by the World Federation of Haemophilia. It is currently the only IHTC Centre in Africa.

• Dr Dewaldt Engelbrecht was awarded a Claude Leon Foundation postdoctoral fellowship and is being hosted by Prof. TL Coetzer.

• Prof. Deborah Glencross was promoted to Full Research Professor.

• Dr P Keene was named ‘Most Influential Lecturer of the Year’ (MBBCh 3 and 4) Wits Medical Students’ Council Awards.

• Dr N Whalley was awarded a Certificate of Appreciation at the Wits Medical Students’ Council Awards.

• Dr P Keene graduated as a SAFRI Fellow, September, 2015.

• Dr N Whalley was selected to attend the SAFRI Fellowship programme starting in March, 2016.

7. ADDITIONAL INFORMATION

Many of the activities in the department overlap with those of the National Priority Program. Please refer to their report for more information.
Anatomical Pathology

Head: Prof. L Banach

1. ABOUT THE DEPARTMENT

The Anatomical Pathology Department comprises five technical staff members and three pathologists, and all pathologists are contracted on a joint appointment with the Walter Sisulu University (WSU). The department provides histopathological and cytological diagnostic services to the Nelson Mandela Academic Complex in Mthatha, which includes tertiary services at Nelson Mandela Academic and Bedford Orthopaedic hospitals, and secondary services at Mthatha General Hospital. The department also offers diagnostic services, and serves as the main referral centre for a large number of peripheral hospitals and primary healthcare facilities in a radius of ~200 km around Mthatha (Region D of the Eastern Cape).

2. DIAGNOSTIC SERVICES

The average number of histopathology and cytology specimens handled in 2015 was around 2 100 per month, a 2.3% increase from 2014. A considerable increase in work volumes was recorded, especially in post-mortems. The cytology work volumes also increased considerably from previous years, particularly in relation to both gynaecological and non-gynaecological specimens, including fine needle aspiration (FNAs).

The department offers systematic consultancy support to special clinical services, such as the Dermatology Clinic, via weekly meetings and follow-ups of critical results.

Despite being understaffed, the department regularly provides consultancy support under the NHLS services at the Nelson Mandela Tertiary Laboratory (NMTL) in Mthatha. The department was able to maintain the standard of its pathology services at the Nelson Mandela Academic Complex, retaining its SANAS accreditation as a tertiary laboratory in 2015.

Table 78: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Technologists</th>
<th>Support</th>
<th>South African*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>1 3 4 1 1 9 10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1 2</td>
<td>- - -</td>
<td>1 2</td>
</tr>
<tr>
<td>Other</td>
<td>1 - 1 - - 1 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>South African*</td>
<td>2 4 5 1 1 13 13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>3 5 5 1 1 5 15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department takes a problem-based learning (PBL) approach to medical undergraduate training and is involved in case selection, facilitation, supporting lectures, tutorials, practical classes and examinations. A comprehensive course is offered during the third year of the MBChB curriculum which fully integrates Anatomical Pathology, Chemical Pathology, Microbiology and Pharmacology. The course is structured as four consecutive modules for the year. The main teaching activity is a small group tutorial presented as two sessions of three hours per week. During the year, 118 students were registered for this course. Further to this, the department is involved in teaching which is integrated into the preclinical and clinical years of the medical career, with regular sessions and final assessments shared with the main clinical services.

Supportive teaching is also provided to second and third year WSU students studying towards a Bachelor in Clinical Medical Practice, with regular sessions as part of the Pathology module. The module runs during the first ten weeks of the academic year.

During 2015, the department also provided academic support to the WSU MBChB programme. It tutored a group of ~20 students in the module on Community-based Education and Service (COBES) for MBChB III. The module included a full afternoon per year spent at the Primary Healthcare Centre for Ngangelizwe, in the outskirts of Mthatha.

Weekly supportive teaching was also given to Medical Technology students during their training in the NMTL.
3.1 Other Training Information
The department received Health Professions Council of South Africa (HPCSA) accreditation for registrar training via MMed in 2014. Two registrar posts have been allocated to the department for 2015. The training started with one registrar in the latter part of the year.

4. RESEARCH ACTIVITIES
The department is mostly engaged in collaborative research projects with the clinical departments in the WSU Faculty of Health Sciences. Due to current academic understaffing and resultant teaching overload, the department was limited in its engagement in independent research projects, community engagement and outreach programmes, and engaged more in the area of ‘educational research’.

4.1 Research Projects
Benign and malignant neoplasms in Transkei, based on the registry and material of registry and NHLS Pathology Laboratory (continuation).
Morphologic findings in HIV/AIDS (continuation). This is now a multi-institutional research collaboration with the University of Stellenbosch.

5. RESEARCH OUTPUT
5.1 Conference Presentations

6. ADDITIONAL INFORMATION
The department remains committed to serving the WSU Medical School by taking on large part of its undergraduate PBL and community-based programmes. It will continue collaborate on teaching and examinations in the clinical and basic years and teaching parallel courses, such as the Clinical Associate Programme. In addition to its academic role, the department still needs to fulfill its role as pathologists at the laboratory, rendering our services to hospital patients through the NHLS. This tightrope between activities continues to threaten service quality, professional development and researcher involvement.
Chemical Pathology

Head: Prof. E Blanco-Blanco

1. ABOUT THE DEPARTMENT

The NMTL Chemistry Department comprises ten staff members and two pathologists, both of whom are contracted on a joint appointment based between WSU and the Department of Health (DoH). The department provides laboratory diagnostic support to the Nelson Mandela Academic Complex in Mthatha, which includes tertiary services at Nelson Mandela Academic and Bedford Orthopaedic hospitals, and secondary services at Mthatha General Hospital. The department also offers laboratory support services as the main referral centre for a large number of peripheral hospitals and primary healthcare facilities in a ~200 km radius around Mthatha (Region D of the Eastern Cape).

Table 79: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th></th>
<th>Pathologist</th>
<th>Technologists</th>
<th>South African*</th>
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<td>1</td>
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<tr>
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<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
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<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
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</tbody>
</table>

2. DIAGNOSTIC SERVICES

The department offers a 24-hour diagnostic service comprising routine chemical pathology assays and a basic repertoire of endocrine assays. The laboratory’s workload increased drastically in 2015, mostly due to processing of samples from special national programmes, such as the anti-retroviral (ARV) rollout. The laboratory processes an average of 5 500 tests per month.

Special support is provided in the administration and maintenance of routine point of care services for blood gases and ancillary tests at three different intensive care units at Nelson Mandela Academic Hospital (NMAH).

The department offers systematic consultancy support to special clinical services, such as the Diabetic and Cardiac Clinic. The service includes routine clinical pathology tests, endocrine tests, drugs testing and other special tests.

The department also supports the Endocrine and Cardiac Clinic of the Medical Outpatients Special Clinic at NMAH on a weekly basis and interacts with clinical departments on regular basis, particularly to follow up on abnormal results.

Despite being understaffed in terms of pathologists and its heavy teaching load, the department regularly provided consultancy support under the NHLS services at Nelson Mandela Tertiary Laboratory in Mthatha. The department retained its SANAS accreditation as a tertiary laboratory in 2015.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department takes a PBL approach to medical undergraduate training and is involved in case selection, facilitation, supporting lectures, tutorials, practicals and examinations. A comprehensive course is offered during the third year of the MBChB curriculum, which fully integrates Anatomical Pathology, Chemical Pathology, Microbiology and Pharmacology. The course is structured as six consecutive modules throughout the year. The main teaching activity for this programme is small group tutorials in two three-hour sessions per week. During 2015, 118 students were registered for this course. Further to this, the department is involved in teaching which is integrated into the preclinical and clinical years of the medical career, with regular sessions and final assessments shared with the main clinical services.

Supportive teaching is also provided to second and third year WSU students studying towards a Bachelor in Clinical Medical Practice, with regular sessions as part of the Pathology module. The module runs during the first ten weeks of the academic year.

An elective module in Chemical Pathology for MBChB final year students was offered to three participants. During this four-week course, students were integrated with the pathologists and participated in all regular activities of the department. An elective six-week module on Clinical Biochemistry is offered to the BSc Honours in Biochemistry students. One student completed it in 2015.
During the reporting period, the department also provided academic support to the WSU MBChB programme. It tutored a group of ~20 students in the module on Community-based Education and Service (COBES) for MBChB III. The module included a full afternoon per year spent at the Primary Healthcare Centre for Baziya, located 60 km from Mthatha.

Postgraduate students included one completing a Postgraduate Diploma in Chemical Pathology (NQF 8) and one doing their MSc in Chemical Pathology (NQF 9). These students are currently engaged in their research projects and have advanced to their second and third years respectively.

Weekly supportive teaching was also given to Medical Technology students during their training in the NMTL.

<table>
<thead>
<tr>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSc Hons/ PGD</td>
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<td>7</td>
<td>7</td>
</tr>
<tr>
<td>MSc</td>
<td>5</td>
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</tr>
<tr>
<td>South African</td>
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</tr>
<tr>
<td>All</td>
<td>12</td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>

4. RESEARCH ACTIVITIES

The department is mostly engaged in collaborative research projects with other clinical departments in the WSU Faculty of Health Sciences. Departmental research is mainly promoted via support and supervision of MSc projects, which are funded by the WSU and Medical Research Council (MRC). Ongoing research towards an MSc Chemical Pathology includes areas such as biomarkers for CVA risks, leptin and thyroid function in low birth weight neonates, biomarkers in prostate cancer and setting up local reference ranges. The department also engages in interdepartmental collaborative research projects in the area of diabetes mellitus.

4.1. Research Projects

Project Title: Establishment of reference ranges for selected analytes in the Eastern Cape, in progress. This study is part of a larger multi-centre collaborative project.

Project Leader: Prof. E. Blanco-Blanco.

Project Title: Establishing adult reference values for selected analytes from South Africa, Nigeria and Kenya.

Project Leader: Prof. Rajiv Erasmus.

5. RESEARCH OUTPUT

Completed research project on ‘The Role of Biomarkers in the Management of Premature Stroke in the Eastern Cape Province’ by WSU MSc student Collin Forka. Supervised by Professors Longo-Mbenza and E. Blanco-Blanco.

5.1 Journal Publications


6. ADDITIONAL INFORMATION

In addition to the regular teaching support to the faculty, Prof. E. Banco-Blanco also served as Chairperson of the Library and Information Services and Resources Development Committees of the faculty and institutional senate. He is also the pathologist representative for the WSU Academic Pathology Committee and Chairperson of the FHS Institutional Academic Research and Planning Committee. He furthermore served as reviewer for the Faculty Science Committee and as a member of Curriculum Development, Staff Development and Quality Assurance committees of the faculty.

Due to current academic understaffing and resultant teaching overload, the department was limited in its engagement in independent research projects, community engagement and outreach programmes, and engaged more in the area of ‘educational research’.
Haematology

Head: Prof. BA Ogunsanwo

1. DIAGNOSTIC AND CLINICAL SERVICES

The department offers comprehensive laboratory services to the Nelson Mandela Academic, Mthatha General and Bedford Orthopaedic hospitals, as well as various secondary hospitals and clinics in the region. It offers both in- and out-patient clinical services to the NMAH under the auspices of the Department of Internal Medicine, and all patients are admitted in the four Medical wards and are jointly managed with the help of interns and medical officers.

The department also offers its expert opinion and care for haemophilia patients from a 200 km radius at the Haemophilia Clinic of the NMAH. It routinely conducts telephonic consultations on haematology matters with medical officers throughout its catchment area, and conducts an average of three to five such consultations a day. Through this patients are then booked into the clinic in the hospital’s Medical Outpatients Department.

2. DIAGNOSTIC SERVICE

The department offers a 24-hour diagnostic service comprising routine and specialised haematology tests. About 300 full blood count samples are processed daily on week days, and much fewer on weekends. The rest of the services consist of other routine haematology tests.

3. TEACHING AND TRAINING

3.1. Undergraduate

The department undertakes the haematology lectures for MBChB II students during their Cardio-Respiratory block. It is also engaged in the PBL and Community-based Education and Service (COBES) curriculum for MBChB III students, which entails the identification of core material, student facilitation, lectures, and assessment of student performance. A total of 118 students were enrolled for this course in 2015. Haematology is incorporated into the Internal Medicine module of MBChB IV and V students. The module takes the form of lectures and tutorials, end-of-block assessments and final exams. Students are divided into six groups that rotate between lectures during the six-week course.

4. RESEARCH ACTIVITIES

Aspects of the following research projects have been ongoing for a couple of years, in collaboration with the Department of Internal Medicine:

- Prevalence of deep vein thrombosis in patients with HIV/AIDS
- Prolonged remission in chronic myeloid leukaemia patients treated with a tyrosine kinase inhibitor
- Retroviral induced aplastic anaemia and other Cytopaenias in Mthatha
- Factor VIII inhibitors in patients with Haemophilia A in the Transkei region
- Immune thrombocytopenic purpura in patients with AIDS: prevalence and response to standard therapy.

5. ADDITIONAL INFORMATION

Due to a chronic shortage of academic staff (only one since 2004), it has been difficult to devote any substantial time to meaningful research. The department could therefore only provide teaching and diagnostic services, which jointly accounted for over 90% of its activity.
Medical Microbiology

Acting Head: Prof. SD Vasaikar

1. ABOUT THE DEPARTMENT

The Medical Microbiology Department comprises five staff members and two pathologists, are contracted on a joint appointment bases between WSU and the DoH. The department provides laboratory diagnostic support to the Nelson Mandela Academic Complex in Mthatha, which includes tertiary services at Nelson Mandela Academic and Bedford Orthopaedic hospitals, and secondary services at Mthatha General Hospital. The department also offers laboratory support services as the main referral centre for a large number of peripheral hospitals and primary healthcare facilities in a ~200 km radius around Mthatha (Region D of the Eastern Cape).

Table 82: Total number of staff per profession and highest qualification

<table>
<thead>
<tr>
<th>Pathologist</th>
<th>Technologists</th>
<th>South African*</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Indian</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>South African*</td>
<td>2</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

2. DIAGNOSTIC AND CLINICAL SERVICES

The department offers a 24-hour diagnostic service comprising routine medical microbiology tests and basic TB services (culture and sensitivity). During 2015, the laboratory’s workload continued to increase, mostly due to processing of samples from special national programmes, such as the ARV rollout. The routine bench analyses an average of 400 specimens per day, while the special TB GeneExpert PCR runs ±700 tests per week, compared to 200 in 2014.

Due to staff shortages, university research engagement and the heavy teaching load, the department provided limited consultancy support to the NHLS services at the NMTL. By maintaining its service levels, the department retained its SANAS accreditation as a tertiary laboratory.

The department offers special support in the infection control units at NMAH, and interacts with clinical departments on regular basis to follow up on abnormal results and advise on the use of antimicrobials.

3. TEACHING, TRAINING AND PROFESSIONAL DEVELOPMENT

The department takes a PBL approach to medical undergraduate training and is involved in case selection, facilitation, supporting lectures, tutorials, practicals and examinations. A comprehensive course is offered during the third year of the MBChB curriculum which fully integrates Anatomical Pathology, Chemical Pathology, Microbiology and Pharmacology. The course is structured as four consecutive modules for the year. The main teaching activity is a small group tutorial presented as two sessions of three hours per week. During the year, 118 students were registered for this course.

Supportive teaching is also provided to second and third year WSU students studying towards a Bachelor in Clinical Medical Practice, with regular sessions as part of the Pathology module. The module runs during the first ten weeks of the academic year.

An elective six-week module on Medical Microbiology is offered to the WSU BSc in Biochemistry and Physiology students, and in 2015 four completed this module.

During 2015, the department also provided academic support to the WSU MBChB programme. It tutored a group of ~20 students in the module on Community-based Education and Service (COBES) for MBChB III. The module included a full afternoon per year spent at the Primary Healthcare Centre Mhlakulo Community Health Centre.

Postgraduate students included one completing a Postgraduate Diploma in Chemical Pathology (NQF 8) and one doing their MSc in Chemical Pathology (NQF 9). These students are currently engaged in their research projects and have advanced to their second and third years respectively.
## Table 83: Total number of trainees per qualification category

<table>
<thead>
<tr>
<th></th>
<th>Total number of trainees</th>
<th>Final year trainees</th>
<th>Successful completion</th>
<th>Percentage of successful completions</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSc Hons</td>
<td>6</td>
<td>6</td>
<td>4</td>
<td>66.6%</td>
</tr>
<tr>
<td>MSc</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>PhD</td>
<td>4</td>
<td>1</td>
<td></td>
<td>0%</td>
</tr>
<tr>
<td>South African</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>33%</td>
</tr>
<tr>
<td>All</td>
<td>13</td>
<td>11</td>
<td>5</td>
<td>45.5%</td>
</tr>
</tbody>
</table>

### 3.1 Postgraduate Students

The following students will be graduating in September 2016:

- One MSc (Medical Microbiology)
- Two BSc Hons (Medical Microbiology).

### 4. RESEARCH ACTIVITIES

The department is mostly engaged in collaborative research projects with the clinical departments in the WSU Faculty of Health Sciences. Departmental research is mainly promoted via support and supervision over student projects.

#### 4.1. Research Units/Study Groups linked to the Department

The HIV Research Group, led by Dr Teke Apalata, received three-year funding from the MRC from April 2015.

#### 4.2. Research Projects

**Project Title:** Evolution of HIV-infected patients receiving HAART and quality of HIV/AIDS care initiated by nurses at primary healthcare level in the Eastern Cape, South Africa  
**Principal Investigator:** T Apalata  
**Co-investigators:** Longo-Mbenza, Norah Katende

**Project Title:** T cell mediated response in HIV-infected patients with cryptococcal meningitis before and after initiation of HAART (in progress)  
**Principal Investigator:** T Apalata

#### 4.3. Grant Funding

- Dr Teke Apalata received a three-year WSU Institutional Research Grant of R175 000 per year.

### 5. RESEARCH OUTPUT

#### 5.1. Journal Publications


### 5.2. Conference presentations

The department presented several papers at the First Univen-WSU International Research Conference held in East London in 2015. These included:

Katende-Kyenda, NL and Apalata, T. An assessment of the level of knowledge about HAART and HIV infected patient’s waiting time at a primary healthcare centre.

Vasaikar SD, Obi CL, Morobe L, Mabotja TKC and Apalata T. Setting up of a molecular laboratory (Pcr) in a resource-limited setting in WSU, Mthatha.


Apalata, T. Cost-benefit analysis of managing healthcare-associated infection at Mthatha Regional Hospital in the Eastern Cape, South Africa.

Muringani, BN, Obi, CL, Apalata, T and Vasaikar, SD. Prevalence of potential enteric pathogens in treated and untreated water sources around the Eastern Cape region.


### 6. ADDITIONAL INFORMATION

Dr Apalata served as co-ordinator of COBES for MBChB III, and Prof Vasaikar is a member of the Curriculum Development, Staff Development and Quality Assurance committees to the faculty, and both served as reviewers for the Faculty Science Committee. Due to academic understaffing and the overload with teaching, the department was limited in its service support, community and outreach.