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Executive Manager’s Foreword

In collaboration with our academic partners, the NHLS has gone from strength to strength.

Dr Johan van Heerden
Executive Manager

Introduction

Since its inception in 2001, the NHLS has been on the forefront of academic achievement, actively promoting the teaching and research mandates of the organisation. The 2012/2013 Annual Report again celebrates these achievements by publishing a separate volume in the report dedicated to these mandates.

In collaboration with our academic partners, the NHLS has gone from strength to strength. This Academic Review acknowledges the much valued contribution by the joint staff (dual appointments by the NHLS and each university) of:

1. The University of Cape Town
2. The University of the Free State
3. The University of KwaZulu-Natal
4. The University of Limpopo (Medunsa)
5. The University of Pretoria
6. The University of Stellenbosch
7. The University of the Western Cape
8. The University of the Witwatersrand
9. Walter Sisulu University.

The relationship between the NHLS and its academic partners is cemented in the concluded umbrella agreement, and the bilateral agreements, which are all on track to be signed during the next financial year.

These agreements 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 and community service activities and achievements. It is clear that the NHLS is not only leading the way in South Africa and the SADC region, but our academic footprint is rapidly expanding into Africa and the rest of the world.

The training of health professionals is dependent on an integrated academic and service platform with the clear understanding and appreciation that in so far as health professional training is concerned, teaching, research and service delivery form a continuum and are inextricably linked.

It is the statutory responsibility of the NHLS to train pathologists, medical scientists, technologists and technicians for the country as a whole. Our close academic partnerships enable the NHLS and universities to produce skilled and dedicated health professionals in pathology.

Research lies at the heart of development and innovation. The collaboration between NHLS and our academic partners is producing a
wealth of ground-breaking, relevant research to propel pathology into the second decade of the 21st century. Combined, the NHLS (including the NICD and NIOH) and the universities boast an impressive research output, which is evident by the amount of grant funding they received, and the number of peer-reviewed publications and presentations at local and international congresses.

An inaugural NHLS Research Summit was held in February 2013 and was attended by more than 150 delegates, including NHLS researchers from all our academic partners, an international speaker and prestigious local keynote speakers.

The summit was instrumental in setting research priorities and steering our vision to be the premier pathology-related research platform on the continent and a major player internationally. The outcomes of the summit will be considered and implemented during the next financial year.

The road ahead is filled with challenges and the 2013/14 year will witness the prioritisation of key objectives. These include, but are not limited to:

1. Improved registrar recruitment and retention
2. Improved registrar pass rate
3. Improving the equity profile of our students
4. Translation of research into operational efficiencies
5. Translation of research to influence national policies
6. Implementing the recommendations of the NHLS Research Summit

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 cooperation in the years ahead.

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Dr Johan van Heerden
Executive Manager
Division of Anatomical Pathology

Head: Professor Dhiren Govender

Diagnostic Services

The Division of Anatomical Pathology provides comprehensive diagnostic histopathological, cytopathological and autopsy services to Groote Schuur (GSH), Red Cross Children’s (RCCH), Somerset, GF Jooste and Victoria hospitals, which belong to the University of Cape Town’s academic hospital complex. The Division also provides diagnostic services to 2 Military Hospital in Wynberg. There are separate SANAS accredited laboratories at Groote Schuur (histopathology and cytopathology) and Red Cross Children’s hospitals. In addition, diagnostic services are offered to the University of Cape Town Private Academic Hospital and consultative and referral services to NHLS and private laboratories in East London, Port Elizabeth, Cape Town, Durban and Pietermaritzburg.

The Groote Schuur Hospital histopathology laboratory received 32,586 surgical pathology cases (including many cases with multiple specimens), the cytopathology laboratory processed 74,927 cases, of which 65,608 were cervical smears, and 9,319 were non-gynaecological cases. The FNA Clinic performed 138 FNA procedures. The electron microscopy unit at GSH processed 432 specimens and the immunohistochemical laboratory performed 17851 tests. During the reporting period 71 adult autopsies were performed. The fetal and perinatal service at GSH examined 156 fetuses and 810 placentas.

The Red Cross Children’s hospital histopathology service included paediatric cases and muscle biopsies. A consultative service for muscle biopsies is based at the Red Cross Children’s Hospital; during the reporting period 176 muscle biopsies were processed, 161 of which were referrals. The electron microscopy unit at RCCH processed 297 specimens. A total of 63 paediatric autopsies were conducted.

Consultants and registrars participated in 50 clinicopathological meetings per month held at Groote Schuur and Red Cross Children’s hospitals.

Research Projects

The divisional staff is currently undertaking over 20 separate research projects, of which the following were initiated during the reporting period:

- The interaction between DC-SIGN and DC-SIGNR with HHV-8(LANA1) and HIV-p24 in Castleman’s disease
  Researchers: Dr D Chetty, Professor D Govender
  Funding: NHLS Research Trust - Pending

- Immunohistochemical evidence of proliferation, hypertrophy and differentiation of glomerular epithelial cells in HIV-associated nephropathy
  Researcher: Dr F Botha, Dr M Duffield
  Funding: NHLS Research Trust - Pending

- Juvenile pilocytic astrocytomas: Search for prognostic markers
  Researcher: Dr N Osman, Dr K Pillay
  Funding: NHLS Research Trust - Pending

Teaching and Training

Undergraduate

The consultant staff are responsible for delivering undergraduate teaching in Anatomical Pathology to MBChB students 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). The Division undertook a major revision of the Anatomical Pathology teaching to MBChB students during the Language of Medicine course in January/February 2013. Newly structured tutorials make use of the recently upgraded Pathology Learning Centre at Medical School. A limited number of students gain access to a special study module in Anatomical Pathology in semester 4, currently the best and earliest opportunity attracting future Anatomical Pathologists into the discipline. For the first time the Division hosted a 5th year MBChB student elective in 2012 and there has been a request for another elective in 2013.

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.

**Postgraduate**

There are 11 registrars (two started in January 2013) and three supernumerary registrars (one started in September 2012). One registrar was successful in the FCPath (Anat) Part 2 examination in October 2012.

Professor D Govender, Dr K Pillay and Professor R Naidoo continued their lecture and tutorial contribution in the BSc (Honours) cancer module.

**Medical technologists:**

Two student intern technologists [1 histology (RCCH) and 1 cytology] were successful in the HPCSA Board examinations in 2012. T Hansen (histology) passed with distinction.

**Professional Development**

**Postgraduate students enrolled:** 21 (1 PhD, 4 MSc, 15 MMed, 1 BSc [Hons])

**Graduated:** 3 (1 BSc [Hons], 1 MMed, 1 FCPath)

**Honours**

The XXIX Congress of the International Academy of Pathology was held in Cape Town in October 2012. This was the first hosting of this congress in Africa. Professor Helen Wainwright served on the Organising Committee. Drs Michael Locketz and Hue-Tsi Wu chaired sessions at this meeting. Dr Komala Pillay was an invited speaker.

The Division successfully hosted a Centenary Paediatric Pathology Day in September 2012. The meeting was jointly convened by Professors Helen Wainwright (NHLS) and Professor ROC Kaschula (UCT).

**Research Output**

**Publications**


Conference presentations (oral and poster)

International: 11
Division Of Chemical Pathology

Head: Professor David Marais

Diagnostic Services

The integrated clinical pathology laboratory at C17 in Groote Schuur Hospital comprises chemical pathology, haematology, immunology, allergology, virology and microbiology. It provides routine diagnostic services to the hospital, other Western Cape provincial healthcare facilities, the University of Cape Town Private Academic Hospital, as well as to a clinical trials service.

The highly automated laboratory, accredited by the South African National Accreditation System (SANAS), offers a 24-hour service. The laboratory endeavours to provide reliable results in a timely manner. Streamlining of the existing tests is being undertaken to ensure cost-effective practice. Routine investigations are analysed on the Roche Modular and Cobas Integra systems. Specialised tests available include protein and lipoprotein electrophoresis (analysed using the semi-automated Sebia Minicap and Hydrasys systems), various manual assays and immunoassays. The radioimmunoassay (RIA) section of the laboratory offers a unique diagnostic service: 4 tests (active renin, aldosterone, 17-hydroxyprogesterone, acetylcholine receptor autoantibody) are not available elsewhere in the Western Cape and one other assay (11-deoxycortisol) is unique in the country. The laboratory endeavours to perform any unusual RIA/IRMA assays requested: leptin, adiponectin, plasma renin activity and atrial natriuretic peptide. The molecular laboratory offers a large repertoire of genetic testing, including pharmacogenetic tests. Newer tests include androgen receptor and mitochondrial polymerase G gene analyses but further genetic investigation can be set up when requested. The biochemical arm of the inherited metabolic disease (IMD) laboratory performs assays within the scope of its staff, equipment and budget, according to the presentation of patients who need diagnosis of severe metabolic errors. Previously reported assays remain on offer while new assays will be undertaken as far as possible in collaboration with special clinics and it is hoped that this unique service will gain more support in future.

The Red Cross Children’s Memorial Hospital chemical pathology laboratory, part of the same business and academic unit, received full ISO15189 accreditation by the SANAS for all routine, manual and specialist inherited metabolic disease diagnostic assays, including analysis of organic and amino acids by gas chromatography-mass spectrometry. Test numbers continue to grow as samples are now analysed from the entire SADC region. An interactive, searchable webpage listing of all the IMD tests remains available at the Red Cross Children’s Memorial and Groote Schuur hospitals at www.madlab.uct.ac.za. This lists all genetic and biochemical assays. High throughput molecular newborn screening tests for glutaricaciduria Type 1 and galactosaemia have been investigated by Dr Tricia Owen, Professor Howard Henderson, Felicity Leisegang and Surita Meldau. The first presymptomatic glutaricaciduria case in South Africa currently receives preventative treatment. The urinary fractionated metanephrine analysis by isotope dilution GC-mass spectrometry remains valuable.

Dr van der Watt has returned to full service after secondment to a special NHLS task team for the national plan to align the NHLS with the Department of Health’s National Health Insurance initiative. He is the chairman of the South African Inherited Metabolic Disease Group, which funded a national teaching visit to 5 academic institutions by Prof James Leonard, Emeritus Professor of Metabolic Disease, at the Institute of Child Health in London.
Watt is the course convener for the toxicology module of a new Master’s Course in Forensic Pathology implemented by Prof Lorna Martin within the Department of Clinical Laboratory Sciences – the first students in this course enrolled in 2012.

Professor David Marais, who took over leadership of the division, completed the move of the lipid laboratory to the Falmouth Building, strengthening and supporting the metabolic studies with cell culture, genetic investigation and other biochemical assays and making this a unique facility in the country. With the support of the Medical Research Council and staff from the Department of Medicine, the laboratory provides tertiary patient care with tests that are not available in routine laboratories. The emphasis is on the genetic causes of familial hypercholesterolaemia, dysbetalipoproteinaemia, hyper-alph-alipo-proteinaemia and Smith-Lemli-Opitz syndrome but additional studies will be undertaken after consultation with the best of the abilities and funding available. Dr D Blackhurst moved the lipid peroxidation laboratory and works on hyperalphalipoproteinaemia. Several novel mutations in endothelial lipase are under investigation.

The National Lottery Board donated money to extend chromatographic investigation for lipid disorders as well as other metabolic disorders with a new technology (direct analysis in real time). This is expected to be delivered in 2013.

**Research Projects**

**Investigation of high molecular weight adiponectin in HIV-infected patients on antiretroviral therapy**

**Researchers:** F Omar, JA King, TS Pillay.

**Funding:** NHLS Research Trust

Therole of multimeric (high molecular weight) adiponectin in metabolic disease resulting from antiretroviral therapy is evaluated by quantifying the circulating levels of both total and high molecular weight (HMW) adiponectin and will establish whether a link exists between HMW adiponectin levels and susceptibility to HIV-induced lipodystrophy. Although total adiponectin levels have been shown to be significantly reduced in patients with HIV-induced lipodystrophy, there is no information on whether HMW adiponectin (the most biologically active form) is altered in HAART-induced lipodystrophy, and whether patients with low levels of the HMW form are more susceptible to lipodystrophy. This project is being written up.

**Design and prototype of an inter-laboratory quality assurance programme for urine bicarbonate**

**Researchers:** R Benjamin, P Berman, JA King.

**Funding:** NHLS K Grant

Renal tubular acidosis is inexpensive to diagnose and treat and may present with failure to thrive; currently such patients should be investigated. Annually about 500 000 cases are identified, of which half are stunted or wasted. Laboratories should be, and are, reluctant to conduct the diagnostic tests (which include urinary bicarbonate) because the available methods – total CO₂ and bicarbonate on a blood gas analyser – have not been validated for urine. External quality assurance does not exist. By running the test, the laboratory risks accreditation and cannot allow the clinician to make confident diagnoses.

The construction of an external quality assurance programme for urine bicarbonate will allow laboratories to assist in the diagnosis of renal tubular acidosis. An external quality assurance programme will facilitate screening of populations at risk as well as the benefit of diagnosis. This was presented during the year and is undergoing preparation for publication.
Determining aldosterone: renin concentration ratio cut-off and plasma renin stability

**Researchers:** F Omar, JA King, B Rayner

Plasma aldosterone: renin activity ratio (ARR) is useful in the diagnosis of primary hyperaldosteronism. Cut-off points vary; 1,000 (pmol/L per ng/ml/h) is used locally. The cumbersome renin activity assay has been replaced in many laboratories by the measurement of renin concentration. As the units and nature of these assays differ, different cut-off values (preferably assay-specific) are required for the plasma aldosterone: renin concentration ratio (ARC) in the diagnosis of primary hyperaldosteronism.

Renin is an unstable analyte due to cryoactivation, requiring special precaution in the handling and storage of specimens. It is necessary to re-analyse samples in dilution when levels exceed the measuring range (4.5–558 mIU/L), necessitating a second freeze-thaw cycle. This study examines the ARC cut-off for primary hyperaldosteronism, using the Diasorin GammaCoat Plasma Renin Activity and Cisbio Renin III Generation assays, and the relationship between these assays. The second objective is to ascertain whether renin concentration is stable after two freeze-thaw cycles.

Reproductive sex steroids: an evaluation of the reproductive cycle of the Great White shark

**Researchers:** A Hewitt, JA King, A Katz, A Kok, C Griffiths

This ongoing study researches the reproductive physiology of the Great White shark to broaden knowledge on its reproductive behaviour and life history. Apart from the scientific value of describing the reproductive behaviour and the mechanisms that control it, the information can be used for the conservation of areas of global significance of reproduction and crucial nursery habitats. Information on the reproductive cycle of this shark is under investigation to identify and quantify reproductively related steroid hormones over a two-year period. This will establish baseline data for the species and will be crucial to understanding the reproductive biology and behaviour of the Great White shark in South African waters. The methodology involves the development of specific and unique radioimmuno assay for steroid hormones, which may also be used in animal models to investigate human endocrine disease and disorders.

Diagnostic utility of serum glypican-3 as a biomarker for screening for hepatocellular carcinoma

**Researchers:** M Setshedi, F Omar, M Ndlovu, M Kew

Hepatitis B- and C-related cirrhosis are the commonest risk factors for the development of hepatocellular carcinoma (HCC). The screening guidelines in patients with cirrhosis include ultrasound of the liver and alpha fetoprotein (AFP) measurement. However, AFP has a low sensitivity and a small number of patients who develop HCC have normal AFP levels. Therefore, the need for a reliable sensitive marker is crucial to enable early diagnosis of HCC. Glypican-3 protein has been investigated as a potential biomarker as it is exclusively expressed in tumours. We aim to measure and compare GPC3 levels in non-cirrhotics, cirrhotics and patients with HCC to determine its diagnostic and prognostic utility in screening for HCC.

Serum prolidase activity as a marker for liver fibrosis

**Researchers:** Dr J Stanfliet, Dr P A Berman, Prof TS Pillay, Dr M Locketz.

**Funding:** NHLS Research Trust

To assess fibrosis, serum prolidase activity has been measured in patients who have histologically confirmed liver fibrosis. The findings are being written up for publication.
Development and assessment of a DNA multiplex screening assay for detection of glutaricaciduria Type 1 and galactosaemia in a large South African cohort  
**Researchers:** Dr GF Van der Watt, Dr EP Owen, Prof HE Henderson  
**Funding:** NHLS Research Trust

Since all known African patients diagnosed with galactosaemia or glutaricaciduria Type 1 in South Africa are homozygous for a single point mutation in each disease, this project will use a multiplexed molecular assay to detect these mutations in low volume samples such as dried blood spots. The subsequent utilisation of this assay will screen for the mutations in a larger cohort of previously obtained dried blood spots. These data will be used to predict the expected disease burden for these disorders in the African population.

Determination of sibutramine in contaminated herbal remedies using a rapid gas chromatography-mass spectrometry (GC-MS) method  
**Investigators:** Dr GF Van der Watt & Mr B Foster

This project follows on queries from various investigators about the potential contamination of a number of herbal remedies with sibutramine, an amphetamine-related amine with anorexigenic properties. A GC-MS method using cation exchange extraction without derivatisation and a 10-m Zebron AAA column (Phenomenex™) was developed to identify and quantify sibutramine within a total preparation and run-time of 20 minutes per sample.

Quantifications of homovanillic acid (HVA) in urine using a simplified rapid GC-MS method  
**Investigators:** Dr GF Van der Watt, Mr B Foster, D Haarburger, R Benjamin

This project aims to provide a fast, accurate estimation of urinary HVA concentration to screen for paediatric neuroblastoma. The method was streamlined to include a single extraction and derivatisation step followed by the quantitation of HVA using a cost-effective vanillic acid internal standard. The method is being evaluated before implementation into the routine diagnostic laboratory to replace an existing non-specific method that is prone to paracetamol interference.

Frequency of R563Q mutations in the epithelial sodium channel (ENaC) in South African populations  
**Researchers:** Dr E Jones, Dr EP Owen, Prof B Rayner

The R563Q mutation, possibly originating from the Khoisan, is found in multiple ethnic groups in South Africa and associates with hypertension. Hypertension resulting from the R563Q mutation is common and responds better to certain drug choices (amiloride); thus, in South Africa, screening for the mutation is indicated.

The C5/6 gene frequency of mutations in the local population  
**Researchers:** Dr EP Owen, Prof HE Henderson, F Leisegang, Dr A Orren  
**Funding:** Medical Research Council (MRC)

Meningococcal infections are frequent in C5- and in C6-deficient patients, and may have severe long-term sequelae: impaired cognitive function, deafness, loss of digits or limbs. The prevalence being about 12% (3% C5 deficiency, 9% C6 deficiency) justifies testing patients with meningococcal infection. DNA from black persons is being investigated for the frequency of mutations resulting in C5 deficiency.

Mutation screening in the CTNS gene in a cohort of cystinosis patients  
**Researchers:** Dr EP Owen, F Leisegang, Dr J Nandhlal.

A cohort of Red Cross Children’s Hospital cystinosis patients is under investigation for pathogenic mutations within this transporter
gene. Initial genomic DNA screening failed to clarify meaningful mutations but screening mRNA revealed a common mutation. The study is extended to the general population.

Screening for single nucleotide polymorphisms and mutations in the XPNPEP2 gene in black South Africans with angioedema induced by angiotensin I-converting enzyme inhibitors

Researchers: Dr EP Owen & Mr R Moholisa

Angioedema is a potentially life-threatening complication of treatment with angiotensin converting enzyme inhibitors (ACEi) and is associated with low plasma aminopeptidase P (APP) activity. The C2399A single nucleotide polymorphism (SNP) at XPNPEP2 was a significant predictor of APP activity in Caucasian subjects.

Increasing recognition of this reaction in local black and coloured patients was attributed to changes in plasma APP activity and genotype. These data suggest that other genetic and biochemical differences in our population might explain the phenotypic variability of the APP activity and ACE activity. This project is being finalised.

Genetic causes of familial hyper-cholesterolaemia phenotype at the Groote Schuur Hospital Lipid Clinic

Researchers: G Solomon, B Ratanjee, Dr D Blom, Dr K Wolmarans, Dr B Brice, Dr R Benjamin, Dr C Chingwanda, Ms M Levey, Dr D Blackhurst, Prof AD Marais

Funding: MRC

Hyperalphalipoproteinaemia

Researchers: Ms G Solomon, Ms B Ratanjee, Dr D Blom, Dr K Wolmarans, Dr B Brice, Dr R Benjamin, Dr C Chingwanda, Ms M Levey, Dr D Blackhurst, Prof AD Marais

Funding: MRC

This project continues from the initial findings in collaboration with Prof M Hayden at the University of British Columbia that identified several subjects with endothelial lipase mutations. High HDL cholesterol concentrations are not always protective against atherosclerosis; the genetic causes are not fully understood but may influence the risk of atherosclerosis. An electrophoretic analysis is being modified to describe the range of HDL species. Collaboration with Prof G Lambert is assessing the cell biology and function of the novel endothelial lipase mutations.

Smith-Lemli-Opitz Syndrome

Researchers: G Solomon, A Mohamed, Prof A D Marais

Funding: MRC

The Smith-Lemli-Opitz syndrome is an uncommon, recessively inherited deficiency in 7-dehydrocholesterol reductase that results in hypocholesterolaemia and congenital malformations as well as developmental delay. As a result of limited equipment, a spectrophotometric assay has been set up and patients from Cape Town and Johannesburg have been diagnosed with the disorder. In the former case, the genotype is now identified while work-up continues in two other families with different mutations.

There is work under way to detect the 7-dehydrocholesterol in amniotic fluid by TLC.
Nutrition in hominins in the Cape Fold Belt region during the middle to late Stone Age

**Researchers:** K Kyriacou, Prof J Parkington, Prof AD Marais  
**Funding:** PAST

This collaborative research between Archaeology and Chemical Pathology seeks to link the findings at excavation sites and middens with nutritional supplies, with special emphasis on energy, n-3 fatty acids, protein and some micronutrients. The detailed fatty acid analysis will examine the availability of n-3 poly-unsaturated fatty acids whilst some micronutrients as well as protein, simple saccharides and starch will be measured in putative foodstuffs.

Oxidative stress markers and anti-oxidant capacity in plasma of subjects with varying risk of cardiovascular disease

**Researchers:** Dr D Ojji, Prof K Sliwa, Prof S Lecour, Dr D Blackhurst

This is a collaborative project samples from a study in the Hatter Institute to determine whether graded cardiovascular risk and disease status correlates with markers of oxidative stress (TBARS) and anti-oxidant activity (ORAC).

Teaching and Training

Undergraduate and postgraduate

Staff members from the laboratory are involved in under- and postgraduate lectures and tutorials in Chemical Pathology. Registrars rotate between the different benches within the laboratories at the Groote Schuur and Red Cross Children’s hospitals to obtain skills across the discipline.

They receive weekly tutorials on basic biochemistry, methodology, management, lipidology, molecular medicine and journal discussions. They also attend weekly journal clubs, endocrinology seminars and ward rounds, as well as post-clinic meetings in lipidology.

There were 5 registrars in chemical pathology, including 2 supernumerary members from Malawi and Nigeria. Clinical pathology registrars rotated through chemical pathology as well, including Dr N Erasmus, Dr C Swart and Dr H Swanepoel. There was no appointment of a registrar in chemical pathology at the beginning of 2012 but Dr Ndlovu joined us in July.

Dr F Omar is the course convenor for clinical pathology. A phlebotomy training course was presented to ensure a high standard and uniformity of sample collection. Dr C Swart started in January and Dr N Erasmus continued her studies, to be joined by Dr H Swanepoel later in the year.

Postgraduate students 2012/2013


Medical technology

During the year under review, 5 medical technology interns and 4 third-year medical technology students were trained in the laboratory. The 4 third-year students passed the final exams and are now employed as student interns. The medical technology interns are awaiting their examination results. Phlebotomy technicians’ student training is co-coordinated by the chemistry laboratory manager. Five phlebotomy technicians wrote and passed their exams in October 2012.
Professional Development

**Postgraduate candidates graduated:**
1 (PhD)
Chem Path MMed Part 3 dissertation and FCPath2

**Postgraduate candidates enrolled:**
18 (9 MMed, 6 PhD, 3 BSc, 7 MMed, 1 MSc)

Research Output

**Congress abstracts 2012**
International: Nine
National: Five

Accredited Publications


Ismail WIW, King JA, Anwar K, Pillay TS. Indinavir and Nelfinavir inhibit proximal insulin receptor signalling and salicylate abrogates inhibition: potential role of the NFkappa B pathway. *Journal of Cellular Biochemistry* (published online 05/02/2013).
**Division of Immunology**

**Head:** Professor Clive M Gray

The Division of Immunology at the University of Cape Town/Groote Schuur, NHLS coastal branch, is involved with a range of activities from identifying the basic mechanisms of infectious disease immunity to translational clinical research on HIV and TB, diagnostic testing in tissue immunology and in clinical immunology and allergy. The vision statement of the division is “Leading Science to Promote World Health.”

The Division of Immunology provides a world-class diagnostic service. The Laboratory for Tissue Immunology (LTI), within the division, is responsible for HLA class I and class II typing for solid organ and bone marrow/stem cell matching. We are the only laboratories in South Africa to have European Federation of Immunogenetics (EFI) accreditation to perform HLA tissue typing, cross-matching and anti-HLA antibody identification. The combination of HLA, cross-matching and single antigen identity of pre-formed antibody testing allows for a virtual cross-match.

Furthermore, 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.

As part of its research function, the division generates and characterises novel and unique transgenic mice as animal models for human diseases and these have been used to make important advances in diseases such as tuberculosis, bilharzia, african trypanosomiasis, candidiasis and cutaneous leishmaniasis, and contributed to a better understanding of immunological mechanisms on a cellular and molecular level.

Basic research in the allergy section has focused on the T cell cytokine responses to allergens as well as the application of novel assays to identify sensitivity profiles. We are moving towards developing humanised mouse models, allowing a more translational platform and research is under way to understand adaptive and innate immune responses during acute HIV infection and in infants exposed to HIV in utero and upon receiving BCG vaccination. The division has an active teaching component in the medical undergraduate syllabus at UCT and provides immunology lectures from years 1-3 in the MBChB undergraduate syllabus.

On-line learning through Immunopaedia (www.immunopaedia.org.za) supplies adjunct material for the undergraduates. Post-graduate immunology through the BSc Honours in Infectious Disease and Immunology programme and Research Immunology cater for more advanced basic and clinical immunology. The thrust of the division is to create a world-class immunology undergraduate and postgraduate programme for training future researchers, doctors and specialists.

**Diagnostic Services**

The main thrust of the diagnostic service of the division is a) provision of HLA typing and cross-matching for bone marrow and solid organ matching, which takes place in the Laboratory for Tissue Immunology; b) autoimmunity and allergy testing, which is performed in the Clinical Immunology and Allergy Laboratory.

Both laboratories were inspected and passed for ISO15189 accreditation with SANAS.

**Laboratory for Tissue Immunology (LTI)**

The LTI is the only tissue typing laboratory in South Africa and on the African continent to be accredited by the European Federation for Immunogenetics (EFI). This international accreditation enables the division to provide the level of tissue typing acceptable to the
World Marrow Donor organisation and other international institutions for HLA typing of patients and potential unrelated and related stem cell donors. The laboratory was inspected by EFI in July 2012 and accreditation was renewed for a further three years. It was recommended that a co-director be appointed who would provide scientific oversight, vision and the ability of the NHLS to stay abreast of new technologies and diagnostics in histo-compatibility.

Over the past year, 1,380 HLA types were performed by serological methods for solid organ donors (330), solid organ renal recipients (390), other organs (33, cardiac and liver), stem cell transplant donors (1,307), stem cell transplant patients (355) and related stem cell donors (380), and related stem cell patients (151). The strategy for typing potential related stem cell transplants was changed in 2012 with a move away from serological screening to DNA typing straight away at low resolution (two digit) to identify patient:donor identical matches at HLA-A*, -B*, -C*, -DRB1* and –DQB1*. We have also made it mandatory that verification of patient and donor HLA be performed prior to transplantation, where a confirmed HLA typing result can only be reported when the initial HLA typing has been repeated on a second independent sample. This is in accordance with EFI standards; a follow-up independent sampling from patient and potential donor is required to confirm the haplotype matching.

The strategy of moving away from serology to DNA typing at low resolution has also been made for all solid organ transplant work-ups. This is important for identifying single antigen specificities of patient pre-formed antibodies when a more precise HLA type is known. DNA typing is determined using a PCR-SSP/SSOP techniques; a total of 7,749 HLA-Class I and II DNA typings were performed, with 1,629typings of these being performed at high resolution (4 digits) for HLA-DRB1*, -DQB1* and –DRB3*4*/5*. These typings also included 1,532 for solid organ recipients, 873 for related stem cell patients, 979 for related stem cell donors, 1,058 for unrelated stem cell patients and 1,330 for unrelated stem cell donors. The laboratory also tested for 280 HLA-B*27 and 43 HLA-B*15 at high resolution. The laboratory is striving to improve techniques and will move towards offering high resolution HLA class I (A, B and C) at high resolution over the next year, using sequence-based typing, it is also exploring the utility of various next generation sequencing platforms.

Clinical immunology and allergy

Over the past year, 21,169 diagnostic tests were performed in the laboratory, where 16,142 tests were for the detection of autoantibodies, which aid clinicians in the diagnosis of autoimmune diseases. Requests for the new tests, which were added in the previous financial year increased steadily. These tests are important in diagnosing anti-phospholipid syndrome with a total of 161 anti-cardiolipin IgM assays, 413 ß-2 glycoprotein 1 IgG and 413 ß-2- glycoprotein 1 IgM assays being performed.

The incidence of allergies has increased and continues to do so, among both children and adults. Some allergies are potentially life threatening and it is therefore important to diagnose such allergies. As such, 5,027 allergy tests were carried out between 1 April 2012 and 31 March 2013.

If patients are found to be allergic to egg white, the laboratory then performs allergy testing to ovomucoid. If ovomucoid is positive, this indicates a risk for reaction to all forms of egg. High levels indicate persistent allergy. Ovomucoid is heat stable and highly allergenic. In addition, if patients are allergic to cow’s milk, the laboratory tests for specific IgE antibodies to milk proteins, as alpha-lactalbumin and beta-lactaglobulin are heat-labile proteins and indicate the risk to fresh milk. Patients positive for these proteins may tolerate long-life milk
following UHT process. In contrast, casein is stable to heat and digestion and indicates risk to all forms of milk. Reflex testing is also performed if patients are allergic to peanuts. A test for specific IgE antibodies to rAra h2 peanut is carried out, and if positive, it indicates that the patient is at an increased risk of severe, systemic reaction to peanuts.

Research Output


National conference presentation

Research Projects

Professor Clive M Gray

**HIV vaccine immunogen design**

**Postdoctoral fellow:** Lycias Zembe  
**Collaborators:** Professor Carolyn Williamson (Medical Virology, UCT); Professor Udaykumar Ranga (Jawaharlal Nehru Centre for Advanced Scientific Research, Bangalore, India)

Innate, adaptive and mucosal immune responses in HIV-1 exposed uninfected infants: a human model to understand correlates of immune protection

**Collaborators:** Dr Heather Jaspan (Division of Immunology, UCT); Professor Ken Rosenthal (McMaster’s University, Canada); Professor Bill Cameron (Ottawa Research Institute, Ottawa, Canada); Professor Alash’le ABimiku (Institute of Human Virology, Nigeria)

**A prospective observational study to analyse host and pathogen contributions in the emergence of extensively drug-resistant tuberculosis.**

**Collaborators:** Dr Dorothy Fallows (Laboratory of Mycobacterial Immunity and Pathogenesis, New Jersey, USA); Professor Gilla Kaplan (Laboratory of Mycobacterial Immunity and Pathogenesis, New Jersey, USA)

Renal transplantation in South Africa: using HIV-positive deceased donors for HIV-positive recipients.

**Collaborator:** Dr Elmi Muller (Department of Surgery, UCT)

Characterisation of virus and host immune responses in the synovial fluid of children with HIV arthropathy

**Collaborators:** Dr Christiana Scott (Red Cross Children’s Hospital, UCT)

Factors affecting HIV susceptibility in the adolescent genital tract

**Collaborators:** Professor Jo-Ann Passmore (Division of Medical Virology, UCT), Dr Heather Jaspan (Immunology, UCT), Dr Doug Wilson (Edendale Hospital, KZN), Professor Robin Shattock (Imperial College, London).

Teaching

**Postgraduate supervision:** 1 postdoctoral fellow; 2 PhD students; 2 MSc students  
**Lectures:** MBBCh undergraduate years 1, 2 and 3; postgraduate immunology course

Publications


Research Projects:

Associate Professor Muazzam Jacobs

Neuron-TB

PhD students: Ngiambudulu Francesco; Philippa Randall
Postdoctoral fellows: Dr Nai-Jen Hsu; Dr Nasiema Allie
Collaborators: Professor Dirk Lang (University of Cape Town), Ms Susan Cooper (University of Cape Town); Professor Lauriston Kellaway (University of Cape Town); Professor Valerie Quesniaux (CNRS-France); Professor Bernhard Ryffel (CNRS-France)

TNF and CNS-TB

PhD students: Boipelo Sebesho; Postdoctoral fellows: Dr Nasiema Allie; Dr Roanne Keeton, Dr Nai Jen Hsu
Collaborators: Professor Lauriston Kellaway (University of Cape Town); Professor Valerie Quesniaux (CNRS-France); Professor Bernhard Ryffel (CNRS-France)

Assessment of vaccine efficacy for malaria and tuberculosis in a co-infection setting relevant for disease-endemic sub-Saharan African regions
Post-doctoral fellow: Dr Roanne Keeton
Collaborator: Professor Stefan Magez (Vrije Universiteit Brussels, Belgium)

Drug discovery for anti-tuberculosis agents from South African medicinal plants
Postdoctoral fellow: Dr Nasiema Allie
Collaborators: Dr Eliyah Madikane (UCT), Professor Pete Smith (UCT), Professor Paul van Helden (US), Professor Peter Folb (MRC), Dr Chris Parkinson (CSIR), Dr N Bagwandine

Investigating antimycobacterial activity of phenothionine derivatives
MSc student: Ms Sumayah Salie
Post doctoral fellows: Dr Nai-Jen Hsu
Collaborator: Dr Anwar Jardine
Investigating HIV-TB coinfection in humanised mice.

**PhD students:** Antoinette Labuschagne

**Collaborators:** Professor Dale Greiner (University of Massachusetts); Professor Don Estes (University of Georgia)

**Teaching**

**Postgraduate supervision:** Three postdoctoral fellows; five PhD student;

**Lectures:** BSc (Honours); molecular medicine; postgraduate immunology course

**Workshops**

Pathpoint 2012
HIV immunology session: Infant HIV diagnostic testing and pathogenesis.
29 September 2012, Century City, Cape Town

**Research output**

**Articles**


**Patents (provisional)**

**Title:** Tricyclic derivatives
**Application Number:** 2012/08875
**Co-applicant:** Dr Anwar Jardine (Department of Chemistry, University of Cape Town)

**Posters**


**Phenothiozine derivatives against M tuberculosis. Sumayah Salie, Nai-Jen Hsu, Dorothy Semenyah, Anwar Jardine, Muazzam Jacobs, Federation of Immunological Societies, 3–5 December 2012.**

**Book Chapters**

**Book Title:** *Innate Immunity and the Eye*; **Author:** Zierhut, Manfred; **Chapter 10-** Role of TNF in Host Resistance to Tuberculosis Infection: Membrane TNF is Sufficient to Control Infection: Ryffel B and Jacobs M; Jaypee Brothers: Medical Publishers, New Delhi, India, 2013; ISBN: 9789350903094.
Medical Microbiology

**Head:** Professor Mark Nicol

**Diagnostic Services**

The diagnostic laboratory has undergone further restructuring in workflow to accommodate substantially increased numbers of specimens due to the closure of the Green Point microbiology laboratory. A central processing bench was established, and streamlined processes established. A visit by an international workflow expert resulted in very complimentary reviews that this was the first laboratory that she had visited where she was unable to improve on existing workflow.

Members of the division are actively involved in infection control and antibiotic stewardship activities, serving on the infection control committees at Red Cross Children’s Hospital and Groote Schuur Hospital, as well as on the Provincial Infection Prevention and Control Committee. The antibiotic stewardship programme, which was based on an antibiotic restriction policy, has been altered to include a more active ward-round-based component as well as on-line tutorials for medical registrars on appropriate antibiotic use.

The diagnostic laboratory continues to provide a service to colleagues engaged in clinical research. During the course of 2011/2012, 12 new clinical studies commenced in the laboratory. As before, the majority of the studies are related to tuberculosis, and include diagnostic, treatment, vaccine and epidemiological studies.

The laboratory investigated 4 outbreaks of highly resistant organisms in hospitals in the Greater Cape Town area, including epidemiological, microbiological and molecular investigations. These investigations have highlighted the rapid emergence of highly resistant bacterial strains in our hospitals.

**Research Projects**

See also the separate report for the MRC/NHLS/UCT Molecular Mycobacteriology Research Unit.

A randomized study of the impact of decentralizing molecular testing for detection of tuberculosis and rifampicin resistance using Xpert MTB/RIF

Professor M Nicol (NHLS/UCT), Dr A Whitelaw (NHLS/UCT), Dr C Boehme (FIND), Dr G Coetzee (NHLS), Dr J Simpson (NHLS), Dr H Cox (MSF).

This is a randomized study of the impact of Xpert MTB/RIF for the diagnosis of TB at a primary care clinic. We completed enrolment into this study, with a total of 3,300 TB suspects at two field sites in the Western Cape – Paarl (6 clinics) and Khayelitsha’s Site B clinic. The first manuscript for this study is currently being finalized.

**Funding:** Foundation for Innovative New Diagnostics, EDCTP, Wellcome Trust

A Prospective Study of Clostridium difficile Infection in a Tertiary Referral Hospital

Dr N Rajabally (UCT/ GSH), Dr A Whitelaw (NHLS/UCT), Dr C Bamford (NHLS/UCT), Dr B Kullin (UCT), A Klein (NHLS), Professor S Reid (UCT), Professor V Abratt (UCT).

This study aims to both describe the incidence and clinical characteristics of *C. difficile* infection at Groote Schuur Hospital, and to ascertain the optimal diagnostic test for *C. difficile* infection. Stool samples are being cultured onto 3 different selective anaerobic media for *C. difficile*, and toxin assays are being performed using commercial lateral flow assays, ELISAs and PCR.

Clinical data are being collected prospectively on patients suspected of having *C. difficile* infection. Isolates will be ribotyped, and will be tested for susceptibility to metronidazole.

**Funding:** MRC, Department of Gastroenterology UCT
The Molecular epidemiology of *streptococcus pyogenes* pharyngitis among children in the vanguard community (Bonteheuwel/Langa), Cape Town, South Africa, and the development of a clinical prediction rule for streptococcal Pharyngitis

Professor B Mayosi (UCT), Professor D Beatty (UCT), Dr J Dale (University of Tennessee), M Engel (UCT), B Muhamed (UCT), Dr A Whitelaw (NHLS/UCT)

The aim of the study is to describe the distribution of emm-types among isolates of *S. pyogenes* causing pharyngitis, in order to assess the possible coverage of a proposed 26 valent vaccine. Isolates have been collected from throat swabs from children presenting with sore throats to community health centres, as well as from asymptomatic children at schools in the region. Analysis of 143 isolates has been performed, and the results are being written up for an MSc dissertation.

**Funding:** NIH / DMID

Drug Discovery for Anti-tuberculosis Agents from South African natural products

Dr Madikane (NHLS/UCT), Dr N Bhagwandin (MRC), Professor I Wid (Stellenbosch University), Professor P van Helden (Stellenbosch University), Dr A Ngwane (Stellenbosch University), Dr L Weisner (UCT), Professor Peter Smith (UCT), Dr E Mutlane (University of Johannesburg), Dr J Panayides (CSIR), Professor N Crouch (South African Biodiversity Institute)

The aim of this project is to develop an anti-tuberculosis drug lead. Several compounds have been developed with improved biological activity against *Mycobacterium tuberculosis* and lowered cytotoxicity against mammalian cell lines. These compounds are being subjected to target identification screens within the South African Tuberculosis Research and Innovation Initiative.

**Funding:** Technology Innovation Agency

Integrated microanalytical extraction-amplification system for detection of tuberculosis in low resource settings

Professor M Nicol (NHLS/UCT), V Allen, Dr L Ah Tow Edries, Dr D Kelso (Northwestern University, USA)

This project involves the development of an integrated specimen collection/processing container and integration into a novel real-time PCR platform for rapid diagnosis of tuberculosis in primary care settings. We have developed and determined the limit of detection of a novel real-time PCR assay as well as developed and field-tested a novel sputum collection device, which is currently being field tested.

**Funding:** Center for Point-of-Care Diagnostics for Global Health (GHDx Center), PATH

Diagnosis of tuberculosis in HIV-infected children – development of microbiological and immunological strategies

Professor M Nicol (NHLS/UCT), Professor H Zar (Child and Adolescent Health, UCT), Dr C Bamford (NHLS/UCT), Professor B Eley (Child and Adolescent Health, UCT), Professor G Hussey (Child and Adolescent Health, UCT), Professor R Wilkinson (Imperial College, London and Institute for Infectious Diseases and Molecular Medicine, UCT), Dr T Connell (Royal Children's Hospital, Melbourne)

This study aims to evaluate a range of novel molecular and immunological tests for their performance in the diagnosis of tuberculosis in children, particularly those infected with HIV. Three components of this project have been published, the first evaluating the performance of Xpert on induced sputum samples, the second on nasopharyngeal aspirates and the third on stool samples. Further studies evaluating the performance of urinary LAM and IGRA assays are under way.

**Funding:** NHLS Research Trust, National Institutes of Health (USA), Medical Research Council, EDCTP
Innate immunity to TB is lineage and host dependent
Professor M Nicol (NHLS/UCT), R Sarkar (UCT), Professor R Wilkinson (UCT, Imperial College, MRC, UK), Dr K Wilkinson (UCT, Imperial College, MRC, UK), Mrs K Wood (UCT)

This study aims to determine whether different lineages of M. tuberculosis induce lineage-specific innate immune responses in macrophages. We used a primary human monocyte-derived macrophage (MDM) model to study characteristic innate cytokine profiles and in vitro growth rate. In the past year we have completed experiments to compare the cytokine responses in donors of different genetic backgrounds, using multiplex (Luminex) cytokine analysis and demonstrated interactions between host and strain genetic background.

**Funding:** National Research Foundation of South Africa Focus Area Award

The effect of early childhood exposure to environmental organisms on the development of wheezing and atopy in young children
Professor M Nicol (UCT/NHLS), Dr M Kaba (UCT), Dr L Ah Tow (UCT), M Duyver (UCT), Dr E du Toit (UCT), Professor H Zar (Child and Adolescent Health, UCT)

The aim of this study is to examine if high levels of exposure to environmental organisms (fungi, bacteria) influence the onset of childhood atopy and wheezing. Home dust samples are being collected antenatally, at 6 and 12 months (1,200 collected to date) using electrostatic dust collectors and evaluated by next generation sequencing to determine bacterial and fungal diversity.

**Funding:** Bill and Melinda Gates Foundation, Carnegie Foundation

The Drakenstein Child Lung Health Study
Professor M Nicol (NHLS/UCT), Professor H Zar (UCT), Dr M Kaba (UCT), Dr E Madikane (NHLS/UCT), Dr E du Toit (UCT), F Dube (UCT), S Mohammed (UCT)

This study is a collaboration between the department of Paediatrics and Child Health, and Medical Microbiology at UCT. We are currently enrolling 500 mother-infant pairs from the Drakenstein region in the Western Cape and following them up over the first two years of life (to date, 450 mothers enrolled). The primary aim of this 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. The first two manuscripts from this study, evaluating the performance of different DNA extraction technologies and swab types, are currently under review.

**Funding:** Bill and Melinda Gates Foundation

The stool microbiota and its relationship to allergy and atopy
Professor M Nicol (UCT/NHLS), Dr M Kaba (UCT), S Claassen (UCT), Dr E du Toit (UCT), Professor H Zar (Child and Adolescent Health, UCT)

The aim of this project is to identify the diversity and main components of the stool microbiota of infants and mothers over a 2 year period at one-monthly intervals. This information will be related to the development of lung disease and allergy. Stool samples are being collected from infants and mothers at birth and monthly thereafter (to date, 900 samples collected). DNA will be extracted and the diversity will be measured using next generation sequencing. Results of a systematic review study on the role of faecal bacterial communities and their association with asthma or recurrent wheezing are currently under preparation for publication.

**Funding:** Bill and Melinda Gates Foundation, Carnegie Foundation
Nasopharyngeal microbiome and pneumonia in young children from Drakenstein sub-district, South Africa
Professor M Nicol (NHLS/UCT), Dr M Kaba (UCT), F Dube (UCT), Dr E Madikane (NHLS/UCT), S Abdulgader (UCT), Professor H Zar (UCT)

The aim of this study is (i) to investigate longitudinally the nasopharyngeal microbiome of a birth cohort of 500 infants (sampled 2-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. To date, more than 2,000 samples have been collected, and 33-plex real-time PCR assays performed on a subset of 450 to determine the most common bacterial and viral pathogens found in the nasopharynx.

**Funding:** Bill and Melinda Gates Foundation, Carnegie Foundation

Bloodstream infection with extended spectrum beta-lactamase (ESBL) producing *Klebsiella pneumonia* at a tertiary hospital in Cape Town
C Moodley (UCT/NHLS/NICD Molecular Epidemiology Unit), Dr C Bamford (UCT/NHLS)

In March 2009 a number of deaths due to bloodstream infection (BSI) with extended spectrum beta-lactamase (ESBL) producing *Klebsiella pneumonia* were reported among children with gastro-enteritis admitted to the acute admissions ward at a tertiary level hospital in Cape Town. Concern was raised that this reflected an outbreak of severe infection with community-acquired ESBL producing organisms. Subsequent investigation revealed that the infections were most likely nosocomially acquired as the children had been admitted for more than 48 hours prior to culture. These conclusions were supported by the findings of PFGE typing of 8 isolates from that time period, showing that all 8 strains were different except for two isolates that appeared to be closely related.

**Funding:** Bill and Melinda Gates Foundation, University of Cape Town, Carnegie Foundation

Risk factors for the acquisition of methicillin-resistant *Staphylococcus aureus* among maternity and neonatal patients in a maternity hospital in Western Cape, South Africa
M Mudau (UCT/NHLS/NICD Molecular Epidemiology/ SAFELTP/University of Pretoria), Dr L Kuonza (SAFELTP/University of Pretoria), Professor M Nicol (UCT), Dr C Bamford (UCT/NHLS)

Molecular typing of 100 clinical isolates of methicillin-resistant *Staphylococcus aureus* isolated at the Groote Schuur Hospital National Health Laboratory Service (NHLS) laboratory between January 2007 and December 2008 (1) revealed six distinct groups, designated A–F. On preliminary inspection, Group C appeared to be linked to maternity and neonatal services. A case control study was conducted to determine risk factors for acquisition of MRSA.

**The antibiotic resistome in apparently healthy children, South Africa**
Professor M Nicol (NHLS/UCT), Dr E Madikane (NHLS/UCT), S Abdulgader (UCT), Professor H Zar (UCT)

This study will be nested within the Drakenstein Child Lung Health Study. The aim of the study is to investigate the longitudinal patterns of *S. aureus* nasopharyngeal colonization in the first year of life, including co-colonization dynamics with other bacterial and viral colonizers/
pathogens of the upper respiratory tract.

**Funding:** Bill and Melinda Gates Foundation, University of Cape Town, Organization for Women in Science in the Developing World

**Development of a real-time assay for the diagnosis of meningitis in children**
Dr C Bamford (UCT/NHLS), Dr E Madikane (UCT/NHLS), J Khumalo (UCT), Dr R Muloiwa (UCT), Dr B Eley (UCT), Dr D Hardie (UCT)

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.

**Teaching and Training**

**Undergraduate**
The division is actively involved in teaching undergraduate medical students, as well as in ongoing curriculum design and review. Although the majority of the teaching involves 2nd and 3rd year students, the division also teaches and examines students in years 4–6. Teaching activities include facilitation of problem-based learning, lectures, tutorials and practicals. 2012 was the second year of an intercalated molecular medicine course, in which 3rd year medical students completed additional lectures, tutorials and practicals (including a module taught by Medical Microbiology) to enable them to take a year off after 3rd year to complete a BSc (Hons). Nine students will take this course in 2012.

**Postgraduate**
The division has an active postgraduate programme, including training at master’s and doctoral level. The Division graduated two BSc honours, one FCPath (Clin Path) and one MMed student in 2012. In addition, 2 infectious diseases registrars completed 6-month rotations in the division.

At present, there are 4 postdoctoral, 7 PhD, 11 MSc, and 3 BSc (Hons) students, 3 Microbiology (MMed Micro) and 1 Clinical Pathology (MMed Clin Path) registrars in the division.

**Professional Development**

Current postgraduate students:
- Postdoctoral: 4
- PhD: 7
- MMed3 (including 1 clinical pathology)
- MSc: 11
- BSc (Med) honours: 3

Postgraduate students who graduated:
- Upgrade from MSc to PhD: 1
- BSc Med (Hons): 1
- PhD: 1

**Research Output**


Division Of Medical Virology

Head: Professor Carolyn Williamson

Diagnostic Services

Medical Virology Diagnostic Laboratory
Head: Dr Diana Hardie

The diagnostic laboratory has maintained its SANAS accreditation status according to ISO15189. It offers a wide repertoire of tests in viral serology and molecular diagnostics with a special interest in molecular diagnosis and an extensive range of 'in-house' and commercial molecular assays. It provides a comprehensive service to Groote Schuur Hospital and Red Cross Children's Hospital, and is the referral laboratory for the Western Cape. It is one of two centres in the Western Cape where HIV viral load and PCR testing are done for the CCMT programme. From April 2012 to March 2013 the laboratory performed over 90,000 HIV viral loads and 10,000 HIV PCR tests. Turn around time (TAT) has been a strong focus and a special effort has been made to shorten the TATs through restructuring and multi-task training.

The use of multiplex PCR for diagnosis of respiratory virus infections continues to provide value to health care. Diagnosis of severe acute respiratory infections (SARI) in young infants is useful for patient management and tracking local epidemiology of these infections. Seasonal prevalence of the different respiratory viruses, in particular that of human metapneumovirus, has been tracked, and this assay also facilitated the recognition of nosocomial outbreaks. Over the next year we plan to expand the range of respiratory pathogens tested for. The laboratory is involved in operational research, in collaboration with the UCT Department of Public Health, to assess the quality and impact of HIV early infant diagnosis in the Western Cape. The goal of this research is to develop a rapid result notification system through CDW to clinics to facilitate follow-up of HIV PCR-positive infants and thus improve service delivery at primary healthcare level. This work also strengthens the direct interaction between the NHLS pathology service and local health authorities.

Outreach

Dr Stephen Korsman

The diagnostic laboratory has an outreach programme to support the laboratories in the Eastern Cape and parts of the Western Cape. Telephonic and electronic support has been provided. In-person outreach was limited by the NHLS financial constraints. George NHLS lab was visited by a pathologist on one occasion.

NICD Cape Town, Centre for Respiratory Diseases and Meningitis Medical Virology Diagnostic Laboratory
Head: Professor AL Williamson

This unit was established in the microbiology and virology diagnostic laboratories at GSH in 2010 to augment the capacity of the routine laboratory to investigate disease outbreaks and to train medical scientists. As of 2013 the unit has been absorbed into the NICD Centre for Respiratory Diseases and Meningitis, where it contributes to the WHO-driven annual viral watch, the influenza subtyping programme, as well as various other respiratory virus-based research studies.

Research Projects

Clinical and Diagnostic Virology Research Group
Head: Dr Diana Hardie

Nosocomial transmission of respiratory viruses within the intensive care unit at Red Cross Children’s Hospital
Investigators: Dr Z Omar, N-C Hu, Dr N Hsiao
Funding: Poliomyelitis Research Foundation (PRF)

This study explored the extent of respiratory virus nosocomial transmission in a paediatric
hospital. Respiratory syncytial virus isolates from the 2011-2012 season were sequenced and some potential nosocomial clusters were identified. In addition, the molecular techniques used to determine the epidemiology of respiratory viruses identified a new subtype of respiratory viruses circulating in our paediatric hospitals.

Evaluation of human milk HIV antibody testing for breast milk donor screening in resource-limited settings using a proxy in-patient population from the Western Cape, South Africa

**Investigators:** S Manicklal, CA de Jager, E Brierley, L Goosen, SM Kroon, M Hsiao

**Funding:** PRF

The major challenge facing community-based milk depots in resource-limited settings is the lack of facilities for venipuncture. This study evaluates the accuracy of HIV antibody screening of breast milk by comparing its performance with formal serum HIV antibody testing. Human milk antibody testing was shown to be reliable for the exclusion of maternal HIV infection in the first month after delivery, as the sensitivity and specificity of human milk ELISA were 100% and 92%, respectively. Although the impact of acute HIV infection was not assessed, the study showed milk antibody screening could be useful in the milk bank setting.

Hepatitis E in patients with acute non-A/B/C hepatitis

**Principal Investigator (PI):** S Korsman

**Funding:** PRF

To determine the prevalence of HEV in patients with acute hepatitis, PCR has been done for HEV in 168 patients. All PCRs were negative. Animal testing is pending.

Invisible bleeding from clean-shave haircuts, detection with blood-specific RNA markers

**PI:** Prof Nonhlanhla Khumalo (dermatology Virology), D Hardie, S Korsman, N-C Hu

The hypothesis that HIV may be spread by uncleaned/unsterilised hair clippers was tested in a pilot study. HIV-infected patients had their hair cut with clippers. Then the clippers were swabbed and washed off, and the supernatant tested for beta-globin RNA and HIV RNA. 1/11 were positive for beta-globin RNA and 0/11 positive for HIV RNA (Abbott Realtime HIV-1 viral load assay; also in-house nested HIV RNA PCR). Publication submitted.

HIV Vaccine Development Group and Human Papillomavirus Research Group

**Institute of Infectious Disease and Molecular Medicine**

**SARChi Chair in Vaccinology:** Professor A-L Williamson

**Development of HIV vaccines**

**UCT Investigators:** Professor A-L Williamson, Professor C Williamson, Dr K Downing, Dr G Chege, Dr E Hurter, M Lambrick

**Collaborators:** D Montefiori, Duke University Medical School, Durham, NC, USA

**Funding:** SAAVI/LifeLab, NRF, HVTN

The first two candidate HIV vaccines, SAAVI DNA-C2 and SAAVI MVA-C, developed at UCT, tested in phase one clinical trial (HVTN 073/ SAAVI 102 – Protocol Chair, Glenda Gray), are moderately immunogenic in humans. This trial was extended to include a Novartis gp140 protein boost. Studies were done in macaques using a similar vaccine regimen to the extended HVTN 072/SAAVI 102. This regimen induced good neutralising antibodies. The next trial that included the two SAAVI vaccines and the Novartis gp140 protein (HVTN 086/SAAVI 103) started recruiting at the end of 2011 (Protocol Chair, Gavin Churchyard) and will be completed in 2013. The potency of the SAAVI DNA-C2 continues to be assessed in the UCTVRG GLP compliant laboratory.

Optimisation of rBCG as an HIV vaccine vector

**UCT Investigators:** Professor A-L Williamson, Dr R Chapman, Dr GK Chege, Professor EG Shephard
BCG, the tuberculosis vaccine, is being developed as a potential HIV vaccine vector. Groups of Chinese rhesus macaques were vaccinated with a mixture of three candidate HIV vaccines (rBCG-Gag, rBCG-RT & rBCG-gp120). A mixture of the three rBCG vaccines induced modest HIV-specific responses in 5 of 8 vaccinated animals. In contrast, no HIV-specific responses were detected in the animals inoculated with either rBCG-Gag only or control BCG before the booster vaccination with SAAVI MVA-C was given. A booster vaccination with SAAVI MVA-C elicited HIV-specific responses in 7 of 8 animals that were primed with a mixture of the three rBCG vaccines and in 3 of 4 animals primed with rBCG-Gag only.

Investigation into different strains of BCG to deliver vaccine transgenes

UCT Investigators: Professor A-L Williamson, Dr R Chapman, S Chetty, Dr G Chege, Dr E Shephard
Collaborators: W Jacobs Jr (Albert Einstein College of Medicine, USA), Aeras, B Ryffel (CNRS, France)
Funding: NRF, NIH

TB vaccine studies have shown that a pantothenate auxotroph (ΔpanCD) of BCG is safe in SCID mice and protects from challenge with M. tuberculosis. In this study, wild-type, ΔpanCD, pfo and a combination ΔpanCDpfo strain of BCG were constructed to express HIV-1 subtype C Gag. Our group has recently shown BCG ΔpanCD Pasteur to be more immunogenic as an HIV vaccine than wild-type BCG when used in conjunction with a Modified Vaccinia Ankara boost (MVA). BCG expressing perfringolysin (pfo) promotes antigen translocation into the cytoplasm and induces stronger CD8+ T cell responses than the wild type. Unique patterns of gene regulation were observed for each of the optimised BCG strains as compared to the wild type.

Development of Avipoxviruses as vaccine vectors

UCT Investigators: Professor A-L Williamson, O Carulei, K Offerman, Dr N Douglass
Funding: NRF

Interest in the Avipoxviruses, notably Fowlpox virus (FWPV) and Canarypox virus (CNPV), has increased due to their successful use as vaccines on commercial flocks and their extensive use and testing as vaccine vectors in humans and animals. A phylogenetic study showed that isolates from wild birds such as penguin, pigeon and lesser flamingo are genetically different from isolates from canaries and domestic chickens. Two local avipoxviruses have been fully sequenced and shown to be unique compared to other published avipoxviruses.

Oral human papillomavirus (HPV) infection in South African men and women recruited for a study on HIV discordant couples

UCT Investigators: Professor A-L Williamson, Dr ZZA Mbulawa, Professor M Hoffman, Professor D Coetzee, Professor J Moodley, DR D Marais, Dr L Johnson
Collaborators: B Allan, Dr ZZA Mbulawa
Funding: PRF, SIDA, CANSA, NRF, MRC

Oral human papillomavirus (HPV) prevalence and factors associated with oral HPV infection were investigated in 221 heterosexually active couples. Oral HPV prevalence was found to be 6.8% in women and 13.5% in men. In women, the risk of oral infection with a specific type was significantly increased if the same type was present in the mouth or genital tract of their partner, or in their own genital tract. In men, the risk of oral infection with a specific type was increased only if the same type was present in the mouth or genital tract of their partner.

World Health Organization HPV LabNet for the African Region

Laboratory Director: Professor A-L Williamson
Laboratory members: B Allan, Dr ZZA Mbulawa
Funding: NRF, NHLS Trust
Human papillomavirus (HPV) is the cause of cervical cancer. HPV vaccination has not been introduced into the public sector in South Africa. As part of the HPV vaccination strategy in South Africa, it is important to have baseline data on HPV so that the impact of vaccination can be assessed as there are very few data on the prevalence of HPV types in South African women. Research is being done with a number of groups in South Africa to provide HPV typing and prevalence data in HIV-negative and HIV-positive women to provide some baseline data for vaccine introduction and also to inform policy on cervical screening.

Sequence analysis of human papillomaviruses

**UCT Investigators:** Professor A-L Williamson, Dr T Meiring, Professor EP Rybicki

**Funding:** PRF, NRF, MRC

Enriched cervical DNA was sequenced from five HIV and HPV co-infected women using the Ion Torrent metagenomic sequencing platform. A total of 904 Mb of data has been generated. The majority of contigs were classified as human papillomavirus (45%) and a number of other circular DNA viruses were identified, including Torque teno virus (15.7%), SEN virus (1.7%) and a novel circovirus (0.3%). Several HPV genotypes (HPV types 34, 43, 56, 74, 90, 103 and 108) were identified including some that were not detected by Roche HPV linear array analysis of the samples.

Analysis of human papillomavirus variants in couples

**UCT Investigators:** Professor A-L Williamson, Dr T Meiring, XK Mndende

**Funding:** PRF, NRF

The objective of this study was to determine the concordance of infection with HPV-16, -58 and -53 variants within heterosexual couples. A total of 12 HPV-16-positive couples, 8 HPV-58-positive couples and 12 HPV-53-positive couples were identified from a cohort of South African heterosexually active couples. In the 12 couples positive for HPV-16, 10 were concordant (ie shared the same HPV 16 variant), and 2 were discordant. For the 8-HPV-58 positive couples; 7 couples shared the same variant while partners in one couple had different variants. From the 12 HPV-53-positive couples, 10 were concordant and two couples were discordant. The majority of couples shared the same variant of the specific HPV types.

Typing of HPV from a cohort of young women from KwaZulu Natal

**UCT Investigators:** Professor A-L Williamson, Dr ZZA Mbulawa, XK Mndende

**Collaborator:** Professor Q Abdool Karim (University of KwaZulu-Natal)

**Funding:** PRF, NRF, NHLS Trust

There is limited information on the prevalence of HPV and the HPV types infecting young South African women. This study aimed to determine the HPV type-specific prevalence in 223 young women in a longitudinal study. Cervico-vaginal lavage (CVL) specimens were collected at baseline and quarterly visits from sexually active HIV-negative women that were ≤30 years of age from KwaZulu-Natal, South Africa. The Roche Linear Array HPV Genotyping assay was used to determine HPV types from 434 CVL specimens. HPV prevalence was found to be: 67.26% (150/223) at baseline, 65.09% (69/106) at the second visit, 60.87% (42/69) at the third visit. HPV prevalence is high in this population compared to other studies performed in HIV negative populations of similar age.

HIV Diversity and Pathogenesis

Group Division of Medical Virology
Institute of Infectious Disease and Molecular Medicine

**Head:** Professor C Williamson

The role of CTL escape mutations in attenuating HIV-1 subtype C infection

**Investigators:** Professor C Williamson, Professor CM Gray, Dr RS Ntale, Dr DR Chopera, Dr NK Ngandu

**Collaborator/Co-Investigator:** Professor S Abdool Karim (University of KwaZulu-Natal).
This study investigated the frequency, timing and pathogenic consequences of early cytotoxic T-lymphocyte (CTL) escape on subsequent HIV-1 disease progression. CTL escape in Gag or Nef epitopes was detected in 69% (35/51) of individuals and was more frequently observed in the acute than early/late infection phases. Participants with viruses escaping CTL responses had significantly higher CD4+ T-cell counts at 3 and 6 months post-infection compared to those whose virus never escaped suggesting that immune responses selecting escape mutations in acute infection provide benefit within the first year of infection. This project forms part of the India-South African programme to inform vaccine HIV-1 subtype C immunogen design.

The Comprehensive Antibody Vaccine Immune Monitoring Consortium (CA-VIMC) was established as part of the Collaboration for AIDS Vaccine Discovery (CAVD). The goal of the CA-VIMC is to facilitate the discovery and timely licensure of a safe, effective and practical HIV-1 vaccine for the world. The HIV Diversity and Pathogenesis group at UCT has been responsible for assembling a panel of 200 functional transmitted/early env genes from southern Africa. The clones are being used to study the genetic and antigenic diversity of HIV-1 strains currently circulating in these regions, and to ask how well the strains are represented by current vaccine immunogens and reference reagents.

Although the HVTN503/Phambili Phase IIB vaccine study in South Africa did not prevent infection, previous studies have shown that sequencing of breakthrough infections provides a sensitive method for detecting a vaccine effect. We characterised HIV-1 breakthrough infections from the Phase IIB Phambili/HVTN503 vaccine trial to determine if the vaccine induced immunity exerted any selective pressure on the virus. 262 full-length HIV genomes were generated from 43 individuals, forty infected with subtype C and three with non-C viruses. The vaccine had no discernible effect on the genetic bottleneck associated with transmission, and we found no evidence of a sieve effect at the protein or CTL epitope level. Further work is underway to investigate amino acid signatures associated with breakthrough infections.
microbicides and other prevention strategies will need to exceed in order to be effective. Neutralising antibodies (nAbs) do not play a role in the initial control HIV replication as they usually only arise weeks to months after control of viremia following infection.

However, there is some evidence in humans that suggests that nAbs are important in controlling viremia in chronic infection. We have identified four individuals with broadly cross neutralising responses, and are currently analysing their viral sequences together with their neutralisation responses to evaluate the impact and duration of effect of these antibodies on controlling viral populations.

HIV super-infection

Investigators: Professor C Williamson
Co-investigator/collaborators: Dr S Travers (SANBI, UWC), Professor SS Abdool Karim (CAPRISA)
Funding: National Research Foundation competitive programme for rated researchers

Super-infection refers to the re-infection of an individual with a second HIV strain after an established primary HIV infection. By studying the timing and incidence of super-infection, together with the infecting viruses, this project aims to investigate why immunity to the first strain does not protect against infection with the second strain; and to inform vaccine testing through an investigation of the role of boosting in enhancing immunity.

We have identified three individuals who were super-infected. We were able to characterise, for the first time, the envelope of viruses that mediate super-infection. We found that the super-infection did not boost immunity to the first virus, and dual HIV infection did not result in greater cross-neutralising activity. These data have implications for the use of polyvalent immunogens in HIV vaccines.

HIV Mucosal Immunology Group
Institute of Infectious Disease and Molecular Medicine
Head: Associate Professor Dr J-A Passmore

Impact of genital inflammation, HIV co-infection and Human Papillomavirus (HPV)-specific cellular immunity on HPV burden in the female genital tract
Principal Investigator: Associate Professor J-A Passmore
Co-investigators: Professor A-L Williamson, Dr F Little, Professor L Denny, Dr P Gumbi
Funder: Cancer Association of South Africa

Genital tract inflammation has been identified as an important co-factor in progression of HPV-associated cervical disease although inflammation has also been shown to facilitate clearance of primary genital tract HPV infections. Genital inflammation is also a significant predictor of enhanced risk for HIV infection.

While inflammation plays diverse roles in the etiology of each of these viral sexually transmitted infections, the intersection of these infections in co-infected individuals results in worse HPV-associated disease outcome. We have identified key biomarkers for genital tract inflammation which are significantly elevated in genital secretions from HIV negative women in discordant relationships with HIV+ partners compared to HIV negative women in concordant relationships with uninfected partners. Interestingly, we found that women who did not spontaneously clear their HPV infections exhibited higher levels of inflammation than women who remained uninfected. While HIV infection was associated with generalised high levels of inflammation over time, signatures associated with HPV infections were very subtle and restricted to only a few cytokines.
Impact of anti-retroviral therapy on HIV shedding, inflammation and the quality of HIV-specific immunity in the female genital tract of women chronically infected with HIV

Principal Investigator: Associate Professor J-A Passmore
Co-investigators: Dr P Gumbi
Funders: Medical Research Council

Initiation of HAART in HIV-infected individuals is associated with rapid and highly effective control of systemic viremia and rebound of blood CD4 cell counts over time. The aim of this study was to evaluate HIV shedding in the female genital tract over time in HIV-infected women on antiretroviral therapy compared to those who are therapy naive and to explore the association between genital HIV shedding and genital inflammation, CD4 restoration and quality of mucosal immunity in the context of ART. We showed that in HIV-infected women HAART is associated with significantly improved CD4 T cell counts both in blood and at the cervix. While HAART effectively suppressed both blood and cervical viraemia, HIV-specific CD8 T cell responses in blood were lost while those at the cervix were preserved.

EDCTP factors affecting HIV susceptibility in the adolescent genital tract

Principal Investigator: Associate Professor J-A Passmore
Co-investigators: Dr H B Jaspan, Professor L Bekker, Professor C Williamson, Professor R Shattock (Imperial College London), Professor T Hope (Northwestern University, USA), Professor F Chiodi (Karolinska Institute, Sweden), Prof CM Gray, Dr D Wilson (Edendale Hospital), Associate Professor Dr N Mulder, Professor E Gray (Perinatal HIV Research Unit)
Funders: EDCTP & Dept Science and Technology

South African adolescents are vulnerable to HIV, disproportionately to the amount of sexual risk behaviour. We postulated that biological factors present at the site of HIV exposure, the genital tract, play a role in increasing susceptibility to infection. HIV in sub-Saharan Africa is primarily transmitted across the genital tract mucosa and knowing that the virus preferentially infects activated cells, we hypothesised that sexually transmitted infections, changes in hormones and foreskin/vaginal microbiome during puberty drives activation and inflammation and recruitment of susceptible target cells. We propose to use the unique opportunity provided by adolescent microbicide and circumcision studies to investigate mechanisms leading to inflammation at genital mucosal surfaces in adolescents. We have assembled a network of clinical sites in Cape Town, Gauteng and Pietermaritzburg which involves a consortium of 14 scientists committed to build capacity for clinical and laboratory mucosal investigations for future adolescent-based HIV prevention studies and to identify factors driving biological risk that will inform new intervention strategies, appropriate for this age group.

Identification of host biomarkers and pathways associated with genital inflammation and susceptibility to HIV infection in women by microarray

Principal Investigator: Associate Professor J-A Passmore
Co-Investigator: Dr L Masson, Professor J Blackburn, Dr Nicola Mulder, Professor S Abdool Karim (CAPRISA), Professor Q Abdool Karim (CAPRISA), Dr N Garrett (CAPRISA), A Grobler (CAPRISA), Dr M Shey (CAPRISA), N Samsunder (CAPRISA)
Funders: Medical Research Council

Tenofovir gel was the first anti-retroviral drug-containing microbicide formulation to show protection against male-to-female sexual transmission of HIV in a large-scale Phase IIb clinical trial. Despite this, it was found that women who had raised concentrations of IL-1β, IL-10, IL-8, MIP-1α, MIP-1β and GM-CSF in their genital tracts were at increased risk of HIV infection, even those who frequently used tenofovir gel. Women who had elevated concentrations of 3 or more
inflammatory cytokines were at 5-fold increased risk of HIV infection [OR (95% CI): 5.5 (2.4 to 12.7), p<0.0001]. Better management of the causes of genital inflammation or augmentation of tenofovir gel with agents to modulate inflammation may reduce susceptibility to HIV infection and increase the efficacy of tenofovir gel. A better understanding of the signalling pathways that regulate inflammatory cytokine production in the female genital tract is, however, critical in order to identify appropriate targets for intervention. The current proposal aims to investigate signalling pathways that regulate inflammation in the female genital tract using host genomic approaches (microarray), to identify novel targets for therapeutic intervention and to confirm these findings using in vitro cervical explant models.

The role of genital tract inflammation in susceptibility to HIV infection and target cell recruitment in the female genital tract: understanding breakthrough infections in the 1% Tenofovir microbicide gel trial

**Principal Investigator:** Associate Professor Dr J-A Passmore  
**Co-Investigator:** Dr M Shey, Prof S Abdool Karim  
**Funders:** PRF

Women from the CAPRISA004 1% Tenofovir microbicide gel trial who seroconverted during follow up were found to have elevated concentrations of IL-1α, IL-1β, IL-8, MIP-1α, MIP-1β and GM-CSF in their genital tracts. Since dendritic cells (DCs) are known to respond to and produce inflammatory cytokines, the aim of this study was to investigate the impact of inflammatory markers and TLR agonists on genital tract-derived DC activation. We found that in vitro addition of inflammatory cytokines and TLR agonists onto cervical explant tissues induced DC emigration. Migrating DCs were activated at both 24 and 48 hours of culture. We also observed increased migration in the ectocervix compared with the endocervix in control tissues. After correcting for background, cytokines and TLR agonists induced similar migration in endocervix and ectocervix. Our interim conclusion from this work is that inflammation may directly influence the efficacy of 1% Tenofovir microbicide gel through enhanced activation of migrating DCs in genital tissues. This may have broader implications for mucosal vaccine efficacy or combination prevention modalities involving microbicides with vaccines. Since DCs are one of the target cells to capture and transfer HIV to other cells, this direct effect could possibly increase the risk of HIV acquisition.

The effect of the contraceptive depot medroxyprogesterone acetate (DMPA) on HIV acquisition and genital tract mucosal protective immune responses to HIV

**Principal Investigator:** Associate Professor J A Passmore  
**Co-Investigators:** Professor Q Abdool Karim, Professor J Hapgood, and Dr S Sengeziwe  
**Funders:** PRF

Recent international observational studies have suggested a relationship between the progesterone-based injectable hormonal contraceptive (HC) use and increased risk for HIV acquisition and transmission. The precise biological and immunological mechanism by which injectable HCs may increase risk to HIV infection is not known. We investigated the relationship between hormonal contraception use, genital inflammation and Tissue Inhibitors of Metalloproteinases (TIMPs) production in the cervicovaginal lavages (CVLs) in HIV-uninfected women. Interim analysis suggests that concentrations of IL-1β, IL-9, IL-12p40, IL-15, IFNα, Eotaxin, Fractalkine and MCP-1 were down-regulated in women using injectable contraceptives (DMPA or NET) compared to women not using HCs. In addition, women using injectables also displayed lower levels of EGF, FGF2, PDGF-AA and TGF-β compared with women with no hormonal
contraception. No significant change was found in TIMP levels from women using injectable contraceptives compared to non-users. Our data suggests that injectables suppress both innate and adaptive arms of the immune system, resulting in a decrease of host resistance to invading pathogens. The immunosuppressive properties of injectable contraceptives evident in the female genital tract could impact on the efficacy of HIV vaccines and prevention strategies.

Teaching and Training

The division participates in the facilitation of problem-based learning for medical students. Other teaching activities include lectures, tutorials, seminars and practicals. The division offers modules in the BSc Med (Hons) programme. In addition, the facility is registered with the HPCSA as a training facility for medical scientists in the field of molecular biology and virology. Two medical scientists in each of these disciplines are currently participating in the training programme. The division has a large postgraduate teaching programme which includes training of Masters (MSc and MMed) and Doctoral students, as well as training registrars.

Postgraduate candidates enrolled:

39 (2 MMed, 13 PhD, 12 MSc, 3 BScHons, 9 Post Docs)

Students graduated:

5 (2 PhD, 3 BScMed(Hons))

Honours

Special awards / honours / promotions

Jo-Ann Passmore has become an Associate Professor

Carolyn Williamson became a member of the Royal Society of South Africa and the South African Academy of Science

Narjis Thawer (MSc student) was awarded a DST fellowship for 2012 South African Women in Science awards

Jo-Ann Passmore was awarded an EDCTP Strategic Primer grant for a study of genital health and mucosal immunology of adolescents in South Africa

Melissa-Rose Abrahams and Gama Bandawe were awarded Fogarty Aids Training Programme fellowships

Research Output

Conference Presentations:

7 international congresses,
2 national congresses,
1 local congress

Jo-Ann Passmore was invited as a plenary speaker to AIDS Vaccine 2012 conference in Boston, USA and she was also invited to present at an international NIH / Division of AIDS workshop on “The need to measure mucosal responses in HIV prevention trials.”

Publications


Meiring TL, Salimo AT, Coetzee B, Maree HJ, Moodley J, Hitzeroth II, Freeborough MJ, Rybicki...


General Haematology and Molecular Haematology

Head: Professor Nicolas Novitzky

Diagnostic Services

The Division of Haematology at Groote Schuur Hospital is a complex unit with multidisciplinary activities that include outpatient clinics, admission beds as well as diagnostic and research laboratories. The clinical services are organised under the umbrella of the Department of Internal Medicine, while the laboratory diagnostic sections are under the broader organisation of the Department of Clinical and Laboratory Sciences and National Health Laboratory Service (NHLS). The laboratory continues to offer comprehensive diagnostic testing for the diagnosis and management of all haematological malignancies. It also offers diagnostic services for a Comprehensive Haemophilia Centre, as well as to a number of tertiary / quaternary programmes. This laboratory also acts as a tertiary referral centre for local hospitals and outlying clinics of the Western Cape, as well for referral samples from the Eastern Cape. The routine and molecular haematology laboratories were again successfully accredited by SANAS.

Teaching and Training

The department remains a primary teaching and training site for medical technologists, technicians, undergraduate medical students of the University of Cape Town (UCT) and registrars (specialising postgraduate doctors) in Haematopathology and Clinical Haematology. Currently there are five haematology pathology registrars and one clinical pathology registrar who are enrolled in the UCT postgraduate programme. Dr Karen Shires continues to provide training in the molecular haematology course for haematology registrars and technologists together with Ms Iva Shankland. Dr Karen Shires and Ms Iva Shankland have provided lectures/practicals in molecular diagnostic techniques for Anatomical Pathology registrars. Dr Karen Shires is part of a team who have developed the Molecular Forensic MSc course. She is the Forensic Genetics course convenor. Consultant pathologists Drs Almero Du Pisani, Jessica Opie and Monalisa Ntobogwana as well as Mr Francois Barton have delivered training courses to NHLS technologists at NHLS Green Point Complex in Cape Town. Dr Almero du Pisani gave a lecture to medical technologists at the monthly Western Cape branch SMLTSA – TTP. Mrs Glenda Davison was awarded a doctorate (PhD) degree from this university. Two medical technologists, Cecile Maree-Hupkes and Adri Rust obtained their B.Tech degrees in biomedical technology. All the March 2013 clinical pathology medical technology students passed the board exam.

Outreach:

Consultant pathologists gave a number of lectures at a 2 day NHLS advanced morphology course for medical technologists from the Eastern Cape (March 2013). Dr Almero du Pisani gave a lecture on AML (4hrs). This course was held at Green Point.

Research Output

Research projects

Cancer Testis Antigen (CTA) expression in Multiple Myeloma
Dr K Shires (supervisor), A Stavridis (MSc student) (NHLSRT, CANSA funding).

This project linked the expression of CTA molecular markers to known prognostic factors in Multiple Myeloma and clearly showed a strong association with poor prognostic factors and advanced disease stage. The assay will be validated for use in the diagnostic arena as a prognostic tool for the disease.
Development of a rapid diagnostic screen for telomerase mutations associated with immunosuppressive therapy failure in South African patients with Aplastic Anemia
Dr K Shires (supervisor), K Xulu (MSc student)

Funding: NHLS Research Trust
This project was designed to create a rapid diagnostic platform for mutations that are known to be associated with the stem-cell aging mechanism responsible for the disease mechanism in a large Aplastic Anemia subgroup. These patients should not be placed on standard immunosuppression therapy and rather transplanted as soon as possible. The novel assay has been developed and is currently being validated.

The search for a CML-specific antigen. An investigation into the changes that occur at the cell surface as a result of transformation with active BCR-ABL
Dr K Shires, Professor N Novitzky

Funding: CANSA
Through the use of phage-display technology, we sought to identify novel CML-associated peptides that would uniquely bind to the surface of BCR/ABL expressing cells. Several peptides were identified through panning and enrichment, which showed a binding preference for both tissue culture cells and granuloctyes from CML patients, indicating potentially useful drug-delivery peptides.

MAGE expression in Multiple Myeloma: A tool for malignant cell identification, disease monitoring and determining disease mechanisms
Dr K Shires (supervisor), K Wienand (PhD student)

Funding: NHLS Research Trust
MAGE C1 was found to be expressed exclusively in symptomatic Multiple Myeloma patients in our previous study and we plan to use this as a tool to both identify the controversial malignant population of cells that are circulating in the peripheral blood, as well as means of measuring minimal residual disease through both flow cytometric and real-time quantitative PCR assays

The effect of alemtuzumab in the immunomodulation of stem cells for transplantation
Professor N Novitzky (supervisor), G Davison (PhD student), R Abdulla and Dr S Mowla.

Depletion of cDS2+ cells is effective in reducing graft vs host disease, but the in vitro effects on the graft have been studied poorly. The project seeks to define the cellular events that follow he use of alemtuzumab “in the bag” by studying blood grafts donated for allogeneic stem cell transplantation.

Developing a flow cytometry method for detecting NPM in AML
Dr K Shires (supervisor), Dr LA Du Pisani (MMed student)

Funding: NHLS
Mutated nucleophosmin 1, when present in isolation, carries a good prognosis in cyogenetically normal AML. The aim of the study was to develop a flow cytometry technique to identify the altered protein due to the mutation and partially validate this technique.

Imported malaria at GSH
Dr LA Du Pisani (supervisor), Dr R Freecks (MMed Student)

The rate of malaria diagnosis in the Western Cape has escalated in the last few years. Malaria is not endemic to this area and virtually all cases are imported. The aim is to study the epidemiology of this parasitic infection as it pertains to this region, to look at how patients were managed and the outcome.
HIV-Associated Burkitt Lymphoma and Antiretroviral Therapy at Groote Schuur Hospital, 2005 - 2010
Dr J Opie (supervisor), Professor N Novitzky (co-supervisor), Dr C Webb (MMed Student).

The number of patients presenting with HIV-BL at Groote Schuur Hospital (GSH) has been steadily increasing over the past decade, despite the roll-out of antiretroviral treatment to HIV-positive South African patients since 2004. This trend has similarly been identified by the Tygerberg Lymphoma Study Group who describe an increase in HIV-related lymphomas from 5% of all lymphomas diagnosed in 2002 to 37% in 2009.2

A smaller international study has also shown an increase in HIV-BL patients from 2% of HIV-associated lymphomas in the pre-HAART era to 13% in the HAART era1. Specific research into the relationship between antiretroviral use and HIV-BL alone has not yet been published from South Africa. The aim of this study is to assess whether immune status and exposure to antiretroviral therapy affect the clinical presentation, diagnosis and management of patients presenting with HIV-associated Burkitt lymphoma at Groote Schuur Hospital between 2005 and 2010.

Clinical presentation, haematological features and clinical outcomes of HIV-associated Hodgkin Lymphoma at GSH, Western Cape, South Africa
Dr J Opie (supervisor) Professor N Novitzky (co-supervisor), Dr L Swart (MMed Student)

The aims of this project include: To establish the incidence of bone marrow (BM) involvement in patients presenting with Hodgkin Lymphoma at GSH and to establish whether BM involvement correlates with HIV status, CD4 counts and LDH and then to compare clinical outcomes of patients with and without BM involvement.

The role of the immune system in the pathogenesis of myelodysplasia (MDS)
Professor N Novitzky (supervisor), G Davison (PhD student)

Funding: NHLS Research Fund
The immune system has been implicated in the pathogenesis of MDS. Investigations have confirmed that T-cells in MDS are not clonal but oligoclonal and that together with monocytes secrete cytokines which stimulate rather than inhibit colony growth of CD34+ stem cells. In addition, dendritic cells are unable to mature adequately and activate allogeneic normal T-cells but can initiate a brisk autologous CD8+ T-cell response. These results suggest that the immune system could be utilised in the development of immune based therapies in MDS patients

Conference Presentations
10th South African Stem Cell Transplantation Society Symposium, 17–18 February 2012, Southern Sun Newlands, Cape Town

N Novitzky, V Thomas, C du Toit & A McDonald. Conditioning with purine analogues leads to good engraftment rates of immunodepleted grafts for aplastic anaemia.

UCT Refresher Couse for FCP Part I candidates, July 2012
J Opie. Overview of haematology physiology

Pathpoint 2012, 28-30 September 2012, Century City, Cape Town

6th Annual Haematology-Oncology 2012 Symposium, Southern Sun, Cape Sun - Cape Town, 2–3 November 2012

Z Mohamed, N Novitzky. A descriptive analysis of HIV-positive patients with multicentric Castleman’s Disease seen at Groote Schuur Hospital Oncology Department from 2005–2011.


N Novitzky, C du Toit, V Thomas and Z Mohamed. Submyeloablative therapy and tandem transplantation for patients with multiple myeloma at the UCT Myeloma Clinic.

Awards

The GSH laboratory won the the Coastal Regional ‘NHLS has got talent competition’.

Publications:


Novitzky N, Thomas V. In the absence of clinically significant graft vs. host disease, myeloablative conditioning may allow an effective graft vs leukaemia effect. Leukemia Research 2012; 36(1): 104–109.


Department Of Anatomical Pathology

Head: Professor Bruce Middlecote

Diagnostic Services

The department provided a diagnostic surgical pathology service to all the provincial hospitals in the Free State and during part of 2012 to some of the provincial hospitals in the North West Province. From time to time work was also sent from the Northern Cape.

A cytopathology service was provided to the Free State and Northern Cape. During the year 25,021 surgical pathology cases and 90,003 cytopathology cases were seen. Eighty-four autopsies were performed. The main challenge for the department is a shortage of pathologists and technologists/technicians.

Research Projects

A comparative investigation of Kaposi sarcoma and non-lesional mRNA expression levels by serial analysis of gene expression.

Collaborators: Dr J Goedhals, Department of Anatomical Pathology, NHLS/UFS; Dr D Goedhals, Department of Medical Microbiology and Virology, NHLS/UFS; Dr PA Bester, Department of Medical Microbiology and Virology, UFS; Dr G Melikian, Division of Infectious Diseases, Department of Medicine, Stanford University, Stanford, CA; Dr MC Botha, Department of Oncology, UFS.

mRNA expression levels in tissue biopsies of Kaposi sarcoma lesions and histologically normal skin will be compared to quantify viral and host gene expression in order to elucidate the pathogenesis of this condition. High quality mRNA will be used for the construction of serial analysis of gene expression (SAGE) libraries for next generation sequencing.

Clinical, pathological and virological correlation of HIV-associated Kaposi sarcoma

Collaborators: Dr J Goedhals, Department of Anatomical Pathology, NHLS/UFS; Dr D Goedhals, Department of Medical Microbiology and Virology, NHLS/UFS; Dr MC Botha, Department of Oncology, UFS

The aim of this study is to try to find a link between the HHV-8 genotype, the clinical presentation of KS and the microscopic picture in HIV-associated KS patients. Patients who have been treated for KS will be identified retrospectively. Their issue samples will be re-examined microscopically and HIV-8 genotyping will be performed. Clinical records will also be reviewed to assess clinical presentation and response to treatment.

Teaching and Training

Undergraduate:
The department presents a module on general pathology to second year medical students. Sessions on systematic pathology, which are integrated into system modules, are conducted with both second and third year students. The total contact time is approximately 140 hours per year. A short course in general pathology is provided to 3rd year physiotherapy and occupational therapy students.

Postgraduate:
Daily departmental and interdepartmental meetings are held. Registrars from forensic pathology rotate through the department for two years. Anatomical pathology registrars rotate through the forensic pathology department on an informal basis. Registrars from oncotherapy, each spend three months in the department.

Professional development
Number of registrars in the department: 8
Number of registrars successfully completing studies: 1 (MMed Anatomical Pathology)
Research Output

Published publications: 5
Conference presentations: International: 3

Scientific publications
Journal articles


Department Of Chemical Pathology

Acting Head: Professor Johannes M Kuyl

Diagnostic Services

The clinical chemistry laboratory is fully accredited by the South African National Accreditation System (SANAS) and is mostly automated centred around the Roche Cobas 6000 automated system. The laboratory processes specimens received mostly from Universitas Hospital, the National Hospital and 3 Military Hospital in Bloemfontein. Specimens are also referred from the laboratories at Pelonomi and Kimberley hospitals. The number of tests performed in the period 1 April 2012–31 March 2013 was more than 900,000 and is increasing. Consultants and registrars attend the endocrine and diabetic clinics and ward rounds on a regular basis.

Research Projects

Biochemical changes after prostatectomy with orchidectomy
Researchers: Dr A Groenewald, Professor S Wentschel (Department of Urology, UFS)

Comparing the biochemical changes in the blood of individuals practising geophagia with those of a matched control group
Researchers: M van Wyk and Professor JM Kuyl

Teaching and Training

The department is actively involved in the training of undergraduate and postgraduate medical students including those from anaesthetics, surgery and family medicine. Part of the postgraduate training occurs in weekly seminars, journal club discussions and wet practical sessions.

Professional development

Postgraduate students enrolled: 3 MMed

Research Output

Publications


Department Of Haematology And Cell Biology

Head: Professor MJ Coetzee

Diagnostic Services

The department offers routine haematology investigations, and an array of specialised tests for haematological malignancies, as well for thrombotic and bleeding disorders. We run a 24-hour service for thromboelastography and platelet function analysis. Ours is the only walk-in finger INR clinic in South Africa, which had 9,280 visits. The Special Haemostasis Unit has been streamlined.

Dr Jaco Joubert has been placed in Kimberley, where he has been able to offer bone marrow investigations locally, and expand the tests. He is helping the recently appointed clinical haematologist there. Together they have improved services, especially the survival rates for leukaemias. Patients from Northern Cape are referred to Universitas. We could improve the Universitas turnaround times by not having to run outreach clinics in Kimberley anymore.

Dr Reinette Weyers, the outreach pathologist in the Free State, continues to refine the diagnostic services and do training. Regularly technologists diagnose haematological emergencies in the smaller laboratories, alert clinicians and move specimens to Universitas quickly, thus enabling these patients to be referred promptly.

However we critically need to upgrade our flow cytometer and automated haemostasis instruments.

A total of 111,177 tests were performed and 522 patients seen at various clinics.

Research Projects

A focus area on haemostasis research was set up in 2012 in the Faculty of Health Sciences of the University of the Free State. The title of this focus area is “Haemostasis in disease: from bench to bedside.” The principal investigator is Professor M Meiring from the Department of Haematology and Cell Biology. Departments that are involved in this focus-area include Haematology, Clinical Haematology, Cardiothoracic Surgery, Cardiology, Neurology, Nephrology, Dietetics, Virology, Biotechnology and Anatomical Pathology. More than 40 projects were running in 2012 in this focus area. Projects where the Department of Haematology is the only department involved include the following:

Thrombotic potential in HIV-associated TTP
Researchers: M Meiring, V Louw, M Webb
Funding: NRF

HIV-associated TTP is a fatal disorder associated with micro-vascular thrombi. The thrombotic potential in these patients is assessed by thrombin generation assays, microparticle quantification, the levels and activity of Von Willebrand factor and its cleaving protease ADAMTS13, tissue factor levels and microparticle thrombin generation assays.

The laboratory diagnosis of Von Willebrand Disease in South Africa
Researchers: M Meiring, M Kelderman, M Coetzee
Funding: NRF

A reference centre for Von Willebrand Disease in South Africa has been established in the Department of Haematology of the University of the Free State. All laboratory tests needed for the full diagnosis of Von Willebrand disease have been set up. These tests are all in-house methods and are developed to be much more cost-effective than commercial kits.
Development of a cost-effective assay to determine VWF propeptide levels in plasma.

**Funding:** NHLS Research Trust  
**Researchers:** P Setlai, M Meirng

The VWF propeptide assay is used to diagnose patients with an increased VWF clearance. In this project the VWF propeptide is first displayed on yeast and purified. Antibodies are then selected against the propeptide by using phage display technology. These antibodies are used in the development of an assay to measure the VWF propeptide in plasma.

Development of an assay to determine the factor VIII binding assay.

**Researchers:** L Cloete, M Meiring  
**Funding:** NHLS RT

The FVIII binding assay is used to diagnose patients with type 2N VWD. Antibodies are selected against human factor VIII by using phage display technology. These antibodies will be used to develop a cost-effective factor VIII binding assay for von Willebrand factor.

Characterisation of a tissue factor inhibiting antibody

**Researchers:** J-G Vermeulen, M Meiring  
**Funding:** MRC

An inhibitory antibody fragment to human tissue factor was developed by Professor M Meiring. This antibody inhibits factor X formation in plasma. It also lengthens the Prothrombin Time dose-dependently. It further normalises the thrombin generation in hypercoagulable plasma. This antibody fragment is characterised by epitope mapping, kinetic profile of action and efficacy testing in a mouse sepsis model.

The effect of inflammatory cytokines on the human umbilical cord endothelial cells.

**Researchers:** W Allers, M Meiring  
**Funding:** NRF

Cultured endothelial cells were used to study the effect of inflammatory cytokines interleukin-6, 8 and tumour necrosis factor, as well as coagulation factors thrombin and tissue factor and combinations thereof on the expression and activity of von Willebrand factor and its cleaving protease ADAMTS13.

Effect of inflammation on endothelial microparticles

**Researchers:** E le Roux, M Meiring  
**Funding:** NRF

Human umbilical cord endothelial cells were stimulated with different combinations of inflammatory cytokines and coagulation factors. Microparticles were quantified and the von Willebrand factor content as well as the microparticle associated thrombin generation were determined.

Teaching and Training

Our registrars now all do the BMedSc (Hons) molecular modules, attend the DNA Diagnostics course in Cape Town, and attend the annual immunology course at Wits University. Two of our recently graduated pathologists have become affiliated lecturers and assist with teaching.

We are teaching medical interns to do bone marrow biopsies, while promoting haematology as a career. We help technologists with research projects for further degrees. The department is applying for the Kimberley haematology laboratory to be recognised as a satellite teaching unit. We are adjusting the Clinical Pathology programme to ensure integrated teaching throughout the residency.
Professional development

Postgraduate candidates enrolled in your department: 15 (3 MMed, 2 PhD, 6 MSc, 4 BSc [Hons]) as well as three intern scientists.

Postgraduate students who graduated during the year: 4 (2 MMed, 2 MSc) as well as one who completed a management short course.

Honours

Dr Reinette Weyers received the prize for the best haematology presentation at the Pathpoint Congress in Cape Town in 2012 with her paper Reaching out: Model of a haematology support service.

Mrs Magda Oosthuizen, our Academic Secretary, was awarded second prize in the ARRQA category in the Central Region.

The Universitas Business Unit received the NHLS national award for the “Laboratory with the Mostest”.

Dr Gerda Marx was one of the first recipients of the University of the Free State Rector’s Prestige Scholars Programme in 2012.

Six invited lectures were delivered.

Research Output

Publications


Viljoen CD. Mandatory labelling of genetically modified food in South Africa: What you should know? South African Association for Food Science and Technology 2012; November issue: 36–37.


Congress presentations

International: 2, National: 5, Local: 6
Division of Human Genetics

Head: Professor Magda Theron

Diagnostic Services

The division is a SANAS-accredited service provider and provide a genetics healthcare platform to the Northern Cape and parts of the Free State. The molecular genetics laboratory is the national referral 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 national referral unit for the diagnosis of Roberts syndrome and Fanconi anaemia. The laboratories render a comprehensive diagnostic service to Universitas Hospital, 3 Military Hospital, Pelonomi Regional Hospital, National District Hospital, Kimberley Hospital, Upington Hospital, Bongani Hospital, Tsepong Hospital, 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 an extensive routine diagnostic screening for inherited breast cancer and referrals throughout South Africa and the African continent are diagnosed. The FISH laboratory renders a pre-and post-natal screening programme based on microdeletions and common chromosomal aneuploidies. The cytogenetic laboratory provides a pre-and post-natal 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.

The department is SANAS accredited and a HPCSA accredited intern medical scientist training facility.

Research Projects

Screening of young and/or familial African breast cancer patients for the presence of BRCA mutations

Researchers: Dr NC van der Merwe, N Peter

Funding: MRC research grant

The incidence of breast cancer is increasing in African women due to the adoption of a more western lifestyle, with an average age at diagnosis of 42.6 years. Hereditary forms of breast cancer due to mutations within the familial breast cancer genes BRCA1 and BRCA2 have unique clinical, molecular, and biological features. In this pilot study, 35 patients representing the Sotho/Tswana population were screened using various mutation detection techniques. Two unique disease-causing mutations have been identified (5.7%); together with rare polymorphisms that are restricted to the African population. The study indicated that a more in-depth search is justified within this population, as they carry unique changes not previously detected internationally based on their unique genetic makeup.

Genetic profile of familial breast cancer within the Coloured population from the Western Cape

Researchers: Dr NC van der Merwe, J Oosthuizen

Funding: Medical Research Council (MRC)

The incidence rate of breast cancer within the Coloured women is 25.6 to 26.6 per 100,000, compared to 14.7 per 100,000 for Black women. A pilot study performed on 124 non-Afrikaner patients from the Western Cape resulted in the identification of the first founder mutation present within BRCA2 for the Coloured/Xhosa populations of South Africa. As only PTT was performed, the full BRCA mutational spectrum for these two groups is not known. As the
Black population is genetically and culturally very diverse, it is expected that each tribal group could foster its own unique mutations, thereby complicating diagnostic screening of South African individuals.

We will be screening these patients representing each of the various tribes for the presence of BRCA mutations in order to determine the mutational spectrum present. Only once the information is known, more population directed mutation panels can be compiled for the appropriate testing of these previously disadvantaged populations for familial BC.

Investigation into the BRCA1 and BRCA2 mutation spectrum present within the African population of central South Africa

Researchers: Dr NC van der Merwe, P Moeti
Funding: MRC

Breast cancer rates and the median age of onset differ between Western European populations (including the SA Afrikaner population with its European heritage) and Africans. Although BC is less common in African women compared to Afrikaners, it strikes at an earlier age and has a higher mortality rate.

Although the majority of SA citizens are Black Africans (38 million), these patients have not had access to diagnostic testing for familial breast cancer so no research information is available regarding the profiles of BRCA1 and BRCA2 mutations within this population. Results of the pilot study by Ms N Peter revealed the presence of unique mutations and rare polymorphisms that caused the disease within 5.6% of this population. The enlarged study will assist in determining whether any of the two disease-causing mutations detected up to date could possible represent a founder mutation within this group.

Familial breast cancer within the Indian population of South Africa

Researchers: Dr NC van der Merwe and Mr HMVE Combrink
Funding: MRC

The Indian population in a country such as South Africa has their historic and genetic origins in India and neighbouring Asian countries. Their population groups and cultures are very complex and diverse differences exist. The fact that they tend to marry within a certain culture increases the possibility of genetic effects being enhanced such as mutations within BRCA1 and BRCA2. Currently, no data is available for the Indians residing within South Africa. The project aims to elucidate the role that BRCA genes play within this population group. As the process for screening for mutations using older technology is extremely labour intensive, the project will also attempt to optimise and implement real-time based high resolution melting (HRM) as the screening method of choice. Once optimised, it will drastically reduce the turn-around-time of performing a complete screen for mutations within these genes. The results obtained from this study will be incorporated within the NHLS diagnostic platform to service the Indian patients residing in KwaZulu-Natal and Gauteng.

Teaching and Training

Intern medical scientists
The division is an HPCSA accredited training facility for intern medical scientists. No intern candidates were contracted during 2012. The vision of the division is the simultaneous incorporation of all intern medical scientists in a full-time Masters or Doctorate programme.

Postgraduate
4 MMedSc students are currently enrolled and will qualify in 2015.
Honours

Professor M Theron served on the Science Committee of the University of the Free State and has been elected as chair of the CPD programme committee of the University of the Free State.

Professor M Theron has been appointed as chair of the Genetics Expert Committee.

Professor M Theron served as coordinator of the HPCSA Medical Science Committee for the assessment of the intern medical science programme.

Dr N van der Merwe was awarded with a self-initiated research grant from the MRC.

Dr N van der Merwe was elected as Chair: Laboratory services of the Faculty Forum of the University of the Free State.

Research Output

Publications


Congress presentations

Local: 3
Department of Medical Microbiology and Virology

Head: Dr E Elliot

Diagnostic Services

The department provides a 24-hour microbiology and virology telephonic consultative service to Universitas, National and Pelonomi hospitals and to Free State as part of the training and outreach platform. It also provides information on request to medical practitioners and health care workers and hospital patients, who are seen on a consultation basis.

Laboratory statistics

Medical Microbiology:

Microbiology test volumes in 2012/2013: 206,363

Serology total tests in 2012/2013: 21,280

Medical Virology:

<table>
<thead>
<tr>
<th>TEST</th>
<th>Number of samples 2012</th>
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<tr>
<td>Serology</td>
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Research Projects

Medical Virology:

Vector-borne and zoonotic viruses research group
Head of research group: Professor FJ Burt.
Collaborators include: Professor R Swanepoel, University of Pretoria; Professor J Paweska, NICD, Johannesburg; Professor M Heise, Carolina Vaccine Institute, USA.

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

Human papilloma virus research group
Head of research group: Professor FJ Burt.
Collaborators: Professor R Seedat (Otorhinolaryngology Department); Dr B Kocjan, Slovenia

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

Human immunodeficiency virus research group
Head of research group: Dr D Goedhals.
Collaborators include: Dr C Jansen Van Vuuren, Dr. D Steyn (Department Internal Medicine, UFS), Dr C Seebregts, MRC, Dr T de Oliveira (Africa Centre, UKZN), Dr J Frater, Professor 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.

Teaching and Training

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

Professional Development

Technologist training
Rotating experiential students: 21
Rotating intern students: 6

Postgraduate students enrolled
M Med: 1
Ph.D: 2
MMedSc: 6
BSc (Hons): 2

Postgraduate students qualified
M. Med. Sc 0
B.Sc. (Hons) 2 (1 Passed with distinction).
Honours

Burt FJ. Roche Floating Trophy for Best Senior Laboratory Presentation at the School of Medicine, Annual Research Faculty Forum 2012.

Mathengtheng L. Floating Trophy for Best Junior Laboratory Presentation at the School of Medicine Annual Research Faculty Forum 2012.

Rangunwala A. Second place in Masters Category of the 3-minute thesis competition held by the postgraduate school, University of the Free State. Identification of antibody directed against nucleoprotein among survivors of Crimean Congo haemorrhagic fever infection.

Research Output

Journal articles


Chapter in book


Conference presentations:

National congresses: 3 presentations
Regional and local congresses: 6 presentations
Department of Anatomical Pathology

Head: Professor Pratistadevi K Ramdial

Diagnostic Services

The Department of Anatomical Pathology reported on 37,903 surgical pathology and 37 autopsy specimens.

A total of 126,538 cytopathology specimens were processed, including 113,312 gynaecological cases, 5,922 non-gynaecological specimens and 7,304 fine needle aspirates. These specimens were processed despite funding issues and major backlogs.

Teaching and Training

Undergraduate teaching

Some 169 hours of lectures and practicals were delivered to undergraduate MBChB students. This included 60 lectures and 22 practicals to second year and six lectures to third year medical students at the Nelson R Mandela School of Medicine.

This included the setting of assessments, end of theme test and end of module examination as well as invigilating, marking and entering of marks. We were also involved in revision and remedial sessions for second and third year students.

The department was also involved in the end of theme and end of module assessments for the second and third years. The department also offered lectures to the clinical science students. This included nine lectures and the setting of assessments.

Postgraduate teaching and training

Cytopathology: Three intern medical technologists passed their medical technologist Board exams in March 2012. One intern medical technologist passed her exam with a distinction in September 2012. Two student medical technicians wrote and passed their medical technician Board examinations in 2012. Three medical technicians completed their fourth year bridging course in biomedical technology and have qualified with National Diplomas in Biomedical Technology.

Histopathology: Two technologists passed the board examinations in March 2012. Three technicians wrote their exams in October 2012 and two passed. During the year, 33 clinicopathological meetings were undertaken with the clinical and surgical disciplines that allowed interaction with clinical colleagues and contributed to improved understanding of disease processes in general, and helped with management of individual patients in particular. The postgraduate training programme facilitated learning and intradepartmental interaction at 30 short topics and 35 “box” slide assessments.

Research Output

Published Papers:


Barr DA, Ramdial PK. Clinicopathological correlates in HIV seropositive tuberculosis cases presenting with jaundice after initiating antiretroviral therapy with a structured review of the literature. BMC Infect Dis 2012; 14: 257 (ahead of print).

In press articles:
Ramdial PK, Sing Y, Ramburan A, Bagratee JS, Naidu TK, Singh B. Lymph node involvement in donovanosis. Pathol Int.

Chapters in Books:


Department of Chemical Pathology

Acting head: Dr Magdalena J Turzyniecka

Diagnostic Services

The Department of Chemical Pathology provides a 24-hour diagnostic service to the academic complex of King Edward VIII (KEH) and Inkosi Albert Luthuli Central Hospitals (IALCH). It also provides outreach and consultative services and is a referral centre for the entire KwaZulu-Natal province for specialist tests such as organic acid and very long chain fatty acid analysis, specialised endocrine assays and protein electrophoresis. The total workload for the period 2012/2013 for KEH was 1.2 million tests and for IALCH was 2.01 million tests, approximately up 10 and 20% from 2011/2012 respectively.

Both KEH and IALCH laboratories are preparing for SANAS accreditation scheduled for the end of 2013, with the KEH laboratory having successfully passed pre-SANAS audit in March 2013. The IALCH laboratory is scheduled for the pre-SANAS visit in June 2013.

There have been several positive changes within the laboratory. The IALCH laboratory implemented newer generation assays for endocrine tests such as oestradiol (eE2), parathyroid (iPTH) hormone and anti-thyroid peroxidase antibodies (aTPO); in March 2013 a quantitative procalcitonin (PCT) assay was introduced to the laboratory repertoire.

In January 2013 the department procured a sweat test system which will enable diagnosis of cystic fibrosis in the entire province. A 100% increase in requests for HbA1c in the second half of 2012 stimulated a tender for a new, higher workload HbA1c analyser which was successfully completed at the beginning of March 2013. Since August 2012, the department has been involved in the implementing of Electronic Gate Keeping (EKG) for IALCH.

The measures planned for the future include introduction of remote signing out of the test results after hours to maintain and improve good turnaround times (TAT), implementation of a lean system and a free one year trial of unity connectivity to improve laboratory analytical performance and introduction of new tests such as free androgen index and salivary cortisol and screening for Down's syndrome.

Research Projects

The department continues with the international VISION study which undertakes evaluation of major vascular events in patients undergoing non-cardiac surgery.

Urinary Cortisol Stability – Effects of different storage conditions and the use of boric acid as a preservative

Researchers: Y Rampursat, M Z Warasally, M J Turzyniecka

Funding: Siemens provided cortisol kits

The laboratory currently uses boric acid as a preservative in urinary collections for cortisol estimation in patients screened for Cushing’s. The study examined stability of urinary cortisol at different storage conditions and the effect of boric acid on the analyte stability with the aim of improving laboratory service delivery and cost effectiveness.

The results suggest that urine samples do not need to be refrigerated during the collection period and addition of boric acid does not significantly affect the stability of cortisol and therefore its use could be discontinued by the laboratory, which would reduce the analytical cost and labour.
An audit of serum and urine electrophoresis results and the requests for immunofixation by different validators

Researchers: M J Turzyniecka and Y Rampursat

Protein electrophoresis is used for the detection of monoclonal immunoglobulins associated with lymphoproliferative diseases and plasma dyscrasias. Immunofixation (IFE) is the only reliable method to characterise monoclonal proteins. Currently, owing to Department of Health directive, reflex IFE is not available in our laboratory for samples other than that requested by haematologists. This reduces analytical costs at the expense of delaying accurate clinical diagnosis. This audit evaluated number and total cost of IFEs when requested by different validators for the same electrophoresis results assuming reflex IFE was available in our laboratory. The audit showed lack of patient and clinician details mainly on requests from referral laboratories and consistency in IFE requesting by different validators which would support need for reflex testing.

A greater demand for HbA1c testing calls for tighter demand management

Researchers: N Pillay and M J Turzyniecka

New national and international guidelines specify when HbA1c testing should take place in case of newly diagnosed and known diabetic patients. The audit retrospectively evaluated data regarding clinical details and patient demographics for 500 SPEP requests performed during June and July 2012. The audit showed poor record of clinical details for externally requested tests together with high number of negative results which suggests that SPEP is used as a screening rather than a diagnostic tool for multiple myeloma. Implementation of demand management should guide appropriate SPEP requesting and reduce the laboratory costs.

A prospective audit of cardiac injury marker ordering in patients with chest pain

Researchers: U Bellbhudder and J Stanfliet

Recent guidelines suggest use of high sensitivity cardiac troponin T or I as the biochemical tests of choice in the investigation of patients with suspected acute coronary syndrome (ACS) in place of other biomarkers such as creatine kinase MB (CK-MB) isoform.

This prospective study conducted at KEH aimed to establish whether clinicians followed the most recent recommendations. The audit showed that ordering patterns in the setting of ACS did not reflect current recommendations, were wasteful and potentially dangerous.
Haemolysis does not cause interference in the Brahms semi-quantitative procalcitonin assay

Researchers: A Sadhabiriss and J Stanfliet

This study aimed to assess the manufacturer’s claim that severe levels of haemolysis will cause interference with Brahms semi-quantitative procalcitonin (PCT) kit

Patient samples with known concentration of PCT were spiked with a prepared haemolysate of known concentration to identify the effect of haemolysis on the assay. The results showed that haemolysis up to Hb 50 g/L did not interfere with the Brahms PCT semi-quantitative assay and even severely haemolysed samples can be assayed using this method.

An audit examining pre-analytical variables resulting in specimen rejection or unsuitability

Researchers: D Naidoo, U Bellbhudder and J Stanfliet

This retrospective audit aimed to determine the most common pre-analytical variables contributing to rejection of specimens received in the Chemical Pathology Laboratory NHLS at KEH during August to December 2012. The main reasons for specimen rejection included haemolysis, insufficient sample volume and EDTA contamination, all of which could be minimised with the appropriate clinicians’ education.

Teaching and Training

Undergraduate

The department contributes to lecturing and reviewing the content of the curriculum of second, third and fourth year medical students at the Nelson R Mandela School of Medicine. It delivered a total of 40 hours of lectures and tutorials covering gastrointestinal, endocrine and renal systems. It was also involved in the end of theme and end of module assessments for the second year.

Postgraduate

The department established regular training for chemical pathology registrars in the form of hands on practical training sessions, weekly tutorials, lectures and calculations sessions together with regular essay writing assessments.

The internal part 1MMed examination was organised at the end of March this year for 2 registrars. The postgraduate academic meetings programme facilitated continuous professional development (CPD) in the form of total 30 journal clubs, seminars and case presentations. In order to facilitate CPD for the pathologist at Greys Hospital in Pietermaritzburg, the department introduced at the beginning of March 2013 teleconferencing of the academic meetings.

In August 2012, Dr Verena Gouden was invited to give a lecture on acid base disturbances at the Acid Base SAACB Workshop at the Wits Medical School. Dr Magdalena Turzyniecka and Mr Zain Warasally gave lectures at SMLTSA KZN Mini Congress in November 2012. Additionally, Dr M Turzyniecka was an invited guest speaker at a symposium in Malaysia at the Universiti Technologi Mara in November 2012.

Technologists and technicians

The department provides in-service teaching and training to student medical technologists and technicians registered for both Chemical and Clinical Pathology.

All 4 student technicians based at KEH and IALCH who wrote exams in September 2012 passed the examination (3 in Chemical Pathology and 1 in Clinical Pathology). Pathologists from the department continue to provide lectures for BTech Biomedical Technology students at the Durban University of Technology (DUT)
Professional Development

Postgraduate candidates graduated:
4 Medical Technicians (2 Chem Path, 2 Clin Path)

Postgraduate candidates enrolled: 2 MMed

Honours

Dr V Gounden received a 2 year NIH fellowship in Clinical Chemistry and is currently in Bethesda, Maryland completing the fellowship in Clinical Chemistry.

Dr M Turzyniecka was elected a secretary of SAACB.

Research Output

Publications

Pillay TS, Turzyniecka M, Naidoo SS. Cost-effective utilisation of basic biochemical laboratory investigations in primary care. *Continuing Medical Education* 2012; 30(7): 249–25

Gounden V. Pre-diabetes and the metabolic syndrome. *Continuing Medical Education* 2012; 30(7): 252–253

Gounden V, Rampursat Y. A case not so crystal clear. *Clinical Chemistry* 2012; 58(8): 1264–1265


The Vision Study Investigators. The vascular events in noncardiac surgery patients cohort evaluation. Association between postoperative troponin levels and 30-day mortality among patients undergoing noncardiac surgery. *JAMA* 2012; 307(21): 2295–2304

Conference presentations:

International: 1
National: 3
Department of Medical Microbiology

Head: Professor Koleka Mlisana

Diagnostic Services

The academic complex consists of laboratories at both Inkosi Albert Luthuli Central Hospital (IALCH) and King Edward VIII Hospital (KEH). Diagnostic services include bacteriological, fungal and mycobacterial identification and susceptibility testing. Specialised testing is also performed on specimens and isolates from other clinics and hospitals in KwaZulu-Natal. The mycology laboratory at IALCH serves as a reference laboratory for isolation, identification and antifungal susceptibility testing on fungal isolates. It now also offers minimum inhibitory concentration (MIC) testing using broth microdilution on selected fungal isolates.

In view of the emergence of drug resistance to carbapenem antibiotics, screening tests for carbapenamase production have been implemented. MIC testing using gradient diffusion methods has been introduced for isolates causing invasive Salmonella disease. Trends in antibiotic resistance are monitored by pathologists and this information is relayed back to the hospital infection control teams.

The IALCH tuberculosis (TB) laboratory is the reference centre for drug susceptibility testing of 1st and 2nd line anti-TB drugs for the province. On average the IALCH laboratory continues to perform 3,273 Auramines and 15,000 TB cultures per month with approximately another 3,000 cultures being processed at KEH. The unit has recently acquired the Epicentre microbiology data management system to assist in managing the 20 Mycobacteria Growth Indicator Tubes used for TB culture. Molecular diagnostics for TB includes the Hain line probe assay (LPA) for identification as well as drug susceptibility of Mycobacterium tuberculosis and identification of mycobacteria other than tuberculosis. The laboratory currently performs approximately 2,600 LPAs per month.

Outreach services have been extended to assist three other peripheral laboratories with support from visiting pathologists as well as permanent pathologist placements at King George Hospital and Mahatma Gandhi Hospital.

Research Projects

A Genotypic Association of Mutations within the rpoB gene and resistance of Mycobacterium tuberculosis to Rifampicin in KwaZulu-Natal

Investigators: K Mlisana (NHLS/UKZN), M Pillay (NHLS), M Pillay (UKZN)

Objectives: Determination of genotypic association of mutations within the rpoB gene and resistance level of M. tuberculosis strains to rifampicin by sequencing and MIC testing.

Of the 34 Rif resistant isolates analysed so far, 25 (73%) harboured a mutation in codon 531 involving a Ser to Leu amino acid substitution. This mutation was associated with a MIC ranging from 4 - 16 ug/ml in 21 these isolates. Five out of six isolates showing substitutions in codons 513 (Gln513 to Pro), had MICs of 2-4ug/ml. Mutations in codons 531 and 526 (His526 to Asp) were associated with a high level of rifampicin resistance in majority (65%) of the isolates whereas codons 513 and 516 (Asp516 to Val) mutations were associated with low level resistance.

De Novo Capreomycin Resistance Is Prevalent, Widespread, and Associated With Increased Early Mortality in Extensively Drug-Resistant Tuberculosis (XDR-TB) Patients in KZN, South Africa

Investigators: MR O’Donnell (Albert Einstein College of Medicine, USA), M Pillay (NHLS), I Master KGV Hospital), YM Coovadia (NHLS & UKZN), NS Shah (Emory University), K Mlisana (NHLS & UKZN), N Padayatchi (CAPRISA)
Objectives: Relevance of CAP resistance among XDR-TB patients not previously treated with CAP containing regimens as well as the clinical impact of CAP resistance on survival and time to culture conversion. To also determine the genetic mechanisms of resistance and the RFLP patterns of Capreomycin resistant MTB strains. 53/216 (24%) isolates were identified and viable for testing. MIC testing for CAP was performed and 48 (90.5%) XDR-TB patients were resistant. 46/48 sputum samples were collected before treatment with CAP was initiated. Codons 1401, 1402 and 1484 of the rrs gene were analysed and showed mutations at A1401G, C1402T and G1484T. Whilst none of the CAP sensitive isolates had A1401G mutation, all 48 resistant isolates had. CAP resistant patients had lower rates of 6-month TB culture conversion (25% vs. 60%) and survival (80% vs. 100%) compared to CAP sensitive patients.

To evaluate the Performance of the new Version 2 Genotype MTBDR+ Assay for the rapid detection of multidrug resistant tuberculosis in smear positive and smear negative culture positive sputum samples.

Investigators: M Pillay (NHLS), YM Coovadia (NHLS & UKZN) and K Mlisana (NHLS & UKZN)

Objectives: To evaluate the performance of the new version 2 Genotype MTBDR+ assay for the rapid diagnosis of pulmonary TB in smear positive and smear negative culture positive sputum samples.

For smear positive, culture positive sputum samples, the Genotype MTBDR+ version 2 assay showed a sensitivity of 97%, 98% and 97% for the detection of MDR-TB, rifampicin and isoniazid mono-resistance respectively. For smear negative, culture positive sputum samples, the assay showed a sensitivity of 78% for the detection of MTB. The sensitivity for the detection of MDR-TB, rifampicin and isoniazid mono-resistance was found to be 94%, 94% and 93% respectively in smear negative culture positive sputum samples.

A rapid detection of XDR-TB: Comparison of the Genotype MTBDRsl Assay with Indirect second-line Susceptibility testing.

Investigators: A Kajee (NHLS), M Pillay (NHLS), YM Coovadia, K Mlisana (NHLS & UKZN)

The Genotype MTBDRsl assay identified fluoroquinolone resistance in 63 of the 66 (95%) sputum samples and in 63 of the 64 (98%) MGIT cultures. Resistance to an aminoglycoside was detected in 62 of the 64 (97%) sputum samples and in 63 of the 64 (98%) MGIT cultures.

For the sputum samples the following mutations were identified: a single mutation A90V (58/138) in the gyrA subunit coding for a fluoroquinolone resistance and a mutation in position A1401G (54/138) of the rrs gene coding for an aminoglycoside/cyclic peptide resistance. The Genotype MTBDRsl detected fluoroquinolone resistance in 65 of the 80 well characterised MGIT cultures with a single mutation (A90V) in the gyrA subunit and a mutation A1401G of the rrs gene.

An evaluation of the Genotype MTBDR+ Assay for the rapid and accurate detection of Mycobacterium tuberculosis/MDR-TB in extrapulmonary specimens received from patients in high TB burden areas within KwaZulu-Natal

Investigators: M Pillay, YM Coovadia, K Mlisana

The Genotype MTBDR+ assay identified MTB in 21 of the 22 (95%) smear positive extrapulmonary samples. The MPT64 antigen assay confirmed the presence of MTB in all 22 cultures. Of the 76 samples that were smear negative, 26 were culture positive.

The Genotype MTBDR+ assay identified MTB in 19 of the 26 (73%) smear negative, culture positive samples. The Genotype MTBDR+ assay has a sensitivity of 95% for the detection of MTB in smear positive fluid aspirates and 73% for smear negative culture positive fluid aspirates.
Biotyping of clinical susceptible MDR- and XDR-TB strains using MALDI-TOF MS.

**Investigators:** S Myende (NHLS), M Pillay, YM Coovadia, K Mlisana, Dr Patrick Govender (UKZN)

**Objectives:** To develop, and optimize a sample preparation protocol, for the discrimination of the members of Mycobacterium tuberculosis complex (MTBC) based on their unique proteomic profile. This method will then be compared to an available protocol which is the inactivated Mycobacteria bead based preparation method (inMbpm).

Reproducible and unique mass spectra were obtained from all strains tested and this enabled the creation of a database for further classification purpose. The optimised method was successful to discriminate members of Mycobacterium tuberculosis complex

Optimization of the sample preparation protocol for matrix assisted laser desorption ionization-time of flight mass spectrometry discrimination of Mycobacterium tuberculosis complex

**Investigators:** M Pillay, S Myende, YM Coovadia, K Mlisana, P Govender (Biochem Dept, UKZN)

Reproducible and unique mass spectra were consistently and exclusively generated using the dilipidation modified sample preparation protocol. A database of typed mycobacteria and clinical strains of M. tuberculosis strains was established.

Bacterial Safety of Flash-heated breast milk using a temperature probe

**Investigators:** M Naicker (NHLS), A Coutoudis (UKZN), K Mlisana (NHLS & UKZN)

Funding: PATH, UKZN Grant

**Objectives:** To evaluate the safety of FoneAstra flash-heat compared to flash-heat without FoneAstra, bacterial growth was compared in breast milk samples before and after pasteurization.

A total of 300 samples were analysed. Bacterial growth was found in 86 of the 100 pre-pasteurised samples and 1 of the 100 post-pasteurised samples without FoneAstra.

Both methods provided safe and effective pasteurisation. FoneAstra offers temperature monitoring, data tracking and can be used as a quality assurance tool for standardising the pasteurisation process.

Incidence of nosocomial infections: An audit of an evidence-based empiric antimicrobial policy in a trauma ICU.

**Investigators:** Y Ramsamy (NHLS), D Muckart (UKZN), K Han (NHLS & UKZN)

A retrospective chart review of all admissions to the trauma Intensive care unit – January 2009–December 2009. Medical data was analysed to establish the incidence of nosocomial infection in the unit. Of 227 patients, 106 (46.6%) had 136 culture positive isolates with a total of 320 pathogens (63% gram negative; 37% gram positive).

Of the gram negative pathogens 56% were Enterobacteriaecae with 25% ESBL positive Klebsiella isolates. Staphylococcal species accounted for 60% of the Gram positive isolates of which 24% were methicillin resistant (MRSA). There were 101 empiric and 14 directed prescriptions issued.

Despite positive cultures antimicrobials were not prescribed in 21 patients who had no clinical evidence of sepsis. Excluding MDR Acinetobacter isolates there were 93.5% appropriate and 6.5% incorrect prescriptions.
Comparison of Etests and Vitek 2® with Broth Microdilution for the Susceptibility of Cryptococcus neoformans

Investigator: Y Mahabeer (NHLS & UKZN); Y Coovadia (NHLS & UKZN)

Funding: NHLS

Broth microdilution (BMD), Etests and Vitek 2 were conducted on 102 C.neoformans isolates from CSF samples. Essential agreements (EA) were defined as results within 2 dilutions. CLSI breakpoints were used to determine categorical agreement (CA). The EA of Etests for fluconazole and voriconazole was 95 and 91% respectively and amphotericin B was 83%. The overall CA for Etests for these drugs was 98%. For Vitek 2®, the overall EA and CA for fluconazole, amphotericin B and 5-flucytosine were 96 and 97% respectively. The Etests and Vitek 2® correlated well with BMD for fluconazole, 5-flucytosine and voriconazole and these are suitable alternatives for susceptibility testing of Cryptococcus neoformans. However, amphotericin B E-tests were less reliable with MIC values lower than BMD.

Evaluation of an Immunochromatographic assay (SD Bioline MPT64 Ag test) for rapid identification of MDR and XDR Mycobacterium tuberculosis isolates in liquid and solid cultures, including evaluation on ageing cultures

Investigators: YM Coovadia (NHLS & UKZN); N Naidoo (NHLS); S Mahomed (NHLS)

Objective: To evaluate the effect of aging cultures on the performance of Immunochromatographic assay by monthly testing of stored liquid and solid XDR and MDR cultures for 3 months.

If AFB were detected then the SD Bioline MPT64 Ag test was performed. Regardless of MPT64 Ag positivity or negativity, the specimen had niacin and nitrate testing. In evaluating ageing cultures, the positive MGIT and corresponding solid culture plates were stored in the hot room and tested every 21 days for 84 days.

In addition, the performance of the test on aging solid and liquid XDR and MDR isolates reported high sensitivity and specificity rates. This indicates that the antigen remains stable in both liquid and solid culture media.

Evaluation of the microscopic observation drug susceptibility assay (MODS) in a busy NHLS TB reference laboratory in KwaZulu-Natal

Investigators: A Kajee (NHLS), M Pillay (NHLS), K Swe Swe Han (NHLS & UKZN), YM Coovadia, KP Mlisana

Funding: NHLS

The MODS assay was performed on 230 well characterised clinical sputum samples comprising of XDR, MDR and mono-resistant strains of M.tuberculosis. The investigator performing the MODS assay was blinded to the culture susceptibility results. Interpretable results were obtained for 220 (96%) of the 230 sputum samples tested. MODS sensitivity was 86% (95% confidence interval [CI], 78-92%), and specificity was 92.8% (CI, 95-99%). The median turnaround time for MDR-TB diagnosis was 9 days (IQR: 6-9) in smear positive and 12–14 days (IQR: 12–15) in smear negative sputum samples with MODS versus 70 days (IQR: 49-96) with indirect proportion method (P < 0.001). MODS is a diagnostic tool of promise for the timely detection of M. tuberculosis resistance to first- and second-line drugs.

Teaching and Training

The department is actively involved in the teaching of medical students and health science students. Training is also given to technicians, technologists and registrars from microbiology, virology and infectious diseases.

Technologists and technicians

Six intern medical technologists and six student medical technologists were trained in the routine microbiology laboratory. Twenty seven student medical technologists received
a training course in the tuberculosis diagnostic laboratory. Three student technicians passed their Board examinations.

**Undergraduates**
The department teaches medical students in basic science and clinical modules. These modules are in the form of large and small group sessions as well as computer-based practical sessions. A semester course in microbiology is conducted for Biomedical Science students which includes lectures and computer-based practical sessions. A series of lectures covering basic microbiology is also delivered to health sciences students.

The department offers an Honours Medical Microbiology programme and had an intake of 18 students in 2012. Microbiology lectures are also given to students enrolled for an honours programme in infection prevention and control.

**Postgraduates**
Two intern medical scientists are currently in training. Registrar training comprises daily informal teaching at the bench and bedside as well as formal tutorials three times a week. In addition, two joint academic meetings are held a week with the Department of Infectious Diseases, UKZN.

**Professional development**
Enrolled Postgraduate Candidates: 16 (4 PhD, 10 MMed, 2 MSc) + 18 BSc Hons

Graduated Candidates: 15 BSc Hons

**Research Output**

**Conference presentations:**
Local Conferences: 8 Presentations

International Conferences: 5 Presentations

**Publications:**


Gray GE, Metch B; Churchyard G; Milisana K; Nchabeleng M; Allen M; Moodie Z; Kublin J; Bekker LG. Does participation in an HIV vaccine efficacy trial affect risk behaviour in South Africa? Vaccine 2013; 31: 2089.


Ntale RS; Chopera DR; Ngandu NK; Assis de Rosa D; L Zembe L; Gamieldien H; Mlotshwa M; Werner L; Woodman Z; Milisana K; et al. Temporal association of HLA-B*81:01- and HLA-B*39:10-mediated HIV-1 p24 sequence evolution with disease progression. J. Virol 2012; 86: 12013


**Department Of Virology**

**Acting Head:** Dr Pravi Moodley

**Clinical Diagnostic Services**

The number of HIV PCR tests (Figure 1) increased considerably due to expansion of Early Infant Diagnosis HIV testing in infants and the changes to the Prevention of Mother-To-Child Transmission Programme guidelines.

The number of HIV viral load tests decreased considerably since the establishment of HIV viral load testing in the Madadeni, Hlabisa and Addington hospital laboratories.

The Enzyme Linked Immuno-Assay (ELISA) for viruses such as HIV; hepatitis A (HAV); hepatitis B (HBV); hepatitis C (HCV); rubella; cytomegalovirus (CMV); Epstein-Barr virus; herpes simplex 1 and 2 (HSV); and toxoplasma serological markers are routinely conducted.

The number of these tests (Figure 1) continues to increase due to more requests for HBV, CMV and toxoplasma from the clinics in the Comprehensive Care Management and Treatment Programme (CCMTP).

All in-house viral PCR (Figure 1) molecular assays have been replaced by commercial assays for the molecular diagnosis of CMV, varicella-zoster virus, HSV and parvovirus, respiratory viruses and enteroviruses. These passed all quality assurance and verifications before being offered as part of the diagnostic service. These more sophisticated assays replaced the conventional cell culture and virus isolation methods which are no longer offered as a diagnostic service.

The department received the best external quality assurance performance in KZN during the reporting period. The department is in the final stages of preparing for the first SANAS inspection in July 2013. The Siemens Ultra Clear RO water purification system and Thermo Scientific 5L 40F Centrifuge was installed in the viral serology section. The antiretroviral genotyping is now available for routine diagnostic purposes. About 25 tests per month were done in the last four months of the year under review.

The registrars spend one day a week in the CCMTP Clinics in various hospitals in Durban as part of outreach to our customers. The department provides monthly outreach to the tertiary complexes in Pietermaritzburg and Ngwelezane hospitals.

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**Figure 1: Trends in workload (2006/2007–2012/2013) to project internal operational requirements and planning to meet customer needs.**
Teaching and Training

Three student medical technologists from 2012 wrote and passed the Virology SMLTSA Board Examinations in March 2013. One medical technologist re-wrote in September 2012 and passed. The current three student medical technologists will write examinations in March 2014. Two medical technicians wrote and passed (N Dladla with Distinction) in October 2012. In 2012, 27 students registered for the 16-credit module, Molecular Virology, BSc (Biomedical Science) at third year level in the Faculty of Science and 21 students passed. There are 30 students registered for 2013.

The department’s contribution to medical student teaching includes lectures and assessments in the first three years of the curriculum. The department plays a much more intensive role in this programme, especially at third year level. Seventy healthcare professionals registered for the module “Introduction to the Virology of HIV” towards the postgraduate diploma in HIV/AIDS Clinical Management in 2012 in collaboration with Nelson R Mandela School of Medicine Enhancing Care Initiative Unit. Sixty three of the 70 passed.

The diverse contribution to teaching and training in the Department of Health and the university allows us to be a competitive teaching and training centre in the province.

Professional Development

Dr Nokukhanya Mdlalose, Dr Tiniyko Khosa and Dr Natasha Thumbiran were invited by Addington Hospital to provide an HIV/Aids overview and Post-exposure HIV Prophylaxis (PEP) / Non-occupational PEP (NOPEP) to nurses in April. Dr Natasha Thumbiran, Dr Tiniyko Khosa and Dr Kerusha Govender was also invited by MEPI and ECI to train nurses in HIV/Aids IN May and July.

Dr Tiniyiko Khosa was invited to teach HIV Basic Science, Socio-economic impact of HIV, HIV Legislation, counselling and testing and Assessment Review by the Regional Training Department in May. Dr Raveen Parboosing was invited by Caprisa (UKZN) to teach in the Advanced Epidemiology course in October.

There are four registrars and four pathologists registered for the MMed in Virology. Dr Raveen Parboosing (pathologist) is registered for PhD and Miss Lavanya Singh (medical scientist) is registered for the MMedSc in Virology. Two registrars passed the FC Path (SA) Virology in October 2012. Dr Mdlalose was invited to be a reviewer for the Basic Science Trach for the South African Durban Aids Conference.

Dr Reshmi Samuel was awarded the MRC self-initiated grant of R190 000.00 and Dr Raveen Parboosing was awarded R280 000 per year from 2013–2016 from the NRF Thuthuka programme.

Research Projects

Hepatitis B and human immunodeficiency virus co-infections in pregnant women in KwaZulu-Natal

Researchers: N Thumbiran, D Moodley, P Moodley and R Parboosing

Funding: NHLS Research Trust Grant

Prevalence of Hepatitis B virus infection in infants: KwaZulu-Natal

Researchers: NB Mdlalose, P Moodley and R Parboosing

Funding: NHLS Research Trust Grant

Impact of HIV, antiretroviral therapy and TB genotype on survival in MDR TB

Researchers: U Laloo, W Sturm, P Moodley, A Moll, T van der Merwe, N Gandhi, G Friedland, NS Shah, J Brust, C Marra

Funding: NIH.
HIVDR prevalence in adults on ART in Gauteng and KwaZulu-Natal
In collaboration with the Department of Health (DOH), National Institute for Communicable Diseases (NICD), National Health Laboratory Service (NHLS), University of KwaZulu-Natal (UKZN), South Africa and United States Centers for Disease Control and Prevention (CDC).
Funding: CDC

Evaluation of referrals for antiretroviral therapy (ART) treatment failure in a public access paediatric ART programme in KwaZulu-Natal
Researchers: R Bobat, M Archary and P Moodley

Epidemiology of HIV, HAV, HCV and HBV in KZN
Researchers: N Tathiah, P Moodley, R Parboosing

Epidemiology of Paediatric HCV
Researchers: R Bobat, M Archary, P Moodley, and R Parboosing
Funding: Department of Virology

Prevalence of HDV in KwaZulu-Natal
Researchers: P Moodley, R Parboosing and L Singh. P
Funding: NHLS Research Trust

Research Output

Publications


Department of Anatomical Pathology Including Cytology

Head: Professor NM Bida

Diagnostic Services

The department provides a comprehensive surgical pathology, autopsy pathology and cytopathology service to the Dr George Mukhari Hospital/University of Limpopo (Medunsa campus) 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 and immunocytochemical stains.

The electron microscopy unit is a facility of the University of Limpopo but is available for use by our department. The laboratory was fully accredited by the South African National Accreditation System in November 2012 without any non-conformances noted. The number of histology cases registered increased from 11,663 in the 2010/11 reporting period to 12,247 in 2011/12. This increase is due to the following:

- Increased area which includes several hospitals in the North West and Mpumalanga.
- Increased patient load at many of our referral centres reflecting the general national trend of increasing hospital admissions resulting from the burden of HIV/AIDS.
- Increasing number of surgical specimens from Polokwane.

The number of cytology registrations decreased from 71,875 in 2010/2011 to 60,254 in 2011/2012. This can be ascribed to the decreased participation in the community health centres for routine pap smears. There is a need to embark on outreach programmes in order to correct this. There was also a problem in the allocation of catchment areas which was resolved.

Common routine special stains such as ZN and PAS are being introduced in the cytology laboratory. During the current reporting period a total of 51 autopsies were performed, 12 of which were paediatric cases.

New diagnostic services

There are plans to expand the scope of our diagnostic services to include immunofluorescence, to be used largely for evaluation of skin and renal biopsies and a requisition has already been submitted. A muscle biopsies bench is currently being considered and should be implemented before the end of the financial year ending 2012. Equipment in this regard is already ordered.

Human Resources

Consulting Staff

The department currently has a complement of three full time consultant pathologists. Dr MJ Chokoe joined the department in January 2012; Dr L Nel joined the department in April 2012 and Dr E Marais joined the department in January 2013.

Registrars

There are currently four resident registrars in the department and one rotating registrars from forensic department.

Auxiliary staff

Ms R Leballo was appointed as a secretary of the department in November 2011. Ms B Payne continues to work as a senior administrative officer in the department. We still have our two audio-typists who capture our histology reports and one copy typist who capture our cytology reports. We need an extra audio-typist, because there is an increase in the specimen volumes in the current reporting period in order to maintain the acceptable turnaround time.
Teaching And Training

Undergraduate

The consultant staff is responsible for delivering whole-year undergraduate teaching in Anatomical Pathology to MBChB students during their third year of study by way of lectures and tutorials. Power point lectures are given electronically to all students and in future blackboards will be utilised.

Autopsy student demonstrations are not performed because the current mortuary is not designed to allow more than 10 individuals at any time so there are space limitations. The lecture hall previously used for student demonstrations is earmarked for revamping together with the old mortuary. Until this is accomplished, mounted wet organ specimens or digital images are used to make up for this.

Teaching in anatomical pathology is also delivered to third year BDS (Dentistry) students from the dental faculty (in the first semester only – some rationalisation of these curricula is being sought to alleviate the teaching burden).

The department is also involved in giving formal lectures 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 are lectured to by registrars.

Postgraduate

There are currently four resident registrars in the department of Anatomical Pathology in various years of study. A comprehensive training programme is in place and was recently fully accredited by the Health Professions Council of South Africa (HPCSA).

- Dr B Ratlabala registered for the MMED in January 2009 and has successfully completed MMED Part 1 examinations.
- Dr N Ntsangani joined the department in November 2012.
- Dr N Tshishonga joined the department in January 2013.
- Dr N Ntsoane joined the department in January 2013.

Dr C Skosana resigned in January 2013 after an unsuccessful attempt at MMED Part 11 examinations. Dr N Ndame resigned in March 2013 after demonstrating a poor performance in formative assessments.

Training of registrars in anatomical pathology requires a good calibre of registrars and for this reason the department has introduced regular formative assessments in order to monitor progress. These formative assessments are also used in the first six months to give guidance in terms of fitness of candidates to continue in their careers based on their performance in the first six months or so.

From time to time registrars from the department of forensic pathology rotate through our department for one year as part of their training.

Technical staff

Our staff is seriously depleted due to resignations in the last six months of the year 2012. One technologist and one scientist resigned in the same period, thus leaving us with only four technologists in the histology section. A student technologist in the histology section passed in 2012. We had four resignations from the cytology section of the laboratory thus bringing our staff compliment to six. In this period we have battled to keep our expected turnaround times due to staff shortages.

One student cyto-technologist passed and another failed. One laboratory assistant passed and one failed. We have experienced a serious reduction in our staff and have been battling
in this period as a result. For this reason, the
embraced the idea of training technicians to
assist in the laboratory and we now have four
technicians who are being trained to assist in
the histology sections of the laboratory.

Professional Development

4 registered for MMED in Anatomical Pathology.
1 registered for PhD

Student medical technologists: 3 (2 in cytology
and 1 in histology)
All three have sat for the final March
examinations.

Student medical technicians: 2

Research Projects

We have dedicated a room for research and
are in the process of developing it. We have
also established a research committee which
meets once a month to develop research ideas.
Currently we are developing protocols in the
areas of:

Breast cancer research

Immunohistochemical profiling of variants of
lobular carcinoma – Dr B Ratlabala

Human papillomavirus (HPV) in conjunctiva

The prevalence of HPV in conjunctival lesions of
a HIV positive cohort – Dr N Ntsangani

Molecular genetic characterisation of HPV in
conjunctiva lesions in immunosuppressed
patients – M Nkosi (PhD thesis)

Research Output

Publications:

Martha M Tlholoe, Monica Kotu, Razia AG
Khammissa, Meshack Bida, Johan Lemmer
and Liviu Feller. Extranodal Natural Killer/T-
cell lymphoma, nasal type: midline lethal
ganuloma. A case report: *Head and Face
Medicine* 2013; 9: 4

TG Tshitake, R Golele, KC Skosana, MN Bida.
Metastatic mesenchymal chondrosarcoma:
A case report and review of the literature, SA
Orthop J 2012; 9(2): ISSN 1681-150X

Conferences

Professor NM Bida was an invited guest
speaker in the international Belgium Week
of Pathology congress where he presented a
paper entitled: Squamo-proliferative lesions of
the skin – the African experience.

We are also collaborating with other
departments such as virology in the area of
HPV research.
**Department of Chemical Pathology**

**Head:** Dr AA Khine

**Diagnostic Services**

The Department of Chemical Pathology serves the 1,500 bed Dr George Mukhari (DGM) Academic Hospital and 17 peripheral clinics in northern Gauteng, Mpumalanga, Limpopo and North West. A number of specialist clinics are operational at the hospital.

Since January 2013 we have introduced new tests in the area of toxic screening, therapeutic drug monitoring and urine drug screening. These tests include the following:

- Cerebrospinal Fluid Identification (CSF) on electrophoresis
- Sex hormone-binding globulin (SHBG) for free androgen index
- Serum lipase for acute pancreatitis,
- ACE and Ca 15-3 tumour markers
- Urine metabolic screening of reducing sugars
- Amino acids using chemical tests
- Thin layer chromatography
- Urine free metanephrines for screening of pheochromocytomas

We provide a 24-hour service and emergency tests are done immediately as they come in. Work flow analysis was done and revised to prioritise the urgent specimens. Specimens shared between different departments of the laboratory are now given specific markers to ensure speedy distribution. All staff members have been trained in short cuts to monitor pending urgent tests on the TrakCare laboratory information system in order to fast track the tests.

Turnaround times of UEC (urea, electrolytes, creatinine), glucose and CSF chemistry are part of the staff Key Performance Indicators (KPI).

A client satisfaction index is also included in the staff KPIs. Expansion of services to other clinics in the surrounding areas is under way. Communications with regional laboratories have been improved with all relevant email addresses and contact numbers for registrars and consultants, including the after-hours and core-laboratory contact numbers, are given to all the regional laboratories for any enquiries.

The head of department has made an email list of all laboratory managers in the region referring tests to this department, including a section of the cytogenetic laboratory which receives on average of 50 specimens a week from the local hospital, as well as all referring hospitals in the three provinces. Standard operating procedures in specimen collection, packing and transportation for cytogenetic specimens have been communicated to staff at all regional laboratories in order to improve the quality of specimens.

**Research Projects**

**The role of Brain Natriuretic Peptide (BNP), NT Pro-BNP and Troponin I in the diagnosis and management of congestive cardiac failure (CCF)**

**Researcher:** Dr J van Graan (registrar)

**Supervisor:** Dr A Rab; Co-supervisor: Dr M de Jongh

**Funding:** NHLS Research Trust

**Status:** Ethics committee approved, awaiting funding from NHLS Research Trust

The aim is to establish the relevance of elevated BNP; NT-proBNP and Tn I levels with respect to the diagnosis and management of CCF. Fifty patients will be recruited into each patient and control group (not in cardiac failure) according to inclusion and exclusion criteria. Blood is collected in EDTA tube for BNP and for NT-proBNP and Tn I in a yellow serum gel tube and spun down within two hours. The specimen will be frozen if not analysed within 24 hours at -200C. It may be stored in this way for up to six months. Data will be statistically analysed.
Envisaged outcome: Positive correlation of measured markers with diagnostic inclusion for CCF and response to therapy which assists the clinicians in patient management and decision-making.

ALT/AST sample stability study (pilot study)
Title: To determine the stability of the sample collected for ALT/AST determination
Researcher: KB Sedumedi, K Mentz

The aim is to determine the actual cut off time in terms of sample separation where results start to vary significantly and to determine the effect of sample storage temperature on the quality of the results. Five serum samples were collected from five healthy volunteers and the samples were separated at different times, stored at different temperatures and analysed at different times on Beckman DxC instrument. Results: AST and ALT showed stability up to 16 and 20 hours respectively. Results obtained from samples separated \( \geq 24 \) hours showed suppressed value. Temperature did not seem to influence the stability of these analytes.

Collaborative research with the Department of Haematology
Title: 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 Hospital over a 6 month period
Researcher: Van der Linde R
Supervisor: Moodley V
Co-supervisor: Sedumedi B
Status: Ongoing, protocol approved by SREC, awaiting MREC approval

The impact of delayed sample separation and analysis on patient management as well as the cost to the clinic and laboratory due to delay in sample delivery to the laboratory for clinics referring to the Dr George Mukhari tertiary laboratory
Researcher: Dr B Phiri (registrar)
Supervisor: Dr K Mentz; Co-supervisor: Dr M de Jongh
Funding: NHLS Research Trust
Status: submitted to ethics committee and awaiting NHLS trust approval

Aim: to estimate the implications on the cost and impact on patient’s outcome during the consolidation of laboratory services at peripheral clinics and district laboratories in Northern Region NHLS DGM. Three clinics with high volume patient load are selected in the study and specimens with request for serum K, ALT and creatinine are included. Results are compared with the specimen transit time and time before analysis and also with quality of specimens. Any result subjected to error due to these pre-analytical delays or poor quality is recorded and doctors/nurses at the referring clinics are contacted. Repeat analysis on the same specimens for verifying abnormal results are recorded. Visits to clinics will be done to collect fresh samples as controls in the study and cost is calculated. If the initial erroneous result was used in the decision-making of patient’s care, implications are recorded and impact on patient’s outcome is analysed.

Envisaged outcome: Evidence-based appraisal in cost and negative impact on patient’s care due to poorly planned referral network or consolidation of services in order to advocate the importance of cost analysis and simulation of referral network model before implementation.
Usefulness of NT-Pro BNP in early diagnosis and management of acute heart failure

Researcher: Dr T Mapheto (Registrar)
Supervisor: Dr B Sedumedi; co-supervisor: Professor P Mntla
Funding: NHLS Research Trust
Status: submitted to ethics committee and NHLSRT

Aim: to explore the usefulness of NT-ProBNP in diagnosis of acute cardiac failure and in response to therapy. The first 100 patients who are clinically diagnosed with acute heart failure will submit blood samples for NT-ProBNP prior to initiation of any treatment; repeat the test upon discharge, at two month and six month follow up visits. The levels are evaluated against clinical and Echo cardiogram findings.

Envisaged outcome: Endorsement in routine use of this marker by showing acceptable positive and negative predictive values of NT-ProBNP for diagnosis of acute cardiac failure and negative correlation (marker level goes down with response to treatment shown in clinical and echocardiogram evidences).

Teaching And Training

Undergraduate

MBCHB 2, 3 and 5
Chemical pathology lectures are given as part of the seminars on practice of medicine modules (POME).

MBCHB 4
Five consultants and senior registrars teach throughout the year in the MBCHB programme including conducting lectures and tutorials in small groups. Course material is revised annually and put onto CD. The curriculum is reviewed yearly by the University of Limpopo Medunsa campus. Assessments are done with four semester tests and three tutorial tests.

A final exam is written and oral with involvement of external examiners. Re-exams are also given once. Some selective lectures that are not included in the core curriculum are also given to these students upon request. Practical sessions in the laboratory applying basic principles of laboratory procedures, pre-analytical requirements, and dry chemistry methods are taught to the students in small groups and assessments are done.

MBCHB 6
MBCHB 6 tutorials are given to block sessions in Internal Medicine six times a year. Next year, this will be increased to six tutorials every week (given by six tutors/lecturers) for a six week block. This is not an examination course and is incorporated into internal medicine and paediatrics.

Bachelor of Dental Science (BDSc) 3
A chemical pathology module is given as formal lectures as well as postgraduate training.

Chemical pathology

Registrars rotate through all the benches in the laboratory for learning and take specific area for signing out results. Registrar training includes verification of clinical results and interpretation, clinical cases consultations, laboratory support to specialist clinics (endocrine, diabetes), participation in the ward rounds in ICU, presentation of journal appraisals, case discussions, in depth academic presentations on current topics and updates, research methodology, scientific writing and data analysis, protocol preparation and submission, application for grants, laboratory management, especially quality management systems, applications of LIS and method validation, inter-pathology seminars (with other disciplines of pathology), inter-departmental seminars (with other clinical departments) and procedures in lab support services.
Registrars are scored on all presentations and monthly written examinations in preparation for their college exam. Progress in their research projects are documented every week at the research meeting. A progress report is prepared by the mentor consultant for each registrar every quarter of the year and submitted to the HOD, then to the Dean and the business manager of the unit. For the primary exams, courses include applied physiology, biostatistics and research methodology (all are given by the respective departments of the university). The intermediate exam includes integrated pathology and molecular biology. The final exam is chemical pathology from the College of Medicine SA. External examiners are involved in the intermediate and final exams.

**Postgraduate training in other clinical disciplines**

Lectures and seminars are given to internal medicine, paediatrics, neurology and whenever requested by other departments.

**Technologist training**

Each pathologist consultant is allocated per routine and special bench for supervising and training technologists. Training focuses on methodologies, quality assessment, validation of results, dilutions and re-runs, repeating tests, method validation and work flow optimisation. A technologists’ journal club has been initiated in the department.

**Professional development**

5 MMed students are registered for this period.
1 BSc (Hons) Human Genetics

**Research Output**

**Publications**

Sedumedi B. Prostate specific antigen: a useful but limited marker for prostate cancer. *CMEJ* July 2012; 30(7): 238


**Congress Presentations**

Pathpoint 2012: Rab A, Budget as a management tool

Pathpoint 2012: Mentz K. Renal stone analysis patients’ findings and Fourier transform infrared spectroscopy method validation.

Department of Haematological Pathology

Head: Professor V Moodley

Diagnostic Services

The Department of Haematological Pathology offers a comprehensive 24-hour diagnostic service to the Dr George Mukhari Academic Hospital (DGM). The laboratory also serves as a tertiary referral centre to the surrounding hospitals and clinics and provides diagnostic services to the Medunsa Clinical Research Unit, supporting clinical trials. During the last year, the switch to the new laboratory information system TrakCare was completed and electronic gate keeping was implemented. The focus within the department was placed on offering a quality service within the shortest possible turnaround time. The concerted effort made by staff to improve service delivery and TAT was evident in the laboratory surpassing the set turnaround time target for the CD4 test (which forms part of the national priority programme), even with the experienced 79% increase in the volume of CD4 tests. Consultants and registrars have become increasingly more involved in the Adult Haematology Outpatient Clinic as well as actively participating in the Paediatric Haematology/Oncology ward rounds. The laboratory underwent successful re-accreditation in January 2013.

Outreach
An outreach programme to the surrounding referral hospitals was initiated with registrars and pathologists visiting the hospitals to present lectures as well as to interact with clinicians.

Research Projects

Continuing
Prevalence of paternity misidentification by the mother as compared to the DNA identification results

Researchers: Y Harris, AS Greef, I Ferreira, DJ Welgemoed

Y-chromosome investigation of a male amelogenin dropout

Researchers: DJ Welgemoed, AS Greef, J Greef, Y Harris

New projects
The haemoglobin chain profile in high flying raptors

Researchers: Y Harris, DJ Welgemoed

Investigating and comparing the haemoglobin profile of horses, donkeys and the hybrid mule.

Researchers: Y Harris, DJ Welgemoed

Teaching and Training

Undergraduate
The department teaches haematology as a fully integrated subject to second and third year MBChB students as part of the practice of medicine curriculum.

Postgraduate
An inclusive practical and theoretical training programme is in place for registrars in haematology over a four-year period. For the first time, registrars wrote the FC Path (Haem) Part I during the year under review. The department is also involved in training registrars from Internal Medicine, Paediatrics and Chemical Pathology. In addition, BSc (Hons) and Masters programmes are presented.

The department was also successfully accredited for the first time to train intern medical scientists.

Technologists
The department provides in-service teaching and training to both haematology and clinical pathology student medical technologists and technicians.

Professional development

Postgraduate candidates graduated: 1 (BSc (Hons))

Postgraduate candidates enrolled: 7 (4 MMed, 1 MSc, 2 BSc (Hons))

Student technologists: 5 (2 Haem and 3 ClinPath)

Research Output

Conference presentations
National: 1
Local: 1
Department of Microbiological Pathology

Head: Professor Maphoshane Nchabaleng

Diagnostic Services

The laboratory serves Dr George Mukhari Academic Hospital (DGM) and surrounding clinics for general bacteriology, mycobacteriology, and serology. It also serves as a referral centre for TB cultures for laboratories in the NHLS Northern region, particularly part of Rekopane Business Unit.

New developments

GeneXpert for TB diagnosis was initiated in November 2012 as part of the national rollout. This has improved the early detection and reporting of TB drug susceptibility testing. There was a noted decrease in test volumes which could be attributed to withdrawal of RPR testing of samples from the annual Antenatal Survey.

DisaLab was replaced with the TrakCare laboratory information system. The software for Microscan, the automated system for the identification and susceptibility testing of bacteria, was improved which resulted in an accreditation score upgrade from 40 to 96. A SANAS assessment was conducted on 16th and 17th January 2013 which confirmed the laboratory accreditation.

The annual workshops on Management of sexually transmitted infections, TB management and infection prevention and control (IPC) were conducted for health care workers from the surrounding clinics and district hospitals in Gauteng, North West and Limpopo respectively. The laboratory continues to support IPC activities and the Pharmacy and Therapeutic Committee (PTC) of the DGM hospital.

Research Projects

There are four strategic 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 in the department – Medunsa Clinical Research Unit (MeCRU) and Setšhaba Research Centre (SRC) – continue to be involved in HIV prevention clinical trials.

Tuberculosis

Genotypic diversity of Mycobacterium tuberculosis strains and association of isoniazid mono-resistance with MDR tuberculosis at the DGM tertiary laboratory

Researchers: AM Mhlongo (PhD student); Professor M Nchabeleng

Collaborators: Dr K Baba (UP), Dr J Molepo (Wits)

Funding: NHLSRT

Molecular characterisation of mixed infections with different strains of Mycobacterium tuberculosis and/or nontuberculous mycobacterium species from clinical specimens at the DGM tertiary laboratory

Researchers: N Makhado (PhD student); Professor M Nchabeleng

Collaborators: Professor B de Jong (University of Antwerp); Professor R Colebunders (University of Antwerp); The aim of the study is to characterise and determine the prevalence of infection with mixed strains of M. tuberculosis and/or non tuberculous mycobacteria in the area served by the DGM tertiary laboratory.

Funding: applied for with NHLS Research Trust

Genotypic characterisation of MDR TB in children at DGM tertiary laboratory

Researchers: EM Sekati (MSc student); Professor M Nchabeleng

Collaborators: Dr J Molepo (Wits)

Funding: NHLS Research Trust
Sexually transmitted infections

Prevalence and diversity of vaginal microbes in pregnant women and in women with adverse pregnancy outcomes

**Researchers:** Dr MC le Roux; Ms BE de Villiers; Dr M Ditsele (MMed); K Matebane (MSc)

**Collaborators:** Dr N Muse

The aim of the study is to detect and compare vaginal microbes in pregnant women and in women with adverse pregnancy outcomes using standard and PCR assays.

**Funding:** NHLS Research Trust

Prevalence of sexually transmitted infections in women receiving termination of pregnancy at Dr George Mukhari Hospital

**Researchers:** Dr MC le Roux; B de Villiers; 

**Students:** Dr M Ditsele (MMed); N Mametja (MSc)

**Collaborators:** Dr Mnisi (Obs and Gynae); Professor TS Monokoane (Obs and Gynae);

In this ongoing project, the emphasis is on the bacterial vaginosis and mycoplasmas viz M.genitalium, and Ureaplasma spp. These isolates will further be investigated for antimicrobial resistance using PCR and sequencing.

**Funding:** NHLS Research Trust

Streptococcus agalactiae, in pregnant women and their babies at Dr George Mukhari Hospital, Pretoria

**Researchers:** Dr MRB Maloba; Professor M Nchabeleng

**Collaborators:** Dr Tsepuane, Professor S Moyo (UNISA), Dr Lebello (UNISA)

The aim is to determine Streptococcus agalactiae colonisation rate in pregnant women and their babies at the DGM hospital and to characterise the isolates.

**Funding:** NRF

Antimicrobial resistance/ IPC

Antimicrobial susceptibility profile of non-ESBL (extended-spectrum beta-lactamases) producing, urinary Escherichia coli isolates at the DGM tertiary laboratory

**Researchers:** Professor M Nchabeleng; B de Villiers; DL Nemutavhanani; M Kwinta (BSc: Hons).

The aim of the study is to determine the antimicrobial susceptibility profile of non-ESBL producing urinary Escherichia coli isolates and determine possible mechanisms of resistance to several antibiotics e.g. cefuroxime.

**Funding:** NHLS Research Trust

Carbapenemases among the local ESBL producing isolates at the DGM tertiary laboratory

**Researchers:** Professor M Nchabeleng; Dr M Le Roux; Dr C Maluleka (MMed)

**Funding:** NHLS Research Trust.

The prevalence and characterisation of beta lactamases among gram negative uropathogens isolated from a selection of secondary and tertiary hospitals in South Africa

**Researchers:** Dr N Mbelle; L Fernandes; Dr M le Roux; B de Villiers;

**Funding:** NHLS Research Trust

The prevalence and characterisation of qnr determinants in extended spectrum beta-lactamase and non-extended spectrum beta-lactamase producing Klebsiella pneumoniae and Escherichia coli isolates from the DGM laboratory

**Researchers:** Dr N Mbelle; L Fernandes; Dr M le Roux; B de Villiers; E Mogoloane (MSc).

The aim of the study is to determine the prevalence and molecular characteristics of qnr determinants in Escherichia coli and Klebsiella pneumoniae clinical isolates obtained from the NHLS at the DGM laboratory.
Characterisation and nasal carriage of Methicillin-Resistant Staphylococcus aureus isolates among patients at DGM hospital and two selected local clinics in Ga-Rankuwa

Researchers: Professor M Nchabeleng; B de Villiers; TM Maleka (MSc)
The aim of the study is to characterise Methicillin resistant Staphylococcus aureus isolates from wound and nasal swabs from patients at DGM hospital, and nasal carriage among selected patients at two local clinics and their house hold members in the Ga-Rankuwa area.

Contract research

Medunsa Clinical Research Unit (MeCRU) Researchers: Dr MP Mathebula; Dr N Carrim-Ganey; Dr G Pila, Professor M Nchabeleng and MeCRU team

Setshaba Research Centre (SRC) Researchers: Dr K Ahmed; Dr R Maboa and SRC team

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

Collaborators: Follow on African Consortium for Tenofovir studies (FACTS)

Funders: DST (SA Gov); BMGF; USAID

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.

Collaborators: DOH

Funders: ISS (Italian Government)

TEACHING AND TRAINING

The department is involved in the teaching of medical microbiology to undergraduate students for several degrees, including MBChB; BDSc; BCur and BSc Diet. The department also conducts a basic molecular biology course.

Professional development

Post graduate students enrolled: 15 (2 PhD; 6 MMed; 3MSc; 4 BSc (Med) Honours)

Post graduate students graduated: 5 (4 BSc (Med) Honours, 1 DTMH, and 1 Postgrad Dip in Health Professionals Education, UCT)

Qualified: 2 medical technicians

Honours

The department was awarded the best non-clinical department prize by final year medical students.

Research Output

Publications:


Conference presentations:

International congresses: 3

National congresses: 3

Local congresses: 10
Department of Virology
(Incorporating the Medical Research Council / UL Diarrhoeal Pathogens Research Unit)

Head: Professor MJ Mphahlele

Diagnostic Services

The laboratory offers routine pathology service to Dr George Mukhari Academic Hospital (DGM) and surrounding private and public clinics. In 2011/2012, centralisation of some diagnostic tests with high work load was implemented to improve service management. Currently, the DGM laboratory performs HIV viral load and Tshwane conducts HIV DNA PCR. There was tremendous improvement of Turnaround time for HIV viral load after introduction of 24hrs service in August 2012. Virus isolation was discontinued due to challenges in securing relevant cell lines.

The laboratory participated in the national antenatal HIV surveillance project of the National Department of Health for the 12th year in succession. Further, the laboratory continues to serve as referral site for a number of laboratories within and outside Pretoria. These include peripheral laboratories in Gauteng, North West, Mpumalanga and Limpopo. There was 17% increase in test volumes mainly due to HIV viral load samples that came from Tshwane, and volumes are expected to increase in 2013. A total of 155,419 samples were received in 2012 compared to 132,626 in 2011.

The laboratory has maintained its SANAS accreditation status for the third time in succession. Assessment was on the 17th January 2013.

Research Projects

The Medical Research Council (MRC) / UL Diarrhoeal Pathogens Research Unit

The unit is a premier research centre in Africa, conducts groundbreaking research work in the field of diarrhoeal pathogens. In addition, the Unit serves as the WHO Rotavirus Regional Reference Laboratory for basic science, surveillance and burden of disease studies, and provides technical support to African countries. The Unit remains the only research unit in Africa that performed phase I through to phase III clinical trials on rotavirus vaccine (GSK Rotarix). The results of the clinical trials served as the basis for inclusion of rotavirus vaccine in the South African Expanded Programme on Immunisation since Aug 2009 and also provided baseline evidence for the WHO SAGE to recommend introduction of rotavirus vaccination programmes in all other African countries.

The HIV and Hepatitis Research Unit

The HIV and Hepatitis Research Unit is actively involved in viral hepatitis studies addressing basic research, epidemiology, and prevention and control of hepatitis viruses. In addition, the Unit has pioneered research in South Africa on co-infection of HIV and hepatitis viruses (HBV and HCV). The HIV and Hepatitis Research Unit performed a number of clinical trials on different hepatitis B vaccines; and the results of these clinical trials served as the basis for inclusion of hepatitis B vaccine in the South African Expanded Programme on Immunisation in April 1995.

South African Vaccination and Immunisation Centre

The Department of Virology hosts the South African Vaccination and Immunisation Centre (SAVIC). The mission of SAVIC is to increase knowledge on vaccine-preventable diseases and to improve the quality and sustainability of immunisation programmes and services in southern Africa, through research, education, training and provision of technical support. SAVIC hosts a dedicated open access website. SAVIC significantly contributes to training programmes of both in-service and pre-service students and staff through dedicated thematic symposia, workshops or special lectures in the field of vaccinology and the Expanded Programme on Immunisation.
Research Projects

HPV types associated with recurrent laryngeal papillomatosis at DGM Hospital, South Africa
Principal Investigator: L Lebelo and Professor MJ Mphahlele
Researcher: M Papala
Collaborators: MN Bida, Department of Anatomical Pathology, University of Limpopo, Medunsa campus / NHLS DGM Tertiary Laboratory, Pretoria; E Raubenheimer, Department of Oral Biology, University of Limpopo, Medunsa campus; and J-P Bogers, University of Antwerp, Antwerp, Belgium
Funding: Poliomyelitis Research Foundation (PRF), National Research Foundation (NRF) and the Flemish Inter-university Council (VLIR-UOS)

Molecular characterisation of human papillomavirus types in South Africa
Principal Investigator: Professor MJ Mphahlele
Researcher: LR Lebelo
Collaborators: MN Bida, Department of Anatomical Pathology, University of Limpopo, Medunsa campus / NHLS DGM Tertiary Laboratory; E Raubenheimer; Department of Oral Biology, University of Limpopo, Medunsa campus; and J-P Bogers, University of Antwerp, Antwerp, Belgium
Funding: PRF, NRF and VLIR-UOS

Molecular determinants and biological characteristics of hepatitis C virus isolates at DGM hospital
Principal Investigators: Dr SG Selabe and Professor MJ Mphahlele
Researcher: MP Gededzha
Collaborators: J Blackard (University of Cincinnati College of Medicine, Cincinnati, Ohio)
Funding: MRC, NRF, National Health Laboratory Service (NHLS) Research Trust and the Stella and Paul Loewestein Charitable and Educational Trust

Complete genome analysis of hepatitis B virus strains isolated from HIV positive individuals at DGM Hospital, Pretoria
Principal Investigators: Dr S Selabe
Researcher: M Muzeze
Funding: PRF, MRC and NRF

Real time PCR for the detection of occult hepatitis B virus in HIV Positive patients
Principal Investigators: AM Musyoki
Researcher: B Motloung
Funding: MRC and NRF

Validation of ELISA (Monolisa antigen antibody ultra assay) for the detection of infection at DGM Hospital, Pretoria
Principal Investigators: Dr SG Selabe
Researcher: Z Mahlangu
Funding: MRC and NRF

Hepatitis B virus infection in health care workers in three metropolitan areas of Gauteng
Principal Investigators: Dr BJ Burnett, SG Selabe
Researcher: TK Sondlane
Funding: Flemish Inter-university Council (VLIR-UOS)

Exploring the evolution of genetic diversity of the human immunodeficiency virus in cancer patients exposed to immunosuppressive therapy
Principal Investigators: Dr SG Selabe and Professor MJ Mphahlele
Researcher: A Musyoki
Funding: MRC, NRF, PRF, and NHLS Research Trust

Investigating paediatric HIV-1 drug resistant outcomes in children with maternal exposure to various prevention of mother to child transmission interventions at DGM Hospital
Principal Investigators: Dr Z Makatini
Researcher: Dr R Maphoto
Funding: Discovery
The investigation of the emergence of nevirapine resistance HIV-1 mutations in HIV-1 positive pregnant women who have had exposure to single dose nevirapine for the prevention of mother to child transmission at DGM Hospital

**Principal Investigators:** Dr Z Makatini  
**Researcher:** Dr K Kuzwayo  
**Funding:** Discovery

Incidence of cytomegalovirus central nervous system infection in the northern Pretoria region

**Principal Investigators:** Dr T Kyaw and Professor DS Magazi  
**Researcher:** Dr KA Mohlala  
**Funding:** NHLS Research Trust and PRF

Human cytomegalovirus viral load dynamics in advanced HIV-infected patients receiving HAART

**Principal Investigator:** Dr T Kyaw  
**Researcher:** Dr T Kyaw  
**Funding:** NHLS Research Trust and PRF

Assessment of cell mediated immune response to human cytomegalovirus antigens in immunosuppressed patients by using quantiferon-CMV assay

**Principal Investigator:** Dr SG Selabe  
**Researcher:** Z Mahlangu  
**Funding:** NHLS Research Trust and PRF

Genotypic Analysis of the circulating Human cytomegalovirus isolates from Pretoria

**Principal Investigator:** Dr T Kyaw  
**Researcher:** S Baloyi  
**Funding:** NHLS Research Trust and PRF

The MRC/UL diarrhoeal pathogens research unit


**Principal Investigators:** Dr LM Seheri, Dr SG Selabe  
**Researcher:** L Netshighefhe  
**Funding:** MRC

Detection and characterisation of circulating NSP4 genotypes in children and animals presenting with rotavirus diarrhoea in the Gauteng and Limpopo provinces

**Principal Investigators:** I Peenze, Dr LM Seheri  
**Researcher:** FRR Mapuroma  
**Funding:** MRC and PRF

Comparison of the VP7 and VP4 sequences of the “epidemic” strains that occur when G2P[4] rotavirus strains are most common versus G2 strains in the past years

**Principal Investigators:** Dr LM Seheri, Dr SG Selabe  
**Researcher:** L Maake  
**Funding:** MRC and PRF

Genomic characterisation and comparison of selected African rotavirus G9 strains detected from 1999–2010

**Principal Investigators:** I Peenze, Dr LM Seheri, Professor MJ Mphahlele  
**Researcher:** MM Nyaga  
**Collaborator:** Professor A van Dijk, Department of Biochemistry, North West University  
**Funding:** MRC and PRF

Epidemiology of rotavirus diarrhoea in children under five years of age attending the public and private healthcare facilities in Swaziland

**Principal Investigators:** Dr LM Seheri, MJ Mphahlele  
**Researcher:** G Maphalala  
**Funding:** MRC and PRF

Characterisation of rotavirus strains circulating in the private pathology laboratory lancet during 2010-2011

**Principal Investigators:** Dr LM Seheri, Professor MJ Mphahlele  
**Researcher:** CM Molatjane  
**Collaborator:** None  
**Funding:** MRC and PRF
Assessing the impact of mixed genotypes infections of rotavirus in genotyping VP7 and VP4 gene segments

Principal Investigators: Professor MJ Mphahlele, Dr LM Seheri
Researcher: R Malabi
Funding: MRC and PRF

Genetic characterisation of G1P[8] rotavirus strain in Pretoria

Principal Investigators: Dr LM Seheri, Professor MJ Mphahlele
Researcher: NS Naidana
Collaborator: None
Funding: MRC and PRF

Rotavirus diarrhoea and molecular epidemiological profile in Windhoek, Namibia

Principal Investigators: Dr LM Seheri, Professor MJ Mphahlele
Researcher: NK Shaanyenage
Funding: MRC

Rotavirus infection in vaccinated and unvaccinated babies

Principal Investigator: Dr LM Seheri, Dr MD Esona
Researcher: NK Magagula
Funding: MRC and NRF

Case-control study to assess the effectiveness of rotarix vaccine in HIV-infected and HIV-uninfected children in South Africa

Principal Investigator: Dr N Page
Researcher: Dr LM Seheri
Collaborators: Dr C Cohen, Dr S Madhi
Funding: GSK/Aspen pharmacare and MRC

Rotavirus sentinel surveillance programme

Principal Investigators: Dr N Page, Dr LM Seheri
Researcher: Dr LM Seheri
Collaborators: Dr C Cohen, Dr S Madhi
Funding: GSK/Aspen pharmacare and MRC

Assessment of the burden of disease associated with rotavirus infection among children less than 5 years of age attending the Brits Hospital and surrounding clinics in the Madibeng District, South Africa

Principal Investigators: Professor MJ Mphahlele, Dr LM Seheri
Researcher: Professor AD Steele
Funding: WHO and MRC

Genetic analysis of animal and human rotaviruses in Limpopo rural communities in South Africa

Principal Investigators: LM Seheri and Professor MJ Mphahlele
Researcher: H Ngoveni
Funding: MRC

The development of new recombinant antigens and scFV phage antibodies for the group specific detection of classical, unusual and new rotaviruses

Principal Investigators: Dr C Potgieter, Dr N Page
Researcher: I Peenze
Funding: MRC

Teaching And Training

The Department of Virology co-ordinates and teaches Medical Microbiology course for DBS III.

The Department of Virology is also involved in teaching Medical Microbiology (coordinated by the Department of Medical Microbiology) to UNDER-GRADUATE students (MBCHB I and III, BDS III, B Cur II, B Dent II and BSc Diet II) and various other courses to POST-GRADUATE students (Honours, MSc Med, MMed and PhD students).

The Virology Diagnostic Laboratory serves as a teaching platform for medical technologists and registrars in virological pathology and other pathology disciplines, and is part of external quality assurance programmes.
Professional Development

Summary

Postgraduate candidates graduated: 6 (5 BSc [Hons], 1 MSc [Med])
Postgraduate candidates enrolled: 22 (12 MSc [Med], 4 MMed, 6 PhD)
Intern medical technologists who past: 2

Postgraduate students graduated in 2012

<table>
<thead>
<tr>
<th>Degree</th>
<th>Name</th>
<th>Student No.</th>
<th>Date of graduation</th>
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<tbody>
<tr>
<td>BSc Med (Medical Virology)</td>
<td>Papala, MP</td>
<td>200728103</td>
<td>19 May 2012</td>
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<td></td>
<td>Motloung, BR</td>
<td>200700830</td>
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<td>Shaanyenange, NK</td>
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<td>Magagula, NB</td>
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<td></td>
<td>Mahlangu, ZP</td>
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Masters degrees by straight research

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<tr>
<th>Degree</th>
<th>Name</th>
<th>Student No.</th>
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<tbody>
<tr>
<td>MSc Med (Medical Virology)</td>
<td>Netshifhefhe, L</td>
<td>200600716</td>
<td>19 May 2012</td>
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Postgraduate students enrolled

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<th>Degree</th>
<th>Name</th>
<th>Student No.</th>
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<th>Year of Study</th>
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<tbody>
<tr>
<td>MSc Med (Medical Virology)</td>
<td>Mapuroma, FPR</td>
<td>200816852</td>
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<td>Muzeze, M</td>
<td>200622128</td>
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<td>Sondlane, TH</td>
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<td>Maake, L</td>
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<td>Nyaga, MM</td>
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<td>Maphalala, G</td>
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<td>Baloyi, SS</td>
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<td>Nailana, S</td>
<td>200729195</td>
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<td>Molotjane, CM</td>
<td>200602072</td>
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<td>Malabi, R</td>
<td>200522825</td>
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<td>Amponsah-DaCosta, E</td>
<td>201117905</td>
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<td>Masutha, NL</td>
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<td>Mohlala, KA</td>
<td>19253890</td>
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<td>Kuzwayo, KC</td>
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<td>Peenze, I</td>
<td>19975316</td>
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<td>Gededzha, M</td>
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<td>Lebelo, RL</td>
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<td>Musyoki, A</td>
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<td>Ngoveni, H</td>
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<td></td>
<td>Kyaw, T</td>
<td>210252771</td>
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Medical Technologists who passed examination

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<thead>
<tr>
<th>Degree</th>
<th>Name</th>
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<tbody>
<tr>
<td>Bio Medical Technology</td>
<td>Sydney Sphamandla Mabizela</td>
<td>Board Exam Passed in September 2012</td>
</tr>
<tr>
<td></td>
<td>Rorisang Candice Moeng</td>
<td>Board Exam Passed in March 2012</td>
</tr>
</tbody>
</table>
Honours

The Department of Virology was awarded a trophy for the Most Committed Department to Faculty of Health Sciences Research Day 2012

Amponsah-Dacosta E. Awarded 2nd place in the category “Best postgraduate student paper”, Faculty of Health Science Research Day, 21–22 August 2012

Maphoto R. 3rd Place for Best Oral Presentation. Faculty of Health Science Research Day 21–22 August 2012.

Maphoto R. Awarded diploma in tropical medicine and hygiene from Wits University in 2012.

Maphoto R. Discovery Fellowship Foundation Award for MMed project titled: Paediatric HIV-1 drug resistant outcomes in children exposed to various PMTC interventions at the DGM hospital, 25 July 2012.

Kuzwayo K. Discovery Fellowship Foundation Award for MMed project titled: To investigate the emerge of NVP resistant HIV-1 mutations in HIV-1 positive woman who have had prior expose to single dose nevirapine for prevention of mother to child transmission at DGM Hospital, Pretoria South Africa, 25 July 2012.


Dr LM Seheri: Overall Best Female Researcher of the University of Limpopo Research Excellence Awards 2012

Dr LM Seheri: Best Upcoming Researcher award in the Faculty of Health Sciences of the University of Limpopo Research Excellence Awards, 21–22 August 2012

Research Output

Publications


Seheri LM, Page NA, Mawela MPB, Mphahlele JM, Steele AD. Rotavirus vaccination within the South African Expanded Programme on Immunisation. *Vaccine* 2012 30S: C14–C20


Conferences

International conferences
Posters: 11
Papers: 10

National conferences
Poster: 11
Papers: 10

International conferences

Papers

11th International symposium on double-stranded RNA viruses. 27 Nov – 1 Dec 2012, San Juan, Puerto Rico.


10th International Rotavirus Symposium, 19-21 September 2012, Bangkok, Thailand


7th African Rotavirus Symposium, 8 November 2012, pre-conference symposium organised back to back with International African Vaccinology Conference, Lagoon Beach Hotel, Cape Town, Western Cape, 9-11 November 2012

Mphahlele MJ. Convenor and Chairperson of the 7th African Rotavirus Symposium, 8 November 2012.

Steele AD. Rotavirus in Africa.


Posters


10th International Rotavirus Symposium, 19-21 September 2012, Bangkok, Thailand


7th African Rotavirus Symposium, 8 November 2012. pre-conference symposium organised back to back with International African Vaccinology Conference, Lagoon Beach Hotel, Cape Town, Western Cape, 9-11 November 2012.


Jere KC, Mlera L, O’Neill HG, Peenze I, van Dijk AA. Whole genome sequence analyses of three African bovine rotaviruses reveal that they emerged through multiple reassortment events between rotaviruses from different mammalian species.


Ngoveni HG, Peenze I, Seheri LM, Mphaelele MJ. Genetic analysis of avian rotaviruses in limpopo rural communities: an unusual detection of human-like group a, group f and group g rotaviruses.


Penze I, Page NA, Botha P, Steele AD, Potgieter CA. Rotavirus group h detected in an asymptomatic piglet stool sample and phylogenetically analysed closest to the Japanese porcine SKA-1 strain.


Shaanyenange NK, Seheri LM, Peenze I, Netshifhefe L, Moche P, Steele AD, Mphaelele MJ. Rotavirus diarrhoea in children less than 5 years of age attending DGM hospital in 2010, following the introduction of rotavirus vaccine.


IX International Congress of Veterinary Virology, 4-7 September 2012, Madrid, Spain


National conferences

Posters

University of Limpopo Faculty of Health Sciences Research Day, 21-22 August 2012, Pretoria

Mohlala KA, Kyaw T, Magazi DS. Incidence of cytomegalovirus central nervous system infections in the Northern Pretoria Region, South Africa.

Mohlala KA, Kyaw T, Makatini Z. Seroprevalence of Cytomegalovirus, Herpes virus and Rubella virus in woman of child bearing age in Northern Pretoria Region.

Amponsah-Dacosta E, Lebelo RL, Mphahlele MJ. Assessing population immunity and chronic carriage to hepatitis B virus in selected provinces in South Africa.

Musyoki AM, Rakgole JN, Msibi T, Motswaledi MH and Mphahlele MJ. High incidence of hepatitis C virus infection in a cohort of HIV positive cancer patients attending at DGM Hospital, Pretoria

Motloung BR, Rakgole JN, Musyoki AM, Selabe SG and Mphahlele MJ. Real-time polymerase chain reaction for the detection of occult hepatitis B virus DNA from human immunodeficiency virus infected patients

Baloyi SS, Kyaw T and Selabe SG. Human cytomegalovirus gene profiling from HIV co-infected in Northwest of Pretoria.

Bana Pele Congress 2012, 22–26 August 2012

Mapotho R, Kuzwayo K, Mawela D, Makatini Z. Paediatric HIV-1 drug resistant outcomes in children exposed to various PMTCT interventions at DGM hospital, South Africa.


Mapotho R, Kuzwayo K, Mawela D, Makatini Z. Paediatric HIV-1 drug resistant outcomes in children exposed to various PMTCT interventions at DGM hospital, South Africa.

MRC Research day, 24–25th October 2012. Cape Town, South Africa

Genetic analysis of avian rotaviruses in Limpopo rural communities: an unusual detection of human-like group A, group F and group G rotaviruses

Papers


Mphahlele MJ. SAVIC’s capacity building of HCWs to strengthen delivery of immunisation services within EPI-SA. Strengthening of Current Immunisation Practices within Pre-service Curricula of Health Professionals in South Africa, OR Tambo Premier Hotel, Kempton Park, Johannesburg, Gauteng Province, 28–29 November 2012.

Maphoto R, Kuzwayo K, Mawela D, Makatini Z. Paediatric HIV-1 drug resistant outcome in children exposed to various PTCT interventions at George Mukhari Hospital, South Africa.

Sondlane TH, Burnett RJ, Selabe SG and Lebelo RL. Hepatitis B virus in health care workers in three metropolitan areas of Gauteng.

Muzeze M, Gedezha MP, Selabe SG and Mphahlele MJ. Complete genome analysis of hepatitis B virus strains isolated from HIV positive individuals at DGM Hospital, Pretoria.

Kyaw T, Kangawaza E and Lecatsas G. High prevalence of cytomegalovirus viraemia in severely immunocompromised HIV-infected patients.

Masutha NL, Mushesh F, Kyaw T. Acute viral hepatitis infection presented with severe hepatic and renal failure in a teenager: Case report.


Courses and workshops attended


MRC/DPRU Staff Members and Students. The 7th African rotavirus Symposium, 8 November 2012, Cape Town, South Africa.

MRC Staff Members and Students. Bioinformatics workshop, organised by University of Limpopo Medunsa Campus, Department of Virology and Jason Blackhard from the University of Cincinnati, USA.


Ngoveni HG. IX International Congress of Veterinary Virology, 4-7 September 2012, Madrid, Spain.

Dr LM Seheri and MM Nyaga. 11th International Symposium on Double Stranded RNA Viruses, San Juan, Puerto Rico, 27 Nov–1 Dec 2012.

Conferences and workshops internally arranged

Department of Virology hosted the very First International Bioinformatics Workshop at Medunsa Campus

The Department of Virology hosted a successful International workshop on Bioinformatics at Medunsa Campus from 19–23 March 2012, in collaboration with the Division of Digestive Diseases, University of Cincinnati College of Medicine, USA. The main organisers were Professor Jeffrey Mphahlele and Nare Rakgole (Department of Virology, University of Limpopo) and Professor Jason Blackard (Division of Digestive Diseases, University of Cincinnati College of Medicine, USA). The aim of the workshop was to educate the participants about newly developed bioinformatics programmes. Attending the workshop were UL’s post-graduate students and academic staff, as well as students and staff from other institutions such as the University of Pretoria, North West University, University of Venda, University of Southern Africa, Botswana Harvard AIDS Institute Partnership and Professor Jason Blackard (USA).

Department of Virology hosted the graduate students from the University of Cincinnati at Medunsa Campus

The Department of Virology hosted graduate students from the University of Cincinnati (UC), USA in June 2012. The visiting honours students embarked on a two week study tour to South Africa with the aim of experiencing real exposure to research on public health and infectious diseases, mainly focusing on HIV/AIDS. Their visit to South Africa also focused on increasing the student’s limited knowledge on the challenges faced when responding to the HIV/AIDS increasing epidemic in resource-limited settings such as Africa.

Workshops held in collaboration with the South African Vaccination and Immunisation Centre (SAVIC)

International Workshop on Vaccinology Training Materials and Handouts, OR Tambo Premier Hotel, Kempton Park, Johannesburg, Gauteng Province, 26–27 November 2012

This workshop was organised by the Network for Education and Support in Immunisation (NESI)/ University of Antwerp and SAVIC, in collaboration with WHO/AFRO. The workshop was a follow-up of the 2009 and 2010 workshops, which were organised to develop generic training materials and handouts for a Vaccinology course. The specific objectives of the current workshop were to further develop and harmonise the vaccinology modules using the reference format and discussion of process of review and validation of the vaccinology
National workshop on strengthening of current immunisation practices within pre-service curricula of health professionals in South Africa, OR Tambo Premier Hotel, Kempton Park, Gauteng, 28–29 November 2012.

The meeting was a follow-up of the "SAVIC Nursing Immunisation Curriculum Review and Update Workshop" held at the Vanderbijlpark, Gauteng, 1 to 4 April 2007. The aim of the meeting was to strengthen the teaching and learning of current immunisation practices within the existing curricula for basic (pre-service) education programmes for doctors, nurses/midwives and other health professionals. The specific workshop objectives were to assess progress with implementation of WHO EPI prototype curricula into pre-service training of health professionals in South Africa and to facilitate country-wide implementation of WHO EPI prototype curricula into pre-service training and learning of all other training institutions which have not as yet implemented the revised curricula. More than 60 participants, including representative from the WHO and from various countries and the vaccine industry attended the meeting.

12th African Region Rotavirus Surveillance Network (AFR RSN) training workshop

The World Health Organization Rotavirus Regional Reference Laboratory (RRL) in South Africa (located within the MRC Diarrhoeal Pathogens Research Unit) and the WHO AFRO, through collaboration with Ministries of Health (MoH), convened the 12th African Region Rotavirus Surveillance Network (AFR RSN) training workshop from 11 to 22 June 2012 at the University of Limpopo Medunsna Campus, Pretoria. The WHO representative, South Africa, Dr Francis Kasolo, WR, officially opened the training workshop. The workshop participants came from Zambia, Zimbabwe, Rwanda, Uganda, Democratic Republic of Congo, Niger, Kenya, Tanzania, Togo, Cameroon, Mauritius, Ethiopia, Nigeria and Kenya. A total of 1,216 positive and 292 negative stool samples were brought to RRL South Africa for analysis. The key objective of the workshop was to generate data on the circulating rotavirus strains in Africa using the WHO generic protocol and regional guidelines. The data is required for rotavirus vaccine advocacy and implementation, as well as future monitoring of vaccine effectiveness. In addition, the main focus of the training workshop was to provide theoretical and practical training relating to rotavirus analysis, testing performance indicators as well as good laboratory practice.

The 7th African Rotavirus Symposium (ARS), Cape Town, 8th November 2012

The 7th African Rotavirus Symposium was the pre-conference symposium at the International African Vaccinology Conference held in Lagoon Beach, Cape Town, South Africa on the 8th of November 2012. The symposium was organised by the MRC/UL Diarrhoeal Pathogens Research Unit in partnership with National Institute of Communicable Diseases, the WHO AFRO and Bill and Melinda Gates Foundation. The symposium brought together nearly 150 African scientists, clinician, pharmaceutical industry (GSK, MSD), health officials and policymakers to discuss the following: rotavirus vaccines and clinical trials effectiveness in Africa, intussusception in Africa, rotavirus surveillance data and strain diversity, progress towards rotavirus vaccine implementation in Africa and how to accelerate vaccine introduction, lesson learnt after vaccine introduction and preparation to evaluate the vaccine impact. The symposium participants were from Africa, the USA, South America, Europe and Asia.
Department of Anatomical Pathology

Head: Dr M Louw

Diagnostic Services

The department provides a comprehensive diagnostic and prognostic service to the Steve Biko Academic, Kalafong, Tshwane District and Mamelodi hospitals. The service extends to all the Tshwane Metro clinics as well as hospitals and clinics in Mpumalanga, parts of Limpopo and North West.

The department also offers a consultation and support service to government institution and private pathology laboratories, Lancet and Ampath.

The government institutions covered by this service include the Oral and Dental Department, Pretoria; 1 Military Hospital, Pathology Department; Faculty of Veterinary Science; Pathology Department: Onderstepoort; and the Department of Forensic Pathology.

Evaluation for diagnostic and prognostic purposes is effected using immunoperoxidase staining, special staining techniques, electron microscopy, molecular biology, polymerase chain reaction investigative modalities. The molecular biology laboratory-histopathology evaluated 400 cases during the financial year beginning February 2011 and ending March 2012.

Institutions serviced by molecular biology Tshwane Academic Division included Lancet laboratories; Dr George Mukhari Hospital, Anatomical pathology and 1Military Hospital. Our department offers a post mortem investigation service to Steve Biko Academic and Kalafong hospitals as well as well as the surrounding private hospitals. Frozen section services are only offered to Steve Biko Hospital.

The department provides a cremation auditing and approval service for the Tshwane Metro and comprehensive cytology service the above mentioned health facilities. Special investigations done on cytological specimens include special staining techniques and immunoperoxidase staining.

Research Projects

Completed research projects (unpublished works):

Norpret study
Researchers: Professor G Dreyer and Department of Anatomical Pathology

Birth asphyxia at Kalafong Hospital – an audit of placental pathology
Researchers: E Marais, S Delport. Available as a dissertation as requirement of the MMed for Dr E Marais

Undiagnosed fatal infections in children: a 10-year review of childhood post mortem findings.
Researchers: C Crause, P Eyal, M Louw - available as a dissertation as requirement of the MMed for Dr C Crause

Teaching And Training

Undergraduate

The department is involved in the training of medical, dental as well as allied health students. Lectures and practical training is delivered to the second, third, fourth and final year medical students. This includes full assessment.

Postgraduate

Currently, the department is training a total of 10 registrars.

Two senior registrars successfully completed their training at the end of 2012 and three senior registrars are due to complete training
in the financial year ending March 2014. Two senior registrars are due to complete training in the financial year ending March 2014/15; two junior registrar due are due to complete training in the financial year ending March 2016 and three newly appointed registrars will complete training in 2018.

For the current academic year, registrars from the University of Pretoria oral and dental department and Forensic Pathology are rotating through our department for training for 24 and 18 months respectively. Registrar training includes monthly rotation with each pathologists, six months of cytology training; post mortem investigation training; weekly training boards in histopathology and monthly training boards in cytology.

It also includes cytology intensive revision, molecular biology, postgraduate anatomy and weekly journal and topic discussions.

Quarterly academic meetings are held with the internal medicine, general surgery, gynaecology and obstetrics, neurosurgical, and paediatric academic departments for discussion of unique and rare clinical cases.

In association with the Steve Biko and Kalafong academic hospitals and Pretoria University, the anatomical pathology department participates in the training and assessment of masters MMed students in internal medicine, paediatrics, general surgery, orthopaedic surgery, gynaecology and obstetrics, ophthalmology, neurosurgery, psychiatry, otorhinolaryngology and radiology.

The department also trains and assesses postgraduate students in occupational therapy and radiography.

**Professional Development**

**Postgraduate students (Registrars) completed:**
Dr C Crause qualified as a histopathologist in May/June and Dr E Marais in October 2012.

**Conferences, workshops, academic presentations attended**

International Anatomical Pathology (AIP) congress was held in September/October 2012.

Dermatopathology Symposium January 2013.

Bushpath. Gastroenterology workshop organised by Pretoria University and Anatomical Pathology Department TAD in collaboration with AMPATH, 21–24 March 2013.

**Research Output**

**Publications**


Research projects awaiting University of Pretoria Protocol and Ethics committee approval:

Role of natural killer cells in endometrial biopsies of infertile women
**Researcher:** Dr M S Muller.

The association between histopathologic, morphologic, p16 and Ki67 immunohistochemical staining patterns and HPV typing of cervical intraepithelial neoplasia
**Researchers:** Dr C Solomon, Dr M Louw, Professor G Dreyer.

The assessment of the prevalence of Epstein-Barr virus in invasive breast carcinoma in our setting
**Researchers:** Dr T Medupe, Dr C Campaini, Dr M Louw.

A retrospective review of thyroglossal cysts in academic hospitals in the greater Pretoria region
**Researchers:** Dr A Van Rooyen, Dr M Louw

CANSA project
**Researchers:** Professor G Dreyer, Dr M Louw, Ms N Heunis, Dr K Richter, Dr C Solomon

A retrospective review study of renal biopsies in Kalafong Hospital 2005–2010
**Researchers:** Dr N Moethilalh, Dr M Louw.
Department of Chemical Pathology

Acting Head: Dr N Oosthuizen

Diagnostic Services

The Department of Chemical Pathology provides diagnostic pathology services to the Steve Biko Academic (SBAH), Tshwane District and Weskoppies hospitals and 60 clinics in the Pretoria region. In addition to providing after-hour laboratory services to Pretoria West and Mamelodi hospitals, the laboratory receives referrals from private and NHLS laboratories nationwide.

Total workload for the period 2012/2013 was 1.1 million tests, up 18% from 2011/2012. During 2012 there were a number of major events in the life of the laboratory, all impacting significantly on daily operations. The first of these was implementation of electronic gatekeeping (EGK) by SBAH in May 2012. Although many of the initial problems have been resolved, ensuring that EGK runs smoothly remains an onerous task.

The second major event was replacement of the existing DISA laboratory information system (LIS) with TrakCare in October 2012. The implementation was challenging for several reasons, not least that Tshwane Academic Division is only the second academic site to go live since the start of the national rollout. Increased test volumes, technical staff shortages, EGK and the new LIS all contributed towards deterioration in turnaround times. Remote sign-out of test results by registrars after hours is just one of the measures introduced in 2012 to address turnaround time delays. Other measures planned for the future are introduction of auto-verification on TrakCare and further automation of analytical processes. The laboratory was inspected by SANAS in February 2013 and retained its accreditation status.

Research Projects

Genetic analysis of inherited forms of hypophosphataemic rickets in South African patients

Researchers: Dr C van Niekerk, Dr NM Oosthuizen, Ms E Pretorius

Collaborators: Prof J Pettifor, Dr K Thandrayen, Department of Paediatrics, University of the Witwatersrand

Funding: NHLS Research Trust (applied for)

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 hypercalciuric forms of inherited hypophosphataemic rickets respectively. Causative genes will be analysed by means of conventional PCR, HRM real-time PCR and DNA sequencing.

The utility of absolute vs relative changes in highly-sensitive cardiac troponin I (cTnI) concentrations in the early diagnosis of acute myocardial infarction (AMI)

Researchers: Dr ESP Dlamini, Dr NM Oosthuizen

Funding: NHLS Research Trust (applied for)

According to current South African guidelines, patients presenting with a cTnI concentration between the 99th percentile and the WHO AMI cutoff require a 50% increase in cTnI 3 hours later in order to diagnose AMI. However, recent studies using the ADVIA Centaur c-TnI-ultra assay suggest that absolute changes have a higher diagnostic accuracy for AMI than relative changes.

Furthermore, other studies have proposed that abbreviating the time between successive samples from 3 hours to 2 hours may allow earlier diagnosis. Using the Beckman Coulter Accu-TnI assay, this study has two aims: firstly
to investigate the utility of absolute vs relative changes in cTnI concentrations and secondly to identify the best time interval for serial measurements for diagnosis of AMI.

Clinical validation of faecal pyruvate kinase M2 (M2PK) for detection of patients with non-bleeding precancerous colorectal lesions

Researchers: Dr LS Masika, Dr NM Oosthuizen
Collaborators: Prof JHR Becker, Department of General Surgery, University of Pretoria
Funding: NHLS Research Trust (applied for)

Although colonoscopy is the gold standard for early detection of colorectal carcinoma and adenomatous polyps, high cost and invasiveness detract from its clinical utility. Currently the best available screening test for colorectal cancer is the immunological faecal occult blood test (iFOBT), but its usefulness is limited to patients with bleeding lesions. M2PK has been proposed as a new marker with higher sensitivity for detection of non-bleeding lesions at risk for malignant transformation.

The aim of this study is to compare urine Hb test strips to the ACTIM iFOBT for detection of bleeding colorectal lesions and to determine the utility of a faecal M2PK ELISA in selecting patients with negative FOBT for urgency in colonoscopy waiting lists.

Teaching and Training

Undergraduate
The department contributes to lecturing and assessment of several systems-based blocks in the MBChB programme, including homeostasis, diseases of childhood, abdomen and breast, traumatology and genito-urinary disorders. The acting head of department is also chairperson of a two-week block for the final-year MBChB students, focusing on diagnostic laboratory medicine.

Postgraduate
The department participates in the teaching and assessment of MMED students in Paediatrics, Neurology, Medical Oncology and Nuclear Medicine during their pathology rotations. MMED students enrolled in the Clinical Pathology training programme spend 18 months in total in the department. For 2013, 6 students enrolled for the BSc Hons in Chemical Pathology.

Technologists
The department provides in-service teaching and training to student medical technologists registered for Chemical Pathology and Clinical Pathology. Of the 3 Clinical Pathology students who wrote exams in March 2012, only 1 passed.

Professional Development

Postgraduate students enrolled:
16 (6 MMED, 4 MSc, 6 BSc Hons)
Postgraduate students graduated:
1 BSc Hons

Research output

Publications

Conference presentations
International: 3
National: 1
Department Of Haematology

Head: Professor R Pool

Diagnostic Services

The Department of Haematology renders tertiary laboratory and clinical services to the Steve Biko Academic (SBAH), Tshwane District, Kalafong hospitals and surrounding clinics. 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. Laboratory services are offered from two separate sites: the SBAH core laboratory and the Institute of Pathology.

Core laboratory

The bulk of the diagnostic work of the department is performed in the core laboratory. Tests with a short turnaround time which have an immediate impact on patient management are done here. More labour intensive tests which are less frequently requested are performed on the Prinshof campus and these include bone marrow examinations, HPLC, haemoglobin electrophoresis, platelet function studies, blood grouping, special haematology, immunohaematology and molecular haematology.

Flow cytometry

The number of specimens submitted for immunophenotyping continued to increase during the period under review. New methods of lysing red cells were investigated. All data (figures and histograms) are now captured on a tablet computer and stored using a “cloud storage” platform.

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. Our 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 538 patients were seen at the clinic. The establishment of a clinical haematology training unit was approved by the HPCSA during the period under review. Members of the department also provided valuable input into the paediatric haematology clinic.

Haemophilia comprehensive care

A total of 310 visits were made to the clinic during the last year with the majority of patients having severe Haemophilia A. There were 118 patients registered at the clinic during the period under review, which included 58 adults and 60 patients under 18 years of age). A warfarin dosage service is provided for patients attending the cardiology clinic at the SBAH.

Research Projects

Researcher: Dr W Gouws

Comparing one stage- and chromogenic factor VIII assays in the diagnosis of patients with Haemophilia A

The one stage method of determining the factor VIII level in haemophilia A patients is currently the method of choice at Steve Biko Academic Hospital’s core laboratory. As proven in the literature, the factor VIII level measured in mild haemophilia A patients is lower with the chromogenic assay than the one stage assay. The severity of the haemophilia A is underestimated when using the one stage assay and this directly influences the management of these patients. In this prospective study the factor VIII levels determined with the one stage clotting assay will be compared to the factor VIII level measured using the chromogenic assay.
**Researcher:** Dr E Beltchev  
Comparative study evaluating the concordance between the results obtained by the Gallios® flow cytometer and ADVIA® 120 or 2120 haematology analyser for the purpose of establishing total nucleated cell count (TNC) in preparation for stem cell transplant.

TNCs are generally obtained from an automated haematology analyser. Most haematology analysers will indicate the presence of NRBCs, but are generally not able to accurately enumerate these NRBCs. Therefore, the presence of NRBCs in a sample must always be confirmed and quantified by conventional manual microscopy of stained blood smears. Disadvantages of manual microscopy include poor sensitivity as well as reproducibility. As flow cytometry allows for an automated, rapid and reproducible quantification of several parameters of a heterogeneous cell population in a single tube, it may be possible to obtain a TNC count, CD34+ absolute count, quantify the major white blood cell (WBC) populations (granulocytes, monocytes and lymphocytes) as well as determine cell viability in one single tube.

**Researcher:** Dr G George  
Validation of the Mission Plus® haemoglobin testing system

This is a hand held, point of care 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.

**Researcher:** A Prinsloo  
Specific bcr-abl mutations in chronic myeloid leukaemia patients

Micro-RNAs (miRNAs) have recently been identified as a class of small functional non-coding RNAs of 18-25 nucleotides which bind to the 3’ untranslated region (UTR) of mRNAs down-regulating gene expression at a post-transcriptional level. These RNA fragments play critical roles in cellular processes including metabolism, apoptosis, differentiation and development. Micro-RNAs are expressed in specific haematological cell types with a regulatory function in early hematopoietic differentiation, erythropoiesis, granulopoiesis, megakaryopoiesis as well as lymphoid development. This is a pilot study to determine if the miR-17-92 polycistron is expressed in vivo with the objective of using quantitative reverse transcriptase (qRT)-PCR to determine expression of miRNA in CML patients and healthy individuals.

**Researcher:** Dr T Chetty  
An investigation into Von Willebrand factor antigen and activity in an HIV-positive population

Two cohorts, one normal and one an HIV-positive, treatment naïve group will be compared as to Von Willebrand activity and antigen as determined on a Sysmex® coagulation instrument. Several other variables such as blood group, CRP level and CD4 count will also be evaluated.

**Researcher:** R Jansen  
Evaluation of a real time PCR assay to detect Prothrombin gene and Factor V Leiden mutation

The aim of this study is to validate an ‘in house’ real-time PCR assay to detect prothrombin and Factor V Leiden mutations. This assay can then be implemented as a quick and cost effective diagnostic test for both these mutations. Previously tested DNA samples will be used to assess accuracy, precision and repeatability. Results will be compared with that of the current diagnostic kit in use.

**Researcher:** T Kalua  
A comparison of three different methods for demonstrating light chain restriction immunophenotypically
Three different methods will be employed to demonstrate immunoglobulin light chain expression on B lymphocytes. Immunoglobulin light chain restriction serves as a surrogate marker for clonality in the diagnosis of B lymphoproliferative disorders and selecting an optimal panel for establishing light chain expression will enhance our laboratory’s diagnostic precision.

**Researcher:** S Mhkwanazi

The establishing a reference range for HbA2. A cohort of HIV-negative male patients will be recruited from the HTC clinic. Along with HbA2 levels, other parameters will also be tested such as FBC, Fe profile, CRP and TSH. The aim of the study will be to establish an HbA2 reference range for the local population.

**Teaching and Training**

**Undergraduate**

**Formal lectures**

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

**Block 280 (Homeostasis) for MBChBII**

Feedback from students on the newly designed lecture series was generally favourable. The course teaches students to understand haematological changes in systemic disease, to recognise the signs and symptoms of primary haematological conditions, to work-up, diagnose and treat the most common haematological diseases and to use the haematology laboratory in a rational and cost effective manner.

This block also includes practical sessions which cover subjects such as the ESR, Hb determinations, haematocrit, red cell indices and blood grouping. A challenge which will have to be faced in the future is the larger intake of MBChB students with an increase of 20% in the total student number envisaged for 2014.

**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 are taught how to take histories and examine patients as well as how to perform the complete laboratory work-up for malignancy. They are exposed to various clinical and laboratory procedures which include bone marrow aspirates and biopsies, immunophenotyping, conventional cytogenetics, fluorescent in situ hybridisation and PCR.

**SA13 (Laboratory Medicine) for MBChBVI**

This is the last formal instruction to student interns on laboratory medicine. Topics covered include the full blood count, 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. The latter topic is particularly important in the light of the “electronic gate keeping” programme which was introduced at the Steve Biko Academic Hospital during 2012.

**Small group tutorials**

Student interns spend two days in the Department of Haematology as part of their internal medicine rotation. During this period they have tutorials on a large number of haematological conditions as well as being taught how to interpret the most commonly requested haematological tests. The second day of the rotation is spent in the haematology clinic where the students engage with 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.
Postgraduate teaching

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. A formal course in management has been included in the curriculum which includes modules on finance, inventory, laboratory design, human resources and quality assurance, among others.

BSc (Hons) Haematology

The degree is based on course work, tutorials, journal presentations and a dissertation. Compulsory modules include applied research methods, medical biostatistics and molecular pathology.

Professional Development

Haematology registrars enrolled: 6
Clinical pathology registrars enrolled: 5

BSc (Hons) students enrolled: 3
BSc (Hons) students graduated: 3
Student medical technologists enrolled: 9

Research Output

Publications


Congress Presentations

Local: 3
Department Of Immunology
(Incorporating the MRC Unit for Inflammation and Immunity)

Head: Professor R Cockeran

Head of MRC Unit: Professor R Anderson

Professor Anderson, who was the previous head of the Department of Immunology, retired in June 2012 and Professor R Cockeran has been appointed the new head.

Diagnostic Services

The Department of Immunology provides a wide range of serodiagnostic tests (allergy, autoimmune and infectious diseases), flow cytometric determination of leukaemias and lymphomas (in collaboration with the Department of Haematology), PLG CD4+ tests, as well as the diagnosis of primary and acquired immunodeficiency disorders, and HLA typing. Over and above these current tests, the department introduced the following tests in 2012/2013: ganglioside auto-antibodies, neuronal auto-antibodies, NMDA antibodies and Aquaporin 4 test.

The amalgamation of laboratories in 2012 resulted in increased test volumes. Major increases were seen in RPR and PLG CD4+ determinations, which increased from 200 to 4000, and 1000 to over 6000 respectively on a monthly basis.

Research

The research activities of the department 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, both infective (HIV/AIDS, tuberculosis, severe pneumococcal disease, severe sepsis) and non-infective (bronchial asthma, rheumatoid arthritis, toxicology of heavy metals in the environmental and occupational setting) origin. Research highlights are described below.

Infectious diseases

Researchers: Professor R Cockeran, Dr MC Colo, Professor AJ Theron, Professor R Anderson, Dr T Rossouw, Dr HC Steel, M Potjo, ND Mutepe, G van Dyk, A. Osman, MT Mothiba, Professor C Feldman, Professor TJ Mitchell, Dr A von Gottberg, Professor K Klugman

Highlights are as follow:

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 strain 172, serotype 23F, effects on additional serotypes are presently being investigated. The major K+ transporter of Mycobacterium tuberculosis appear 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 intra-vascular and intra-granuloma survival. More recent research is focused on the potential of antimicrobial agents to target biofilm formation and non-replicating biofilm-encased organisms.

An 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, is underway.
This study will recruit a total of 100 mother-infant pairs. Researchers in the department of immunology have been an integral partner in the establishment of a South African drug resistance database, as well as the assessment of the strengths and weaknesses of the new South African HIV-1/AIDS treatment guidelines.

**Inflammation**

**Researchers:** Professor AJ Theron, Dr HC Steel, Dr MC Cholo, Professor R Cockeran, Professor R Anderson, M Makgobu, Professor GR Tintinger, Dr PWA Meyer, Dr B Hodkinson, Professor M Ally, E Musenga, Professor A Wadee, Professor M Tikly

The major research highlights for this research programme are:

Tetracycline antibiotics appear to interact pro-oxidatively with human neutrophils by acting as calcium ionophores, thereby potentiating the harmful pro-inflammatory activities of these cells.

The heavy metal manganese (at concentrations representative of occupational exposure) potentiates the production of toxic reactive oxygen species, hydrogen peroxide and hypohalous acid, by activated neutrophils and monocytes-derived macrophages, as well as pro-inflammatory cytokines by the latter cell type. This is a consequence of the superoxide dismutase mimetic activity of the metal and may underpin its neurological and respiratory toxicity.

Predisposition of rheumatoid arthritis and seropositivity for citrullinated peptide antibodies (aCCP) are associated with a high level of certain circulating cytokines, especially vascular endothelial growth factor and interferon-gamma and appear to identify a sub-set of patients at risk for developing severe disease. Current research is focused on the identification of other biomarkers as predictors of response to therapy and outcome.

**Teaching and Training**

**Undergraduate**

Teaching and training in basic and applied immunology are offered to student medical technicians, technologists, scientists, medical and dental students, as well as to students enrolled in various BSc courses.

**Postgraduate**

Training is offered at BSc (Hons), MSc and PhD levels, while registrars and clinical assistants from medical microbiology, virology, haematology and clinical pathology rotate through the department’s research and diagnostic laboratories. The department of immunology also provides access to equipment and supervision of researchers from other departments and academic institutions.

**Professional Development**

Technicians specialising in immunology can now be registered at the HPCSA in this discipline. The department of immunology’s laboratory manager, Dr PWA Meyer, was awarded the best laboratory manager in the northern region.

Intern Medical Scientist: 1 completed and is now registered as a medical scientist

**Postgraduate candidates graduated:**
7 (6 MSc – 2 with distinction, 1 PhD)

**Postgraduate candidates enrolled:**
14 (7 MSc, 7 PhD)

**Research Output**

Funding received from the MRC, NRF, EU, and UP, resulted in the following publications:

Tintinger GR, Anderson R, Feldman C. Pharmacological approaches to regulate neutrophil activity. *Seminars in Immunopathology* 2013. (Epub, manuscript no: SSIM-D-12-00058)

Ally MTM, Hodkinson B, Meyer PWA, Musenge E, Tikly M, Anderson R. Serum matrix metalloproteinase 3 (MMP3) in comparison with acute phase proteins as a marker of disease activity and radiographic damage in early rheumatoid arthritis. *Mediators of Inflammation* 2013 (in press, manuscript no: MI183563)


Cassol E, Malfeld S, Mahasha P, Slavik T, Seebregts C, Poli G, Cassol S, van der Merwe SW, Rossouw T. Lack of CD4+ T cell restoration in the small compared to large intestine of African HIV patients on antiretroviral therapy. *Journal of Infectious Diseases* 2013 (in press, manuscript no: MS#509257)


Pepper Michael S. Partial relief from the regulatory vacuum involving human tissues through enactment of chapter 8 of the National Health Act and regulations thereto. *South African Medical Journal* 2012; **102**(9): 736–737


De Vries J, Pepper MS. Genomic sovereignty and the African promise: mining the African genome for the benefit of Africa. *Journal of Medical Ethics* 2012; **38**(8): 474–478

Published Abstracts


Congress presentations

International: 5
National: 2
Department of Medical Microbiology

Head: Professor Nontombi Mbelle

Diagnostic Services

The department continues to provide comprehensive diagnostic laboratory services for Steve Biko Academic and Tshwane District hospital. It provides referral diagnostic and clinical services for Kalafong and Mamelodi hospitals, as well as several primary health care clinics in the Tshwane District. It also serves as one of the referral laboratories for the northern branch. The GeneXpert automated diagnostic test that can identify Mycobacterium tuberculosis (MTB) and resistance to rifampicin (RIF) was rolled out in October 2012 resulting in significant reductions in TB PCR and culture testing. The TrakCare laboratory information system was implemented in October 2012 and the electronic gate keeping project in the Steve Biko Academic Hospital in September 2012.

Several ward rounds are held with clinical departments such as the infectious diseases division of the department of internal medicine; the departments of surgery, adult and paediatric intensive care units. The department remains actively involved in infection prevention and control programmes for the hospitals served and partners national, provincial and district infection prevention and control initiatives.

It further continues to serve as an enhanced surveillance site for the National Institute of Communicable Diseases (NICD), actively participating in the Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa (GERMS SA) surveillance programmes for enteric pathogens, mycology, parasitology and respiratory and meningal pathogens as well as the pneumococcal vaccine surveillance programme.

Research

Research in the department is laboratory based and 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 MTB 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 and anti-mycobacterial activity of vitamin D and antimicrobial peptides. 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 nucleic acid amplification test (NAAT) in resource constrained high burden settings.

Researchers: S Omar (PhD student), NE Maningi (PhD student), GI Manenzhe (PhD student); L Khathi (MSc student), MR Mohlabeng (MSc student), F Osman (MSc student), Dr K-A Strydom, Dr M Matabane and Dr Moncho (MMed students), S Atanga (MSc student) and S Matukane (MSc student)

Supervisors: Professor MM Ehlers, Dr MM Kock, Professor B Fourie, Dr K Baba, Dr MR Lekalakala, Dr F Ismail and Dr NA Ismail.

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

Funding: NHLS Research Trust, Faculty of Health Sciences, UP Research Committee - (RESCOM), DTTC/USAID/TREAT TB
Antibiotic Resistance Research Programme
Research projects conducted in this research programme focus 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. Of interest is the relationship with zoonotic bacteria that might result in significant public health consequences. Organisms focussed on are mainly Enterobacteriaceae and methicillin resistance Staphylococcus aureus.

Researchers: I Barakzai (MSc student), N Schoonraad (MSc student), W Strasheim (MSc student), R dos Santos (MSc student), MB de Jesus (MSc student), JE Louw (MSc student), HS Jung (BSc Hons student), M Lowings (BSc Hons student) and N Nhlengethwa (BSc Hons student)

Supervisors: Dr MM Kock, Professor MM Ehlers, Dr K Baba, Professor S Essack, Dr RM Lekalakala.

Funding: NHLS Research Trust; RESCOM; Professor MM Ehlers, BMAZD IRT, UP

Sexually Transmitted Infections Research Programme
Research in this area focuses on the detection, identification and characterisation of sexually transmitted pathogens with a current emphasis on Trichomonas vaginalis, Neisseria gonorrhoeae and Ureaplasma species, using molecular and phenotypic tools.

Researchers: BI Osizigbo (MSc student), MJ Redelinghuys (MSc student), I Ruskasha (MSc student completed), A Kulasinghe (BSc Hons student completed), N Nhlengethwa (BSc Hons student completed)

Supervisors: Dr MM Kock, Professor MM Ehlers

Collaborators: Dr T Crucitti (Institute of Tropical Medicine and Hygiene, Antwerpen, Belgium), Dr H Lombaard (Head: Maternal and Foetal Unit, Department of Obstetrics and Gynaecology, University of Pretoria/Gauteng Department of Health)

Funding: MM Kock University of Pretoria research development grant; NHLS Research Trust; RESCOM grants, UP; MRC grant.

Surveillance research programme
This programme focuses on the continuous monitoring and surveillance of clinical pathogens such as 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.

Researchers: TG Maphanga (MSc student completed), AM Salawu (MSc student), T Adelowotan (PhD student), R Schwim (BSc Hons student) Dr GS Mahlangu and Dr Beki Temba Magazi (MMed students)

Supervisors: Professor MM Ehlers, Dr RM Lekalakala, Dr K Baba and Dr MM Kock

Funding: RESCOM; Professor MM Ehlers, incentive funding for rated researchers, NRF, NHLS Research Trust.

Miscellaneous research projects
Effects of different antiretroviral drugs on selected lactic acid bacteria isolated from commercial probiotic supplements
Researcher: Ms ML Baloyi (MSc student)

Supervisors: Professor MM Ehlers and Dr P Strydom

Collaborators: Agricultural Research Council, Animal Products Institute, Irene.

The detection of atypical pathogens of pneumonia in patients admitted in the medical intensive care unit with the diagnosis of pneumonia from the remnants of the broncho-alveolar lavage and endotracheal aspirates specimens using molecular assays
Researchers: Dr E Hoosein (MMed student); Dr BT Magazi (MMed student)

Supervisor: Dr MR Lekalakala
Improving the microbiological diagnosis of HIV-associated opportunistic pneumonia using a novel semi-quantitative multiplex real-time PCR assay

**Researcher:** Dr N Ismail (PhD Student)

**Supervisor:** Professor B Fourie

Comparison of BD Phoenix and VITEK 2 for the identification of yeast isolates

**Researcher:** TG Mohamed (BSc Hons student)

**Supervisors:** Dr F Ismail and Dr K Baba

Prevalence and characterisation of Group B Streptococcus among pregnant women in Pretoria

**Researcher:** Dr M Said (MMed student)

**Supervisors:** Dr F Ismail and Mr Y Dangor

Honours

Professor MM Ehlers again received NRF C2 rating as a scientist for the period 2012 to 2016.

Dr Visser was second prize winner for oral presentations at the faculty of Health Sciences Academic Day

Mr Kulasinghe received first prize in the poster section at the Faculty of Health Sciences Academic Day

Teaching and Training

Undergraduate

The department provides teaching and training to medical technologists, undergraduate medical and dental students, as well as to allied health care 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.

Postgraduate

Training programmes are offered for BSc honours, Masters and PhD training. Support is also offered to rotating registrars from internal medicine, paediatrics and neurology departments. The department also co-ordinates the clinical pathology training programme over and above the structured training programme of microbiology registrars.

Professional Development:

Postgraduate candidates enrolled:

4 BSc Hons, 12 MSc, 6 PhD, 6 MMed (medical microbiology); 4 MMed (clinical pathology)

Postgraduate candidates graduated:

8 BSc Hons (3 cum laude); 3 MSc (1 cum laude); 1 PhD; 1 MMed (medical microbiology)

Research Output

Publications:


Visser A, Mostert C. Causes of hyperferritinaemia classified by HIV status in a tertiary care setting in South Africa. *Epidemiology and Infection* 2012; 1–5

Visser A, Hoosen A. Haemophilus influenza type b conjugate vaccines – A South African perspective. *Vaccine* 2012; 305: C52–C57

Visser A, Hoosen A. Combination vaccines in the South African setting. *Vaccine*, 2012; 305: C38–C44


Said HM, Kock MM, Ismail NA, Baba K, Omar SV, Osman AG, Hoosen AA, Ehlers MM. Comparison between the BACTEC MGIT 960 system and the agar proportion method for susceptibility testing of multidrug resistant tuberculosis strains in a high burden setting of South Africa. *BMC Infectious Diseases* 2012; 12: 369

Handbook chapters:


Conference attendance and participation:

International: 6
National: 8
Local: 21
Department of Medical Virology

Head: Professor LM Webber

Diagnostic Services

Virology diagnostic services are offered to the Steve Biko Academic Hospital and Tshwane District Hospital as well as other regional hospitals and surrounding clinics. The laboratory also serves as regional referral laboratory for HIV-1 DNA PCR assays which are essential for early diagnosis of HIV infection in infants. The laboratory has maintained its accreditation status and continually reviews workflow to optimise turnaround times.

The department actively participates in outreach activities including one of the pathologists assisting weekly at the HIV Clinic at the Tshwane District Hospital and FF Ribiero Clinic; pathologists and registrars attending clinical ward rounds at the Steve Biko Academic Hospital; and pathologists, registrars and medical scientists presenting lectures, workshops and providing other academic support to healthcare professionals in the Pretoria and other geographical regions.

Research

The Department of Medical Virology has four main research focus areas. This includes the bloodborne virus research programme which addresses clinical and epidemiological aspects of HIV-1, hepatitis B virus and hepatitis C virus; and the human papillomavirus and cervical cancer research programme which addresses cervical cancer screening in South Africa,

It also includes the enteric virus and environmental research programme, which includes projects on the molecular epidemiology of gastroenteritis viruses, the recovery, detection, characterisation and molecular epidemiology of food- and waterborne viruses; and viral zoonoses, which is housed in the University of Pretoria-based BSL3 laboratory on the Prinshof Campus.

Bloodborne virus research projects

New projects

Evolution of HIV-1 minority variants in ARV-naive patients and patients receiving highly active antiretroviral therapy

Principal Investigator: Dr S Bowyer
Collaborators: M Mzingwane (PhD student), Dr S Mayaphi, Dr AH Mazanderani, Dr L Debusho
Funding: HIV Research Trust; Poliomyelitis Research Foundation (PRF) (application submitted), NHLS Research Trust (application submitted)

The proportion of Human Immunodeficiency Virus Type-2 (HIV-2) among patients that tested positive for HIV1/2 ELISA at the Tshwane Academic Division of the National Health Laboratory Services (TAD NHLS)

Principal investigator: Dr R Mafuyeka
Co-investigators: Dr S Mayaphi and Professor LM Webber
Funding: PRF (application submitted), NHLS Research Trust (application submitted)

Ongoing studies

An open phase II study in HIV-1 infected untreated male adult patients to evaluate safety and tolerability and the in vivo effects on T-cell population and viral load of a GnRH-analogue administrated by intranasal administration during 28 days when combined with a single intramuscular testosterone depot injection to restore a normal serum testosterone level

Principal investigator: Professor LM Webber
Co-investigators: Dr H Kinkel, Dr O Winquist, Dr N-G Pehrsson, Dr H Lomberg.
Funding: Karolinska University Hospital, Stockholm, Sweden

Identification of primary (acute) HIV-1 infections in an HIV hyperendemic setting

Principal investigator: Dr S Mayaphi
Co-investigators: Professor DJ Martin, Dr TM Rossouw, Dr SAS Olorunju
Funding: NHLS Research Trust
The genetic diversity of HIV in vivo: South African patients with low pre-treatment viral loads

**Principal investigator:** Dr M Erasmus  
**Supervisor:** Professor L Webber  
**Collaborators:** G Malherbe, Dr T Rossouw  
**Funding:** Discovery Foundation Academic Fellowship Award, NHLS Research Trust

Optimising and developing more sensitive assays for surveillance, diagnosis and characterisation of unique variation in African isolates of hepatitis B (HBV), hepatitis C (HCV) and HIV in mono- and HIV co-infected patients

**Project leader:** Dr SM Bowyer  
**Co-investigators:** Dr S Mayaphi, Professor LM Webber  
**Researchers:** LS le Clercq, Dr O Laguda-Akingba  
**Funding:** PRF

Using the power of position specific scoring matrices to analyse viral variation and evolution in Africa

**Project leader:** Dr SM Bowyer  
**Researcher:** LS le Clercq

Human Papillomavirus and Cervical Cancer Research Projects

**Ongoing studies**

Screening for cervical neoplasia with a combination of HPV testing and cytology in an urban community in South Africa

**Principal investigator:** Professor G Dreyer  
**Co-investigators:** Dr KL Richter, Dr M Louw  
**Funding:** CANSA grant (via HPV Cervical Cancer Research Fund)

Cervical cancer screening in South Africa: Incorporating HPV E6/E7 mRNA testing

**Principal investigator:** Dr KL Richter  
**Co-investigator:** Professor G Dreyer  
**Funding:** Discovery Foundation (HPV Cervical Cancer Research Fund); Big Cat AORTIC grant (HPV Cervical Cancer Research Fund); NHLS Research Trust

Enteric Virus and Environmental Research Projects

**New projects**

Molecular epidemiology of sapoviruses and novel noroviruses in South Africa

**Principal investigator:** Professor MB Taylor  
**Researcher:** TY Murray (née Yasvoin)  
**Funding:** PRF; NRF incentive funding for rated researchers

The detection and molecular characterisation of clinically important enteric viruses in selected surface waters sources in Kenya

**Principal investigator:** Professor MB Taylor  
**Co-investigator:** Dr JM Mwenda  
**Researcher:** NM Kiulia  
**Funding:** NRF, South Africa / Kenya Research Partnership Programme

Recombinant expression and characterisation of the capsid protein of clinically important norovirus GI and GII strains

**Principal investigator:** Dr J Mans  
**Co-investigator:** Professor MB Taylor  
**Researcher:** JC Botha  
**Funding:** PRF

**Ongoing studies**

Development and application of cost effective techniques for the sensitive recovery and detection of enteric viruses in surface and treated drinking water samples

**Principal investigator:** Professor MB Taylor  
**Researchers:** Dr W van Zyl, Dr M Wolfaardt, Dr J Mans, TY Murray; GA de Ridder, F Ngwana, and V Ruhanya  
**Funding:** Rand Water/THRIP, Sedibeng Water and Midvaal Water
An investigation into the link between water quality and microbiological safety of fruit and vegetables from the farming stage to processing production and marketing

**Project leader:** Professor L Korsten (Dept of Microbiology and Plant Pathology, University of Pretoria).

**Co-investigators:** Professor MB Taylor; Professor E Buys (Dept of Food Science, University of Pretoria); Professor B Pillay (Dept of Microbiology, University of Kwazulu-Natal [Westville Campus])

Researchers: V Ruhanya, GA de Ridder, R Said, N Ndindwa

**Funding:** Water Research Commission solicited research project K5/1875/4

**Molecular characterisation of noroviruses detected in water, fresh produce and clinical specimens**

**Principal investigator:** Professor MB Taylor

**Researcher:** Dr J Mans, TY Murray

**Funding:** Medical Research Council self-initiated research grant

**Miscellaneous Research Projects**

**New projects**

Retrospective study / case series of CMV disease in patients with HIV/AIDS admitted in a medical intensive care unit

**Principal investigator:** Dr S Mayaphi

**Co-investigators:** Dr Marieke Brauer, Dr Daniel Morobadi, Dr Ahmad Haeri-Mazanderani, Dr Rendani Mafuyeka, Dr T Marshall, Professor G Tintinger, Professor Anton Stoltz

**Honours**

TY Murray (née Yasvoin) (PhD student under Professor MB Taylor’s supervision)

Awarded a full scholarship from the Water Institute of Southern Africa (WISA) to attend the 6th IWA International Conference for Young Water Professionals 10–13 July 2012 Corvinus University, Budapest, Hungary.

Awarded a prize for her presentation “First detection of human sapoviruses in river water in South Africa” at the Fountain of Knowledge UP Water Institute Members’ Forum Conference 9 November 2012 Law Building, Hatfield Campus, University of Pretoria

C van Eeden (PhD student under Professor M Venter’s supervision)

Received a student travel award from the Belgium Ambassador to South Africa to attend the 13th Conference of the International Society for Veterinary Epidemiology and Economics (ISVEE XIII) 20–24 August 2012 MECC, Maastricht, The Netherlands.

Received the Norval-Young award to participate in the International 11th Biennial Conference of the Society of Tropical Veterinary Medicine 19–22 September 2012 Orvieto, Italy

NM Kiulia (MSc student under Professor MB Taylor’s supervision)

Received a Bill & Melinda Gates travel award to attend the 11th International Symposium on Double-Stranded RNA viruses 27 November 2012 to 1 December 2012 Caribe Hilton Hotel, San Juan, Puerto Rico

Professor MB Taylor was awarded a C2-rating (established researcher) for the third time by the National Research Foundation. This rating is effective for the period 2013–2017.
Faculty of Health Sciences Faculty Day  
28–29 August 2012

S van Niekerk was awarded second place in the category Researcher: Basic Sciences [Oral] for her presentation entitled “Alpha viruses as a cause of neurological disease in farm and wild animals in Southern Africa”

Dr A Haeri-Mazanderani was awarded second place in the category Researcher: Clinical [Oral] for his presentation entitled Determining the human cytomegalovirus (HCMV) viral load cut-off value for initiation of ganciclovir treatment in HIV/AIDS patients in medical ICU

Faculty of Health Sciences Gala Dinner  
17 November 2012

Professor M Venter was awarded first runner-up in the category “Best-overall publication: Clinical” in the Faculty in 2011 for the publication: Contribution of common and recently described respiratory viruses to annual hospitalisations in children in South Africa.

Professor M Venter was awarded first runner-up in the category “Best-overall publication: Non Clinical” in the Faculty in 2011 for the publication: Identification of deletion mutant respiratory syncytial virus strains lacking most of the G protein in immunocompromised children with pneumonia in South Africa.

Professor M Venter was awarded second runner-up in the category “Best publication: Team Effort” in the Faculty in 2011 for the publication: Fatal neurologic disease and abortion in a mare infected with lineage 1 West Nile virus, South Africa.

S van Niekerk was awarded second runner-up in the category “Best publication: Young researcher (<35 years) Clinical” in the Faculty in 2011 for the publication: Replacement of previously circulating respiratory syncytial virus subtype B strains with the BA genotype in South Africa.

Teaching and Training

Undergraduate

The academic staff presents formal lectures, symposia and tutorials to undergraduate MBChB and BChD students in the 2nd, 3rd, 4th, 5th and 6th years. Teaching in the department also includes formal lectures to undergraduate allied health professions (BCur, BDietetics, and BPhysT) students.

Technologists and technicians

The department provides weekly lectures/tutorials to the Intern Medical Technology, the Intern Medical Technician students and Medical Technologists.

Postgraduate

The department is an HPCSA accredited training facility and offers formal lectures, tutorials and practical training to basic science postgraduate students, M Med (Path) Medical Virology/Medical Microbiology registrars and M Med students from other disciplines rotating through Pathology. The CPD accredited M Med (Path) Medical Virology tutorials, which are held weekly, are attended by clinicians and pathologists from the private sector. JCPD accredited journal club and research forum meetings are held on a weekly basis. Numerous presentations were given to other academic departments, societies and NGOs.
Professional Development

Postgraduate candidates enrolled:
23 (3 BSc [Hons]; 7 MSc, 8 PhD, 4 M Med (Path) Medical Virology, 1 Post-doctoral fellow)

Postgraduate candidates graduated:
4 (1 PhD, 3 BSc [Hons])

Research Output

Publications


Conference presentations

International: 16
National: 9
Local: 16
**Division of Anatomical Pathology**

**Head:** Professor JW Schneider

**Diagnostic Services**

The division provides a comprehensive diagnostic service to Tygerberg Hospital and approximately half of the Western Cape public health sector. Consultation services are offered to NHLS laboratories in the Eastern Cape and the private sector. The division also offers special services and expertise including electron microscopic support for service and research, a fine needle aspiration (FNA) clinic, rapid on site cytology diagnostic services, and consultation services especially in the fields of dermatopathology, electron microscopy, neuropathology, renal pathology and perinatal pathology. Specialised services include the application of flow cytometry in the diagnosis of lymphomas using material obtained from FNA of lymph nodes.

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 and other higher educational institutions, including the University of the Western Cape and the MRC. During the reporting period, the surgical pathology laboratory processed 20,219 cases, the electron microscopy laboratory processed 391 cases, and the immunohistochemistry laboratory performed 13,475 immunohistochemical stains and 1,102 direct immunofluorescence stains. Staff conducted 18 adult and 77 paediatric autopsies. The cytopathology unit processed 61,869 gynaecological cases, 4,487 non-gynaecological cases and 9,012 fine needle aspirations, including the performance of 3,848 on site FNA on patients in the FNA clinic and on 329 patients in theatre. The cytopathology laboratory maintained and the histopathology laboratory obtained SANAS accreditation.

The Pathology Research Facility facilitates the development and introduction of new diagnostic molecular pathology tests through national and international collaboration. In addition to supporting clinical geneticists, various molecular tests are offered for the diagnosis, prognostication and therapeutic interventions of various haematological malignancies, colorectal carcinoma and carcinoma of the breast.

During 2012, the division expanded the paediatric pathology service to meet the growing demands from neonatologists, paediatricians, paediatric surgeons and obstetricians to obtain a better understanding of poor foetal outcome in order to improve the management of pregnant women in both the public and private sectors.

The division sustained its ongoing support of diagnostic services to pathologists in the Eastern Cape through assistance with excessive routine workloads and diagnostic consultations, including a telepathology service to pathologists in Mthata and East London.

**Research Projects**

**New research projects for 2012–2013 with ethics approval**

Infection with the human immunodeficiency virus changes the laboratory and clinical expression of lymphoreticular malignancies

**Researchers:** R van Wijk (Division of Haematological Pathology, University of Stellensbosch (US)), Professor A Abayomi (Division of Haematological Pathology, US), Professor P Jacobs (Division of Haematological Pathology, US), Dr N Mohamed.

**Funding:** NIH
Aim of this study: A critical comparison of tissue microarray and conventional histopathology including immunohenotyping infection in the study of human immunodeficiency virus associated lymphomas.

Spectrum of autoimmune bullous skin disease at Tygerberg Hospital: 4 year review

Researchers: N Adam (MBChB student, US), Professor JW Schneider, Dr W Visser (Division of Dermatology, US).

Aim of the study: To identify the clinicopathological spectrum of autoimmune bullous skin disease diagnosed positively on direct immunofluorescence at Tygerberg Hospital over a 4 year time period.

An audit of the completion of surgical pathology requisition forms and its impact on diagnostic accuracy and turn-around time of the final pathology reports in the Division of Anatomical Pathology at Tygerberg Hospital

Researchers: Dr T Wantenaar, Professor JW Schneider, Professor RT Erasmus (Division of Chemical Pathology, US).

The primary objective of this audit is to establish how the clinical information submitted influences the pathological assessment of the specimen and the compilation of the pathology report and diagnosis. The secondary objective is to establish the completeness and accuracy of the request forms submitted to the anatomical pathology laboratory. The third objective is to ascertain whether or not the cases that lacked clinical information impacted on the turnaround time of the particular case.

Leadership for transformative learning and interdependence

Researchers: Professor J Bezuidenhout, Professor J Blitz (Family Medicine and Primary Care, SU), Professor M de Villiers (Deputy Dean Education, Faculty of Medicine and Health Sciences, SU), Dr F Waggie (University of the Western Cape); Professor G van Zyl (Dean, Faculty of Health Sciences, University of the Free State).

Funding: FRILT grant and Teaching Development Grant

The overarching aim is to identify the relevant competencies required for transformational and shared leadership in health teams and design and implement a suitable leadership programme.

Nature AND nurture: Understanding how to enhance attributes and attitudes of undergraduate students towards engaging in research, particularly among underrepresented groups and in a resource constrained environment

Researchers: Professor J Bezuidenhout, S van Schalkwyk, Professor J Blitz (Family Medicine and Primary Care, SU), Professor M de Villiers (Deputy Dean Education, Faculty of Medicine and Health Sciences, SU), M Blackie (Stellenbosch University) J Frantz (University of the Western Cape); Professor V Burch (University of Cape Town).

Funding: FRILT grant

The overarching aim is to develop a framework for nurturing undergraduate research and designing and implementing interventions that will enhance attitudes and attributes of undergraduate students towards participating in research as undergraduate students and in future as practitioners.

How do historical figures of medicine compare with modern role models in healthcare as defined by the literature?

Researchers: Willem-Johan Steyn (MBChB VI, US); Professor J Bezuidenhout.

The overarching aim of this study is to explore the relevance of historical role-models in medicine in the 21st century.
Who is the student? Defining the socio-cultural identity and learning preferences of undergraduate students in the first year of Health Sciences studies

**Researchers:** M Christodoulu, Professor J Bezuidenhout, Professor J Blitz (Family Medicine and Primary Care, SU).

**Funding:** FRILT grant, Teaching Development grant

To explore aspects of student identity that may be relevant to graduate attributes and transformative learning in order to develop interventions and strategies that will support students to become leaders and change agents.

Investigation of the relationship between genetic and environmental risk factors associated with obesity and insulin resistance in South African patients with non-alcoholic fatty liver disease (NAFLD)

**Researchers:** Professor MJ Kotze, LR Fisher, J Pretorius, D de Klerk, Dr M Hoffmann (Division of Chemical Pathology, US), Professor L van der Merwe (Statistical Consultation, MRC); C Daniels, Dr FC Kruger (Gastroenterology Unit, Durbanville Medi-Clinic)

**Funding:** Chronic Disease Initiative in Africa (CDIA)

Non-alcoholic fatty liver disease patients recruited for this study are subdivided into four clinical subgroups relating to disease severity (fatty liver disease, non-alcoholic steatohepatitis, no/mild fibrosis, severe fibrosis) to identify biomarkers that may distinguish between patients at increased risk of cardiovascular disease vs liver disease. This ethically approved sub-project of the parent study, entitled “Non-alcoholic fatty liver disease: genotype and phenotype expression” focuses on gene-environment interaction as may be reflected by abnormal blood biochemistry levels and was approved by the SU Ethics Committee as an addendum to the parent project. It led to the development of a risk score for NAFLD currently investigated further as part of a comprehensive cardiovascular screen.

Implementation of Genomic Healthcare

**Researchers:** Professor MJ Kotze, Professor SJ van Rensburg (Division of Chemical Pathology, US), Dr DP van Velden, D Geiger; Dr F Cronje, Professor J Marnewick (Oxidative Stress Research Centre, Faculty of Health and Wellness Sciences, Cape Peninsula University of Technology, Cape Town [CPUT]); Professor M Collins and Dr A September (Sport Science Institute, UCT).

**Funding:** NRF, Winetech and THRIP (2nd cycle)

Chronic, multi-factorial conditions caused by a complex interaction between genetic and environmental risk factors frequently share common disease mechanisms, as evidenced by an overlap between genetic risk factors for cardiovascular disease (CVD) and Alzheimer’s disease. A method has been developed and implemented for assessment and treatment of CVD risk factors in midlife as a preventable cause of cognitive decline, morbidity and mortality in old age. A second cycle (extension) of the parent project entitled “Development and application of a pathology supported genetic assay to assess the impact of hereditary factors on health outcomes in individuals subjected to a wellness screen” was approved by THRIP that will focus on the inflammatory component of the metabolic syndrome and increased risk of osteoarthritis that shares disease pathways with a genetic tendency for sport injuries.

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, Professor J Bezuidenhout, Professor SJ van Rensburg (Division of Chemical Pathology, US), Dr R Pienaar, Professor MJ Kotze

**Funding:** CANSA, NRF

This study is focused on the elucidation of molecular mechanisms which underlie differences in breast tumour pathology that
may correlate with adverse effects related to environmental exposures, including treatment options. Identification of disease subtypes allows for classification of patients into different treatment groups based on disease mechanism and not only symptoms. The overall objective of the study is to facilitate prevention of cumulative risk in breast cancer patients through development of a comprehensive pathology supported genetic testing (PSGT) service informed by molecular tumour subtyping. Ultimately, pathology and genetic tests will be assessed together in a multiplex assay that may be extended to include exome sequencing where clinically indicated.

Tygerberg Hospital adult cancer registry database

**Researchers:** Dr M Zeier (Department of Medicine, US), Dr J Taljaard (Department of Medicine, US), Prof JW Schneider, Professor A Ellmann (Division of Nuclear Medicine, US), Professor H Botha (Department of Obstetrics and Gynaecology, US), Dr M Heunis (Division Clinical & Radiation Oncology, US), Professor JB Nachega (Center for Infectious Diseases, US), Dr F Bassa (Department of Medicine, US).

The primary aim of the study is to establish a hospital-based cancer registry database for Tygerberg Hospital that can contribute to the South Africa National Cancer Registry. Secondary aims include determination of demographic variables for this cohort, establishment of treatment patterns for this cohort and training at all levels on passive cancer case reporting.

**Honours**

Professor J Bezuidenhout has been appointed deputy editor of the African Journal of Health Professions Education.

She was selected as African Collaborative, in collaboration with UWC and Free State, Institute of Medicine, USA Global Forum on Innovation in Health Professional Education Collaborative Initiative.

Professor J Bezuidenhout received an NHLS reward in the category pathologist for her contributions to the development of health professions training at a national and international level.

She was the recipient of a Teaching Fellowship from Stellenbosch University.

**Teaching and Training**

**Undergraduate**

In addition to the module on essentials of Disease Processes, consultants also lecture in clinical modules in the second, third, fourth and fifth years of the MBChB programme. The division is involved with a practical module in the fourth and fifth years where students visit the laboratories, receive training in the performance of FNAS and other basic procedures, and perform case studies that involve all the pathology disciplines. Other undergraduate teaching activities include supervision of MBChB students’ research assignments, teaching of basic pathology to students in physiotherapy and occupational therapy, participation in the Faculty Committee for Undergraduate Teaching, MBChB Programme Committee, and close involvement with the continuous development of the MBChB programme.During the past year, pathologists from the division served as external examiners for undergraduate medical students at Walter Sisulu University in Mthatha.

**Postgraduate**

There are 11 anatomical pathology registrars in the division and a further two registrars in oral pathology (University of the Western Cape). Registrars in forensic medicine receive one year of training from anatomical pathology consultants on the same platform.
Other postgraduate teaching activities include lectures to BSc Hons (reproductive biology) students, involvement with development of and teaching in the MPhil (Health Professions Education) research methodology module, teaching of MMed students in family medicine on how to perform FNAS, participation in the Faculty Committee for Postgraduate Teaching, and teaching of anatomical pathology and normal histology to registrars from clinical disciplines to assist them with preparation for part 1 MMed or College of Medicine of SA examinations.

The HPCSA-registered MSc (cytopathology) programme runs over a minimum of two years and has a modular design in keeping with modern international trends. The programme is offered by distance education and it includes student contact via satellite broadcasting and WebCT. Ongoing national and international moderation of the programme confirmed the high quality and standard of this programme, which is the only cytopathology degree programme in Africa.

Medical technologists and technicians
The division provided training for 2 student cytotechnologists and 1 histotechnologist.

Outreach
The division is involved with the training of medical staff and healthcare workers at regional hospitals and clinics to develop the skills and confidence to perform FNAS for cytology and academic support is offered to pathologists in the Eastern Cape. A DVD with Professor CA Wright as the presenter has been produced to facilitate FNA training of healthcare workers. There is close collaboration with pathologists at Walter Sisulu University, using telepathology to exchange teaching material and to offer comments on diagnostically challenging cases. The division also provides specialised pathological tests and consultations on various tissue samples from the NHLS anatomical pathology laboratories at Nelson Mandela Academic Hospital in Mthatha and in Port Elizabeth.

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, training clinicians and nursing sisters in the optimal technique in FNAB to ensure that better quality specimens reach the cytology laboratories. Pathologists and registrars from the division offered a FNA training session at the International Child TB Training Conference that was held at Goudini Spa, Cape Town, South Africa 30 September–4 October 2012. The division provided two months of specialist dermatopathology training to a visiting dermatologist from Kenya.

Professional Development

Postgraduate students graduated:
1 MMed, 1 M (Pathology)

Postgraduate students enrolled: 2 PhD, 11 MMed, 5 MSc (Cytopathology), 3 M (Pathology)
Research Output

Publications


Louw M, Brundyn K, Schubert PT Wright CA, Bolliger CT, Diacon AH. Comparison of the quality of smears in transbronchial fine-needle aspirates using two staining methods for rapid on-site evaluation. *Diagnostic Cytopathology* 2012; 40(9): 777–781

Nteene LM, Wright CA. A comparison of specimen adequacy in fine needle aspiration biopsies performed by pathologists, trained nursing staff and clinicians. *Tropical Doctor* 2012; 42: 97–98


Conference presentations

International: 22
National: 9
Local: 13

**Division of Chemical Pathology**

**Head:** Professor R Erasmus

**Diagnostic Service**

The Division of Chemical Pathology is SANAS accredited and provides a comprehensive 24-hour service to Tygerberg Hospital and some of the clinics and secondary hospitals in the Western Cape region.

This service has been expanded with effect from April 2011 to include Eerste River Hospital and more peripheral clinics. The division is one of the referral centres for samples from the Eastern Cape, particularly from Nelson Mandela, Livingstone and East London hospitals.

New test validation and introductions include Vitamin D, automated ADA and Procalcitonin.

**Research Initiatives And Projects**

The division has developed four research themes which have evolved over the past four years.

The clinical audit and laboratory management team is lead by Dr Zemlin, who is also involved in leading a study on free light chains in patients with HIV. Dr Hoffman leads the team on reference range values, while Dr Rensburg is involved in establishing a research group on point of care testing.

Dr Ali is studying the pathophysiology of fat accumulation in various disease states. Professor Van Rensburg leads the group on multiple sclerosis and schizophrenia. Many of these research groups have external collaborators.

**Research Projects**

- Establishing reference values for common biochemical analytes in African countries
  - **Researchers:** Erasmus RT, Hoffman M, Wassung J, Matsha T, Ichihara K.
  - **Funding:** NHLS, Beckman Coulter, Pathcare

- Distribution of paraxonase 1 genotype and phenotype: correlation with lipid and lipoprotein profile, oxidative status and atherosclerosis in a South African population
  - **Researchers:** Erasmus RT, Matsha T, Hassan S, Macharia M
  - **Funding:** MRC

- Molecular investigation of genetic factors associated with insulin resistance and obesity in a South African population
  - **Researchers:** Erasmus RT, Matsha T, Hassan S, Vergotine Z
  - **Funding:** MRC

- Predictors of cardiovascular risk and glucose tolerance in a mixed ancestry population
  - **Researchers:** Matsha T, Erasmus RT, Hassan S, Soita D
  - **Funding:** Cape Peninsula University of Technology

- Carotid intimal thickness and modifiable cardiovascular risk factors in a mixed ancestry population
  - **Researchers:** Matsha T, Erasmus RT, Hassan S, Kisten Y
  - **Funding:** Cape Peninsula University of Technology

- HbA1c as a screening tool for diabetes mellitus and prediabetic conditions and the investigation of traditional and future biochemical predictors of cardiovascular risk in a local urban community of Cape Town
  - **Researchers:** Zemlin AE, Erasmus RT, Matsha TE, Hough FS
  - **Funding:** Cape Peninsula University of Technology and NHLS
HIV and inflammation study (HAIG) – ADMA levels  
**Researchers:** Ipp H, Zemlin AE, Hudson CA  
**Funding:** NHLS, Harry Crossley, MRC

Chronic kidney disease and its association with the MYH9 gene in a South African population  
Matsha T, Yako Y, Masconi K, Hassan S, Erasmus R  
**Funding:** Stellenbosch University, Cape Peninsula University of Technology

Non-conformances in the laboratory  
**Researchers:** Zemlin AE, Osegbe ID, Kimengech KK, Erasmus RT.  
**Funding:** Stellenbosch University

ADA and total IgG as cost-effective markers of immune activation and inflammation in asymptomatic HIV infection for application in resource-limited settings  
**Researchers:** Ipp H, Zemlin AE, Glashoff RH, van Wyk J, Vanker N, Reid T, Bekker L  
**Funding:** NHLS, the Poliomyelitis Research Foundation (PRF), Harry Crossley

Free light chains in treatment-naïve HIV subjects  
**Researchers:** Zemlin AE, Ipp H, Rensburg MA, Maleka S, Erasmus RT  
**Funding:** NHLS, K-funding

Mechanism of Lipodystrophy in patients with HIV  
**Researchers:** Ali A, Erasmus RT, Van Helden P, Baker B, Peterson R  
**Funding:** Stellenbosch University

Hormonal regulation of Vaspin  
**Researcher:** Ali A

Cinnamon in the life of patients with type 2 diabetes  
**Researchers:** Ali A, Baker B, Peterson R

The effect of Vit D on fat accumulation and insulin resistance  
Ali A, Matsha T, Erasmus RT  
**Funding:** Stellenbosch University

The development of a comprehensive gene-based, pathology supported intervention program for improved quality of life in patients diagnosed with multiple sclerosis (MS)  
**Researchers:** Janse van Rensburg S, Kotze MJ, Geiger D, Davis W, Moremi K, Rensburg M, Cronje F, De Klerk MMJS, Erasmus RT  
**Funding:** NHLS K-funding

Dietary supplementation with eicosapentaenoic acid in patients with schizophrenia: Clinical efficacy and changes in cell membrane fatty acids  
**Researchers:** Janse van Rensburg S, Kotze MJ, Geiger D, Luckhoff H, Erasmus RT  
**Funding:** NHLS K-funding, Harry Crossley

POCT evaluations  
**Researchers:** Rensburg MA, Erasmus RT

The prevalence and clinical significance of acanthosis nigricans in diabetic and non-diabetic women of mixed ancestry  
Hoffmann M, Hough FS, Visser W, Ferris W  
**Funding:** Harry Crossley, K-Funding

The cardiovascular risk marker asymmetric dimethylarginine is elevated in asymptomatic, untreated HIV-1 infection and correlates with markers of immune activation and disease progression  
Hudson C, Zemlin A, Ipp H  
**Funding:** Harry Crossley

Teaching and Training

Undergraduate  
Teaching and training of undergraduate medical students continues to be an important part of the division’s goals and priorities. The basis of disease module is chaired by Dr Megan Rensburg. This module is presented to
the MBChB I students and forms the basis of teaching of Pathology. The division in recent years has introduced case-based learning in which smaller groups are involved. The MBChB IV and V students also 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.

Postgraduate
The division is involved in co-ordinating 2 postgraduate modules. These are laboratory management (Dr Zemlin) and molecular diagnostics (Dr Hoffmann). The division this year also is taking part in organising the diagnosis and screening module of the Masters Degree in clinical epidemiology organised by the Centre for Evidence Based Health Research.

The division was involved in supervising 4 BSc Honours, 3 Masters, 4 MMed (including 2 Clin Paths), and 6 doctoral students. In line with the vision of the division to encourage newly qualified specialists to register for doctoral studies, a second specialist was registered for a PhD (Dr Hoffmann).

The laboratory management module was completely re-organised by the programme committee, and will soon be offered as an international course. The division continues to attract senior technologists and pathologists from West and East African countries to its training programme on laboratory management. The division was also involved in giving workshops on laboratory management in South Africa, Zimbabwe and Zambia.

The division established a research focus group on Point of Care Testing and Personalised Medicine. Members of the division are on several national (NHLS Expert Committee) and international committees (International Federation of Clinical Chemistry). Specialists, postgraduate students, and medical technologists from the division attended several courses during 2012 as part of continuous professional and skills development.

Outreach And Community Interaction
The division continued to provide outreach services to Karl Bremer Hospital and in Paarl.

Professional Development
Five honours, three masters and one doctoral student graduated with one masters’ student receiving the degree cum laude. The doctoral student who completed the doctoral studies was the first African female to finish from the division, as well as the department of Pathology.

Members of the division are actively involved in the South African Association for Clinical Biochemistry (SAACB), the International Federation of Clinical Chemistry (IFCC), Federation of South African Societies of Pathology (FSASP) and the Multiple Sclerosis Society. Members of the division successfully organised the last annual Pathology Congress, Pathpoint, which was held in Cape Town and attracted a record number of international faculty. Members of the division were involved as external examiners at the University of Kuwait, University of Zimbabwe, Walter Sisulu University, North West University, Wits University and also acted as examiners for the College of Medicine of South Africa (Chemical Pathology).

20 manuscripts were reviewed for the following journals: J Clinical Pathology, Acta Clinica Chimica, Journal of Clinical Chemistry and Lab Medicine, South African Journal of Medicine. Invited talks were given at the annual Africa Health Conference, the Malaysian Association for Clinical Biochemistry (MACB) conference, and at Teknologi Mara University in Kuala Lumpur, Malaysia.
Number of postgraduate students:

- MMed (current): 2
- BSc (current): 4
- Masters (current): 5
- HonsBSc graduated: 5
- PhD (current): 5
- MSc graduated: 3
- PhD (graduated): 1

Research Output

Publications


Van Der Merwe N, Bouwens CSH, Pienaar R, Van Der Merwe L, Yako Y, Geiger DH, Kotze MJ. CYP2D6 genotyping and use of antidepressants in breast cancer patients: Test development
for clinical application. *Metabolic Brain Disease* 2012; **27**: 319–326


Erasmus RT. Guest Editorial. *CME Journal* 2012; **30**(7): 229


Rensburg MA. Troponins and acute coronary syndrome. *CME JOURNAL* 2012; **30**(7): 261–262


Published Abstracts


Book Chapter


Conference attendance and presentations

National conferences: 15
International conferences: 5
Invited speaker invitations: 2
International workshops: 2
Division of Haematological Pathology

Head: Professor A Abayomi

Diagnostic Service

The Division of Haematology is SANAS accredited and provides a comprehensive 24-hour service to Tygerberg Hospital and some of the clinics and secondary hospitals in the Western Cape region. This service has been expanded with effect from April 2011 to include Eerste River Hospital and more peripheral clinics. The Division is one of the referral centres for samples from the Eastern Cape, particularly from Nelson Mandela Hospital, Livingstone Hospital and East London 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. Some of the specialised haematology tests performed at Tygerberg include hereditary thrombophilia screening assays, and flow cytometry and genetic tests used in the diagnosis of haematologic malignancies.

The following molecular based tests have been introduced by the division in conjunction with the Pathology Research Facility: FLT-3 is an important poor prognostic indicator in patients with acute myeloid leukaemia. We have validated a RQ-PCR method to assess response to treatment by measuring BCR-ABL transcript levels in patients receiving treatment for CML.

In addition, the Division of Haematology has received National Institute of Health (NIH) funding (part of the H3Africa initiative) for the development of a Cape Town pilot biorepository under the direction of Professor Abayomi, in collaboration with NHLS, Stellenbosch University, South African National Bioinformatics Institute (SANBI – University of Western Cape), RUCDR (Rutgers University), and the Scripps Research Institute for Regenerative Medicine.

The Division is also involved in a collaborative study named Paediatric HIV Exposed and Uninfected infant study (HEU) with the Immunology Unit at NHLS Tygerberg.

Research Projects:

The Tygerberg Lymphoma Study Group
Malignant lymphoma incidence and HIV-related lymphoma subtypes in the Western Cape of South Africa
Researchers: A Abayomi, R Grewal, A Sommers, G Sissolak, F Bassa, D Maartens, P Jacobs, C Stefan, LW Ayers. In collaboration with the Innovation Center of the University of Ohio, and the sub-Sahara Africa Lymphoma Consortium (SSALC/NCI).
Funding: The NIH through the Sub-Sahara Africa Lymphoma Study and the AIDS Cancer Specimen Repository (ACSR).

A continental and international multidisciplinary approach to improve the understanding of the how HIV is transforming the incidence, pattern, prognosis of Malignant Lymphoma and define a cost effective policy model and strategic approach to management in the Western Province of South Africa and the sub-Continent.
Development of cost-effective 10 colour flow cytometry panel which will aid in the characterisation of HIV-related lymphoma’s (HRL) in TAH catchments area of South Africa

**Researchers:** C Swanepoel, L Stephens, R Grewal, B van Rooyen, B Nkambule and A Abayomi

**Funding:** The NIH through the Sub-Saharan Africa Lymphoma Study, ACSR, D43 Scholarship.

In the Western Cape, South Africa, the HIV-related Lymphoma’s (HRL) incidence and mortality rates have risen dramatically with the prevalent HIV/AIDS epidemic. HRL are the most complex and challenging for the pathologist and findings from a retrospective study that are currently being conducted in the Tygerberg Hospital (TAH) shows that it makes up almost 30% of new cases at TAH. Majority of these cases are diffuse large cell, Burkitt and Plasmablastic lymphomas with atypical presentations and morphology.

For this reason, there is a need in understanding the impact of HIV on the development of different subtypes of lymphoma as this may play a role in the future treatment or the outcome of all malignancies in South Africa. Therefore as part of a 5 year prospective study an expanded immunophenotypic and molecular panel will be used to improve the understanding of how HIV is transforming the lymphoma incidence, pattern and prognosis in the TAH catchments area of South Africa.

One of the objectives would be the implementation of multi-colour flow cytometry in the immunophenotypic characterisation and staging of HIV related lymphomas. Monoclonals not routinely used will be incorporated into selected panels by consensus and based on current and evolving evidence. The development of a cost effective flow cytometry panels may aid to improve diagnostic capacity in resource constrained settings.

**HIV Activation and Inflammation Group (Haig)**

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-G Bekker, Annie Zemlin, Tim Reed, Stanley Loots, Samuel Mburu, Bongani Nkambule

In collaboration with Division of Virology, University of Stellenbosch; Desmond Tutu HIV centre IIDMM, University of Cape Town; and Division of Chemical Pathology, University of Stellenbosch.

**Funding:** SHARP/ PRF Funding

This project aims to delineate affordable and easily measurable markers of the activation and inflammatory status of the immune system in asymptomatic HIV-infection, in order to identify patients who may be at increased risk of progressive disease or adverse events. This would lead to the design of a panel of affordable 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 and thereby ultimately, assist 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.

**Haemostasis and platelet activation in HIV**

**Researchers:** B Nkambule; G Davison; Dr H Ipp

In collaboration with the Department of Biomedical Science, Cape Peninsula University of Technology.

**Funding:** K-funding; NHLS Grants

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 to compare platelet activation in HIV patients with uninfected controls.
Pilot study of innate immune abnormalities in HIV exposed uninfected infants.

**Researchers:** Principle Investigators: M Cotton, MM Esser, T Kollmann, D Speert  
**Collaborators:** H Ipp; C de Beer; J Steenkamp; S Naidoo.

A collaboration with Department of Paediatrics; Tygerberg, University of Stellenbosch; the Division Microbiology and Immunology, University of Stellenbosch, the Division of Haematology, University of Stellenbosch and the Division of Infectious and Immunological Diseases, Department of Paediatrics, University of British Columbia.

**Funding:** Innate immune assessment is to be provided through Burroughs Wellcome Funds from Professor Tobias Kollmann.

The primary aim is to investigate the innate immune response in 25 HEU, and 25 HIV unexposed infants at 2 and 6 weeks of life. HIV PCR will be repeated on all babies at 12 weeks of life. The secondary aim is to process the study results for recommendations of HEU infant follow up. The objectives will be to determine the difference between HEU and UE infants in innate immune function and, if documented, the significance of this difference.

**Free Light chains in patients with HIV:** Establishing local reference ranges and their association with stage of disease, chronic antigen stimulation and effect of HAART in patients with HIV infection

**Researchers:** M Jansen van Vuuren, Professor Erasmus, M Esser, J Germishuys, M Rensburg, H Ipp and A Zemlin

A collaboration between the Division of Chemical Pathology, University of Stellenbosch; the Division Microbiology and Immunology; University of Stellenbosch, and the Division of Haematology, University of Stellenbosch.

**Funding:** NHLS grants

This is a pilot study which will be conducted prospectively and aims at evolving a new paradigm for the diagnosis of TB. The results could add important strategic focus for managing TB in resource constrained environments. The diagnosis of active symptomatic TB in immune competent patients is relatively straightforward but can be challenging in immune compromised patients. We aim to diagnose TB on peripheral blood using flow cytometry by detecting intracellular cytokines released by CD4 T cells following exposure to TB specific antigens. A flow cytometry based simple assay would not involve major infrastructure changes due to widely available flow cytometry platforms nationwide currently utilised for enumerating CD4 counts in HIV patients.

**TB Cytokine Group**

**Rapid, cost effective, blood 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:** R Grewal, S Ndoroma, L Mutema, A Abayomi, C Swanepoel, F Bassa, J Taljaard.

A collaboration between the Division of Haematology, University of Stellenbosch and the Division of Infectious Diseases, University of Stellenbosch.

**Funding:** NHLS and Harry Crossley Project

To establish local reference ranges and to determine the association of free light chain levels with stage of disease, chronic antigen stimulation and effect of HAART in patients with HIV infection

**Biobanking**

**Development of Africa H3 Biorepositories to facilitate studies on biodiversity, disease and pharmacogenomics of African populations**

**Principal Investigator:** A Abayomi

**Co-investigators:** C Swanepoel; E Fakunle; B van Rooyen; R Grewal; A Christoffels; C Rossouw; Michael Sheldon; A Brooks,
A collaboration between NHLS, Stellenbosch University Faculty of Medicine; the Division of Haematology, Stellenbosch University; South African National Bioinformatics Institute (SANBI), University of the Western Cape; the Department of Chemical Physiology, Centre for Regenerative Medicine, The Scripps Research Institute, La Jolla, USA; RUCDR Infinite Biologics, Rutgers University, Piscataway, USA.

This grant supports a two-year pilot effort to establish an H3Africa biorepository that will receive, store, and distribute biological research samples obtained in the H3Africa Initiative. This H3 Africa pilot biorepository is directed by Professor Akin Abayomi, from NHLS (Tygerberg Hospital Business Unit) and the Faculty of Medicine of Stellenbosch University in collaboration with SANBI; Rutgers University (RUCDR), IFASEMB and the SCRIPPS Research Institute for regenerative medicine.

During the pilot phase, the biorepository team will set up governance, operations and test biorepository protocols for human tissues such as nucleic acids and blood. To achieve the Phase I goal, the biorepository will assess its current practices to identify its strengths and weaknesses, upgrade repository practice and infrastructure and conduct Phase II implementation and quality control tests. At that point, the biorepository’s progress will be reviewed and, if the group is found to have made sufficient progress, it will be scaled up to a full-scale H3 Africa biorepository which will be funded for an additional five years. The goals for the Phase II scaled up biorepository will be to build upon the progress made in Phase I to provide, by the end of 3 years of funding (in both Phase I and II), a fully functioning biorepository capable of receiving and distributing samples from and to African countries utilising international standards.

Renewable resources as a means to ensure sustainability in a biobank

Researchers: C Swanepoel, B van Rooyen, R Grewal, E Fakunle, M Sheldon and A Abayomi

An important aspect that underpins most biobanks in the developed world is the establishment of renewable cell lines to maximise their biological resources. This ensures an unlimited source of genetic material for future studies and also eliminates the need to resample patients when they are not available. Establishment of renewable cell lines can either be achieved via through Epstein–Barr Virus (EBV) transformations which give rise to lymphoblastoid cell lines (LCLs) or via the new cutting edge technology, induced pluripotent stem cells (iPSC’s) reprogramming which would become the method of choice in the near future. These type of technologies is not commonly practise in SA most likely due to the ethical and religious views on immortalising cells, therefore a need exist to provide these type of approaches as a service as it would provide long term benefits in the future by providing a platform for disease modelling and drug screening development.

The aim is to optimise the development of renewable cell lines as a sustainable resource for future research in genomics studies

Stem Cell Research Group

The isolation and expansion of Mesenchymal stromal cells for use in cell based therapeutic applications

Researchers: C Swanepoel, B van Rooyen, R Grewal, and A Abayomi

Mesenchymal stromal cells (MSC) are rare multipotent progenitor cells found in bone marrow stroma. Its self-renewal capabilities, ability to differentiate into various cell types as well as its immunosuppressive properties, make these cells an excellent model for future therapeutic applications in MSC-derived
tissue-repair. However, their rarity in the body necessitates the need for in vitro expansion. Eighty to a hundred million cells with a 90% viability can be generated from 1-4ml bone marrow aspirate depending on proper isolation, culturing and subculturing techniques. At present, there is no well-defined protocol for the isolation or characterization of these cells. While many isolation methods exist, none are optimal and the most common methods include plastic adherence, density gradient centrifugation and immunomagnetic selection. The aim of the pilot study is to determine optimal culturing conditions for the isolation and expansion of MSC from bone marrow using the combination of density gradient centrifugation and the plastic adherence capabilities of the MSC cells followed by the identification of a homogenous MSC's population using flow cytometry based techniques.

High priority cell based therapeutic options aimed at ameliorating HIV/AIDS and ultimately aiming for infrastructure development to sustain regenerative and curative therapies

**NHLS Principal Investigators:** A Abayomi, R Grewal, C Swanepoel, B van Rooyen, B Duma.

**Non-NHLS Collaborators:** Professor Alan Christoffels, SANBI; K Moodley, Director Centre for Medical Ethics and Law, Faculty of Medicine, Stellenbosch University; F Bassa, HOD Clinical Haematology, Division of Clinical Haematology, Faculty of Medicine, Stellenbosch University.

International Collaborators: Professor Jeanne Loring and Dr Eyitayo Fakunle at The Scripps Research Institute, Center for Regenerative Medicine, La Jolla, USA; Professors Andrew Brooks and Michael Sheldon from RUCDR Infinite Biologics at Rutgers, The State University of New Jersey, Piscataway, USA; Professor Robert Gallo and collaborators from the Institute of Human Virology, Baltimore, USA; Dr Kambiz Shekdar, Chromocell Corporation, and the Rockefeller Institute, USA; and Dr Joseph O’Neill, Institute of Human Virology, Baltimore, USA.

This proposal is a request for supplementary funding to support an existing NIH H3Africa consortium biorepository grant and establish within this facility, indigenous capacity to refine, test and develop cellular therapies to ameliorate and cure HIV infection. The NIH H3Africa grant award has commenced to develop a full scale biobank facility in Cape Town to support South African, Regional and Continental large scale genomic research and cell based therapies for prevailing and endemic public health disease conditions. The NIH grant was awarded to this group in 2012 for a potential 7 year funding period to a total tune of approximately 10 million USD, for infrastructure and operational development.

The NHLS have defined within its strategic agenda to be the custodians of large scale human Biorepository technology and regenerative medicine in South Africa. Similarly the Department of Science and Technology (DST) have identified the importance of all types of Biorepository capacity development inclusive of human biobanks and will exercise overarching oversight and efforts to identify and preserve and study South Africa’s biodiversity in its entirety.

Outline of high priority HIV related projects being conceptualised by the H3Africa Cape Town Biorepository team are as follows:

In the absence of any foreseeable preventative vaccine options, cellular therapies and therapeutic vaccines are emerging as a strategy for ameliorating the natural history of HIV and producing longevity with or without concomitant HAART. A biorepository is a facility that can accelerate such treatment strategies by providing the infrastructure to:

i. Modify patient cells for HIV resistance by (CCR5) genetic modification in autologous multipotent stem cells as a laboratory research and development strategy as a
Contribution to the growing philosophy of achieving HIV cure in selected patients with severe HIV related complications.

ii. Develop the capacity to grow characterize and culture autologous Mesenchymal Stromal Cells (MSc) for therapeutic trials aimed at altering the immune activation profile in HIV patients as an emerging strategy to modifying the natural history of HIV and TB infection and as an adjuvant therapy to HAART.

iii. Investigate the role of Protein 17 protein (P17) a key HIV product necessary for viral survival as a potential therapeutic target for ameliorating the pathogenesis and oncogenic role of HIV Clade C in humans.

It should also develop the necessary platforms to engage and help define the ethical and legislative governance structures to implement such research and potential clinical interventions in South Africa.

Other

A new paradigm utilizing established Multiplex Flow Cytometry for cost effective viral load monitoring and the identification of sanctuary sites with a view to support evolving strategies aimed at eradication of HIV infection and its multiple associated viral infectious agents namely HPV and HCV

Principal investigator: A Abayomi,
NHLS Co-Investigators: W Preiser, M Andersson
Local Collaborators: J Nachega, Director Centre for Infectious Disease, Tygerberg Hospital.
International Collaborators: B Patterson, MD (CEO, IncellDx, Inc.) and K Shults BSc. (Director of Research, IncellDx, Inc Menlo Park, California, USA), and T Elbeik, Ph.D. (Elbeik Associates, LLC, Consulting and Project Management, San Francisco, California, USA).

In the June 2010 report “The Long Run Costs and Financing of HIV/AIDS in South Africa,” the Republic of South Africa has over 5 million people infected with HIV with an estimated 5 million new infections by 2030. By following the current treatment paradigm (antiretroviral therapy monitored by CD4 counts and plasma viral load) it is estimated that in 2012 resources amounting to between R20 and R25 billion are needed for a multitude of different programs to combat HIV, and the amount will continue to increase to an estimated R30 to R40 billion annually by 2022.

This is further compounded by unprecedented increases in TB, HPV, and HCV. It is therefore clear that the conventional paradigms to treat HIV has its limitations, is not financially viable and compounds the economic and political instability of the Republic of South Africa and surrounding regions. New approaches for the monitoring and treatment of HIV are needed. Specifically, tests that identify the cellular location and active state of HIV is critical to adapt current therapies, and develop 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 the HIV along with cell surface markers of HIV pathogenesis to facilitate the development of new and significantly more effective treatment options, including targeted and eradication of HIV in the Republic of South Africa. This technology, known as Simultaneous Ultrasensitive Subpopulation Staining/Hybridization In Situ or SUSHI, was invented by Professor 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 are detectable. Identifying the cell source of actively replicating HIV allows for targeted therapy (immunologic and pharmacologic) and eradication, a strategy unattainable by current plasma viral load or CD4 counts assays.

SUSHI is a single platform based assay and is superior, and more economical than conventional yet 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, are 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 R&D research. 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, with utility in support of effective treatment throughout all regions of the Republic of South Africa, irrespective of existing infrastructure.

Climate Change and environmental health
Professor Akin Abayomi is 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 chapter is a collaboration with SANBI and the Department of Environment and Water Affairs. It is a follow up study of the long term mitigation scenarios on climate change.

**Teaching and Training**

**Undergraduate**

Teaching and training of undergraduate medical students continues to be an important part of The Division's goals and priorities. The Haematology module was chaired by Dr B.Walker. This module is presented to the MBChB III students and encompasses the important basics of haematological disease. We are also involved with lectures and tutorials as part of the Essentials of Disease processes module which is presented to MBChB I students. The MBChB IV and V students also 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 registrar's in the division actively participate in this program which runs throughout the academic year.

**Postgraduate**

In the past year the Division has recruited three new haematopathology registrars. The Division also contributes towards training a clinical pathology registrar every year. During 2012, the Division, managed to train two PhD and one Masters Science student. Dr H Ipp supervised some of the students who graduated and continues to be actively involved with the supervision of many science students in collaboration with other divisions and departments. Professor Abayomi, Dr R Grewal and Dr B Walker were also involved with supervising students.

The division also contributes towards training of internal medicine registrars rotating in clinical haematology every 3 months. Specialists, postgraduate students, and medical technologists from the Division attended several courses during 2012 as part of continuous professional and skills development.
Outreach and Community Interaction
Professor Abayomi and Dr Grewal went on a one week exchange outreach to departments of Haematology at the Abuja National Teaching Hospital, Abuja General Hospital and Bingham University Medical School in Nigeria. Ward rounds and 2 lectures were delivered:Haematology curriculum in post graduate studies in South Africa.
New advances in diagnostic haematology

Professional Development

Number of postgraduate students:

MMed (Haem Path) current: 7
FCHAem Part 1: 4
Hons BSc graduates in Haematology : 0
PhD (current): 2
MSc graduated: 1
MMed graduated: 1
Clinical pathology: 1

Research Outputs

International invited speakers


A Abayomi. Management of Lymphoma in HIV and non-HIV patients in low-to-middle income countries in Africa; Haematology curriculum planning for Africa ; and Basic concepts of flow cytometry. 2nd ASCO-AOI-ASCP MCMC Faculty List, 21–24 January 2013, Eldoret, Kenya.

National invited speaker

A Abayomi. Attended the ICON Meeting for Protocol Development at ICON headquarters in Durbanville, Cape Town.

A Abayomi. Attended the ICON Meeting for Protocol Development for Haematological Disorders.


A Abayomi, R. Grewal; B. Walker. 4th International Pediatric Haematolgy/Oncology Workshop, 19-20 March 2012, Tygerberg Hospital.

A Abayomi, R. Grewal. Attended 1st Annual ARESA Research Ethics Seminar, presented by The Centre for Medical & Ethical Law, University of Stellenbosch, 30–31 August 2012.

A Abayomi , R. Grewal. Attended Advanced TB diagnostic Research at University of Cape Town Lung Institute, 6–9 March 2012.

A Abayomi, R. Grewal. Attended Good Clinical Practice Refresher Course at Tygerberg Hospital on 23 May 2012.


A Abayomi. Developing Biorepository capacity in Africa to support indigenous research. ASLM Conference, 1–7 December 2012, Cape Town.
Posters

International
The 17TH Congress of European Haematology
Association congress Amsterdam, Netherlands
June 14-17, 2012. Haematologica vol 97 s1
June 2012

Large unstained cells on routine haematology
analyzer correlate with immune activation
levels in asymptomatic treatment-naïve HIV
infection. H Ipp, N Vanker, A Abayomi

Serum free light chains in patients with HIV: Their
association with markers of disease stage and
severity, and the effect of antiretroviral therapy. A Zemlin, H Ipp, J Germishuys, M Rensburg, M Esser, M Janse van Vuuren, R Erasmus

Platelet flow cytometry and markers of immune
activation in asymptomatic, treatment-naïve
HIV infection, B Nkambule, H Ipp, R Glashoff

National

Annual Academic Year Day: Stellenbosch
University 15–16 August 2012

Large unstained cells on routine haematology
analyzer correlate with immune activation
levels in asymptomatic treatment-naïve HIV
infection. N Vanker, H Ipp

Decreased responsiveness of monocytes to LPS
in chronic HIV-1 infection as detected utilising
an optimised whole blood LPS stimulation assay. K Poovan, D De Swart, H Ipp, RH Glashoff

Elevated levels of the cardiovascular risk marker
asymmetric dimethylarginine (ADMA) in patients with HIV and their correlation
with other markers of immune activation. CL
Hudson, AE Zemlin, H Ipp

Serum protein electrophoresis patterns in
patients with HIV not on antiretroviral therapy. S Maleka, A Zemlin, H Ipp, J Germishuys

Oral presentations / referate

Stellenbosch University Academic Day

Increased anaemia-associated erythrocyte
apoptosis (erythroptosis) in chronic HIV
infection: Relationship with immune activation
and oxidative stress. S Loots, D De Swart, H Ipp, RH Glashoff

Exvivo characterisation of markers of b-cell
activation, exhaustion, and apoptosis in
asymptomatic HIV-infected individuals. TD
Reid, H Ipp, RH Glashoff

Serum free light chains in patients with hiv
not on antiretroviral therapy. S Maleka, A Zemlin, H Ipp, J Germishuys

PathPoint Congress (September 28–30, 2012)

Increased catalase activity and lipid peroxidation
markers with decreased total antioxidant status
in treatment-naïve asymptomatic HIV-infection. S Mburu, JL Marnewick, A Abayomi and H Ipp
Platelet flow cytometry and markers of immune activation in asymptomatic, treatment-naïve HIV infection. BB Nkambule, RH Glashoff and H Ipp.

Recent abstract bibliography


Publications

Abstracts


Large unstained cells on routine hematology analyzer correlate with immune activation levels in asymptomatic treatment-naive HIV infection. H Ipp, N Vanker, A Abayomi

Serum free light chains in patients with HIV: Their association with markers of disease stage and severity, and the effect of antiretroviral therapy A Zemlin, H Ipp, J Germishuys, M Rensburg, M Esser, M Janse van Vuuren, R Erasmus

Platelet flow cytometry and markers of immune activation in asymptomatic, treatment- naïve HIV infection. B Nkambule, H Ipp, R Glashoff.

Journals


Grewal RK and Abayomi A. Bone marrow morphological features and diagnostic value in paediatric disseminated tuberculosis in the setting of increased HIV prevalence. Accepted SAMJ October 2012


Journal articles in development:

Evaluation of a high throughput flow cytometer that integrates sample preparation and analysis in one system for Lymphocyte Subsets analysis in the setting of an HIV patient management facility in a developing country.

The HIV Pandemic: Cellular therapies, stem cells and biobanking.

Migration of b-clade HIV-1 epidemics between North America and the Caribbean.

Book chapters


Conference presentations

National conferences: 6
International conferences: 5
Division of Medical Microbiology and Immunology

Head: Professor A Whitelaw

Diagnostic Service

The Division of Medical Microbiology has been SANAS-accredited since February 2009 and offers a high quality diagnostic service in microbiology, immunology and serology.

This was a challenging year for the division. Professor Wasserman resigned as head of the division in May 2012, and Dr Heidi Orth was acting HoD until December 2012, when Professor Andrew Whitelaw was appointed. In addition, the microbiology laboratories in the Western Cape underwent a process of consolidation during 2012, as part of the NHLS strategic plan to consolidate certain specialised fields.

The microbiology laboratory at the Green Point Complex was closed and microbiology samples from the greater Winelands and surrounding northern districts were diverted to the NHLS Microbiology Laboratory at Tygerberg Hospital.

Our service delivery area thus expanded to include four regional hospitals (Karl Bremer, Paarl, Worcester and Helderberg), 17 district hospitals (such as Khayelitsha, Eerste River, Hermanus and Vredenburg) and over 122 primary healthcare clinics. Samples from these new areas accounted for 55% of the samples received recently with the remaining 45% coming from Tygerberg Hospital itself.

The impact of this increased workload was felt to a great extent. The number of tests registered at our laboratory in October 2012 compared to October 2011 increased by 63%.

Since the closure of Green Point laboratory in August 2012, we registered an average of 57% more tests compared to the same 3-month time period in 2011.

The Immunology Unit was actively involved in the consolidation plans for the CD4 ARV roll-out and maintains a high quality service with increasing sample volumes despite new laboratory sites being developed. Further significant increase in volumes of RPR and FTA were noted for the syphilis diagnostic bench, with syphilis testing increasing by 20% in the reporting period. The increase in tests was also due to the closure of the Greenpoint laboratory. The acquisition of an automated Syphilis screening instrument will be a necessity in future.

SANAS granted continued accreditation status to immunology when the laboratory was inspected in August 2012.

Consultants and registrars from the division continue to offer a comprehensive consultative service, including 24 hour on-call availability, ward rounds in ICUs, and clinical meetings. In March 2013, the division commenced with an antibiotic-stewardship outreach programme at Khayelitsha District Hospital and Worcester Provincial Hospital. Members of the division regularly talk at local society workshops and hospital CME functions. The consultant of the Immunology Unit provides a clinical service in immunology in collaboration with the paediatric and adult infectious diseases services at Tygerberg Hospital. A further weekly clinical service is provided at the Paediatric and Adolescent Rheumatology Clinic at Tygerberg Hospital. 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.

In February 2013 the laboratory received the GeneXpert instruments, as part of the national rollout and is now offering this service to Tygerberg Hospital. New tests in immunology include the Toxoplasma IgG avidity, Intrinsic Factor, as well as the Thyroid Stimulating Receptor Antibody Tests.
Members of the division are involved in a number of provincial and national bodies. These include the discipline-specific expert committees, the SA Society of Clinical Microbiology, the NHLS Microbiology Advisory Committee, the Western Cape Provincial Quality Improvement Committee, the Infection Control Society of Southern Africa, and the Federation of Infectious Disease Societies of Southern Africa. The Immunology Unit is represented at the NHLS Expert Committee for Immunology, The South African Immunology Society (SAIS) Education Committee, The Primary Immunodeficiency Working Group of Allergy Society of South Africa (ALLSA), The Board of the African Society for Primary Immunodeficiencies (ASID), The Board of the HIV Outreach Programme and Education (HOPE) NGO.

Research

This division has focused on four well defined research themes which include the laboratory diagnosis of tuberculosis; the epidemiology and pathogenesis of staphylococcal infections; the immunopathology in HIV-exposed infants; and the investigation and profile of primary immunodeficiency in South Africa.

Research Projects

Birth cohort study to focus on the immune and environmental risk parameters of HIV-exposed infants

**Investigators:** Dr M Esser; Professor M Cotton (KIDCRU)

A funding application with the Peter Wall Institute of Advanced Studies from and in collaboration with the University of British Colombia, Vancouver was successful for a birth cohort study to focus on the immune and environmental risk parameters of HIV-exposed infants which commenced in July 2012. Sub-studies on CMV prevalence, toxoplasmosis prevalence, placental morphology, immune activation markers of neonates, CD4 and viral loads, nutritional observation and neurodevelopmental outcome are part of this multidisciplinary study.

The Primary Immunodeficiency Registry of South Africa

**Investigator:** Dr M Esser

The registry continues to promote the networking for laboratory diagnosis and treatment of patients with primary immunodeficiencies. More than 200 patients are recorded nationally to date and ethical permission and collaboration of WITS University was added in 2012. The Immunology Unit Tygerberg provides the only dedicated clinical and laboratory service for Primary Immunodeficiency in South Africa.

Population structure, host cell interaction and pathogenesis of Staphylococcus aureus strains isolated at Tygerberg Hospital, South Africa

**Investigators:** Professor E Wasserman, W Oosthuysen, Dr H Orth, Professor B Sinha

This study continues the collaboration concerning the pathogenesis of staphylococcal infection with researchers at Würzburg University, Germany, and is funded by the NRF and the German equivalent. The aim of the study is to describe the population structure of a collection of S. aureus strains isolated from clinical cases at Tygerberg Hospital. The strains are characterised by various strain typing methods including MLST, spa-typing and pulsed field gel electrophoresis and the main genetic virulence markers are identified. Virulence assays (adherence and invasion, as well as the ability to induce cell death) are also investigated. Mr Oosthuysen submitted the work as a PhD thesis at the end of 2012.
A phenotypic and genotypic characterisation of strain types, virulence factors and agr groups of colonising S. aureus strains associated with bloodstream infection

**Investigators:** Professor E Wasserman, Dr K Hoek, K Karayem

**Funding:** MRC

This study aims to determine the epidemiology and correlation between S. aureus causing bloodstream infections and nasal colonisation. Furthermore, the study will investigate agr group types, determine agr functionality and investigate the virulence factor(s) that may facilitate invasion of these colonizing strains. This will provide clinically useful information for the purposes of infection control and the prevention of invasive S. aureus disease.

**The rapid diagnosis of Cryptococcal meninigitis using the lateral flow assay on CSF**

**Investigators:** Dr A Lourens, Dr C Samuel

**Funding:** NHLS, K-projects

The study aims to evaluate the performance of the commercial lateral flow assay (LFA) on CSF samples for the diagnosis of cryptococcal meningitis using the latex agglutination test and culture as the reference standards. The second part of the study is aimed at comparing the performance and reproducibility of the cryptococcal LFA on CSF samples when performed as a point-of-care (POC) test in 3 district hospitals compared with the CLAT, culture and LFA performed in an accredited laboratory.

**An audit of blood culture standards at a secondary hospital in Cape Town**

**Investigators:** Dr MS Abrahams, Dr H Orth

Blood culture contamination is a common problem, leading to increased laboratory costs, and potentially inappropriate antibiotic therapy. Although guidelines for blood culture collection exist, the degree to which they are followed is uncertain. The aim of this audit is to assess adherence to best practice guidelines for the taking of blood cultures and to determine the institutional blood culture contamination rate at a local secondary level hospital.

**Molecular Diagnosis of Mycobacterium tuberculosis from Urine specimens of patients with suspected Tuberculosis disease**

**Investigator:** Dr K Hoek

This study aims to develop a novel molecular diagnostic test to detect small trans-renal DNA fragments from M. tuberculosis in urine specimens from patients suspected with tuberculosis disease. The use of urine as diagnostic specimen for the identification of mycobacterial DNA is an attractive prospect in patients with paucibacillary disease (HIV infected) or in whom sputum is difficult to obtain (children) and is less invasive than current alternatives.

**Evaluation of Bioplex 2200 in detecting auto antibodies in patients with SLE**

**Investigator:** Dr M Esser, Dr E Richter

Immunofluorescent auto-antibody screen is the current gold standard because of high sensitivity and availability of titres. However, interpretation of positive/negative and patterns are subjective, not standardised and there is a high intra- and inter- laboratory/observer variability, as also inconsistencies in classification. The method is time and labour intensive and requires experienced staff. Automated systems have been developed to address these issues and the study is evaluating one or more of these systems on clinically profiled SLE patients.
ARVs are now accessible and have been provided by the SA Government since 2003. The first obstacle in caring for HIV infected children in South Africa has thus been overcome. However, for antiretroviral therapy to work, patients must adhere to a daily regimen of ARVs for life. This study aims to investigate the factors leading to virological failure in children on ARVs at local Western Cape Clinics (such as Delft Clinic) and then based on these findings to develop an intervention strategy using Hope Community/other Health Workers. The study will thereafter focus on optimising the role of the HOPE Community Health Worker.

Point of care CD4 testing to assess maternal ARV eligibility – the paediatric visit as intervention opportunity for failed maternal care

In the study of evaluating maternal care using point of care testing (POCT) for CD4 counts at Tygerberg Hospital, 52 patients were enrolled, counselled, and given a referral letter back with the provisional Point of Care PIMA finger-prick CD4 count. More than one third of patients identified with the PIMA result qualified for ARVs.

A comparative study of neuroprotective strategies in neonatal hypoxic ischaemic encephalopathy

Perinatal hypoxic ischaemic insult causes varying degrees of neonatal encephalopathy. It is the leading cause of death in term newborns in South Africa. Serum cytokines IL-1β, IL-6 and MIP-1α will be assayed and compared to brain cytokines as less invasive markers of brain injury and to monitor response to intervention by standard cooling protocols and or morphine.

Immunological parameters of HIV exposed uninfected infants with severe infectious morbidity

HIV exposed but uninfected infants as well as adults have a high frequency of HIV-specific T regulatory cells in their peripheral blood. The aim of this project is to document the presence of HIV specific immune response in HIV uninfected infants and to add to the understanding of the role Regulatory T cells (Treg) in HIV infection. We hypothesise that HIV specific Treg function decreases the risk for infection following perinatal HIV exposure. HIV infection is characterised by hyper-activation of the immune system and chronic inflammation, so correlates of protection from infection may indeed relate to immune suppression with important implications for prevention of infection with HIV.

Teaching And Training

Undergraduate

This division maintained its extensive involvement in training undergraduate students in different modules. This involves an extensive lecture programme, weekly laboratory rotations for MBChB students, hosting elective students, as well as lectures to the BSc Dietetics students.

Trainee medical technologists from the Cape Peninsula University of Technology underwent practical training and received lectures from technologists in this division. The 100% pass rate for medical technologists and technicians that trained in the immunology section and wrote the Board examination up to this report has been maintained and the student that qualified in 2012 obtained 80% in the board examination.
Pathology registrars from diverse divisions as well as the Infectious Diseases Fellows from Tygerberg, UCT and Red Cross Children’s Hospital rotate through the Immunology Unit as part of their immunology laboratory training. UWC experiential students are regular rotators in the Immunology Unit.

Postgraduate
During the period under review, four microbiology registrars were registered in the department. In addition, two clinical pathology registrars rotated through the division, as do infectious disease registrars as part of the CMSA certificate in ID training. The division also contributes to the training in infection control offered by the Unit for Infection Prevention and Control at Stellenbosch University. The training offered to registrars and infection control students includes formal tutorials, practicals and mentorship. Members of the division are involved in supervising BSc (Hons), MSc and PhD students, as well as contributing to the lecture and tutorial programme offered to the BSc (Hons) students.

The first HPCSA registered intern scientist in Immunology commenced training, in collaboration with Synexa Life Sciences, in the Immunology Unit.

Professional development

Postgraduate candidates graduated: 4
1 FC Path (P Naicker), 2 MScMedSc (S Naidoo, R Adams), 1 Hons BSc (N Williams)

Postgraduate candidates enrolled: 6
(4 MMed (Micro), 2 doctoral, 2 Hons BSc)

Dr Rena Hoffman, a consultant from the division, obtained her MPhil degree in Health Science Education from Stellenbosch University at the end of 2012.

Members of the division attended a number of workshops and courses during the review period, including the SA TB congress, the Pathpoint congress, the African Society for Immunodeficiency Congress, the European Society for Immunodeficiency Congress, the European League against Rheumatism Congress, the ALLSA Congress, the Federation of African Immunology Societies Congress and various industry sponsored workshops, education workshops and communication skills workshops.

Close collaboration with the African Society of Immunodeficiencies was again established with a teaching school for primary immunodeficiencies hosted at the Allergy Congress in Cape Town in June 2012 by Dr M Esser. A national working group for Paediatric Infectious Diseases – PIDSA – was constituted under the auspices of the Allergy Society of South Africa, with Dr Esser chairing the group.

Honours

Two students from the Division of Medical Microbiology, Will Oosthuysen (PhD) and Dr Shareef Abrahams (MMed), both won awards for the best oral and best poster presentations respectively at Stellenbosch University’s Faculty of Medicine and Health Sciences Annual Academic Day 2012.

At the 2nd ASID Congress March 2012 in Hammameth, Dr Esser was elected chair of the society and president for the 3rd ASID congress in South Africa June 2013.
Research output

Publications:

Journal Articles (subsidised)


Esser M. Primary Immunodeficiency - missed opportunities and treatment challenges. *Current Allergy & Clinical Immunology* 2012; 25(4): 184–188


Streicher Em, Muller B, Chihota V, et al. Emergence and treatment of multidrug resistant (MDR) and extensively drug-resistant (XDR) tuberculosis in South Africa. *Infection Genetics and Evolution*, 2012; 12: 686–694

Wolzak Nk, Cooke Ml, Orth H, Van Toorn R. The Changing Profile of Paediatric Meningitis at a Referral Centre in Cape Town, South Africa. *Journal of Tropical Pediatrics* 2012; 58(6): 491–495

Journal Articles (non-subsidised)


Conference presentations

International: 7
National: 4
Local: 4
Division of Medical Virology

Head: Professor W Preiser

Diagnostic Service

The diagnostic section’s workload again increased significantly – by more than 24,042 tests year-on-year, to a total of 192,537. Most of this increase is due to the antiretroviral roll-out programme, with test requests for HIV viral load increasing by 34%, for HIV PCR by 19.3%, and for genotypic HIV drug resistance by 29%.

In 2012 the laboratory tested 336 respiratory samples as part of the influenza surveillance programme. In contrast to the previous year where pandemic influenza A(H1N1) 2009 dominated, the 2012 season was dominated by influenza A(H3N2), followed by influenza B. Once again, about 10,000 serum specimens from the Western Cape were tested as part of the HIV and herpes simplex virus (HSV) annual antenatal survey.

In-house real-time PCR tests for mumps virus and enteroviruses as well as sequencing of the HIV integrase gene are now accredited, while measles virus PCR and enterovirus and adenovirus genotyping were added to the repertoire, but not yet accredited.

Tygerberg is the only NHLS laboratory in the coastal region to routinely perform cell culture and offer virus isolation. It thus provides training also for registrars and student medical technologists from Groote Schuur Hospital laboratory. Tygerberg is also the only laboratory in the whole country still performing Coxsackie virus neutralisation assays and one of only two NHLS laboratories to perform HIV drug resistance testing for routine diagnostic purposes.

The annual SANAS accreditation visit confirmed the excellent quality of the work done by the diagnostic section. In addition, all areas performed well in various external quality assurance programmes. Turnaround times were affected by HIV viral load registrations being done by core laboratory, instrument breakdown and staff shortages. We hope to improve the situation by the appointment of approved new posts.

Outreach visits to NHLS laboratories and hospitals in various localities of the Western Cape and to NHLS Mthatha had to be postponed due to financial restraints.

Research Projects

The division’s research focuses on HIV-1 as a major health problem in South Africa and the region, encompassing projects on genetic, immunological and clinical and translational aspects; this is complimented by research on selected other relevant topics.

Molecular characterisation and diversity of HIV
Researchers: Professor S Engelbrecht, Dr RH Glashoff, Dr E Vardas, Dr GB Jacobs (post-doctoral fellow), E Wilkinson (PhD student), S Isaacs (MSc student), W Msimanga (MSc student), C Tamandjou (BSc Hons student)
Collaborators: Professor S Seedat, Department of Psychiatry, Tygerberg; Dr T de Oliveira, Africa Centre for Health and Population Studies, University of KwaZulu-Natal; Professor J Joska, Department of Psychiatry, UCT; Professor R Paul, Department of Psychology, University of Missouri, St. Louis, USA.
Funding: Poliomyelitis Research Foundation (PRF), University of Stellenbosch, NHLS Research Trust, National Institutes of Health (NIH), Medical Research Council (MRC)

One of the features of HIV-1 is its extreme genetic diversity, which impacts on diagnostic assays, antiretroviral treatment, prevention and vaccine development. It is well known that HIV-1 subtype C strains predominate in South Africa. However, an unusually large number
of subtypes and unique HIV-1 recombinants (URFs) have recently been identified from South African patients, including complex recombinants (ACD and AFG). This may be an indication that the homogeneous subtype C epidemic in the country is changing. It is essential to study HIV-1 non-subtype C viruses on an ongoing basis in order to gain a better understanding of their characteristics and the viruses in circulation in South Africa.

The construction and characterisation of infectious HIV-1 subtype C proviral clones is another important activity. Much of what we have learned about HIV biology has been with the use of studying infectious HIV proviral molecular clones in in vitro assays. These assays are normally based on HIV-1 subtype B as this is the predominant strain circulating in North America and Europe. Therefore we are constructing and characterising new infectious HIV-1 subtype C infectious clones, based on the strains circulating in South Africa. These clones will be used in various cell culture and phenotypic assays in our laboratory.

**Immunological aspects of chronic HIV-1 infection: cellular role players in immune activation and targets for immunotherapeutic intervention**

**Researchers:** Dr RH Glashoff, Dr H Ipp (haematopathological pathologist enrolled for part-time PhD), Dr C de Beer, D de Swardt (PhD student), K Poovan (MSc student), T Reid (MSc student), S Loots (MSc student), K Reddy (MSc student)

**Collaborators:** Dr A Zemlin, Division of Chemical Pathology Tygerberg; Professor L G Becker, Desmond Tutu HIV Foundation, UCT; Professor E Vardas, Lancet Laboratories, Johannesburg; Dr L Azzoni, Wistar Research Institute, Philadelphia, USA; Dr M Malnati, San Raffaele University, Milan, Italy.

**Funding:** DST SHARP, PRF, NHLS Research Trust

Several projects are currently studying immune activation and inflammation in chronic HIV infection, its impact on immune cell numbers, phenotypes and function and the potential for immunotherapeutic intervention to minimise activation-associated pathology. 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.

Recently we have shown that dendritic cell depletion in chronic HIV-1 infection is exacerbated by active pulmonary TB and ARV therapy does not lead to full restoration of these cells. The TNFα receptor 2 (TNFR2) is significantly upregulated on DCs and the interaction of this receptor with TNF may prime these cells apoptosis. We have also recently shown that the expanded inflammatory monocyte subset in chronic HIV-1 may play an important role in clearance of dying red blood cells. Apoptotic erythrocytes are also markedly increased in HIV-1 infection, and these cells are preferentially taken up by the inflammatory monocyte subset. This work thus defines an important new pathway which could be driving expansion of inflammatory monocytes.

A major thrust of the research is to define novel cost-effective surrogate markers of immune activation for use in the South African setting and also to investigate the neuropeptide vasoactive intestinal peptide (VIP) as a potential therapeutic agent. Included in these studies are HIV-TB co-infected individuals and individuals on short-term antiretroviral therapy (ART) to assess the impact of both on immune cell activity and marker expression.

The complete list of sub-projects include: modulation of apoptosis of CD4+ T cells from HIV-infected individuals with the neurotransmitter vasoactive peptide (VIP) and other biomediators; blood dendritic cells (DCs) in HIV-infected individuals in South Africa and the impact of TB co-infection and.
immune modulation; B-lymphocyte activation and exhaustion in chronic HIV infection: novel surrogate markers of generalised immune activation and selective modulation of aberrant B cell responses using vasoactive intestinal peptide (VIP); erythrocyte apoptosis (erythropoiesis) and anaemia in chronic HIV infection: relationship with immune activation and viraemia; monocyte/macrophage function in chronic HIV infection: impact of immune activation and modulation with vasoactive intestinal peptide (VIP); monocytes in chronic HIV infection: expression of gut-associated chemokine homing receptors, bcl-2 and PPAR-α and their relationship to immune activation; and, impact of TB co-infection on expression of T cell inhibitory markers PD-1 and TIM-3, and their relationship to immune activation.

Antiretroviral drug resistance: epidemiological, clinical and diagnostic aspects

Researchers: Dr G U van Zyl (virological pathologist enrolled for part-time PhD), Professor W Preiser, Professor S Engelbrecht, R Fisher (PhD student), M Claassen (medical technologist), D Hart (MSc student), D Njenda (MSc student)

Collaborators: Professor M Cotton, Paediatric Infectious Diseases Unit Tygerberg; Drs M Zeier and J Taljaard, Adult Infectious Diseases Unit, Tygerberg; Dres C Scheller, J Bodem and Professor A Rethwilm, University of Würzburg, Germany; Drs E Goemaere, G van Cutsem, C Malavazzi, Médecins Sans Frontières, South Africa; D Smith and R Haubrich, University of California, San Diego; S Travers and N Wood, University of the Western Cape; Dr T de Oliveira, Africa Centre / University of KwaZulu-Natal; Professor R Shafer, Stanford University.

Funding: PRF, NHLS Research Trust; Department of Health CCMT Grant; Centre for AIDS Research (sub-award); University of California San Diego (sub-award)

The use of nevirapine (NVP) for the prevention of mother to child transmission of HIV (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, when patients require therapy. Furthermore, deep sequencing methods used detect minor resistant variants may not reliably quantify these variants due to PCR or sequencing error. In this project a new platform to quantify these minor variants is being investigated. Sequencing is currently in progress and analysis of results will follow in the latter half of the year.

Stavudine (D4T) as a component of first-line therapy in the national antiretroviral roll-out programme was replaced by Tenofovir (TDF) in adults and by Abacavir (ABC) in children from April 2010. To study the effect of these changes on resistance patterns, therapy information from request forms and resistance mutations detected in the laboratory were analysed. This audit of resistance frequencies in more than 1500 specimens submitted to the division's diagnostic service shows a change in the NRTI mutation patterns between 2007 and 2012. The guideline change was associated with a rapid increase in TDF use from < 2% between 2006-2008 to 41% of patients in 2011 and an increase in the frequency of the K65R mutation. Similarly, in children ABC use increased with an associated increase in the L74V mutation. This study has been accepted for publication.

A new study will investigate the fitness benefit of the reverse transcriptase mutation A62V when co-occurring with M184V and K65R in HIV-1 subtype C. In an audit of HIV-1 drug resistance results in a subtype C population we found an unexpected association of A62V with M184V and K65R. This suggests fitness interactions. We are constructing molecular clones that harbour combinations of these mutations to assess the fitness interactions by phenotypic characterisation and growth competition assays.
Viral hepatitis

Researchers: Dr M I Andersson, Professor W Preiser, Dr RH Glashoff, T Maponga (MSc student), N Chotun (MSc student)

Collaborators: Dr S Ijaz and Professor RS Tedder, Health Protection Agency, London, UK; Dr E Nel, Department of Paediatrics Tygerberg; Professor S Moore, Paediatric Surgery Tygerberg; N du Toit, Department of Oncology Tygerberg; Drs B Robertson, W Spearman and Professor M Kew, UCT; Drs P Veersamy and V Fredlund, UKZN; Dr R Santella and Professor J Jacobson, Columbia University, New York

Funding: Wellcome Trust, PRF, NHLS Research Trust.

Viral hepatitis and related conditions form an emerging research theme. A study into the prevalence and character of hepatitis B virus (HBV) infection in HIV-infected pregnant women in the Western Cape has been completed and published. Another related study comparing HBV infection in HIV-infected and HIV-uninfected pregnant women has been submitted for publication.

A cross-sectional study of the prevalence of HBV infection in HIV-exposed infants tested at Tygerberg Hospital has been concluded and is being written up for publication. The prevalence of HBV infection in infants born to HIV-positive mothers is being investigated through a retrospective cohort study making use of banked samples from a study performed by the International Maternal Paediatric Adolescent AIDS Clinical Trials Group.

The possible emergence of HBV drug resistance driven by antiretroviral drug exposure is being studied in patients at Tygerberg Hospital, and studies of possible mother-to-child transmission of resistance HBV variants are being prepared.

Immune aspects of HIV-1- hepatitis B virus (HBV) co-infection are studied to determine the impact of HIV-1 infection on fibrosis and markers of immune activation or inhibition in HBV-coinfected individuals. In particular we are investigating whether gastrointestinal tract (GIT) leakage in HIV-1 infection impacts on markers of immune status in HBV infection. GIT leakage products are thought to be a major factor in HIV-1 pathogenesis, however the importance of increased gut leakage products on other markers of immune status in the context of HBV infection have not been examined. An important aspect of this research is an examination of liver fibrosis and how it is related to other immune factors, and why co-infection exacerbates fibrosis in HBV infection.

A new 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 characterization of HBV, aflatoxin adduct testing and patient survival time post diagnosis. Finally, a case report that we recently published pointed to hepatitis E virus (HEV) infection possibly playing a more important role in South Africa that previously thought. We are currently studying the prevalence of HEV infection in a cohort of HIV infected patients at Tygerberg Hospital, using serological and PCR testing to identify seroprevalence and any cases of chronic HEV infection.

Opportunistic viral infections and related conditions

Researchers: Dr C de Beer, Dr G U van Zyl, Professor W Preiser, Dr RH Glashoff, Professor S Engelbrecht, Ms N Chotun (MSc student), Ms S Isaacs (MSc student), Ms J van Staden (BSc Hons student), Ms I Smit (BSc Hons student)

Collaborators: Dr M Esser, Immunology Unit NHLS Tygerberg; Dr M Zeier, Infectious Diseases Clinic Tygerberg; Professor H Botha, Gynaecological Oncology Unit Tygerberg; Professor M Cotton, Paediatric Infectious Diseases Unit Tygerberg; Professor G Theron,
Department of Obstetrics and Gynaecology
Tygerberg; Dr E Nel, Department of Paediatrics
Tygerberg; Professor S Moore, Paediatric Surgery
Tygerberg; N du Toit, Department of Oncology
Tygerberg; Professor L Warnich, Department of
Genetics, Stellenbosch University; Drs M Joffe, P
Ruff and A Sparaco, Wits; Professor T Kollmann
and D Speert, University of British Columbia,
Vancouver, Canada; Dr Anna Giuliano, Moffitt
Cancer Research Institute, Tampa, USA; A
Giesen, University of Heidelberg, Germany

Funding: Wellcome Trust, PRF, NHLS Research
Trust, NIH, Moffitt Cancer Research Institute,
Bill & Melinda Gates Foundation, Harry Crossley
Foundation.

To assess the magnitude of efavirenz (EFV)-
associated neuropsychiatric side effects and any drug level or pharmacogenetic
associations with toxicity, patients who are
initiated on a combination antiretroviral
treatment are recruited and neuropsychiatric
findings recorded at baseline and on follow-
up visits. EFV hair levels are used to measure
drug exposure and genetic polymorphisms
associated with the metabolism of EFV are
detected by collecting DNA from saliva.

To identify factors associated with poor
compliance, in order to better identify those
patients who fail HIV therapy, the prevalence of non-psychotic psychiatric disease is being investigated in a cohort of HIV-positive patients
attending Tygerberg Hospital. Questionnaires
are used to identify substance misuse, psychiatric symptoms, dementia and levels of
compliance and HIV viral load is determined.
Analysis of 80 patients recruited so far shows
that poor compliance is associated with depression.

While the rate of mother-to-child transmission of HIV has been reduced remarkably over the
past few years, increasing evidence suggests
immune abnormalities in uninfected children
born to HIV infected mothers (HIV exposed
uninfected; HEU). Even in the absence of
PMTCT of HIV, HEU infants far outnumber
HIV-infected infants. These HEU infants and
children are being recognised as a frequently
overlooked higher risk group for infectious and
non-infectious morbidity than their unexposed
counterparts. Some of the known risk factors
contributing to excess morbidity of HIV-infected
and HEU infants include poor placental transfer
of maternal antibodies, perinatal exposure to
antiretroviral drugs and increased exposure to
pathogens from immune-deficient individuals
in the household.

Follow-up and care of HEU infants should be
an integral part of child health programmes.
The above studies all aimed to investigate
different immune parameters and function in
HEU infants and compare it to the unexposed
control group. Innate immunity was assessed
by investigating different Toll-like receptors
and adaptive immunity was assessed through
measuring the antibody levels before and after
routine vaccinations. Immune activation, B cell
memory and apoptosis markers was evaluated
by flow cytometric assays to provide insight into
the difference found in the adaptive immune
responses between the two groups.

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 human immunodeficiency
virus (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.

An internationally collaborative evaluation of human papillomavirus (HPV) vaccination in young women as a preventative measure against HIV-1 acquisition is being conducted in preparation for a larger Phase III trial planned for 2014/2015. 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 prevalence of other STIs (syphilis, gonorrhoea, chlamydia and HSV-2) is also being determined. The study will be completed in the second half of 2013, and the data generated will be invaluable in both our understanding of the status of HIV-1 and HPV co-infection and the impact of other STIs as risk factors in HIV-1 acquisition. The results from the study will inform the design of the planned larger study for 2014/15.

Development and improvement of diagnostic laboratory technologies

Researchers: Professor W Preiser, Dr G U van Zyl, Dr C de Beer, Professor S Engelbrecht, Dr J Maritz (MMed student), Dr H Newman (MMed student), H la Grange (MSc student), D Njenda (BSc Hons student), L Breunig (University of Würzburg, Germany)

Collaborators: Dr J Dempers, Department of Forensic Pathology and Western Cape Forensic Services, Tygerberg; Professor C Wright, Anatomical Pathology, Port Elizabeth; Professor A Stich, Medical Mission Institute, Würzburg, Germany.

Funding: PRF, NHLS Research Trust, NHLS K-funding, Harry Crossley

Preliminary data indicates that a high percentage of cases show evidence of bacterial and viral pathogens. Histological findings suggest infection in 28% 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 that more cases occur in the winter, but the results so far do not support the reported increased incidence of SUDI cases in December. The study was able to confirm the presence of bacterial and viral pathogens in SUDI cases, but the extent of contributing to death needs to be elucidated. The division continues to work on alternative assays for important markers for the diagnosis and therapeutic monitoring of viral diseases, especially HIV.
A new study is investigating the use of a screening strategy using qualitative PCR on pooled patient specimens to diagnose virologic failure and, if present, detect HIV-1 drug resistance. The aim is to screen patients on antiretroviral therapy through mini-pool PCR reactions that would detect virologic failure > 1000 copies/ml and then PCR and sequence individual specimens from positive pools to detect the presence of drug resistance. This is likely to yield a cost-effective strategy for detection of virologic failure and resistance.

Immunohistochemistry (IHC) and immunocytochemistry (ICC) as indispensable techniques for the diagnosis of viral disease in organs and tissues require the use of appropriate positive and negative controls. Obtaining such control material poses a challenge as it currently relies on using patient specimens. In Honours projects, control materials were developed using infected and uninfected cell cultures, processed either as "mock tissue" blocks or liquid-based cytology preparations.

### Potentially zoonotic and emerging viral diseases

**Researchers:** Professor W Preiser, N L Ithete (PhD student), N Sampson (MSc student), A Adams (BSc Hons student)

**Collaborators:** Professor S Matthee, Department Conservation Ecology & Entomology, Stellenbosch University; Professor D Krüger, Institute for Virology, Charité, Humboldt University, Berlin, Germany; Dr J F Drexler, Professor CH Drosten, Institute for Virology, Universitätshklinikum Bonn, Germany

**Funding:** Deutsche Forschungsgemeinschaft (DFG), PRF, NHLS Research Trust, Harry Crossley Foundation

This project aims to identify and characterise novel viruses occurring in small mammals, ie rodents, shrews and bats, in southern Africa that could result in zoonotic transmission and human disease. Animal tissues are screened for the presence of viral genome. In addition, patients matching a clinical case definition of possible disease are tested using molecular and serological assays and serosurveys are conducted to assess the prevalence of virus-specific antibodies in different populations as a marker of previous exposure.

### Various projects

**Researchers:** Professor W Preiser, Dr C de Beer, S Fortuin (Hons BSc student)

**Collaborators:** Professor H von Briesen, Fraunhofer-Institut für Biomedizinische Technik, Germany.

**Funding:** Bill & Melinda Gates Foundation

The division continues to be the primary site for the Global HIV Vaccine Research Consortium (GHRC), which is one of the grantees of the Bill & Melinda Gates Foundation within the CAVD. This consortium is developing and standardising cryotechnology and cryoprocedures through establishment of a fully functional cryolaboratory in Medical Virology, Stellenbosch University. Stellenbosch University is also the only primary site in the Collaboration for Aids Vaccine Discovery (CAVD) and is responsible for sample collection of recently infected HIV strains.

PBMC isolation is done according to specifically developed protocols in the ChameleonLab system. Plasma and serum are stored at -80°C, and PBMCs are 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 samples are being used by global collaborators involved in vaccine and neutralisation assay development and optimisation.
Excess PBMC, plasma and serum samples from these patients are processed and stored for local research and research projects for postgraduate students. The first of these additional projects was completed in 2012 for a HonsBSc (Medical Virology) degree and will be used for three more projects in 2013.

Honours

Professor Preiser spent a two-month sabbatical period at Columbia University in New York through the NIH D43 grant, which included attending the EPIC summer school.

Teaching and Training

Staff members in the division teach in various modules of the faculty’s MBChB and allied health sciences programmes. On the diagnostic platform, registrars in medical virology, medical microbiology and clinical pathology are being trained. One newly appointed virology registrar joined the division in February 2013. Seven intern medical technologists were in training during 2012.

In total, eight PhD students, 10 MSc students, eight BSc (Honours) students and four medical virology MMed candidates (registrars) were enrolled during the reporting period. In addition, staff co-supervised a number of postgraduate students in other divisions.

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 basic aspects of immunology and advanced aspects of immunology, and the Diploma in Tropical Medicine and Hygiene course at the London School of Hygiene and Tropical Medicine. The international research training group “HIV/AIDS and associated infectious diseases in southern Africa,” in cooperation with the University of Würzburg in Germany and UCT, funded by the NRF and the Deutsche Forschungsgemeinschaft, has been terminated. The final IRTG symposium was held in Stellenbosch in March 2013. As the only such international structured PhD training programme for the whole of Africa it had received considerable attention from various roleplayers.

An international three-day lecture course “Epidemiology and Evolution of Emerging Viruses in Africa” was organised and held near Tygerberg in March 2013. Presenters and participants came from a variety of institutions in South Africa, other African countries and Germany. This course was followed by the investigators’ meeting marking the beginning of the second funding phase of the international collaborative project on hantaviruses in small African mammals.

In March 2013, a small laboratory training workshop was conducted in collaboration with the Fraunhofer Institute for Biomedical Technology in Germany as part of the GHRC Collaboration. Dr Anja Germann from the IBMT presented this lecture and practical laboratory course on HIV Elispot assays which four students attended, three from Medical Virology students and one a former student.

Professional Development

During the reporting period, four MSc, four BSc (Honours) and one MMed students graduated while another MMed student qualified through the CMSA examination and was appointed as virology pathologist at NHLS Tygerberg; in addition one intern medical scientist qualified to register as a scientist with the HPCSA.

One intern medical technologist of the 2011 intake passed the Board exam, both the 2012 intake candidates are awaiting results and two interns commenced training in 2013. After qualification, the successful candidate was placed at the NHLS at Dora Nginza. One technologist resigned during the period under review.
Research Output

Journal articles


Kabue JP, de Swardt D, de Beer C, Glashoff RH. Short-term antiretroviral therapy fails to reduce the expanded activated CCR5-expressing CD4(+) T lymphocyte population or to restore the depleted naive population in chronically HIV-infected individuals with active pulmonary tuberculosis. AIDS Res Hum Retroviruses 2013; 29(5):769-777


Conference presentations
International: 12
National: 15
Department of Anatomical Pathology

Head: Professor A Stepien

Diagnostic Services

The department received 4,933 surgical pathology specimens which is less compared to the previous financial year. The decline was as a result of prolonged protests at the hospitals that we serve. These hospitals include the Nelson Mandela Academic Hospital Complex in Mthatha as well as several referring hospitals in the north-eastern part of Eastern Cape.

In addition we handled 61 post mortem cases, most of them from the Forensic Services Department, which co-operates with the department of forensic pathology regarding histopathological diagnosis. We also performed four autopsies.

Cytology handled 9,310 cases in total during the period under review. The diagnoses requiring pathologists’ confirmation were still referred to the NHLS in Port Elizabeth and Cape Town.

Teaching And Training

We have 97 students enrolled in the MBChB III, Problem-Based Learning programme in 2012 after one deregistered. All 97 passed the final examination, a 100% pass rate. No postgraduate training in anatomical pathology has taken place yet, but our programme has been accredited and the preparatory work for admission of students should be finalised in 2013.

Research

Most of the current research is a continuation from previous years and includes the study of benign and malignant neoplasms based on the registry and material of registry in Transkei; and NHLS pathology laboratory morphologic findings in HIV/AIDS.

Research output

Publications


García Jardón M, Blanco Blanco E, Kwizera E. MBChB III students’ perception of the educational environment at the medical school at Walter Sisulu University. Submitted to be published in the 5th International WSU Research Conference Proceedings 2012

Conferences

Professor Mirta Garcia Jardon MBChB III students’ perception of the educational environment in at the medical school at Walter Sisulu University. 5th International WSU Research Conference ICT East London, 23–24 August, 2012
**Department of Haematology**

**Head:** Professor BA Ogunsanwo

**Diagnostic and Clinical Services**

The department offers comprehensive laboratory services to the Nelson Mandela Academic, Mthatha General and Bedford Orthopaedic hospitals, as well as to various secondary hospitals and clinics in the region. The department offers both in-patient and out-patient clinical services to the Nelson Mandela Academic Hospital under the auspices of the Department of Internal Medicine. We also offer expert opinion and care for patients at the Haemophilia Clinic of the Nelson Mandela Academic Hospital. In addition we routinely conduct telephonic consultations on haematology matters with medical officers across our regional catchment area.

**Research Projects**

**Ongoing research**

- Prevalence of deep vein thrombosis in patients with HIV/AIDS
- Prolonged remission in CML patients treated with a tyrosine kinase inhibitor
- Leukaemia in evolution: cytogenetic evaluation as a tool for early diagnosis
- Retroviral induced Aplastic Anaemia and other Cytopaenias in Mthatha
- Factor VIII inhibitors in patients with Haemophilia A in the Transkei region
- ITP in patients with AIDS: prevalence and response to standard therapy

**Teaching and Training**

**Undergraduate**

- MBChB III Students:
  - Staff members of the division are engaged in the Problem-Based Learning (PBL) and Community based education and service (COBES) curriculum. This entails the identification of core material; student facilitation; lectures; and assessment of student performance. We experienced a 100% past rate in 2012 with all 97 of our students passing. One student deregistered.

- MBChB IV & V Students

- MBChB IV: Incorporated into Internal Medicine (105 students in 2012)
- MBChB V: Incorporated into Internal Medicine (92 students in 2012)

**Research Output**

National conference presentations: 1
Division of Medical Microbiology

Acting Head: Professor SD Vasaikar

Diagnostic And Clinical Services

The department offers comprehensive laboratory services to the Nelson Mandela Academic (NMAH), Mthatha General and Bedford Orthopedic hospitals, as well as to various secondary hospitals and clinics in the region. The department offers services in bacteriology and runs a separate TB laboratory capable of GeneXpert, mycology, parasitology and serology testing. The epidemiological reports for antibiotic sensitivity patterns at NMAH are presented to the NMAH Infection control committee and to the multidisciplinary TB task team and committee.

Research

Research Projects

Characterisation, antibiograms and activity of medicinal plants against Streptococcus pneumoniae and Haemophilus influenzae isolates from clinical samples of patients in the ECP
Researchers: I Morobe, Professor CL Obi, Professor SD Vasaikar, Professor A Oyedeji, Professor JN Eloff, Professor T Hattori
Funding: Walter Sisulu University (WSU)

Phenotypic and molecular characterisation and activity of medicinal plants against local isolates of S. aureus and S. epidermidis in the Eastern Cape province, South Africa
Researchers: NS Mthethwa, Professor CL Obi, Professor SD Vasaikar, Professor A Oyedeji, Professor JN Eloff, Professor T Hattori
Funding: National Research Foundation

Genes encoding antibiotic resistance, pathogenicity and phylogenetic profiles of local isolates of Klebsiella species
Researchers: Professor CL Obi, Professor SD Vasaikar
Funding: WSU

Immunopathogenesis of vulvovaginal candidiasis in HIV-infected women, PhD (UKZN) student research project
Researchers: Dr T Apalata, Professor P Moodley
Funding: University of KwaZulu-Natal

Molecular characterisation of Aeromonas spp, E. coli, non-tuberculosis Mycobacteria and activity of medicinal plants against isolates from water and stool in the Eastern Cape region
Researchers: B Muringani, Professor CL Obi, Professor A Oyedeji.
Funding: WSU

Immune response to specific mycobacterium tuberculosis antigens among parasites infected school children in Mthatha: Role of Vitamin D and deworming
Researchers: N Nxasana, SD Vasaikar, K Baba
Funding: WSU

Composition of microorganisms involved in bacterial vaginosis and effects of immune mediators in non-HIV and HIV infected women
Researchers: K Bidla, Dr T Apalata, Professor SD Vasaikar
Funding: WSU, NRF

Phenotypic and identification of genes encoding for resistance in Acinetobacter species from clinical specimens in Mthatha, South Africa
Researchers: TKC Mabotja Professor SD Vasaikar, Dr T Apalata
Funding: WSU, NRF
Antigonooccal activity and cytotoxicity of selected medicinal plants from rural Eastern Cape, SA.

Researchers: L Faye, Dr T Apalata, Professor Vasaikar SD

Funding: Department of Agriculture

Enhancement of surveillance for invasive respiratory, meningeal and diarrhoeal diseases in South Africa. Group for Enteric, Respiratory, Meningitis disease surveillance in South Africa (GERMS-SA). Collaborative research with NICD

Researchers: Professor SD Vasaikar, Dr T Apalata

Teaching And Training

Undergraduate
MBChB students

Members of the division are engaged in the Problem-Based Learning programme and community-based education and service curriculum. These curriculums entail the identification of core material, student facilitation, lectures and assessment of student performance. In total 97 of the 98 students passed in 2012 and one student de-registered.

Nursing Science: BCUR II:
Total students 73, passed 73 (100%) modules of medical microbiology for Bachelor of Medical Sciences and Bachelor of Medical Clinical Practice second year

Postgraduate:
Postgraduate courses offered include PhD (Health Sciences), MSc (Medical Microbiology), BSc Honors (Med Micro).

Professional development
Currently there are 4 PhD students (3 in 4th year and 1 in 2nd year) and 3 MSc Hons (1st year), 1 BSc Hons. (1st year part-time student)

Research Output

Journal articles


Conference presentations
International congresses: 2
National congresses: 12
Department of Anatomical Pathology

Head: Professor MJ Hale

The Department of Anatomical Pathology of the University of the Witwatersrand 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, Chris Hani Baragwanath, Helen Joseph and Raheema Moosa. In addition, the department is responsible for offering similar care to all provincial hospitals in Gauteng and North West Province.

Diagnostic Services

During the period 1 April 2012 to 31 March 2013, the department based at the Charlotte Maxeke Johannesburg Academic Hospital saw a total of 44,053 cases. A total of 148 neuropathology cases were processed.

A total of 425 renal pathology specimens were processed. Oral pathology diagnosed a total number of 1,559 cases. A total of 240 specimens required electron microscopy and an average of 3,000 immunohistochemistry tests were performed each month. A total number of 1,372 polymerase chain reaction (PCR) tests were performed including 192 B-cell rearrangement studies and 187 T-cell rearrangement studies, 752 mycobacterial DNA studies, 96 Bartonella studies, 103 HHV8 (herpesvirus 8) studies, 6 Parvovirus studies and 36 rt-PCR studies (synovial sarcomas). 55 post mortems were performed from the Charlotte Maxeke Johannesburg Academic and Helen Joseph Hospitals. A total of 1,758 bone marrow trephines were processed.

A total of 110 consultations and reviews received internationally from Namibia and Kenya and nationally from Pietersburg, Cape Town, East London, Port Elizabeth and Bloemfontein were seen by consultants in the department. These also included consultations from private practice laboratories in Johannesburg, Pretoria, Durban, Port Elizabeth and Cape Town.

The histopathology unit situated at Chris Hani-Baragwanath was responsible for a further 17,024 routine histology specimens, 21 post mortems and an average of 6,372 Immunohistochemistry tests per year. Our cytology department reported 121804 Pap smear cases, 13,360 non-gynaecologic exfoliative cases and 11017 FNA cases including palpable masses, radiologic-guided FNAs and intraoperative FNAs.

The Anatomical Pathology laboratory at the Charlotte Maxeke Johannesburg Academic Hospital is still an accredited laboratory and will be re-accredited by SANAS in October of this year. The laboratory at Chris Hani-Baragwanath Hospital in also a SANAS accredited laboratory and was successfully re-accredited in February of this year. The Cytology laboratory is also a SANAS accredited laboratory and was successfully re-accredited in April of this year.

Research

Ongoing research:

Sub-Saharan Africa Lymphoma Consortium (SSALC)

Funding: US National Cancer Institute

Principle Investigators: Professor W Stevens, Head of Molecular Medicine and Haematology, University of the Witwatersrand and NHLS and Dr Y Perner, Principal Pathologist, Department of Anatomical Pathology, University of the Witwatersrand and NHLS.

Collaborator: Professor LW Ayers, Department of Pathology, College of Medicine and Public Health, The Ohio State University, Polaris Innovation Centre, Columbus, USA.
The subtypes and distribution of non-Hodgkin’s lymphoma in Southern Africa, especially in patients with AIDS, is largely unknown. The Mid-Region AIDS and Cancer Specimen Resource, (ACSR), has launched the “Sub-Saharan Africa Lymphoma Consortium,” (SSALC) to address this deficiency.

Approximately 200 cases of lymphoproliferative disorders were retrieved from the Anatomical Pathology archives. These were reviewed with a panel of expert haematopathologists at Ohio State University in June 2010.

In addition, a core biopsy from each paraffin embedded tissue block was subjected to tissue microarray analysis (TMA). On completion of the review and TMA analysis, it is anticipated that areas of diagnostic discrepancy will be highlighted and clarified. TMA technology is available as a research tool in the review of further lymphoma diagnoses. This research is ongoing.

The histopathological analysis of cellular elements, accessory molecules and cytokines in Mycobacterial granulomas from HIV positive and negative individuals

**Funding:** Department of Immunology research funds (NHLS Research Trust)

**Investigators:** Dr R Wadee (Department of Anatomical Pathology), Professor MJ Hale (Department of Anatomical Pathology), Professor AA Wadee (Department of Immunology), School of Pathology, NHLS and University of the Witwatersrand.

The immune response to infection with Mycobacterium tuberculosis involves interactions between macrophages, cytokines, accessory molecules and T-helper cells. Mycobacteria evade the host’s immune response whilst granulomas are important in the host’s defences. These responses may be associated with immune-pathology especially in patients with HIV.

This study will investigate the cell mediated immune mechanisms in granulomas and will assess the presence of macrophages and other cellular elements including CD4+ and CD8+ lymphocytes and accessory molecules in granulomata. The accessory molecules will include Human Leukocyte Antigen (HLA) Class I and II. The study aims to identify the presence of several pro-inflammatory and anti-inflammatory cytokines in granulomas.

The study will compare the various molecules, cellular elements and cytokines in granulomas from HIV positive and HIV negative individuals. Control specimens will be in the form of a foreign body granuloma.

**Evaluation and impact of screening and treatment approaches for the prevention of cervical neoplasia in HIV+ women in Burkino Faso and South Africa (HARP)**

**Sponsor:** London School of Hygiene & Tropical Medicine (LSHTM), London, UK

**Investigators:** Reproductive Health Research Unit at Wits University, Cytology Unit and Dept of Anatomical Pathology at Wits University and NHLS, National Institute for Communicable Diseases, London School of Hygiene and Tropical Medicine, University of Ouagadougou, Montpellier University.

**Funding:** European Commission/ FP7-HEALTH. 2010.2.4.1-4

The aim of this study is to improve cervical cancer prevention programmes for HIV+ women in Africa by evaluating the effectiveness of cervical screening strategies and by developing algorithms leading to earlier detection and management of cervical cancer in this high risk population.

**A three year retrospective audit on thyroid FNA.**

**Investigators:** Dr L Fatman, Cytology Unit

All thyroid FNAs from January 2007 to December 2010 will be correlated with histology. The specific emphasis will be...
on atypical follicle cells of undetermined significance to further define this category and help determine better diagnostic criteria to improve patient management. This research is in the process of being written up.

To determine the optimal cervical screening and management of HIV+ women.

**Investigators:** Cindy Firnhaber, Jennifer Smith, Pam Michelow, Tanvier Omar, Simon Levin, Mark Faesen, Allen Rinas, Sophie William, Doreen Schulze.

**Departments:** Clinical HIV Research Unit/Right to Care, University of the Witwatersrand, NHLS, University of North Carolina.

**Funding:** PEPFAR

To determine the efficacy of cytology, visual aided inspection and HPV DNA testing for the detection high grade squamous intra-epithelial lesions (HSIL) /invasive cervical cancer in HIV-seropositive women. A second aim is to compare the efficacy of cryotherapy and loop electrosurgical excision procedure (LEEP) procedures for the treatment of high-grade cervical intra-epithelial neoplasia (CIN2/3) among HIV-seropositive women. The third aim is to determine the utility of subsequent HPV DNA testing as a marker of effective treatment following the treatment of CIN 2/3 among HIV-seropositive women.

**Immuno-staging of HPV Cervical Lesions in HIV infection**

**Investigators:** E Papasavvas, PhD, M Feldman, MD, Andrea Foulkes, PhD, Deborah Glencross, MD, Simon Levine, MD, Tanvier Omar, Anna-Lise Williamson, PhD.

**Aims:** To investigate the association between cervical lesion stage, innate, adaptive and immune-inhibitory mechanisms in ART-treated HIV+/HPV-16+ women, by testing the hypothesis that low grade lesions are positively associated with functional innate and adaptive HPV-specific responses in absence of negative immune regulation mechanisms.

**Prevalence of anal dysplasia using anal cytology testing and associated risk factors**

**Investigators:** Eefje Jong and Cindy Firnhaber at Right to Care - Helen Joseph Hospital, Pam Michelow at Cytology unit Dept of Anatomical Pathology, NHLS, Wits University.

**Funding:** CFAR (grant of $20,000)

An increased incidence of anal cancer is reported in HIV+ patients. Several risk factors such as low CD4 count, high viral load, concurrent abnormal pap smear and anal intercourse are associated risk factors. However, extremely limited data is available on the prevalence and risk factors on anal dysplasia in low-resource countries. The proposed research will provide epidemiologic data in this regard.

**Molecular profiling of colorectal cancer in a cohort of South African patients**

**Principle Investigator:** Michelle McCabe, School of Pathology, Division of Anatomical pathology, NHLS and University of the Witwatersrand

**Supervisor:** Dr Perner, School of Pathology, Division of Anatomical pathology, NHLS and University of the Witwatersrand

**Collaborators:** Dr L Cronje

**Project description:** This project aims to define the molecular pathogenesis of CRC according to currently known parameters in a random cohort of South African individuals who have had biopsy samples or colorectal resections reported by the Charlotte Maxeke Johannesburg Academic Hospital (CMUJAH).

This data will provide insight into the CRC molecular subtypes prevalent in South Africa, a heretofore largely unassessed aspect of the disease, with a view to developing a cost-effective method for assessing the molecular profile of these tumours for prediction of response to individualized treatment and prognosis in patients with this disease.
ACTG A5282 trial
Dr P Michelow

The AIDS clinical trials group (ACTG) is the largest HIV clinical trial organization in the world, playing a major role in setting standards of care for HIV+ patients. The ACTG is funded by the United States Department of Health and Human Services and the United States National Institutes of Health through the National Institute of Allergy and Infectious Disease.

This is a similar study to the HARP study in that cervical cytology and HPV testing will be compared in HIV+ women in low-resource communities. The ACTG A5282 trial has 11 study sites (3 in South Africa, 1 in Zimbabwe, 1 in Botswana, 1 in Zambia, 1 in Malawi, 1 in Haiti, 1 in Peru, 2 in India). I am not involved in the actual trial. My role is to undertake quality assurance of the cytology for all 11 sites. A random selection of five Pap smears from all 11 sites will be sent to me for review at 6 monthly intervals for the duration of the study. This trial is underway and will take 2-3 years.

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 University of the Witwatersrand
**Project Leader:** S Naidoo, School of Pathology, Division of Anatomical Pathology, NHLS and University of the Witwatersrand
**Source of funding:** National Health Laboratory Services Research Trust Grant

**Typing of Epstein Barr Virus using EBNA2 genotyping**

A specific and reliable method for the detection and typing of the Epstein-Barr virus using the DNA of paraffin embedded tissue samples as the template was optimised. The region within the EBNA-2 gene discriminating between EBV type 1 and 2 was amplified with the nested primers EBNA-2C and EBNA-2G for type 1 and EBNA-2C and EBNA-2B.

The study assesses the detection of EBV type 1 and type 2 in HIV associated Non-Hodgkin’s B Cell lymphomas using a qualitative EBNA2 PCR amplification.

**MYC rearrangements in extra-oral plasmablastic lymphoma**

**Researcher:** Dr Y Perner, School of Pathology, Division of Anatomical Pathology, NHLS and University of the Witwatersrand,
**Supervisors:** Professor S Meer, Dr P Willem
**Funding:** NHLS Research Trust

**Aim:** To assess the presence of MYC rearrangements in a cohort of extra-oral plasmablastic lymphomas (PBL).

**Methods:**
30 PBL cases from the NHLS Anatomical Pathology archives will be reviewed histologically, representative of extra-oral tumours from individuals of both known and unknown retroviral status. A tissue microarray (TMA) will be created using a manual tissue arraying instrument (Beecher Instruments, Silver Spring, MD).

An immunophenotypic profile will be established against which all lymphoma diagnoses will be assessed. MYC rearrangements will be assessed on TMA by interphase fluorescence in-situ hybridization. Translocations commonly associated with DLCL will be explored by FISH, specifically t(8;14), t(11;14), BCL2 and BCL6 rearrangements. The relationship to Epstein Barr virus and clonality studies will be examined by CISH.

**Results:** The study is currently underway and results are pending. An NHLS Research Trust Fund grant has been awarded to conduct this project.
Human papillomavirus infection of the oesophagus and its association with squamous cell carcinoma: A retrospective study of cases seen at Chris Hani Baragwanath Hospital in 2009 and 2010

**Researcher:** Dr. D. van der Byl, School of Pathology, Division of Anatomical Pathology, NHLS and University of the Witwatersrand  
**Supervisor:** Prof. M.J. Hale, School of Pathology, Division of Anatomical Pathology, NHLS and University of the Witwatersrand  

Funding was obtained from the Departmental funds.

A study to determine the presence of HPV in the oesophagus and assess any association it may have with squamous cell carcinoma of the oesophagus. PCR was performed on cases of oesophageal squamous cell carcinoma that were diagnosed between 01 January 2009 and 31 December 2010 at Chris Hani Baragwanath Hospital. Ten cases of normal oesophageal biopsies were included as controls. Of the 96 cases, 2 showed evidence of condylomatous atypia on light microscopy. PCR for HPV was negative in all 95 of the squamous cell carcinoma cases tested and in the ten control cases. Despite the high prevalence of HPV in South Africa, HPV was not detected in any of the cases.

**New Research:**

Duodenal eosinophil count in patients presenting with functional dyspepsia at Chris Hani Baragwanath Academic Hospital.

**Researchers:** Principle investigator: Dr Mohamed Hussein Abdulsamad, Department Of Internal Medicine Faculty Of Health Sciences, University of the Witwatersrand.  
**Collaborators:** Professor R Ally, Department of Internal Medicine, Faculty of Health Sciences, University of the Witwatersrand. Dr EJ van den Berg, Department of Anatomical Pathology, NHLS and Faculty of Health Sciences, University of the Witwatersrand.

The aim of the study is to assess the duodenal eosinophil count in biopsies of patients with functional dyspepsia. It is hypothesized that eosinophil infiltration in the duodenum may be common in adult patients with non-ulcer dyspepsia, and that duodenal eosinophilia may be a diagnostic marker for non-ulcer dyspepsia. Confirmation of this would lead to changes in...
the evaluation of duodenal biopsies in these patients and in their management. The study involves routine biopsy material and therefore funding has not been obtained.

The demographics of Kaposi sarcoma and CD 117 immunohistochemical expression in a retrospective cohort of cases at Chris Hani Baragwanath Academic Hospital

**Researcher:** Dr R D Mohanlal, MbChB, DMH, FCPath (Anat), Pathologist, NHLS, Chris Hani Baragwanath Academic Hospital.

**Supervisor:** Dr S Pather

I will be collecting demographics of all cases diagnosed with Kaposi sarcoma at the Chris Hani Baragwanath Academic hospital from 1 January 2005 to 31 December 2009 using SNOMED search. Details such as age, gender, biopsy site, co-morbid pathology, CD4 count will be recorded on a datasheet and analysed. A cohort of 50 cases will be randomly selected from those cases confirmed with HHV8 immunohistochemistry. These will be stained with CD117 and the staining recorded together with HHV8 staining. Any trends in staining across tumour stage and patient CD4 counts will be noted and analysed. I will apply from funding from the NHLS Research Trust grant.

Epstein Barr Virus positivity using Epstein Barr Virus-encoded ribonucleic acid (EBER) in-situ hybridisation in classical Hodgkin lymphoma: a review of 30 cases from the Johannesburg Academic Hospital Complex.

**Researcher:** Dr E McAlpine, Division of Anatomical Pathology, School of Pathology, Wits University and NHLS.

**Supervisors:** Drs Y Perner and S Pather, Division of Anatomical Pathology, School of Pathology, University of the Witwatersrand and National Health Laboratory Service.

Hodgkin lymphoma is a unique haematolymphoid neoplasm which shows Epstein-Barr virus (EBV)-positivity in a varying number of cases depending on factors including tumour subtype, socioeconomic status, geographical location and Human Immunodeficiency virus (HIV) status of the host.

A retrospective histopathological review of cases of classical Hodgkin lymphoma was performed on archived surgical specimens from the Division of Anatomical Pathology, Johannesburg Academic Hospital Complex. Cases from January 2008 to December 2011 were included. The following details were recorded from each case: age, gender, topographical site, lymphoma subtype, HIV status and CD4 count (if HIV-positive). EBV status was also recorded if available. The 30 most recent cases underwent EBV testing.

Assessment of the hTERC gene amplification on chromosome 3q26, as a specific biomarker of cervical carcinoma in HIV-positive South African patients

**Researchers:** G Baker, Dr T Omar, Dr P Willem

This research study aims to develop a FISH assay to detect copy number changes in the hTERC gene which may be advantageous to use in conjunction with a cytology Pap smear. The main objective of this study is to determine the frequency of 3q26 amplification in South African HIV-positive cervical cancer specimens and assess its value as a predictor of progression to invasive cancer. Should the predictive power of 3q26 amplification be validated in SA HIV-positive women, this test could be used in a sequential pre-screening strategy on all Pap smears from HIV-positive patients. This will ensure that an informed decision regarding treatment can be made for these patients. This is a retrospective study using stored and archived biopsy specimens with a known HIV status. Samples include Normal, HPV infected, CIN I, II and II cases and those cervix biopsies with invasive carcinoma. FISH will be performed and the predictive value of 3q26 amplification will be evaluated against subsequent disease progression/regression.
Ascertaining the contribution of pulmonary TB to non-hospital deaths in a high HIV prevalence and high TB burden setting

Researchers: N Martinson, T Omar, E Variava, M Rakgokong.

Southern African countries have extremely high rates of TB, most related to HIV. In South Africa, TB is the leading cause of death but a third of all deaths occur at home. There is little information on whether people who die at home have TB. Our study aims to identify the proportion of people who die at home from natural causes and who have infectious TB. 100 people who died at home in the Klerksdorp area have undergone post mortem bronchial washings, and lung biopsies to assess for the presence of TB. Material is being evaluated by microscopy, culture, histology, Gene-Xpert and PCR.

Teaching and Training

Undergraduate
Consultants and registrars within the department contribute extensively in lecturing and offering practical theme sessions to GEMP 1 and 2 and all registrars participate as facilitators in the 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. Dental and pharmacy students as well as students of physiotherapy and occupational therapy attended half-courses in anatomical pathology during their third year of study.

Postgraduate
Anatomical Pathology lectures are given over four blocks during the academic year to MSc students in Physiotherapy and Occupational therapy and the department is involved in the teaching of pathology for the Diploma in Tropical Medicine and Hygiene offered by University of the Witwatersrand.

All registrars in the Department of Anatomical Pathology are registered for the degree of MMed (Anatomical Pathology) with the University of the Witwatersrand.

In addition to their surgical pathology training, registrars in Anatomical Pathology follow a formal academic programme drawn up annually by the department.

The cytology unit trains registrars in Anatomical Pathology, medical officers, technologists, technicians, and laboratory assistants.

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 the students assignments/tasks to complete. The students are also trained on the bench by supervisors and senior technologists. From Tuesdays to Thursdays of every week, the students are given one and a half hour 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.

Professional Development

Number of postgraduate students: 27 (MMed)
At the end of March 2013 we had 23 registrars enrolled for the MMed.
Dr Yvonne Perner, Dr Tanvier Omar, Dr Reubina Wadee and Dr Lerato Nokoane, all consultants in the department are also registered for the MMED at the University of the Witwatersrand

Number of postgraduate students that qualified:
1 (FCPath Anat) – Dr Lauren Blackburn
Honours

Visitors to the Department:
Professor Ondrej Hes visited and gave a lecture to the Department in January 2013. Professor Hes is Professor of Pathology and Head of the Special Diagnostics Laboratory in Sikl's Department of Pathology at the Charles University Medical Faculty Hospital, Pilsen, Czech Republic. He is a member of the International Society of Urogenital Pathology’s Working Group for the Classification of Renal Tumours.

Dr Russell Harley visited and gave a lecture to the department in October 2012. Dr Russell specializes in anatomic pathology in Charleston, South Carolina.

Dr Ann Marie Nelson visited and gave a lecture to the department in October 2012. Dr Nelson is from Washington, USA and specialises in anatomic and clinical pathology.

Dr Michael Wilson visited and lectured to the department in October 2012. Dr Wilson is from Denver USA and specialises in anatomic and clinical pathology.

Publications:


Conference attendance/contributions:

International Conferences:
Professor Martin Hale presented at the USCAP conference held in Baltimore from the 2–8 March 2012.

The IAP (International Academy of Pathology) 2012 International Congress took place from the 30 September–5 October 2012 in Cape Town. Professor Martin Hale was the chairman of the organizing committee for the congress. 25 of the consultants and registrars in the department attended and presented posters and lectures at the congress.

Courses and Symposia:
Professor Wayne Grayson hosted the 9th Annual Johannesburg Dermatopathology Symposium on 19 January 2013 at the Faculty of Health Sciences, University of the Witwatersrand.
Department Of Chemical Pathology

Acting Head: Doctor Nereshni Lutchman

The chemical pathology laboratories provide a comprehensive clinical chemistry service to the academic hospitals in the Johannesburg region and consultative services to doctors regarding appropriate cost-efficient use of the laboratory. As a very expensive repertoire of tests and specialised testing are performed in the academic complex, consisting of laboratories at both the Charlotte Maxeke Academic Hospital (CMJAH) and the Chris Hani Baragwanath Academic Hospital (CHBAH), this unit serves as a reference laboratory for the NHLS laboratories.

The automated laboratories at both sites are high volume 24-hour continuous service laboratory. Both laboratories moved to single platform total laboratory automation solutions which included routine chemistry, haematology and microbiology. During this time, intensive training and continued refinement of laboratory processes have taken place. The complex is currently facing many challenges. These include the impending implementation of the TrakCare Laboratory Information System and ongoing staff shortages of skilled personnel. Despite these challenges, the laboratory endeavours to provide results of the highest quality as reflected by the comprehensive external quality control initiatives, and the maintenance of SANAS accreditation.

This compromises the placement of blood gas machines in the critical, high care and admission wards. Currently there are 15 Arterial Blood Gas analysers, making it the largest hospital point of care service (HOSPOCT) in the country. In addition to the blood gas service CHBAH launched the first point of care service in the Diabetic Clinic in the country.

The Diabetic Clinic service was successfully extended to the paediatric and antenatal diabetic clinics. The test menu has also been extended to include microalbumin. CHBAH is always invited to extend the POCT to Soweto during the SAPS wellness awareness projects.

Clinicians have complimented the CHBAH HOSPOCT as it is in line with the established global POCT guidelines.

Recently, a satellite emergency laboratory was established in the new Emergency Unit housing both surgical and medical casualties. The test menu, designed in conjunction with the clinicians, offers critical biochemical tests only and allows for much improved turnaround times for results to reach clinicians. Plans are in place to extend the satellite type of service to cover the new Jabulani Hospital in Soweto.

CHBAH established a research laboratory and currently has a medical scientist who is registered for an MSc with Wits. Several Wits Ethics-approved research projects are being run in collaboration with clinicians from CHBAH.

The specialised testing unit has continued its involvement with the intensive care staff at both CMAH and CHB in providing testing for toxic substances in critically ill patients. In addition, the menu of tests being performed in this unit has increased significantly in keeping with international trends. The acquisition of new up-to-date technologies will serve to continue this trend.

The CAMH biochemistry routine laboratory runs on average 160,000 tests per month while the laboratory at the CHB performs on average 170,000 tests per month.

The CBHAH complex has successfully transitioned to an automated platform in 2012. This complex has also successfully established a point-of-care testing (POCT) service in the wards in order to improve patient care.
Senior staff in the department, in addition to their routine service work, serve on several NHLS and other committees such as the Chemical Pathology Expert Committee, Point-of-care Working Group, Standardisation Committee, College of Medicine, and the HPCSA. The pathologists are further involved in serving on university committees and teaching at undergraduate and postgraduate levels.

Research Projects

The focus areas of research are obesity, diabetes mellitus, cardiovascular disease, metabolic syndrome, the metabolic aspects of HIV and its therapy and toxicology.

Pathophysiology of obesity and type 2 diabetes

Genetics of obesity: S Mnyosi, Dr C van Niekerk, Professor N Crowther

Mutations in the melanocortin 4 receptor (MC4R) have been shown to cause morbid, early-onset obesity in humans. The MC4R receptor resides in the hypothalamus and is bound by α-melanocyte stimulating hormone (MSH), a potent anorexigenic neurotransmitter. The present study is investigating the occurrence of mutations in the MC4R gene in obese and lean white and black South African subjects. This study has shown that polymorphisms in the MC4R gene do not contribute to the high prevalence of obesity in the South African black population.

The development of an exercise programme for treatment of the metabolic syndrome

Researchers: G Torres, Professor N Crowther and Professor G Rogers (Department of Physiology, University of the Witwatersrand Medical School)

Funding agency: South African Sugar Association

A number of studies have shown that vitamin D may have a number of extra-skeletal effects, and this has led to a large increase in the number of requests for vitamin D serum level measurements in clinical biochemistry laboratories across the globe, including South Africa. However, there are a number of
different commercially available assays for the measurement of total serum vitamin D levels and their suitability is largely unknown. This project will compare some of these assays against a gold standard method performed using HPLC.

Metabolic and anthropometric changes during the menopause transition in African females

Researchers: N Jaff, Professor N Crowther, Professor S Norris (Wits/MRC Developmental Pathways to Health Research Unit, Department of Paediatrics, University of the Witwatersrand)

Funding agencies: MRC and NHLS

Studies in European populations have shown that during the menopause transition changes in body fat distribution, lipid levels and insulin sensitivity occur. These changes may predispose to cardiovascular disease (CVD) and type 2 diabetes. However, it is not known whether similar changes occur in African females. Therefore, the current project will use subjects recruited from the birth to 20 study and measure body fat distribution and CVD risk factors in pre-, peri- and post-menopausal females.

Type 1 diabetes and maturity onset diabetes of the young

Pathophysiology of type 1 diabetes in African subjects

Researchers: Dr C Padoa, Professor N Crowther, Professor P Rheeder (Division of Clinical Epidemiology, University of Pretoria)

Funding agencies: NHLS, MRC

Very little is known about the aetiology or the genetics of type 1 diabetes in black African subjects. The main genetic input into the disease comes from the HLA region of the genome and the present study is investigating HLA haplotypes and other gene polymorphisms and their association with diabetes in African type 1 diabetic patients as well as the prevalence of autoantibodies to insulin and other islet beta-cell autoantigens. The present data shows that in African subjects the age of diagnosis of diabetes is older than in White patients, with 20-30% of African subjects being diagnosed with type 1 diabetes between 20-25 years of age. Differences in the prevalence of certain autoantibodies have also been observed between African and European diabetic subjects.

MODY in South African populations

Researchers: K Prigge, Dr C Padoa, Professor N Crowther, Professor R Erasmus (Department of Chemical Pathology, University of Stellenbosch) and Dr M Hoffmann (Department of Chemical Pathology, University of Stellenbosch)

MODY is a genetic form of diabetes that accounts for up to 5% of all cases of type 2 diabetes in European populations. However, no data is available for the presence of MODY in African populations. The present study is developing molecular diagnostic tools for identifying MODY cases referred to us from diabetes clinics based in Johannesburg and Stellenbosch.

Pathophysiology of atherosclerosis and heart disease

Triglyceride and cholesterol synthesis from glucose and fructose

Researchers: R Immelman, Professor N Crowther, Professor J Paiker

Funding agencies: NHLS, MRC, South African Sugar Association

In vitro studies have shown that glucose can be used for the synthesis of cholesterol but no in vivo studies have been performed to confirm this in vitro data. The present study uses 13C-glucose to determine the input of carbon units from glucose to in vivo cholesterol synthesis in humans.
High dietary fructose intake is associated with elevated serum triglyceride levels. Therefore, the current study is also using 13C-labelled fructose to determine whether fructose contributes carbon atoms for the synthesis of both triglycerides and cholesterol. Data collected thus far shows that glucose does contribute to triglyceride but not cholesterol synthesis.

**Abdominal fat accumulation and associated metabolic disorders**

**Researchers:** Dr N Naran, Professor N Crowther.  
**Funding agencies:** MRC and NRF

Heart disease and diabetes are more common in the Indian than African population of South Africa. Furthermore, studies have shown that Indian subjects tend to have greater abdominal fat accumulation than African subjects. The present investigation is therefore studying ethnic differences in body fat distribution and relating this to differences in insulin sensitivity and lipid metabolism. The contribution of diet, daily physical activity and socio-economic status to abdominal fat mass is also being investigated. The study thus far has shown that lipid accumulation in the liver is associated with increased visceral fat mass.  
**Funding agencies:** MRC and NRF.

**HIV/AIDS**

**HIV associated nephropathy (HIVAN)**  
**Researchers:** Dr J George, Professor S Naiker, Dr R Duarte (Department of Nephrology)  
**Funding agency:** NHLS

HIVAN is a leading cause of end stage renal disease among HIV-positive subjects. The aetiology of the disease will be studied in HIV-positive subjects using kidney biopsy samples. The infiltration of immune system cells into the renal tissue will be analysed as will the chemokine and CD4 receptor and chemokine co-receptor expression of renal tubular cells.

The genetics of body fat re-distribution and lipid abnormalities in ART-associated lipodystrophy  
**Researchers:** Mr T Tlomatsana, Dr N Naran, Professor N Crowther

Not all subjects who receive ART develop lipodystrophy and therefore it is possible that some subjects are more susceptible to this side effect of ART than others. Previous studies have investigated the possibility of gene polymorphisms that may account for this. Therefore, a number of candidate gene polymorphisms are being studied in patients with and without ART-associated lipodystrophy to determine whether gene variation can increase the risk of lipodystrophy in subjects receiving highly-active anti-retroviral therapy (HAART). Our data shows that a polymorphism in one of these candidate genes, the TNF alpha gene does associate with lipoatrophy in this patient group.

The role of cystatin C in the assessment of renal function for patients initiating HAART  
**Researchers:** Dr T Seape, Dr J George.

The recent revision of ARV guidelines for the management of HIV infected patients in South Africa has included the use of Tenofovir, a nucleotide reverse transcriptase inhibitor. Tenofovir may be nephrotoxic and has been associated with the onset of acute renal failure following initiation of therapy. The guidelines suggest assessment of renal function before initiation of Tenofovir. Cystatin C is a more sensitive marker of small changes in glomerular filtration rate (GFR) and overall is a better estimator of GFR than serum creatinine. The aim of this study is to assess the use of cystatin C as a better alternative to GFR for the determination of kidney disease in HIV patients initiating HAART.
Toxicology and renal function

Toxic effect of plant extracts

Researcher: T Snyman

Funding agency: NHLS

Some plants used as herbal remedies in South African traditional medicines (muthi) contain toxic agents known to cause liver pathology. The effect of these agents on apoptosis rate in two human hepatocyte cell lines – HepG2 and HUH7, are being studied and methods developed to block their liver toxicity. Data shows that these agents cause both apoptosis and necrosis.

Teaching and Training

Technologists

The large variety of testing methods employed in the chemistry laboratories at both sites enables them to serve as ideal environments to provide teaching and training at all levels. Tutorials, lectures, CPD accredited activities, and seminars form part of the weekly routine which further enhances the training capabilities of these laboratories.

Undergraduate

The Department contributes to the Graduate Entry Medical Programme (GEMP), with teaching extended to the final year medical students (GEMP 4) in the form of weekly tutorials. All the medical staff, including the consultants and registrars, as well as the majority of the scientists who participate in the GEMP 1 and 2 teaching programme by acting as block and case coordinators, present lectures, facilitate weekly cases, give tutorials and set exams, as well as invigilate and mark exam papers.

Postgraduate

The Department has nine registrar posts in chemical pathology and takes on up to an additional two clinical pathologists. Registrars’ daily tasks include validating chemistry results and troubleshooting methods as well as providing a consultative service for general laboratory problems when required. Registrars rotate through all units of the laboratory, where they are exposed to a variety of clinical and technical disciplines. A consultant is in charge of each unit and oversees the training in that unit by means of tutorials and case discussions. Registrars are also obliged to attend related clinics where they manage patients. This further enhances their training, and helps them develop insight into the clinically appropriate and cost-efficient work-up of patients as well as providing them with insight into the logistical problems of providing a laboratory service. They provide support to the Day Ward in the provision of dynamic function tests.

The registrars also provide cover to the laboratories at Donald Gordon Medical Centre, which allows them to gain experience in fields such as transplant medicine. Under supervision they are involved in providing continuing medical education to doctors in outlying hospitals. Registrars are heavily involved in undergraduate teaching though facilitation at problem-based learning sessions and in tutorials to GEMP IV students. Two registrars successfully completed the Fellowship examinations in 2012 and one of them has been redeployed to the Free State.

Honours

Dr Nitien Naran won the Best Oral Presentation prize in the category “Diseases of Lifestyle” at the Wits Research Day, September 2012. He also presented a paper at the Pathpoint 2012 congress, Cape Town, September 2012.

Dr Marketa Toman presented a poster at The Faculty of Health Sciences Research Day (19.9.2012) and was awarded a prize for the Best Poster Presentation in the “Diseases of Lifestyle” category.
Professor Nigel Crowther received an award at the annual meeting of the Federation of South African Pathology Societies for the best poster/oral presentation in the field of clinical biochemistry. The title of the presentation was: “The current waist circumference cut point used for the diagnosis of metabolic syndrome in sub-Saharan African women is not appropriate.” The presentation was co-authored with Professor Shane Norris.

Dr Nereshni Lutchman won a scholarship to John Hopkins Bloomberg School of Public Health to attend the Graduate Summer Institute of Epidemiology and Biostatics.

Professional Development

Number of postgraduate candidates enrolled in the department: 20 (11 PhD, 3 MSc, 6 MMed).

Number of postgraduate students who graduated during the year: 1 (1 PhD).

Number of registrars who completed the college requirements for FCPath: 2

Research Output

The research output of the department in terms of publications and presentations at conferences has been well maintained.

Journals

Crowther N, Norris SA. The current waist circumference cut point used for the diagnosis of metabolic syndrome in sub-Saharan African women is not appropriate. *PLoS One* 2012; 7(11): e48883


Crowther NJ. Early determinants of chronic disease in developing countries. *Best Pract Res Clin Endocrinol Metab.* 2012; 26: 655–665


Conference presentations

Presentations at national congresses: 5
Division of Human Genetics

Head: Professor Arnold Christianson

The Division of Human Genetics, National Health Laboratory Service (NHLS) and University of the Witwatersrand provides a limited menu of medical genetic diagnostic laboratory services for the country and minimal clinical genetic services for Gauteng Province.

Diagnostic Services

The diagnostic laboratory services of Human Genetics are provided by the molecular genetics, cytogenetics, applied polymorphisms, biochemistry, and human genome diversity and disease research laboratories. The human genome diversity and disease research laboratory provides a genetic ancestry testing service to the public.

The continuing reduction of the division’s laboratory staff compliment, exacerbated by other problems, has severely affected the division’s ability this year to undertake and maintain its mandate to service, both clinical and laboratory needs. This in turn has adversely impacted on the academic platform for teaching, training and research.

Services undertaken

The number of tests conducted per laboratory 2011/2012 to 2012/2013

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>2011-2012</th>
<th>2012-2013</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Genetics</td>
<td>6851</td>
<td>5809</td>
<td>-15.21</td>
</tr>
<tr>
<td>Cytogenetics</td>
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<td>2364</td>
<td>-4.60</td>
</tr>
<tr>
<td>Applied Polymorphisms &amp; Biochemistry</td>
<td>6259</td>
<td>5448</td>
<td>-12.96</td>
</tr>
<tr>
<td>Clinical Genetic Services</td>
<td>1972</td>
<td>1882</td>
<td>-4.56</td>
</tr>
</tbody>
</table>

Molecular Genetics

The Molecular Diagnostic Laboratory remains the largest diagnostic laboratory in the country performing tests for single gene disorders. The laboratory offers testing for more than 40 genetic conditions, offering its service to the public and private sectors. It continues to perform almost 80% of tests nationally. In addition, the laboratory is actively involved in research and development of new tests but due to the critical staff shortage and the pressures of the routine diagnostic service the laboratory undertook minimal research. Tests performed decreased by almost 15% from the previous financial year. Despite adverse circumstances experienced by the laboratory, it once again maintained its high standard of biannual external quality assurance obtained through the American College of Pathologists (CAP). Due to the critical staff shortage the laboratory was unable to train intern medical scientists during this period. The laboratory received 2 new staff members after September 2012 which has helped to reduce the significant backlog of tests.

Genotyping Facility

The SNP Genotyping Facility in the Division of Human Genetics is jointly funded by the National Research Foundation (Research Infrastructure and Support Grant), Wits University and the NHLS. This facility has been available for research and collaboration with scientists locally, regionally and nationally. The facility has two major sections – a semi-automated robotic system for DNA quantification and normalisation (Tecan EVO150), and a medium-throughput genotyping platform (Illumina BeadXpress).

Several publications have emanated from the data generated through the genotyping facility and more will be published in 2013. Genotyping was done for researchers from...
the University of Cape Town, Stellenbosch University and the University of the North West. The five year grant period of the platform has concluded and the BeadXpress has been put into hibernation until such time as it is required for further research. The Tecan was not functional in 2012 due to the theft of the computer and a 12 month process to reinstate it to a working condition. It is expected to be operational again in 2013.

During the reporting period, data was generated for research studies related to kidney disease, obesity and hypertension, population genetics, bone mineral density and abalone genetic diversity.

Cytogenetics

The Cytogenetics laboratory continues to provide a pre-and post-natal laboratory service. This laboratory processed samples of peripheral blood, amniocenteses, chorionic villi, products of conception, and skin fibroblasts. FISH studies are performed on samples for specific microdeletions or other chromosomal rearrangements. The laboratory maintains its high standard quality assurance by obtaining good results from the proficiency testing through the American College of Pathologists (CAP).

Cytogenetics has been severely affected by continuing staff losses of trained individuals who are difficult to replace as there are few trained cytogeneticists in the country. Prenatal samples from women of advanced maternal age, products of conception and blood from infants with suspected Down syndrome, Trisomy 13 and 18 continue to be diverted to the Applied Polymorphism section for rapid detection of Down syndrome and other “common” chromosomal aneuploidies by QF-PCR.

Applied Polymorphisms and Biochemistry

The laboratory’s main activities include parentage testing, QF-PCR for the detection of chromosomal aneuploidies and tests for certain inherited biochemical abnormalities. Test numbers have decreased by approximately 13% since last year and most of the decrease can be attributed to a decline in the demand for QF-PCR (a fall-off of about 28%). Paternities saw a 6% decrease while biochemical testing saw a 2% increase. This section remains short staffed, with only four out of seven posts being occupied. This has had an adverse impact on turnaround times and progress towards accreditation.

Clinical Genetic Services

The clinical diagnostic service continues to see patients with a wide spectrum of genetic disorders, including antenatal and clinical cases. Weekly clinics are held at Charlotte Maxeke Johannesburg Hospital, Chris Hani Baragwanath Hospital, Rahima Moosa Hospital and at Donald Gordon Medical Centre. Regular clinics are also held in specialist clinics in the teaching hospitals, including haemophilia (at Charlotte Maxeke Johannesburg Hospital and Chris Hani Baragwanath Hospital), the breast cancer clinic at Chris Hani Baragwanath Hospital and a haematology/oncology genetic clinic at Chris Hani Baragwanath Hospital. Fewer clinics are being serviced due to significant staff losses of medical geneticists and genetic counsellors. The unit has been reduced to less than half its previous size. Further rationalisation of the clinics undertaken is inevitable.

Very successful outreach clinics in East London and Port Elizabeth provided local patients with genetic services and local doctors with CPD in medical genetics. Airfares, accommodation and car hire for the outreach clinics were sponsored by the Wings and Wishes organisation.
The first two registrars in the primary specialty of medical genetics, registered in 2009, were successful in obtaining their College of Medicine examinations and completing their MMed dissertations. Both were trained in the Clinical Unit. Unfortunately there are no substantive posts in the country to employ these two medical geneticists or future qualifying medical geneticists in the country.

The clinical section continues to provide many educational talks at the academic teaching hospitals, at a number of private hospitals and other venues to specialists and lay people on a wide array of medical genetics topics. These continue to be well received and have a positive impact on the sections interaction with health professionals and patient referral.

HGDDRL

Genetic Ancestry Testing
A major translation of our research is the service we provide to the public in the form of genetic ancestry testing. This activity contributes to the public understanding and education of science.

Research

The research undertaken in the division reflects the wide interests of its senior staff. Research is being undertaken on policy issues related to the implementation of medical genetic services, particularly laboratory services in middle and low-income countries. Research and development on medical genetic tests for locally relevant medical genetic disorders continues as before. Members of the academic staff are part of the Wits Molecular Biosciences Research Thrust: Health for Africa and participate in workshops and research forums organised under the umbrella of the Thrust. MSc and PhD students and several postdoctorals fellow from the division are doing genomic research while based at Wits Bioinformatics, a joint faculty initiative (Science and Health Sciences). A staff member, Prof M Ramsay, is the interim director of the Sydney Brenner Institute for Molecular Bioscience (SBIMB), one of the 6 21st Century Wits Institutes. The SBIMB is also a joint faculty initiative (Science and Health Sciences). Further, the Human Genetics Diversity and Disease Research Unit continues to make use of population and evolutionary genetics to understand how changes in the human genome are associated with the epidemiology of disease, and reconstruct human history and human origins.

Research projects

Gentee– Genetic Testing In Emerging Economies

Researchers: Professor A Christianson, Professor J Kromberg
Collaborators: Professor I Nippert, University of Munster, Germany

GenTEE is a continuation of the work initiated in the CAPABILITY programme. It is funded by the Institute for Health and Consumer Protection, a European Union funded organisation. It is an international pilot study assessing medical genetic services, particularly laboratory services, in eight countries with emerging economies – Argentina, Brazil, China, Egypt, India, Oman, Philippines and South Africa. An international report summarising its content has been completed and will be published soon.

Inherited breast and ovarian cancer: a review of the available genetic counselling and testing services in Johannesburg

Researchers: M Jefferies, S Macaulay, T Wessels

In South Africa, testing for inherited breast and/or ovarian cancer is limited to those individuals with a high risk family history and those relatives of individuals with identified mutations in the predisposing genes, BRCA1 and BRCA2. This study aimed to assess the
genetic counselling service offered to patients, particularly in terms of BRCA1/2 testing. Seventy-four percent of patients attended genetic counselling for predictive or diagnostic BRCA mutation testing. Testing was offered to 78% of patients, with an uptake of 81%, 90% of which was performed nationally. Ninety-four percent of respondents to a telephonic questionnaire stated they would refer to the genetic counselling service. Results from this study will assist in improving the genetic counselling services offered by the division.

Pregnant women’s perceptions and knowledge regarding alcohol use during pregnancy

Researchers: Cle Roux, S Macaulay, T Wessels
Funding: MFREF (Wits)

Foetal alcohol syndrome (FAS) is a major cause of intellectual disability, with the highest rates reported in South Africa. This study aimed to investigate and compare the knowledge and awareness of pregnant women from the state and private medical sector, regarding alcohol use during pregnancy and its effects on the foetus. This was achieved by asking randomly selected participants at Charlotte Maxeke Johannesburg Academic Hospital and two private antenatal centres in Randburg and Bryanston, to complete a structured questionnaire. Overall, this study found that pregnant women from various backgrounds have limited knowledge of the harms caused by alcohol use during pregnancy. Misconceptions about acceptable levels of maternal alcohol consumption and its effects were also evident.

South African women’s experience of genetic counselling

Researchers: M Morris, Sr M Glass, T Wessels

Client satisfaction is commonly researched in clinical settings as it aids in obtaining desirable outcomes for patient care. There has been limited research on client satisfaction in genetic counselling. South Africa provides a unique situation for genetic counselling because of the multicultural and linguistic diversity. The aim of this qualitative study was to explore mothers’ experiences of genetic counselling in Johannesburg, South Africa. The study made use of interpretative phenomenological analysis (IPA) and voice-recorded focus groups. The groups were conducted in a suitable African language and facilitated by an experienced psychologist. All recordings were transcribed and translated into English. During data analysis, themes were extracted, inter-connected and interpreted to create a comprehensive picture of the mothers’ experiences. Themes included a general lack of awareness; experiences of the genetic counselling process; addressing communities and families about genetic disease and the dissatisfaction experienced within the existing healthcare system.

The characteristics of the genetic counselling process in an antenatal multicultural setting

Researchers: TM Wessels, Professor C Penn
Funding: NRF, Thuthuka

The aim of the study was to investigate the nature of antenatal genetic counselling encounters within a multicultural setting. Results have shed some light on the structure of the sessions and the interactional features and showed that genetic counselling is a complex interaction where the different phases of the interaction have very distinct features. The phases of the session included: opening, information gathering, information giving, decision making and counselling segments. The healthcare setting and referral system were shown to influence the interactions and the strategies the counsellors employed. Techniques traditionally advocated were found to be somewhat inefficient in this healthcare context and a contextual model of genetic counselling was proposed. This work will contribute to T Wessels’ PhD which is awaiting examination.
The molecular aetiology of inherited breast cancer in the South African black population

**Researchers:** W Chen, Dr R Kerr, Professor A Krause

**Funding:** NHLSRT, University of the Witwatersrand – Faculty Research Trust

Hereditary breast and ovarian cancer (HBOC) caused by mutations in the BRCA1 or BRCA2 genes have been well studied in other populations. Little is known about the genetic aetiologies of HBOC in the South African black population. The South African black population exhibits a higher than expected incidence of breast cancer, often presenting with early onset and rapid progression of disease. Possible founder mutations may exist within this population. This study aims to investigate 33 South African black individuals presenting with breast cancer. These individuals will be selected based on a predefined high risk profile. Sanger sequencing analysis and Multiplex Ligation-dependent Amplification analysis will be performed to screen for any mutations present in BRCA1 or BRCA2. Three patients tested positive for BRCA mutations.

Ashkenazi Jewish Genetic Testing: Utilisation Of Services, Genetic Knowledge And Perceptions Of Stigma

**Researchers:** K Stoler, C van Wyk, Professor A Krause

Genetic carrier testing programmes originated in different ethnic groups to establish whether an individual or his/her partner carries an inherited recessive genetic mutation that could cause a serious genetic condition in a couple's offspring if both are carriers. A number of conditions have a higher incidence in the Ashkenazi Jewish (AJ) population due to founder effect. This research study focused on the AJ genetic testing programmes available to the Jewish community in Johannesburg, South Africa. It explored the uptake of genetic carrier testing, individuals' understanding of genetics and risk factors, and psychosocial implications of participating in a genetic carrier testing programme.

The study highlighted the limited understanding, absence of stigma and need for genetic services to be promoted further in the AJ community through educational programmes.

Genotype-Phenotype Correlation In South African Black And Afrikaans Individuals With Fanconi Anaemia

**Researchers:** Professor A Krause, Dr C Feben, T Haw

**Collaborators:** Dr L Wainwright, Professor J Poole, Professor D Stones, Dr C Sutton

**Funding:** MRC

Fanconi anaemia (FA) is an inherited disorder which leads to premature death from bone marrow failure or malignancy. FA is caused by allelic mutations in one of at least 13 different genes. The Afrikaans and Black populations in South Africa both have founder FA-causing mutations. This unique genetic homogeneity provides opportunities to establish whether genotype-phenotype correlations exist in Fanconi anaemia.

We aim to describe the clinical features of patients homozygous for Black and Afrikaans founder mutations. Awareness of the clinical features of FA in South African populations will hopefully lead to more efficient diagnosis of FA. 35 Black patients have been examined as part of an MMed project and 8 Afrikaans patients have been seen to date. Many black patients had growth and pigmentary abnormalities. Renal abnormalities occurred in 37% of the patients. We intend to recruit further Afrikaans patients for the project in 2013.
Pathogenic mutations and novel variants in msh6 in a South African colon cancer cohort

**Researchers:** V Bekker, P Pitamber, W Chen, Dr R Kerr, Professor A Krause  
**Funding:** NHLS Research Trust, University of the Witwatersrand: Faculty Research Trust

The two most common cancers that show a heritable component are breast and colorectal cancer (CRC). Research and some diagnostic services for breast cancer exist in South Africa, but little research and no diagnostic service for familial CRC is available in this country. This project is part of a bigger project, the overall aim of which is to set up diagnostic mutation screening for hereditary non-polyposis colorectal cancer (HNPPC). To date, four major genes have been shown to be involved in the aetiology of HNPPC: MSH2, MLH1, MSH6 and PMS2. Together, mutations in MSH2 and MLH1 account for about 90% of all HNPPC in European populations and MSH6 accounts for the remaining 10%. A previous student has completed an investigation of MSH2 and MLH1. This project aimed to set up mutation screening for MSH6, using DNA sequencing. Six patients were screened for MSH6 mutations, one of whom tested positive.

**Genetic aetiology of Li-Fraumeni syndrome in black African patients**

**Researchers:** M Kruger, S Macaulay, W Chen, Professor A Krause  
**Funding:** University of the Witwatersrand: Faculty Research Trust

Li-Fraumeni syndrome (LFS) is a rare, early onset cancer pre-disposition syndrome. LFS is associated with germ-line mutations in the tumour suppressor gene TP53. Germ-line TP53 mutations have treatment and management implications. Patients with germ-line TP53 mutations must avoid radiotherapy as this may cause secondary radiotherapy-induced malignancies. Five black African patients, with LFS associated cancers, were screened for mutations in TP53. Sequence analysis of the coding region of TP53 identified missense mutations in 3/5 patients. A novel mutation was identified in a family from the DRC (p.Phe109Ser). A known pathogenic mutation (p.Arg337His) was identified in a five year old patient with adrenocortical carcinoma. Genetic testing for at-risk family members is available once the mutations have been confirmed in a diagnostic setting. This study describes the first African patients with LFS.

**Genetic factors influencing inhibitor development in a cohort of South African haemophilia a patients.**

**Researchers:** Dr A Lochan, S Macaulay, W Chen, F Essop, Professor J Mahlangu, Professor A Krause, S Macaulay, Professor J Mahlangu  
**Funding:** NHLS Research Trust, University of Witwatersrand

A critical complication of factor VIII (FVIII) concentrate replacement therapy in Haemophilia A (HA) treatment is inhibitor development. The objective of the study aims to characterise and correlate HA disease severity, inhibitor development, intron 22 inversion mutation status, ethnicity and FVIII haplotype in a South African severe HA (sHA) cohort. Of the 249 HA records reviewed, 238 were included for analysis. One hundred and twenty four (52%) were black and the remainder were white. Ninety (38%) patients had the intron 22 inversion mutation (of which 52 were black) and 30 (12%) had inhibitors (of which 22 were black). The H2 haplotype was the commonest in blacks. Preliminary data suggest a correlation exists between this haplotype and inhibitor development.

To screen for a novel FKRP-related muscular dystrophy mutation and identify a possible founder haplotype in South African Afrikaner patients with a dmd/bmd phenotype

**Researchers:** F Essop, C Prentice, M Mudau, Professor A Krause  
**Funding:** NHLS
Muscular dystrophy incorporates a wide range of inherited disorders that involve muscle weakness. The FKRP-related muscular dystrophies involve mutations in the fukutin-related protein (FKRP) gene. A previously unreported FKRP mutation (c.1100T>C) was found in exon 4 of the FKRP gene in two Afrikaner patients, clinically diagnosed with DMD/BMD. 39 white South African patients (clinically diagnosed with DMD/BMD, but negative for common DMD/BMD mutations) and 100 Afrikaner controls were screened for the c.1100T>C mutation. Six Afrikaner patients were found to be homozygous for the mutation and 5 were heterozygous for the mutation. The carrier frequency was estimated to be 1 in every 50 individuals in the general Afrikaner population. Microsatellite analysis showed a possible founder haplotype, suggesting that the c.1100T>C mutation is likely to be a founder mutation in the South African Afrikaner population. FKRP founder mutation screening should be considered in Afrikaner patients who test negative for DMD/BMD.

The effect of excessive paternal alcohol intake on the epigenetic signatures and associated gene regulation at paternally imprinted loci in mice

Researchers: J Knezovich, Professor M Ramsay, Professor M Weinberg
Collaborators: Professor A Ferguson-Smith (University of Cambridge)
Funding: NHLS Research Trust, University of the Witwatersrand – Faculty Research Trust

Epigenetic factors regulate gene expression and are vital components in regulating cell cycle and developmental processes. They are sensitive to the presence of alcohol, which mediates its effects through alterations to DNA methylation, histone modifications and/or RNA intermediates. Imprinted genes rely on DNA methylation to silence alleles in a parent-of-origin specific manner and are important in foetal development.

This study investigates epigenetic signatures at paternally imprinted loci. An association with paternal pre-conception alcohol exposure and gene expression will be examined. It is hypothesised that excessive alcohol exposure will alter epigenetic elements at ICRs associated with genes in sperm DNA and that this would be transmitted to the offspring with concurrent dysregulation of imprinted gene expression.
Transgenerational inheritance of DNA methylation alterations at the h19 imprinting control region following chronic maternal ethanol exposure in mice

**Researchers:** M Ungerer, Professor M Ramsay  
**Funding:** NHLS Research Trust, University of the Witwatersrand – Faculty Research Trust

Foetal alcohol syndrome is characterised by growth and neurodevelopmental deficit. Epigenetic modification is a potential mechanism of alcohol teratogenesis due to its effect on DNA methylation. A mouse model was used to study transgenerational inheritance of DNA methylation alterations at the H19 imprinting control region (ICR) following maternal ethanol exposure. Its contribution to changes in parturition, growth and behaviour was assessed. Mean methylation at the CTCF1 binding site was reduced in the F1 ethanol-exposed group (P=0.021) and trended towards significance in the F2 and F3 ethanol-exposed generations (P=0.083). Phenotypic analysis revealed reduced F1 fertility following alcohol exposure (P=0.003) and alcohol’s effect on growth and behaviour were apparent. These findings support an epigenetic mechanism in alcohol teratogenesis and potential transgenerational effects.

The WNT signalling pathway in systemic sclerosis

**Researchers:** J Frost, Professor M Ramsay  
**Collaborators:** Professor M Tikly (Division of Rheumatology, University of the Witwatersrand)  
**Funding:** Connective Tissue Disease Research Fund (University of the Witwatersrand Medical School)

Systemic sclerosis (SSc) is a complex immune disease involving the vasculature and extracellular matrix. Familial clustering and occupational prevalence indicate both inherited and environmental causes. SSc is characterised by thickening and tightening of the skin. The WNT signalling pathway, involving a family of secreted glycoproteins, directs cell proliferation, cell fate during development and tissue homeostasis, and has been implicated with altered gene expression in SSc.

**Epigenetic mechanisms (changes in gene expression) are pivotal to immune system function and failure to maintain epigenetic homeostasis in the immune response may lead to immune dysfunction and autoimmunity in genetically predisposed individuals. This project examines gene expression, methylation status and protein expression of WNT pathway related genes in black South African patients with SSc.**

Dense genotyping of risk loci in black South Africans with rheumatoid arthritis: an association study

**Researchers:** Dr N Govind, J Frost, Professor M Ramsay,  
**Collaborators:** Professor M Tikly (Division of Rheumatology, University of the Witwatersrand)  
**Funding:** Medical Research Council of South Africa (MRC) and Connective Tissue Disease Research Fund (University of the Witwatersrand Medical School)

Genome wide association studies (GWAS) have identified numerous rheumatoid arthritis (RA) risk loci. However, little is known about the genetics of RA in black South Africans. To test associations in black South Africans with RA, samples were genotyped on the Immunochip. After QC, 117 353 SNPs were tested for association in 263 cases and 365 controls. The strongest associations were found in the MHC region with 64 SNPs reaching statistical significance (most significant with HLA DRB1 and HLA DQA1). In addition there were suggestive associations of 2 SNPs on chromosome 1. In keeping with previous studies the HLA class II region confers the strongest genetic risk. Further studies are required in African RA patients.
Exploring the role of genetic variation at the leptin and the leptin receptor genes (lep and lepr) in obesity and hypertension in a black South African cohort

**Researchers:** T Ngcugcu, Professor M Ramsay  
**Collaborators:** Professor A Woodiwiss and Professor G Norton (School of Pathology)  
**Funders:** National Institute of Health (Fogarty) fellowship through Wits Non-communicable Diseases Research Leadership Programme (NCD), University of the Witwatersrand – Faculty Research Trust, NHLS Research Trust

Obesity and hypertension are common non-communicable disorders, on the increase in South Africa and worldwide, which often occur together. Leptin regulates appetite by binding leptin receptors in the hypothalamus to signal satiety. The LEP and LEPR genes, encoding leptin and its receptor, respectively, are compelling candidate genes. The African Programme on Genes in Hypertension (APOGH) cohort with data for height, weight, skinfold thickness, waist and hip circumference and brachial, aortic (central) and 24 hour ambulatory blood pressure, was studied. LEP and LEPR related SNPs were genotyped in 905 individuals.

Preliminary analysis shows that the LEP SNP rs7799039, previously associated with elevated systolic and diastolic blood pressure in Tunisian men and American women, is not significantly associated in the APOGH cohort.

Renal disease associated with HIV infection among Africans is on the increase, with the lifetime risk of end stage renal disease (ESRD) being threefold higher than among Europeans. Two genes, MYH9 and APOL1, have been identified as risk loci for non-diabetic forms of kidney disease. Their role in HIV positive South African blacks with kidney disease was explored by studying 96 SNPs in 90 patients with kidney disease and 100 matched HIV positive and healthy controls without kidney disease. Genotyping was done using the Illumina BeadXpress system and the rs71785313 SNP was genotyped using TaqMan Assay. The data are being analysed for association with kidney disease in this Southern African population.

The genetics of primary open-angle glaucoma (POAG) in black South Africans: Candidate gene association studies  

**Researchers:** Dr S Williams, T Zwane, Professor M Ramsay  
**Collaborators:** Professor T Carmichael (Division of Ophthalmology, Wits); Dr M Hauser (Duke Center for Human Genetics)  
**Funding:** Carnegie Foundation

POAG is an important cause of irreversible visual loss. This research was designed to identify genetic risk factors for POAG in black South Africans. POAG patients (250) and unaffected controls (250) were enrolled at St John’s Eye Hospital in Soweto and were evaluated in case-control association studies for genetic risk factors in candidate genes. Common genetic variants were identified in...
COL1A1, ZNF469 and MYOC that were marginally associated with POAG. An association was identified with diabetes mellitus and a SNP in WDR36. Combining the data with other African datasets identified associations with TMCO1 and CAV1/CAV2. The genetic risk associated with candidate genes evaluated in this study and POAG in black South Africans is small, suggesting the need for more studies in this population.

**MYOC variants in primary open angle glaucoma (Poag) in black South Africans**

**Researchers:** Dr S Williams, T Wainstein, A Hobbs, Professor M Ramsay  
**Collaborators:** Professor T Carmichael (Division of Ophthalmology, Wits)  
**Funding:** MRC

Mutations in the MYOC gene are important as causal factors in some forms of POAG. This study revealed that South Africans with POAG may have a MYOC mutation that either causes or contributes to their risk for developing POAG in approximately 3.3%. The commonest mutation is a frameshift mutation (Tyr453del) that is incompletely penetrant. Mutation screening successfully identified high-risk individuals who can be monitored to detect early signs of the disease. The Gly374Val mutation is predicted to be damaging to MYOC. It is an uncommon cause of POAG in this population. This study has important implications for the management and counselling of black South African patients with POAG and their families.

**The identification of genetic markers of obesity risk and body composition in a South African black population**

**Researchers:** V Pillay, Dr Z Lombard, Professor N Crowther, Professor H Soodyall  
**Collaborators:** Professor M Ramsay, Professor S Norris (MRC/WITS Developmental Pathways for Health Research Unit)  
**Funding:** NRF Thuthuka, NIH (H3Africa Collaborative Centre), University of the Witwatersrand – Faculty Research Trust

The research aims to identify genetic markers associated with susceptibility to obesity risk in a black South African population of over 40 years (caregivers of the Birth to Twenty (Bt20) cohort). An association study will focus on loci previously associated with obesity measures (body mass index, body fat %, waist to hip circumference) in Europeans, to determine whether they are also role players in an African population. Genotyping will be done using the Illumina Human CardioMetabochip with ~200,000 SNPs identified through genome wide meta-analyses for metabolic and atherosclerotic / cardiovascular diseases and traits to fine map loci previously associated with body composition and to assess association in an African population.

**Genetic diversity in black South Africans from Soweto**

**Researchers:** A May, Professor M Ramsay  
**Funding:** Novartis, Basel, Switzerland

Due to the genetic diversity of its peoples, Africa is attracting research attention. However, few studies have explored southern Africa, which comprises mostly southeastern Bantu-speakers. We present a detailed exploration of genetic diversity in 94 unrelated southeastern Bantu-speakers from Soweto. Participants were typed for approximately 4.3 million SNPs using the Illumina Omni5 beadchip. PCA and ADMIXTURE indicated that southeastern Bantu-speakers are distinct from other Africans.

We compared our results to participants in a rheumatoid arthritis case-control study. Controls showed good clustering with our sample, but some cases demonstrated notable admixture. Sowetan population structure thus appears unique, and may have clinical implications. Our data represent a suitable reference for southeastern Bantu-speakers and constitute a prelude to the Southern African Human Genome Programme.
Genetic risk factors for painful HIV-associated sensory neuropathy (hiv-sn) in black southern africans

Researchers: L Hendry, J Mellet, Dr Z Lombard
Collaborators: Professor P Kamerman (School of Physiology, University of the Witwatersrand), A Wadley (School of Physiology, University of the Witwatersrand), Professor P Price (School of Pathology and Laboratory Medicine, University of Western Australia), Dr C Cherry (Burnet Institute, Melbourne, Australia)
Funding: Wits URC, Wits FRC, Belgian Embassy Masters fellowship

HIV-SN is a common complication associated with HIV-infection, with a common symptom being pain. Variation at specific loci within genes has been suggested to alter susceptibility to developing HIV-SN and pain, and the intensity of the pain experienced. The current research involved conducting an in-depth study, in a black Southern African population, of previously identified genes. SNPs identified in the literature were supplemented with population appropriate tagSNPs. Following genotyping and association analysis, it was found that some SNPs and haplotypes associated with HIV-SN susceptibility, pain susceptibility and pain intensity, but none of the results were consistent with that which has been found in previous studies in non-African populations, emphasising the importance of conducting genetic association studies in separate ethnic groups.

Reconstructing the maternal ancestry of the Malagasy

Researchers: P Patel, A Hobbs, Professor H Soodyall
Collaborators: Professor T Jenkins, G Campbell (Montreal, Canada)
Funding: MRC and National Genographic Project

This study employs genetic markers to elucidate the maternal origins of the Malagasy using 981 samples. Phylogenetically informative SNPs were screened for using single base extension assays. Non-coding hypervariable regions (I and II) were sequenced using previously published protocols. The intergenic COII/tRNALys 9-bp deletion used in conjunction with sequence data was useful at distinguishing sequences derived from African and Asian sources.

In addition, sequencing of coding region SNPs (1473C-T and 3423T-A) definitive of the “Malagasy motif” was conducted. Using the recommended nomenclature for mtDNA haplogroups, 41.28% of mtDNA lineages were traced to African sources and 58.72% to non-African origins. The 9-bp deletion occurred at 22.73%. This study corroborates historical, linguistic and archaeological data concerning the parental origins of the Malagasy.

Reconstructing the origins of the Abelungu people from the Eastern Cape

Researchers: D Deveredicis, Professor H Soodyall
Collaborator: J Kalis (University of Umtata)
Funding: MRC and National Geographic Society

Since Y chromosome DNA is inherited patrilineally, like surnames, we have used Y chromosome DNA markers to test the oral history of the Mlungu clan, that they are descended from “two brothers” of European origin. If their claim is correct, then we would expect to find the same Y chromosome DNA haplotype in their descendants.

In addition, this haplogroup would be placed on a branch of the human Y chromosome phylogenetic tree that has non-African (either European or Asian) origins. So far, we have found a high proportion of non-African Y chromosomes among men tested, but the female gene pool examined using mtDNA is sub-Saharan African. Overall, this study brings together anthropological and genetic studies in refining the oral narrative of local populations.
Tracing the genetic ancestry of coloured communities in the Eastern Cape

**Researchers:** R Mahabeer, T Naidoo, Professor H Soodyall

**Funding:** MRC

We conducted field work in PE and surroundings following an invitation by the Khoe-San Political Strategic Task Team for PE and Uitenhage between 28 September–1 October, 2012. We sampled 119 individuals of whom 75 were males and 44 female volunteers. Majority of the people sampled self-identified as Coloured, but claimed Khoe-San ancestry. Thus far 53.3% (40/75) Y chromosomes have been resolved into haplogroups which are more commonly found outside of Africa (haplogroups G, H, I, KN, R*, R1b). The commonest haplogroup suggestive of African ancestry was E3a which was found at a frequency of 30.6%. We are currently completing the mtDNA analysis. This data will be combined with our previous studies on groups from the Eastern Cape to better understand the genetic structure of Coloured groups from this region.

High resolution SNP analysis of Eurasian haplogroups r1a and r1b in Southern Africa

**Researchers:** L Gaskell, T Naidoo, Professor H Soodyall

**Funding:** MRC

Haplogroups R1a and R1b comprise two of the most common Y chromosome clades in Eurasia, with R1a found most often in Eastern Europe and Asia, while R1b obtains its highest frequencies in Western Europe. Some of the subclades within R1a and R1b, however, display geographic structuring at a higher level of resolution. Genotyping of these subclades would allow one to determine, more precisely, the ancestral origin of an R1a or R1b Y chromosome. Two multiplex single base extension (SBE) assays were developed to resolve the R1a and R1b haplogroups into their subclades. Thus far we have found that within haplogroup R1a (95 individuals), most individuals fell into haplogroup R1a1a1 (R-M417) (87/95) with the rest belonging to haplogroup R1a1a1b1a1 (R-M458) (8/95). Haplogroup R1b (255 individuals) contained more diversity. Of the eight subclades, haplogroup R1b1a2a1a1a (R-U106) was most common (85/255), followed by R1b1a2a1a1b3 (R-M529) (57/255). Haplogroups R1b1a2a1a1b (R-S116) (42/255) and R1b1a2a1a1b2 (R-U152) (44/255) displayed similar frequencies, while low frequencies were found for R1b1a2a (R-L23) (12/255), R1b1a2a1a1 (R-L11) (7/255), R1b1c (R-V88) (7/255) and R1b1a2 (R-M269) (1/255).

Age of the association between Helicobacter pylori and man

**Researchers:** Dr CM Schlebusch, Professor H Soodyall

**Collaborators:** S vd Merve (University of Pretoria), Y Moodley (Max-Planck Institute, Berlin, Germany)

**Funding:** MRC

When modern humans left Africa circa 60,000 years ago, they were already infected with Helicobacter pylori, and these bacteria have subsequently diversified in parallel with their human hosts. We investigated the diversity of H.pylori in Africa, where both humans and H.pylori originated. Three distinct H. pylori populations are native to Africa: hpNEAfrica in Afro-Asiatic and Nilo-Saharan speakers, hpAfrica1 in Niger-Congo speakers and hpAfrica2 in South Africa. Rather than representing a sustained co-evolution over millions of years, we find that the coalescent for all H. pylori plus its closest relative H.acinonychis dates to 88–116,000 years. At that time the phylogeny split into two primary super-lineages, one of which is associated with the former hunter-gatherers in southern Africa known as the San. H. acinonychis, which infects large felines, resulted from a later host jump from the San, 43–56,000 years ago.
These dating estimates, together with striking phylogenetic and quantitative human-bacterial similarities show that H. pylori is approximately as old as are anatomically modern humans. They also suggest that H. pylori may have been acquired via a single host jump from an unknown, non-human host. We also find evidence for a second Out of Africa migration in the last 52,000 years.

**MTDNA control region variation affirms diversity and deep structure in populations from southern Africa**

**Researchers:** Dr CM Schlebusch, Professor H Soodyall  
**Collaborators:** M Lombard (University of Johannesburg)  
**Funding:** MRC

The current San and Khoe populations are remnant groups of a much larger and widely dispersed population of hunter-gatherers and pastoralists, who had exclusive occupation of southern Africa before the influx of Bantu-speakers from 2000 years ago and sea-borne immigrants within the last 350 years. Use mitochondrial DNA (mtDNA) we examined the population structure of various San and Khoe groups, including seven different Khoe-San groups (Ju/hoansi, !Xun, /Gui+/Gana, Khwe, ≠Khomani, Nama and Karretjie People), three different Coloured groups and seven other comparative groups. MtDNA hyper variable segments I and II (HVS I and HVS II) together with selected mtDNA coding region SNPs were used to assign 538 individuals to 18 haplogroups encompassing 245 unique haplotypes. Data was further analysed to assess haplogroup histories and the genetic affinities of the various San, Khoe and Coloured populations. Where possible, we tentatively contextualise the genetic trends through time against key trends known from the archaeological record. The most striking observation from this study was the high frequencies of the oldest mtDNA haplogroups (L0d and L0k) that can be traced back in time to approximately 100,000 years ago, found at high frequencies in Khoe-San and sampled Coloured groups. Furthermore, the L0d/k sub-haplogroups were differentially distributed in the different Khoe-San and Coloured groups and had different signals of expansion, which suggested different associated demographic histories. When populations were compared to each other, San groups from the northern parts of southern Africa (Ju speaking: !Xun, Ju/hoansi and Khoe-speaking: /Gui+/Gana) grouped together and southern groups (historically Tuu speaking: ≠Khomani and Karretjie People and some Coloured groups) grouped together. The Khoe group (Nama) clustered with the southern Khoe-San and Coloured groups. The Khwe mtDNA profile was very different from other Khoe-San groups with high proportions of Bantu-speaking admixture but also unique distributions of other mtDNA lineages.

**Genome variation in seven khoe-san groups reveals adaptation and complex African history**

**Researchers:** Professor H Soodyall  
**Collaborators:** CM Schlebusch & M Jakobsson (Uppsala University, Sweden); M de Jongh (UNISA)  
**Funding:** MRC

We genotyped approximately 2.3 million SNPs in 220 southern Africans and found that the Khoe-San diverged from other populations >100,000 years ago, with a divergence time almost twice as long as any other living population in the world. While genetic data supports the common origin of the different Khoe-San speaking groups, there was evidence of genetic structure (differences) among Northern and Southern Khoe-San groups dating back to 35,000 years ago. These data could not unambiguously resolve the geographic region of origin of modern humans to a single region in Africa, though southern Africa was a likely region of origin.
Several genes associated with development and morphology was highly selected for in global populations, but genes implicated in immunity were highly selected for among the southern African populations.

Crossing the sub-Sahara: The phylogeography of haplogroup B2b

Researchers: T Naidoo, A Hobbs, R Mahabeer, S Harris, D De Veredicis, Professor H Soodyall
Collaborators: CM Schlebusch (Uppsala University, Sweden), DE Platt (IBM, USA), and the Genographic Consortium
Funding: MRC, NRF, NHLS Research Trust and National Geographic Society

The present study examined Y chromosome DNA variation within haplogroup B2b, defined by seven bi-allelic markers and 17 microsatellites, in more than 4,500 males from sub-Saharan Africa. These data were used to elucidate the complex patterns involved in the evolution of haplogroup B2b and the human movements involved in its spread across sub-Saharan Africa. We identified 365 Y chromosomes belonging to haplogroup B2b. Many of the subclades of haplogroup B2b exhibited substantial population specificity: B2b1 and B2b4a occurred among the Khoe-San and their descendent populations in southern Africa; B2b2 was found only in the Mbuti from northeastern Democratic Republic of Congo; while B2b3 and B2b4b were restricted primarily to the Western Pygmy groups (Baka, Bakola, Biaka and Mbenzele) of Cameroon, Central African Republic and Gabon. Paragroups B2b* and B2b4* however, displayed wider distribution and were present in populations across central, east and southern Africa. Haplogroup B2b was found throughout most of sub-Saharan Africa; from Cameroon in the west to Kenya in the east, and in southern Africa (including Madagascar - 2.8%). The highest frequencies were observed in hunter-gatherer populations, with frequencies of 51% in the Hadzabe, 44% in the Mbuti, and 33% in the Ju’hoansi. The distribution of haplogroup B2b and its subclades across sub-Saharan Africa appears to be characterised by the movement of hunter-gatherer populations following the end of the last glacial maximum.

Teaching And Training

The Division of Human Genetics contributes to both undergraduate and postgraduate teaching in the Faculty of Health Sciences, University of the Witwatersrand. The clinicians, counsellors and medical scientists remain active in training of lay groups in support and counselling skills.

Professor JGR Kromberg assists with research supervision and mentoring of young inexperienced staff. She has instituted a monthly research meeting in the division for staff and students to discuss the progress of their research on an ongoing basis.

Members of the clinical section of the division serve on the first constituted College of Medical Genetics for South Africa.

Undergraduate level

In the MBBCh course, undergraduate teaching is provided to medical students in Molecular Medicine in second year and in medical genetics in GEMP 1, 2 and 3. The Division also gives human and medical genetics lectures to undergraduates in physiotherapy, speech therapy, pharmacy and occupational therapy.

Postgraduate level

The division continues to teach a BHSc (Hons) in Human Genetics. MSc and PhD degrees by research continue to be undertaken and a second year programme for the MSc (Med) in Genetic Counselling was offered in 2012. In 2007 medical genetics became a primary specialty. Primary specialty training in medical genetics was initiated in January 2009, and the first two registrars wrote
and passed their Part 2 CMSA exams in Medical Genetics in August/October 2012. In addition, they both completed the requirements and obtained their MMed in Medical Genetics. A third registrar is due to write Part 2 CMSA exams in April 2013. No intern posts were available for the training of genetic counsellors or medical scientists in 2012 and 2013.

Amoratorium on teaching and training of medical geneticists and medical genetic counsellors was put in place in 2013. The decision was taken for several reasons. Firstly, the continuing reduction of staff in the clinical unit was making teaching untenable, particularly as the staff reduction is increasing the remaining individuals’ commitment to the already excessive workload. Add to this the situation in the laboratories in which the technology available is from the 1990s, and the staff shortages have made it increasingly difficult to assure the quality of work. Finally, posts for genetic counsellor internships were not made available and substantive posts for newly qualified registered medical geneticists and counsellors are not available in the country.

Postgraduate teaching is given to registrars in psychiatry, paediatrics, pathology, internal medicine, family medicine and MSc students in occupational therapy, medical ethics and neuro-developmental paediatrics and midwives and nurses.

**Professional Development**

Postgraduate candidate (1 April 2012 - 31 March 2013):
- 45; 4 BHSc (Honours), 13 MSc (Med) Human Genetics, 4 MSc (Med) Genetic Counselling, 3 MMed, 8 PhD, 3 postdoctoral fellows.

Postgraduate candidates who graduated (1 April 2012 - 31 March 2013):
- 10; 3 BHSc (Honours), 3 MSc (Med) Human Genetics, 2 MMed.

**Research Output**

**Journal articles**


Chapters in Books


Conference presentations

International: 6
National: 3
Local: 12
Department of Molecular Medicine And Haematology

Head: Professor Wendy Stevens

The Department of Molecular Medicine and Haematology had another successful year of providing world-class laboratory medicine, professional development and educational innovation and research. Progress was seen in all areas of departmental activities notwithstanding the provision of haematology and molecular medicine diagnostic services, basic and translational research, and undergraduate, postgraduate and registrar teaching and mentoring.

The department continued to attract postgraduate students and expanded its current national and international diagnostic footprint and scientific collaborations. Importantly, the department accelerated translational breakthroughs in areas such as TB diagnostics nationwide, and impacted on health systems strengthening and public policy. This was due to the commitment of our community of exceptional clinicians, researchers, teachers, students and staff.

The excellence displayed by this team was acknowledged at the recent National Awards ceremony for the National Health Laboratory Service (NHLS) where the group was awarded the Best Academic Laboratory Award; The Innovation Award and the CEO’s award. In addition, this department has provided the bulk of the research and development activities to support the activities of the National Priority Programme (NPP).

Diagnostic Services

In the period under review, overall total diagnostic test volumes in the department increased by 16% when compared to the previous financial year. This increase largely relates to the HIV related tests such as the HIV PCR viral load assays which have grown 37% year on year, from 312 595 viral load tests in the previous financial year to 441 554 samples in the current financial year.

The average turnaround time for all test methods remains resolute in that for the second consecutive year, 97% of set targets were met during this financial period. The overall performance on EQA for all test methods in the department was scored 86% within consensus. All diagnostic service laboratories within the department retained their SANAS accreditation status for the 12th consecutive year in 2012.

Research and Development

The department received significant sponsored research funding for academic and National priority related projects during the current financial under review. This included national and international funding donors, such as the Global Fund, Centres for Disease Control (CDC,) Gates Foundation, FIND, the South African Department of Science and Technology, among numerous others.

Overall, during the current financial period the staff contributed to 80 peer review publications in addition to two textbooks. Most of the articles were published in internationally accredited journals. The department staff also participated in 57 conferences both national and international, presenting both oral and poster presentations, as well as organizing workshops. These exclude the invited oral presentations by senior members with respect to activities for the NPP.

Teaching and Training

As part of the School of Pathology of the University of the Witwatersrand and NHLS, the department continued its teaching and
training activities in the fields of medical technology, haematology pathology, clinical haematology and molecular medicine. Students taught and trained in the department included those doing GEMP I and II, Bachelor of Medical Science, trainee medical technicians, trainee medical technologists, intern science students, trainee medical scientists, BSc(Hons), MSc and PhD postgraduate students, haematopathology registrars, clinical pathology registrars and clinical haematology registrars.

In addition, all the student technologists and registrars who wrote their board examinations have passed. Furthermore, several successes and commercial opportunities have arisen from the collaboration with the engineering department in running the Biomedical Engineering degree.

The table below depicts the number of postgraduate degrees that were awarded during the financial period under review and those that are in progress:

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<tr>
<th>Degree</th>
<th>Completed FY 13</th>
<th>In Progress</th>
<th>Total</th>
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<td>5</td>
<td>10</td>
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<tr>
<td>MSc</td>
<td>3</td>
<td>22</td>
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</tr>
<tr>
<td>PhD</td>
<td>4</td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td>Grand Total</td>
<td>12</td>
<td>50</td>
<td>62</td>
</tr>
</tbody>
</table>

The department continues to have a diverse range of diagnostic, research and teaching activities that are separated and managed in functional units that are described alphabetically and in no order of importance in the text below.

The highlights below provide a small glimpse into the breadth of activities, advances and innovations during the last financial period.

**Antiviral Gene Therapy Research Unit**

**Director:** Professor Patrick Arbuthnot

**Research Projects**

The Antiviral Gene Therapy Research Unit has continued to focus its research activities on the use of nucleic acids to inhibit viral replication. The long term objective remains the advancement of this approach for the treatment of viral infections that are particularly important to sub-Saharan Africa.

Previous research has been concerned with harnessing the RNA interference pathway to inhibit HBV, HIV-1 and rift valley fever viruses. Progress on these topics has been good and highly effective antiviral sequences have been thoroughly characterised.

These results have been summarised in previous reports and continue to be the topic of research publications. To address the problem of delivery of silencing nucleic acids to target tissues, engineering viral and non-viral vectors has been undertaken. Particularly, we have been investigating the utility of recombinant adenoviruses, adeno-associated viruses and lentiviruses for delivery of gene silencers to target tissues such as the liver.

An important new development has been the use of so-called ‘designer nucleases’ to target and disable hepatitis B virus gene expression.

These engineered DNA-digesting enzymes are particularly powerful as they are capable of recognizing specific HBV sequences and introducing mutations at intended sites. During the coming year, we will continue to focus on these topics.
Teaching and Training

Members of the Antiviral Gene Therapy Research Unit continue to be involved extensively in the teaching of undergraduate medical students and also of BSc Honours candidates. The main responsibility is to the training of postgraduates, and these duties are summarized below.

Graduating Students 2012

Liam Thompson Title: Signalling aptamers for the detection of HBV serological markers in patients at risk of hepatocellular carcinoma.

Current Postgraduate students

<table>
<thead>
<tr>
<th>Student name</th>
<th>Degree (year registered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juliette Delhove</td>
<td>PhD (2012)</td>
</tr>
<tr>
<td>Musa Marimani</td>
<td>PhD (2010)</td>
</tr>
<tr>
<td>Kristie Bloom</td>
<td>PhD (2010)</td>
</tr>
<tr>
<td>Justin Hean</td>
<td>PhD (2010)</td>
</tr>
<tr>
<td>Carol Crowther</td>
<td>PhD (Thesis Submitted)</td>
</tr>
<tr>
<td>Fiona van den Berg</td>
<td>PhD (2009)</td>
</tr>
<tr>
<td>Fidan Karatas</td>
<td>PhD (2011)</td>
</tr>
<tr>
<td>Tristan Scott</td>
<td>PhD (2009)</td>
</tr>
<tr>
<td>Dejana Ivacik</td>
<td>PhD (2010)</td>
</tr>
<tr>
<td>Tafadzwa Mlambo</td>
<td>MSc (2010)</td>
</tr>
<tr>
<td>Neliswa Nhlabatsi</td>
<td>MSc (2010)</td>
</tr>
<tr>
<td>Michelle Robinson</td>
<td>MSc (2011)</td>
</tr>
<tr>
<td>Timothy Dreyer</td>
<td>MSc (2013)</td>
</tr>
</tbody>
</table>

Professional Development

Dr Mohube Betty Mowa was appointed a lecturer in the School of Pathology during May of 2012. This position was made possible through the transformation and equity initiative that is directed by the University Vice Chancellor. Betty continues to make excellent progress with her research work and is enthusiastically involved with student supervision. Abdullah Ely recently received promotion to Senior Researcher and he too is making excellent progress as a young researcher.

Conference Attendance 2012/3

Researchers from the AGTRU were well represented at South African and international conferences during 2012/3. International meetings where our work was presented include the American Society for Gene and Cell Therapy annual conference (Philadelphia, USA), Keystone Symposium on Gene silencing by small RNAs (Vancouver, Canada), European Society of Gene and Cell Therapy (Versailles, France), International Meeting on the Molecular Biology of Hepatitis B viruses (Oxford, UK) and the German Gene Therapy Society Conference (Hamburg, Germany).

Automated Haematology Laboratory

Pathologist in Charge: Dr Elise Schapkaitz

Diagnostic Services

The unit forms part of a Total Automated clinical pathology service, which serves the Charlotte Maxeke Academic Hospital and surrounding clinics. The unit continues to serve as a national reference laboratory for both the private and public sectors. The laboratory provides a 24 hour service for the full blood count and differential count.

Current research Projects are listed below:
1. Local Clinical Validation of modified ISLH guidelines
2. Guidelines for checking samples and reviewing Slides in Routine Haematology
3. Evaluation of the Peripheral blood Smear (PBS) Review Rate at the Charlotte Maxeke Johannesburg Academic Hospital Laboratory Complex
4. Evaluating the rules/criteria and the impact of these defined triggering values on the PBS review rate. The objective is to reduce the workload of PBS review, while not compromising patient care by reporting false negative results.
5. Determination of the false negative rate.
6. Evaluation of morphologic flags on the Advia 2120 automated analyser with specific reference to paediatric haematology oncology samples
7. Validation of the Advia(2) 2120 automated method for measurement of the ESR
8. Validation of the Humased automated method for measurement of the ESR
9. Validation of the Reticulocyte haemoglobin content (Chr) on the Advia(2) 2120 haematology analyser

Teaching and Training

Training is provided for the following staff categories: Registrars, technologists/technicians, CPD

Training Objectives are as follows:
• Understand total laboratory automation
• Understand automation in haematology
• Understand IQC, EQA and troubleshooting
• Become familiar with rules for checking samples and for manual review of slides
• Become familiar with quality management

MMED Project (D Pillay):
• Diagnosis of haematological malignancies in the era of Total Laboratory Automation: Comparison of the Advia 2120 to immunophenotyping and morphology

Research Output
1. Evaluation of Quality indicators at the Charlotte Maxeke Johannesburg Academic Hospital Laboratory Complex
2. Laboratory errors impact on patient care. Management strategy is to identify and monitor pre-analytical (sample rejection), analytical (repeat testing, IQC and EQA performance) and post analytical critical areas (critical value policies and reporting and TATs). Assess the role of intervention e.g. training on laboratory performance
3. Evaluation of Critical value Reporting at the Charlotte Maxeke Johannesburg Academic Hospital Laboratory Complex
4. Technological solutions to Improve Critical Value Reporting at the Charlotte Maxeke Johannesburg Academic Hospital Laboratory Complex

Bleeding Disorders Research Unit

Director: Professor Johnny Mahlangu
Research coordinators: Dimakatso Mafokwane, Nontobeka Nkonyane, Malebo Motiane

Diagnostic services

In the year under review, the unit received 127 referrals with unknown bleeding diathesis from Gauteng, Mpumalanga and North West provinces. Confirmed diagnoses included congenital haemophilia (25), von Willebrand disease (8), acquired haemophilia (4) or platelet disorders (7). The remainder either did not have a bleeding diathesis or had an as yet uncharacterized bleeding disorder.

Research projects

Ongoing research in the unit includes clinical trials (15), investigator initiated collaborative research projects (11) and postgraduate research (3).
Teaching and training
Teaching in the unit included lectures to medical registrars, haematology registrars, undergraduate students as well as technologists and technicians. There are currently 3 masters students doing projects in the unit.

Professional development
All unit staff attended good clinical practice instruction

CD4, HIV- and Immunohaematology and Flow Cytometry
**Pathologist in charge:** Prof Debbie Glencross

Diagnostic services
The CMJAH Flow Cytometry laboratory comprises three separate units including CD4/ HIV Immunology, the Leukaemia and Lymphoma Diagnostic and the Immunohaematology/ Transplant and Cross Match services. During 2012, the Helen Joseph CD4 laboratory was consolidated into the CMJAH CD4 laboratory to rationalize CD4 services around Johannesburg. In addition to routine CD4 enumeration of ~15000 samples per month, additional service includes workup for primary immunodeficiency, a Leukaemia/ lymphoma Diagnostic service well as cross-matching for transplantation, HLA typing and antibody screening, cytokine analysis and diagnosis of paroxysmal nocturnal hemoglobinuria (PNH).

In September 2012, the CD4 unit began implementation of reflex Cryptococcal Antigen (CrAg) screening in all CD4 samples with counts < 100 cells/µl in support of the national Department of Health initiative to diagnose and treat patients with cryptococcal infection. Professor D Glencross also heads up the NPP CD4 programme, assisted by Dr L Coetze, who coordinates CD4 service delivery, standardisation, implementation and training of CD4 services across the NHLS.

Research
Current research projects focus on immunological aspects in a range of diseases including cancer, HIV, TB, neonatal sepsis, as well as the immunological pathways involved in sleep, bee-venom desensitization, immune-reconstitution and transplantation. Most of these projects are grant-funded and incorporate both local and international collaborations. Other studies include ongoing evaluation of new and emerging CD4 technologies as well as various immunological HIV sub-studies and CD38 monitoring in the context of antiretroviral treatment for HIV/ AIDS. In collaboration with Dr Helen Payne as Wellcome Trust Research Training Fellow, the unit has undertaken a large neonate and childhood normal range study in south Africa.

Teaching and Training
This unit participates in both undergraduate lecturing, including both the Molecular Medicine II and III as well as the GEMP 1 courses, and postgraduate tutorials, for the MMED part 1 (pathology) and MMED part 2. In addition, the unit is responsible for input into the BSc Honours courses, runs the bi-annual 2-week Immunology course, is responsible for Registrar Leukaemia/ lymphoma training and also coordinates and runs 6 NHLS NPP CD4 training courses per annum as well as coordinating on-site training and laboratory audits.

There are three MMed masters students registered including Drs Kilfoil, Mannaru and Havyarimana. The NPP CD4 training workshops, held up to 4 times per annum, are coordinated through this unit. Dr Elizabeth Mayne and Ms C Worsley serve as members of the NHLS Immunology Expert Committee (both are registered PhD candidates). Dr Mayne represents the dept for Registrar Teaching and Training Committee (representing haematology and immunology), is an Executive of the South African Immunology Society (head:
teaching and learning subcommittee) and the South African Transplant Society and a committee member of the University of the Witwatersrand Postgraduate Teaching and Learning Committee, 3rd year working party.

**Professional development**

Denise Lawrie, Laboratory Manager of this unit obtained her PhD and will graduate in July 2013.

**Honours**

This laboratory is very proud of CD4 staff members Lilia Moreira and Nonhlanhla Vera Sibiya, who received awards during the recent NHLS Awards for Runner up, Best Lab Supervisor and Runner up, Best Technician, respectively.

Dr Elizabeth Mayne received the Phyllis Knocker Bradlow Award for Excellence (top award of the Colleges of Medicine for examination performance and post examination contributions to medicine). She also received a NRF Thuthuka grant (3 year major PhD funding) as well as a Discovery Academic Excellence Award.

**Clinical Haematology – NHLS 2012**

**Pathologist in charge:** Prof Barry Jacobson

**Consultants:** Prof Johnny Mahlangu, Dr Susan Louw,

**Specialist Sisters:** Sister Theodora Sheila Kruger, Sister Johanna Sithole (BNurs)

Clinical haematology provides a consultative service to indigent patients both in-patients and out-patients at the Charlotte Maxeke Hospital Johannesburg Academic Hospital as well as private patients both at the Charlotte Maxeke Hospital and at the Donald Gordon Hospital.

Professor Mahlangu heads the Adult Haemophilia Clinic which provides comprehensive care for these patients at the Charlotte Maxeke Hospital.

An active teaching programme is provided for Registrars who rotate through Clinical Haematology. There is a formal two year Registrar training programme offered in conjunction with Professor Moosa Patel’s unit in the Charlotte Maxeke Hospital to obtain certification in the sub-speciality of Clinical Haematology.

The Anti-coagulation Clinic was started 15 years ago by Professor Jacobson and patients are counselled and monitored by Sister Johanna Sithole and Sister Theodora Sheila Kruger. They are also instructed in home treatment with low molecular weight heparin. They are actively involved in a national programme to train nursing staff in anti-coagulation.

**Summary of research and plans**

- Increase number of clinical consultants at NHLS, Charlotte Maxeke Hospital.
- Flying and thrombosis.

**Meetings held**

Southern African Society of Thrombosis and Haemostasis annual conference. Approximately 150 people attended including Physicians, Clinical Haematologists, Haematopathologists, Radiologists, Pulmonologists, General Surgeons, Vascular Surgeons, Cardiac Surgeons, Neurologists, Neurosurgeons, Urologists, Paediatricians, Gynaecologists and Anaesthetists. Registrars in training from these disciplines also attended.

**Collaborations**

Dutch collaboration with Cirion investigator group, Slotervaart teaching hospital Amsterdam, The Netherlands.

**Invited as Guest Speaker in 2012 (Prof Jacobson)**

• 24 March – Botswana presentation to physicians – How to investigate and manage a patient presenting on VTE.
• 25 May – Livingstone Hospital - Resource Centre. Invited guest speaker. An approach to the investigation, diagnosis and management of Venous Thromboembolism (V.T.E.)
• 19 July – SA Heart Annual Congress. Sun City. Invited guest speaker.
• 28 October – Southern African Society of Thrombosis and Haemostasis. Speaker: Rebound thrombosis after stopping anticoagulation - Fact or Fantasy?

Current Post-graduate projects undertaken in Clinical Haematology include:
Dr Nikki Delport – Achieving therapeutic anti-XA levels in critically ill patients receiving standard dose enoxaparin.
Dr Estee Benade - Validation of coagucheck P.O.C. device.
Dr Elize van Rooy – Determination of coagulation disturbances secondary to unpressurised flight.

Chris Hani Baragwaneth Hospital: Haematology
Pathologist in charge: Dr Nazeer Alli
Diagnostic services:

The haematology department continues to provide a basic laboratory service to the hospital and clinics in surrounding areas. Specialised tests have been centralised at CMAJH laboratory and Wits Medical School as a cost effective measure. However, CD4 counts are done on site.

The laboratory boasts one of the most automated platforms in the country (Roche diagnostics), which is comprised of two full blood count analysers, two slide makers-stainers, two coagulation analysers, an automated ESR analyser, a digital microscopy system and a stockyard. The sophisticated software allows for auto-review of differential counts which has reduced the numbers of slides for manual microscope review by 40%.

Academic activities:

a) Training and teaching:
   i. Registrars and student technologists rotate through the department as part of their curriculum.
   ii. An in-house CPD accredited teaching programme for resident staff is in place.

b) Clinical activity:
   i. Participation in haematology clinics (Mon & Tues).
   ii. Attendance of ward rounds.

c) Multi-disciplinary meetings are held fortnightly with paediatric oncology and adult haematology departments.

d) Research activity:
   e) 1 MSc graduate, Nov 2012

Early Infant Diagnosis (EID) Unit
Pathologist in charge: Prof Gayle Sherman
The Early Infant Diagnosis (EID) unit aims to assist in delivery of quality HIV diagnostic services for infants and children in collaboration with the national and provincial...
departments of health and other partners by training, provision of technical assistance, research, monitoring and advocacy.

Sister Tsakani Mhlongo performs EID training on Early Infant Diagnosis for doctors, nurses, counsellors and facility managers nationally. The training spans specimen collection to interpretation of HIV PCR and rapid test results in children with a view to ensuring that all identified HIV-infected infants access care (Table 1).

Table 1: Number of healthcare workers trained on EID during 2012/3

<table>
<thead>
<tr>
<th>Month</th>
<th>Number of Health Careworkers trained</th>
<th>Provinces</th>
<th>Number of Facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2012</td>
<td>30</td>
<td>GP</td>
<td>23</td>
</tr>
<tr>
<td>May 2012</td>
<td>137</td>
<td>LP, GP, MPU</td>
<td>98</td>
</tr>
<tr>
<td>June 2012</td>
<td>134</td>
<td>GP, NW, MPU</td>
<td>97</td>
</tr>
<tr>
<td>July 2012</td>
<td>78</td>
<td>MPU, GP</td>
<td>64</td>
</tr>
<tr>
<td>Aug 2012</td>
<td>148</td>
<td>GP, MPU</td>
<td>135</td>
</tr>
<tr>
<td>Sept 2012</td>
<td>155</td>
<td>GP, MPU</td>
<td>141</td>
</tr>
<tr>
<td>Oct 2012</td>
<td>112</td>
<td>KZN, GP, MPU</td>
<td>65</td>
</tr>
<tr>
<td>Nov 2012</td>
<td>112</td>
<td>NW, LP, GP</td>
<td>103</td>
</tr>
<tr>
<td>Dec 2012</td>
<td>32</td>
<td>GP</td>
<td>31</td>
</tr>
<tr>
<td>Jan 2013</td>
<td>56</td>
<td>NW, MPU</td>
<td>47</td>
</tr>
<tr>
<td>Feb 2013</td>
<td>204</td>
<td>NW, MPU, GP</td>
<td>163</td>
</tr>
<tr>
<td>Mar 2013</td>
<td>Training of master trainers for national DoH 2013 guideline implementation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1198</td>
<td>967</td>
<td></td>
</tr>
</tbody>
</table>

The training materials used viz. the SOP for “Taking blood from infants for the HIV PCR test” and poster for dried blood spot (DBS) collection, were developed by the EID unit and are freely available on the NHLS website. Hard copies of these training aids are distributed nationally during training or on request.

**Technical assistance** is provided for policy development on infant diagnosis nationally e.g. to the Department of Health (DoH) and the HIV Clinicians Society, and internationally to the World Health Organization and via the Laboratory Working Group of the Inter-Agency Task Team. The unit is represented on both the PMTCT and Paediatric Technical Working Groups at the DoH, participated in formulating the 2013 South African PMTCT and Paediatric treatment guidelines and assisted in cascading training on the new guidelines nationally. The unit provides clinical support for problematic cases nationally to ensure that children on lifelong HAART are definitely HIV-infected.

**Monitoring** of the national Early Infant Diagnosis (EID) programme is achieved in collaboration with the NHLS Corporate Data Warehouse. Two PCR reports are distributed monthly to managers from national down to facility level detailing PCR tests performed against targets of exposed infants per province/district to measure EID coverage, proxies for early vertical transmission and numbers of PCR positive infants per facility requiring tracking into care. The monitoring function is constantly being improved to assist in addressing challenges experienced in the field.

**Research** activities, funded by UNICEF and PEPFAR, include the assessment of laboratory and field-based HIV tests for use in diagnostic algorithms for infants and children. Clinical research is conducted in collaboration with Prof A. Coovadia at Rahima Moosa Mother and Child Hospital. Currently two Masters and one PhD student are under supervision in the unit.
Evolutionary Medicine

Pathologists in charge: Dr Pierre M Duran
http://www.wits.ac.za/pathology/emu

This group continued with their main research focus, which is the emergence of biocomplexity in disease. There are currently three PhD and three MSc projects under Dr Pierre's supervision. These include the evolution of multicellularity, origin of life and death genetic programmes, cancer and molecular systems dynamics. There were several highlights to the year for Pierre's research lab: (i) two of Pierre's students won conference awards in 2012 (see * Dylan Chapman and Nisha Dhar’s presentations below); (ii) Pierre was awarded a NASA grant together with his collaborators in the USA.

Haemostasis and Thrombosis laboratory
Pathologist in charge: Dr Susan Louw
Test volumes
This laboratory conducts on average 5 500 tests per month with most of the tests being resulted within their expected turnaround times.

INR / Anticoagulation clinic activities includes the following:
- Monitoring of warfarin therapy of 100+ patients per day (serving in excess of 5 000 patients)
- Blood results and patients are assessed, dose of warfarin is adjusted and medication dispensed
- INR clinic training course for nursing sisters are conducted on a 6 monthly basis:
  - Attended by both private and public sector.
  - 1 nurse specialist resigned at the end of 2011 leaving 2 permanent staff members in the clinic
- Assays being validated for the assessment of activity of the new oral anticoagulants

Research Projects:
The relationship between HIV infections and DVTs: MMed completed: Dr. S Louw

<table>
<thead>
<tr>
<th>Title</th>
<th>Degree / Department</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemostatic Management System (HMS): Guiding blood product replacement and anticoagulation therapy in cardiac bypass surgery.</td>
<td>MSc  - (Haematology / T. Ramatsui)</td>
</tr>
<tr>
<td>Need to dose adjust prophylactic LMWH therapy in trauma patients.</td>
<td>Mmed  - (Anaesthetics / J Vlok)</td>
</tr>
<tr>
<td>Coagulation profile in HIV infected children undergoing dental surgery</td>
<td>Mmed  - (Anaesthetics / A. Zeijlstra)</td>
</tr>
<tr>
<td>D-dimer levels in HIV infected pregnant women</td>
<td>Poster presentation for congress  (P. Kumalo)</td>
</tr>
</tbody>
</table>

Projects approved by the post-graduate committee:
- Pathogenesis of thrombotic thrombocytopenic purpura (TTP) in HIV
- Clopidogrel resistance in Black South African patients

Teaching and Training:

Undergraduate medical students training:
This unit is involved in facilitating problem-based learning sessions with undergraduate medical students; lectures/tutorials for undergraduate medical students.

Postgraduate registrar training including:
Weekly coagulation journal club, small group discussions and training on a daily basis and assessments at end of each rotation
D-dimer outreach programme to train peripheral laboratories: Dr Susan Louw

Research and development
1. Assays being validated for the assessment of activity of the new oral anticoagulants
2. Validation and implementation of Nijmegen assay
3. Testing to measure activity of new anticoagulants

Haematology, Helen Joseph Laboratory, NHLS

Pathologists: Dr Sarolta Keresztes and M. Bernice Dhlamini

Diagnostic services:
Helen Joseph laboratory belongs to the NHLS Central area together with Edenvale, South Rand, RMMCH, Braamfontein and Sizwe laboratories. Situated at Helen Joseph Hospital, which is a large academic hospital with 550 beds. The laboratory is a clinical routine laboratory consisting of three sections, including haematology, chemistry and microbiology with the main function to provide routine diagnostic service to the hospital and to several outline hospitals and clinics.

The staff of haematology section currently includes two pathologists, one supervisor, three medical technologists, one haematology technician and one laboratory assistant. A small satellite laboratory at Rahima Moosa Mother and Child Hospital operating with one medical technologist provides basic tests to the hospital during the day. After hours, work is referred to the Helen Joseph Laboratory. A large INR clinic is operated by 1 INR clinic sister with the supervision and support of the pathologist providing anticoagulation therapy monitoring to hospital patients.

In addition to giving diagnostic services to the hospital, the laboratory is a referral centre providing consultative service for the outlier, smaller laboratories by reporting on referred peripheral smears and bone marrow samples. The pathologists provide consultative service to clinicians, reports on bone marrow samples (80-100/month) and oversee a large INR clinic (500-600 patients) located on the laboratory premises. The haematology section performs altogether 10-15 000 test/month. The laboratory participates in internal and external QC programmes and is actively working towards SANAS accreditation, with the aim to provide a quality service. A new computer system (TrakCare Lab) has been introduced in the laboratory aiming for a more efficient, user friendly and customer oriented service with anticipation of improved accessibility of patient’s results by customers.

Research projects:
An on-going collaborative project is to provide FBC and reticulocyte parameters for monitoring iron status of pregnant HIV-1 negative, as well as positive women who are part of an ARV therapy trial at the antenatal clinic at Chris Hani Baragwaneth Hospital.

Supervision of GEMP 3 research project (The correlation between the Absolute lymphocyte count and CD4 count in HIV positive pregnant women. The clearance certificate for ethics (M120347) is also done by Dr MB Dhlamini.

Teaching and Training:
The laboratory is involved in undergraduate teaching by facilitating the GEMP 1 programme.

Postgraduate teaching includes registrar training who are rotating on a monthly basis to the laboratory. They participate in the routine work while receiving practical training, mainly in morphology. The laboratory is providing on-going training for students preparing for the medical technologist or technician exams. All students who wrote exams in 2012 have passed.
A haematology outreach programme is being developed and contribution is given in the form of lectures to outline laboratories/hospitals. The differential course, as part of this programme is also contributed to by lectures. CPD meetings are held weekly, as part of the Continuous Education Programme.

**HIV Molecular**

**HIV and Haematology Molecular Diagnostics Unit**

**Director:** Dr Sergio Carmona  
**Laboratory Manager:** Mr. Perry Hlalele

The laboratory continues to grow in the three areas of routine and research. It currently provides HIV diagnostic and monitoring through EID PCR and viral load quantification (HIV PCR Lab), HIV genotyping for drug resistance diagnosis (HIV DR laboratory) and molecular support for a set of haematological disorders (haematology PCR laboratory). The activities and achievements of these labs are presented as follows.

**A. HIV PCR Laboratory**

**Diagnostic service:**
The Johannesburg PCR laboratory is one of the busiest NHLS PCR laboratories in the country currently processing approximately 40,000 viral load samples and 2,000 early infant diagnosis HIV Qualitative samples per month, reaching close to 441,554 and 23,900 samples per annum. With the consolidation of laboratories in the region, the workload continues to increase. The laboratory also supports numerous clinical trials from several networks including HPTN, ACTG, IAVI through CLS.

**B. Genotyping Laboratory**

**Pathologist in charge:** Dr Sergio Carmona  
**Co-directed by:** Prof Maria Papathanasopoulos  
**Laboratory Manager:** Dr Kim Steegen

**Diagnostic service:**
The genotyping laboratory currently focuses on HIV Antiretroviral Drug Resistance (HIVDR) testing for the public sector which provides clinicians with valuable knowledge on HIV-1 drug resistance and guides in patient management. The laboratory processed 820 samples during the latest financial year. A similar service is provided for various international clinical trial research network groups such as ACTG, PASER and IAVI.

**Research and Development Activities**
In-house assay development and evaluation
In order to meet the needs of the public sector, we validated a new in-house assay that will give more robust results. Additionally a more cost-effective one-step in-house assay is being validated as well. At the same time these assays will also be validated on Dried Blood Spots (DBS), which is a more convenient sample matrix for remote clinics.

**Affordable VL and HIVDR test**
A novel affordable two-step approach, using either plasma or dried blood spots as the sample input, was assessed to identify virological failure and subsequently detect key HIVDR mutations in order to improve quality of HIV care in resource-poor settings. This two-step approach included a real-time PCR based viral load test and a short RT sequencing step and was evaluated in the genotyping laboratory. A good concordance with reference assays was noted, with these assays being simple to perform and are more affordable, viable options to commercial alternatives. Both tests may be used and adapted in either regional or reference laboratories, and their compatibility with DBS sampling extends the access of HIV-1 virological monitoring to more remote settings.
Bioinformatics collaborations
The laboratory is part of the SATuRN network, which has been set up in South Africa to perform surveillance testing on HIV-1 drug resistance in the public sector. Our laboratory will perform resistance testing for this network as well as be involved in data analysis of the resistance data, in collaboration with Dr Tulio de Oliveira. The laboratory is collaborating with Professor Simon Travers from the South African National Bioinformatics Institute, University of Western Cape for the development of a fast, accurate bioinformatics program for the analysis of 454 ultradeep sequencing data for research purposes. The laboratory is collaborating with TherapyEdge and using their Deepchek program for data analysis for diagnostic purposes.

Global Fund
Professor Stevens has, in collaboration with Right to Care, received a grant from the Global Fund in 2011. The HIV genotyping laboratory will be involved in two components of this project, namely conducting a cross-sectional HIVDR drug surveillance study in South Africa and expand the HIVDR testing capacity in South Africa. This project will start early 2012.

C. Haematology PCR Lab
Pathologists: Dr Sergio Carmona
Laboratory Manager: Dr. Michelle Bronze

The unit is engaged in performing routine PCR testing for haematological diseases

<table>
<thead>
<tr>
<th>Current tests run</th>
<th>New assays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunoglobulin heavy chain gene</td>
<td>MPLS15 mutation detection,</td>
</tr>
<tr>
<td>rearrangement assay</td>
<td></td>
</tr>
<tr>
<td>T-cell receptor gene rearrangement</td>
<td>Jak2 exon 12 mutation detection</td>
</tr>
<tr>
<td>assay</td>
<td></td>
</tr>
<tr>
<td>Parvovirus B19 detection assay</td>
<td>IDO gene quantification</td>
</tr>
<tr>
<td>Jak2V617F mutation assay</td>
<td>Jak2V617F detection using real-time PCR</td>
</tr>
<tr>
<td>Factor V Leiden and Prothrombin</td>
<td>A novel parvovirus B19 assay to detect a broader</td>
</tr>
<tr>
<td>assay</td>
<td>diversity of viral genotypes is also being</td>
</tr>
<tr>
<td></td>
<td>developed</td>
</tr>
</tbody>
</table>

HIV Pathogenesis Research Laboratory (University of the Witwatersrand funded posts)

CoDirectors: Prof Maria Papathanasopoulos and Dr Alexio Capovilla

Diagnostic services
Prof Papathanasopoulos is co-director of the Genotyping Unit and contributes to diagnostic services of the Unit.

Research projects
The laboratory conducts research to increase the knowledge base of HIV-1 subtype C pathogenesis that can be translated into novel drug discovery and vaccine design. The group is funded by the South African HIV/AIDS Research and Innovation Platform (SHARP) (DST/TIA), DST/TIA India-SA bilateral on HIV Vaccine Development, NRF India-SA bilateral on HIV Integrase inhibitors, Advanced Materials Division, Mintek, South African NRF, Medical Research Council (MRC) and the Poliomyelitis Research Foundation. The following research projects were completed and/or are ongoing by the Research Scientists and postgraduate students.

HIV-1 Vaccine Research
1. Investigating novel CD4-liganded HIV Envelope glycoproteins as candidate HIV vaccine immunogens.

Basic Mechanistic/structure/function studies
1. Thermodynamic, kinetic and structural analysis of HIV-1 receptor interactions with CD4-based ligands.
2. Investigating the function and mechanism of thioredoxin-mediated CD4 isomerisation in the ‘immunovirological’ synapse.
3. The expression, purification and characterization of native CD4 domains 1 and 2 (D1/D2).
4. The development of novel protocols.
for the cost-effective production of HIV immunodiagnostic reagents.
5. Comparison of the HIV-1 Vpu interaction with CD4 and CD74.
6. Determination of the Importance of the Vpr-Dynein Interaction in HIV-1 Motility toward the Nucleus.

**HIV-1 drug development**

1. The development of domain-specific monoclonal CD4 antibodies as novel anti-HIV therapies.
2. Investigation of the LEDGF-integrase interaction as a target for HIV-1 drug intervention.
3. Evaluation of the NIH Clinical Collection for potential HIV-1 integrase inhibitors.

**HIV-1 antiretroviral drug resistance**

1. In vitro selection and characterisation of human immunodeficiency virus type-1 subtype C integrase strand transfer inhibitor resistant mutants.
2. Coreceptor usage of HIV-1 subtype C from patients failing HAART.
3. High throughput sequencing to provide us with a clearer understanding of HIV-1 quasispecies dynamics, and allow us to identify the minority quasispecies and their relevance on clinical virological outcomes in a short time period (both for ARV drug resistance, tropism research and identification of latent reservoirs and viral eradication strategies).

**TB drug resistance**

1. Genotypic characterization of MDR and XDR Mycobacterium tuberculosis identified through the GenXpert national programme.

**Teaching and training**

Prof M. Papanastasopoulos, Dr A. Capovilla and Ms N. Cerutti are all involved in undergraduate teaching (Mol Med II, GEMP) and BSc(Hons) and MMed’s; they supervise postgraduate students (see below for numbers).

**Professional development**

PhD student, Mr Mark Killick won 1st prize for oral presentations for the Faculty of Health Sciences at the Wits 4th cross faculty symposium.

Number of postgraduate candidates currently enrolled:
8 PhD, 5 MSc, 1 BSc(Hons)

Number of postgraduate students who graduated in the last financial year:
2 MSc, 2 BSc(Hons)

**Morphology and Specials**

**Pathologist in charge:** Dr Narisha Ramparsad

**Diagnostic Services**

The morphology and specials unit provides diagnostic services for a wide range of tests including the following more common tests: bone marrow aspirate and trephine interpretation as well as haemoglobin electrophoresis.

This unit conducts clinicothopathologic meetings in conjunction with the adult and paediatric oncology units on a monthly and bimonthly basis, respectively.

Consolidated patient reports including other molecular testing done is provided to clinicians following these meetings. Samples are received from other national laboratories and international laboratories, for testing as well as review.
**Research Projects**

The laboratory has been involved in point of care testing (POCT) projects including the Hemocue POCT project and the CSIR project.

1) Hemocue project: Various staff members have been instrumental in the implementation phase of this project, involving quality assurance, training, instrument maintenance, stock control as well as interface development (in conjunction with the NHLS/TrackCare and hospital IT departments). To date, over 370 health care workers have been trained, with between 500 –1000 tests performed monthly.

2) CSIR project: The laboratory is supporting the CSIR in the development of a lenseless technology system for morphology identification and differential counts of peripheral blood samples. In addition, using high resolution imaging, the laboratory is also involved in the creation of a morphology database which will be used for future training.

**Teaching and Training**

The unit is involved with undergraduate and postgraduate training. Undergraduate training includes, lectures to medical students, facilitating at the Graduate Entry Medical Programme, technician/technologist training. Postgraduate teaching revolves around lectures and tutorials, morphology case presentations, on the bench training for registrars and journal clubs.

**Professional Development**

1 MSC awarded– The Role of Alpha Thalassaemia in Unexplained Microcytosis at the Wits Academic Hospitals

**Red Cell Membrane Unit**

**Director:** Prof Theresa L. Coetzer

This diagnostic unit investigates blood samples from patients with haemolytic anaemia and characterises the underlying red cell membrane protein defect. It is the only unit in the country offering this service.

**Plasmodium Molecular Research Unit**

**Director:** Prof Theresa L. Coetzer

The main research aim of this unit is to investigate molecular aspects of the malaria parasite, Plasmodium falciparum, with the ultimate aim of identifying and validating novel drug targets.

Funding was provided by grants from the NRF and the University of the Witwatersrand.

**Research Projects**

**Protein trafficking**

Mrs Belinda Bezuidenhout, PhD student

Ms Melanie Friend, MSc student

Ms Alisje Steyn, MSc student

The transport mechanisms of P. falciparum proteins to internal organelles are poorly understood. Several domains of a putative transporter gene have been cloned into expression vectors and the recombinant proteins used to biopan a P. falciparum phage display library, which identified several binding partners. Transgenic parasites expressing the transporter protein fused to a GFP fluorescent tag revealed that the protein localised in vivo to distinct foci, implicating the protein in the transport of cargo molecules from the Golgi to cellular...
destinations. Several mini-genes of selected invasion proteins have been cloned into vectors that have been modified to contain a parasite stage-specific promoter. Transgenic parasites have been generated containing the mini-protein of interest fused to green or red fluorescent tags and these are currently being analysed.

**Kinases**

Dr Kuben Naidoo  
Ms Sasha Roets, MSc student

Phosphorylation plays a major role parasite biology. P. falciparum glycerol kinase is a key enzyme in membrane phospholipid metabolism and gene knockout studies revealed that the enzyme is required for optimal intra-erythrocytic growth and development of the parasite. Studies on a parasite protein kinase, PfPK8, indicated that the recombinant protein phosphorylated exogenous substrates and interacted with the host red cell membrane, implying a role during invasion or development within the red cell.

**Programmed cell death (PCD)**

Mr Warren Viera, PhD student  
Mr Dewaldt Engelbrecht, PhD student  
Mr Dale Liebenberg, MSc student  
Ms Anthea Hean, MSc student

PCD in the intra-erythrocytic stages of P. falciparum may provide it with the means to limit its burden on the human host allowing the transmissible forms of the parasite to develop. Several candidate P. falciparum PCD genes have been identified by bioinformatics. Selected genes have been cloned and expressed as recombinant proteins and subjected to biopanning against P. falciparum phage display libraries, which revealed several binding partners, currently under investigation. Transgenic parasites expressing GFP-tagged proteins in vivo have been created and localisation studies are underway. The biological effect of PCD was investigated by exposing parasites in in vitro cultures to physiologically relevant stress factors, including febrile temperatures. A range of biochemical markers were evaluated, indicating that P. falciparum may exhibit a unique phenotype.

**Gene regulation**

Dr Sonja Lauterbach, postdoctoral fellow

Transcription factors in P. falciparum are not well characterised. PfMyb2, a DNA binding protein, previously identified in the unit, may play a role in RNA processing, and splicing assays are currently being established. Ongoing studies to knock out the gene by double homologous recombination have produced viable parasites, but integration of the plasmid only occurred on one side of the gene and thus PfMyb2 is likely essential.

**Professional development**

Postgraduates registered in 2012:  
• 1 postdoctoral fellow, 4 PhD, 5 MSc  
• Postgraduates who graduated in 2012: 1 PhD

**Honours**

1. Professor Theresa Coetzer:  
   o Appointed co-director of the newly established Wits Research Institute for Malaria (WRIM)  
   o Invited to present the University of the Witwatersrand Faculty of Health Sciences Prestigious Research Lecture

2. Dewaldt Engelbrecht, a PhD student in the unit, won two prizes at the University of the Witwatersrand Research Days:  
   o Best student oral presentation in Molecular and Comparative Biosciences at the Faculty of Health Sciences Biennial Research Day  
   o Best oral presentation at the Molecular Biosciences Research Thrust Annual Research Day
Somatic Cell Genetics Unit

**Head of Unit:** Dr. Pascale Willem

The Unit performs highly specialised tests to detect, characterise and monitor acquired genetic alterations in the context of disease. The unit also develops, evaluates and implements novel molecular diagnostic techniques with an emphasis on carcinogenesis.

**Diagnostic Services**

Conventional cytogenetic analyses, FISH, reverse quantitative real-time PCR, reverse transcription PCR, sequencing, microarray analysis as well as sequencing of BCR-ABL and c-KIT mutations and PDGFR alpha in gastrointestinal stromal tumours are performed. The unit offers a wide variety of specialized molecular cytogenetic tests and the diagnostic volumes continue to grow year on year since the past ten years, due to the continuous increased in the number of molecular target of therapy being identified.

**Research Projects**

The unit is investigating new methods of molecular diagnostic in line with National Health priorities. In particular molecular diagnostic of 3q26 gain in cervical cancer a powerful predictor of disease progression is being evaluated and implemented.

The main aim of research projects in the unit is to identify molecular markers of disease which have a diagnostic/prognostic value as well as being potential targets of existing or future therapy.

**Molecular pathogenesis of oesophageal squamous carcinoma (OSCC):**

Oesophageal squamous carcinoma (OSCC) is an aggressive cancer endemic to South Africa. Using an integration of genome wide array technology and molecular cytogenetics, we have identified several genes commonly rearranged in 51 OSCC cases and 5 cell-lines. In particular, the ephrin receptor A3 gene, EPHA3, showed mono-allelic deletions in 74.5 % of patients’ specimens and in 2 out of 5 OSCC cell-lines making it a likely key gene at play in the pathogenesis of this cancer. The EphA3 protein is part of an ephrin receptor tyrosine kinase family, deregulated in a variety of cancers. This project aims to investigate the tumour suppressive role of EPHA3 in OSCC.

**Genome wide investigations of genes aberrations in HIV associated B-cell lymphomas**

Human Immunodeficiency Virus (HIV) infection strongly associates with an increased risk of acquiring high-grade B-Cell lymphoma. As South Africa has more than 5 million people living with HIV infection, this region can expect a sharp increase in the diagnosis of high-grade lymphomas.

Histological types of B cell lymphoma considered as AIDS defining lymphoma, include Burkitt lymphoma (BL), diffuse large B cell lymphoma (DLBCL), plasmablastic lymphoma (PBL) and pleural effusion lymphoma (PEL). These diseases are aggressive and generally have a poor outcome. This project aims to investigate the genome wide composition of PBL lymphoma of the oral cavity as well as ABC DLBCL, and to identify the biological pathways involved in the pathogenesis of this disease with a view to characterize targets of existing or new therapy. This is a multidisciplinary project involving the anatomical pathology department (WITS), the University of Pretoria and the Irving Cancer Institute at Columbia University (New York).

Funds were received from the following resources: NHLS Research Trust, Griffin Research Trust, CANSA and the University of Columbia (New York).
Teaching and Training

Intern training was as follows:

<table>
<thead>
<tr>
<th>Intern Students</th>
<th>Completed</th>
<th>In Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Technologist</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Medical Scientist</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Laboratory assistant</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

Post-Graduation training was as follows:

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<tr>
<th>Student</th>
<th>Completed</th>
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</tr>
</thead>
<tbody>
<tr>
<td>MSc Student</td>
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<td></td>
</tr>
<tr>
<td>PhD</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

Teaching And Training

Pathologist: Dr Penny Keene

NHLS Students

The pass rate for laboratory students (registrars, intern scientists and student technologist) have improved compared to the previous financial periods. The technician’s category however still remains a challenge. The table below delineates the outcome of the various board exams over the past four years.

Performance of trainees in the various board exams

<table>
<thead>
<tr>
<th>Category</th>
<th>Number wrote exams</th>
<th>% Pass rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FY 10</td>
<td>FY 11</td>
</tr>
<tr>
<td>Registrar</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Technologist</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Technician</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Laboratory Assistants</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

Bachelor of Science Honours Students

Senior Lecturer: Dr Natalie Whalley

Report for Molecular Medicine Honours Haem4004 2012

Five students registered for Haem4004 in 2012. They all passed, with two first class passes (80%, 75%), two second class passes (61%, 60%) and one third class pass (58%) being achieved. The external examiner, Prof Jan Verschoor from Pretoria University, was satisfied with and complementary about the standard of the course. The top achiever for 2012 was Tarryn Bourhill.
Honours 2013

There are five students registered for BSc (Hons), four full-time and one part-time, registered for 2013.

Conference Presentations FY 13 – April 2012 to March 2013

Crowther C: Sustained inhibition of hepatitis B virus replication in vivo using helper-dependent adenovirus vectors to deliver U6 Pol III antiviral RNAi expression cassettes. Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Scott T (PhD student): Inhibition of Rift Valley fever virus replication using anti-viral short hairpin RNAs.” Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Ivacik D (PhD student): “Potent knockdown of viral replication following lentiviral vector-mediated delivery of liver-specific micro RNA mimics targeting HBV” Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Bloom K (PhD student): Targeted inactivation of Hepatitis B virus with Designer Nucleases awarded Best oral presentation for the Infectious Diseases category. Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Marimani M (PhD student): Inhibition of hepatitis B virus replication using guanidinopropyl modified siRNAs. Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Justin Hean (PhD student): Altritol/inosine-containing siRNA development to improve silencing efficiency against Hepatitis B virus replication. Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Mlambo T (MSc student): Expression of anti-HBV primary micro-RNA shuttles using an inducible promoter system. Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School

Nhlabatsi (MSc student): Determining the silencing efficacy of anti-HIV Dicer-independent shRNAs. Neliswa Wits Faculty of Health Sciences Research Day, 19 September 2012, Wits Medical School


Ivacik D. Lentiviral vectors mediate efficient delivery of micro RNA mimics that silence HBV replication. The 4th WITS Cross Faculty Graduate Symposium, Friday 19 and Monday 22 October 2012

Robinson M (MSc student). Controlling the expression of viral genes using an RNA-based molecular switch that is responsive to endogenous viral protein output. The 4th
Scott T (PhD student). Pathogenic effects of Rift Valley fever virus NSs gene are alleviated in cultured cells by expressed antiviral short hairpin RNAs. The 4th WITS Cross Faculty Graduate Symposium, Friday 19 and Monday 22 October 2012

Mlambo T (MSc student). Inducible expression of primary micro-RNA mimics for the inhibition of HBV replication. The 4th WITS Cross Faculty Graduate Symposium, Friday 19 and Monday 22 October 2012

Nhlabatsi N (MSc student). Determining the silencing efficacy of anti-HIV Dicer-independent short hairpin RNAs. WITS Research day December 2012

Nhlabatsi N, Arbuthnot P, Weinberg M. Determining the silencing efficacy of anti-HIV Dicer-independent short hairpin RNAs. WITS Research day December 2012

Mlambo T, Mowa B, Arbuthnot P. An inducible and liver-specific RNAi-activating expression system for the inhibition of HBV replication. WITS Research day December 2012


Bloom K (PhD candidate). Using engineered TALE nucleases and repressor TALEs to achieve effective inactivation of hepatitis B virus replication in vivo. Invited speaker at 19th annual meeting of the German Society for Gene Therapy (Deutsche Gesellschaft fur Gentherapie) in Hamburg, Germany. 28th of February to the 2nd of March.

Ivacik D (PhD candidate). Poster: A recombinant lentiviral vector system for delivery of liver-specific micro RNA mimics targeting HBV. 19th annual meeting of the German Society for Gene Therapy (Deutsche Gesellschaft fur Gentherapie) in Hamburg, Germany. 28 February to 2 March.

Glencross DK, Coetze LM, Cassim N and Stevens WS. Poster: Development of a ‘full coverage’ tiered laboratory service can ensure optimized laboratory and point of care CD4 testing. African Society of Laboratory Medicine (ALSM), Cape Town, South Africa. December 2012

Cassim N, Coetze LM, Stevens W and Glencross DK. Poster: Evaluating the costs of implementation of the community laboratory and/or point of care testing as part of a tiered CD4 laboratory service model in the Pixley ka Seme district. African Society of Laboratory Medicine (ALSM), Cape Town. December 2012.


Coetzee LM, Drury S, Swanepoel G and Glencross DK. Poster: using the tiered service approach to assess gaps in laboratory service delivery in the eleven pilot districts of the National Health Insurance (NHI). Dec 2012 African Society of Laboratory Medicine (ALSM), Cape Town, South Africa

Coetzee LM, Drury S, Swanepoel G and Glencross DK. Oral: Laboratory-type CD testing performed on a mobile unit can provide equivalent quality testing real-time. Dec 2012 African Society of Laboratory Medicine (ALSM), Cape Town.


Mahlangu J. Role of short term prophylaxis in areas with no access to long-term prophylaxis. Global Haemophilia Network meeting on Collaboration and Innovation, Barcelona 3–5 March 2012(oral)

Julius H, Ramparsad N, Mahlangu J. Point of care diagnostic: Opportunities and challenges for implementation, 1st African Society of Laboratory Medicine Congress, Cape Town, 1–7 December 2012 (poster)

Mahlangu J. Oral presentation: Opportunities for haemophilia collaboration in south africa, national haemophilia foundation medical and scientific advisory committee annual meeting, Protea Hotel, OR Tambo, 16–17 November 2012.


Alli NA, Wessels P, Rampersad N, Clark B, Thein SW. Poster: Hb Rothschild in a case presenting with cyanosis. RCPA Pathology update: 38th annual meeting, 22nd–24th Feb, 2013, Melbourne, Australia


Steegen K, Levin L, Ketseoglou I, Bronze M, Carmona SC, Papathanasopoulos MA, Carmona SC, Stevens W. High level resistance to didanosine observed in South African children failing an abacavir or stavudine based first-line regimen. 20th Conference on Retroviruses and Opportunistic Infections. 3–6 March, 2013, Atlanta, USA.


Killick M, Capovilla A and Papathanasopoulos MA. Immunogenicity of native and CD4 liganded monomeric and trimeric envelope glycoproteins based on HIV-1 Subtype C consensus Founder virus sequences. AIDS 2012 Vaccine Conference. 9–12 September, 2012, Boston USA.


Choudhury R, Durand PM. Laboratory detection of programmed cell death in the model unicellular organism Chlamydomonas reinhardtii.

Book chapters


Publications


Hamlyn EHS, Rees V, Venter W, Palanee T, Stevens W, Ingram CF, Papathanasopoulos M. Increased levels of CD4 T-cell activation in individuals with CXCR4 T-cell activation in primary HIV-1 infection. AIDS 2012; 26(1):

Hamlyn E, Ewings F, Rees V, Venter W, Palanee T, Stevens W, Ingram CF, Papathanasopoulos M. Plasma HIV viral rebound following protocol-indicated cessation of ART commenced in primary and Chronic HIV infection. PLoS One 2012; 8


<table>
<thead>
<tr>
<th><strong>Abbreviation</strong></th>
<th><strong>Definition</strong></th>
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<tbody>
<tr>
<td>ACTG</td>
<td>AIDS clinical trials group</td>
</tr>
<tr>
<td>ARMS-PCR</td>
<td>amplification refractory mutation system PCR</td>
</tr>
<tr>
<td>ART</td>
<td>antiretroviral therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>antiretroviral</td>
</tr>
<tr>
<td>CANSA</td>
<td>Cancer Association of South Africa</td>
</tr>
<tr>
<td>CAPRISA</td>
<td>Centre for the AIDS Programme of Research in South Africa</td>
</tr>
<tr>
<td>CCHF</td>
<td>Crimean-Congo haemorrhagic fever</td>
</tr>
<tr>
<td>CCMT</td>
<td>Comprehensive Care Management and Treatment</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control and Prevention</td>
</tr>
<tr>
<td>CDW</td>
<td>Corporate Data Warehouse</td>
</tr>
<tr>
<td>CMJAH</td>
<td>Charlotte Maxeke Johannesburg Academic Hospital</td>
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<tr>
<td>CMV</td>
<td>cytomegalovirus</td>
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<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>CPD</td>
<td>continuing professional development</td>
</tr>
<tr>
<td>CPUT</td>
<td>Cape Peninsula University of Technology</td>
</tr>
<tr>
<td>CRC</td>
<td>colorectal cancer</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
</tr>
<tr>
<td>CSIR</td>
<td>Council for Scientific and Industrial Research</td>
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<tr>
<td>CVD</td>
<td>cardiovascular disease</td>
</tr>
<tr>
<td>DST</td>
<td>drug susceptibility testing</td>
</tr>
<tr>
<td>EQA</td>
<td>external quality assurance/assessment</td>
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<tr>
<td>EU</td>
<td>European Union</td>
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<tr>
<td>DGGE</td>
<td>denaturing gradient gel electrophoresis</td>
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<tr>
<td>DGM</td>
<td>Dr George Mukhari Hospital</td>
</tr>
<tr>
<td>DST</td>
<td>Department of Science and Technology</td>
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<tr>
<td>EID</td>
<td>early infant diagnosis</td>
</tr>
<tr>
<td>ESBL</td>
<td>extended-spectrum beta-lactamase</td>
</tr>
<tr>
<td>FA</td>
<td>Fanconi's anaemia</td>
</tr>
<tr>
<td>FBC</td>
<td>full blood count</td>
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<tr>
<td>FISH</td>
<td>fluorescence in situ hybridisation</td>
</tr>
<tr>
<td>FNA</td>
<td>fine needle aspiration</td>
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<tr>
<td>GC-MS</td>
<td>gas chromatography-mass spectrometry</td>
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<td>GEMP</td>
<td>graduate entry medical programme</td>
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<tr>
<td>GERMS-SA</td>
<td>Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa</td>
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<tr>
<td>GSH</td>
<td>Groote Schuur Hospital</td>
</tr>
<tr>
<td>HA</td>
<td>haemophilia A</td>
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<tr>
<td>HAART</td>
<td>highly active antiretroviral therapy</td>
</tr>
<tr>
<td>HBV</td>
<td>hepatitis B virus</td>
</tr>
<tr>
<td>HBC</td>
<td>hepatitis C virus</td>
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<tr>
<td>HEU</td>
<td>HIV-exposed uninfected</td>
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<tr>
<td>HHV</td>
<td>human herpesvirus</td>
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<tr>
<td>HLA</td>
<td>human leucocyte antigen</td>
</tr>
<tr>
<td>hMPV</td>
<td>human metapneumovirus</td>
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<tr>
<td>HPV</td>
<td>human papillomavirus</td>
</tr>
<tr>
<td>HVTN</td>
<td>HIV Vaccine Trials Network</td>
</tr>
<tr>
<td>IALCH</td>
<td>Inkosi Albert Luthuli Central Hospital</td>
</tr>
<tr>
<td>ICU</td>
<td>intensive care unit</td>
</tr>
</tbody>
</table>
Glossary

IMD  inherited metabolic disease
IPC  infection prevention and control
IRMA  immunoradiometric assay
KEH  King Edward VIII Hospital
KIDCRU  Children's Infectious Diseases Clinical Research Unit
LTI  Laboratory for Tissue Immunology
MDR-TB  multidrug-resistant tuberculosis
MIC  minimum inhibitory concentration
MGIT  mycobacterium growth indicator tube
MLPA  multiplex ligation-dependent probe amplification
MRC  Medical Research Council
MRSA  methicillin-resistant Staphylococcus aureus
MSSA  methicillin-susceptible Staphylococcus aureus
NAAT  nucleic acid amplification test
NIAID  National Institute of Allergy and Infectious Disease
NICD  National Institute for Communicable Diseases
NIH  National Institutes of Health
NRF  National Research Foundation
PBMC  peripheral blood mononuclear cell
PCR  polymerase chain reaction
PFGE  pulsed-field gel electrophoresis
PRF  Poliomyelitis Research Foundation
QF-PCR  quantitative fluorescent polymerase chain reaction
RA  rheumatoid arthritis
RCCH  Red Cross Children's (Memorial) Hospital
RFLP  restriction fragment length polymorphism
RIA  radioimmunoassay
RSV  respiratory syncytial virus
RT-PCR  real-time polymerase chain reaction
SAAVI  South African AIDS Vaccine Initiative
SABMR  South African Bone Marrow Registry
SADC  Southern African Development Community
SANAS  South African National Accreditation System
SARI  severe acute respiratory infection
SCC  staphylococcal cassette chromosome
SLE  systemic lupus erythematosus
SME  sub-acute measles encephalitis
SNP  single nucleotide polymorphism
STI  sexually transmitted infection
TB  tuberculosis
TMS  tissue microarray analysis
T-RFLP  terminal restriction fragment length polymorphism
UCT  University of Cape Town
UFS  University of the Free State
UKZN  University of KwaZulu-Natal
US  Stellenbosch University
WHO  World Health Organization
Wits  University of the Witwatersrand