

# FACULTY OF HEALTH SCIENCES

## BIENNIAL RESEARCH REVIEW

### 2010 TO 2011



FACULTY OF HEALTH SCIENCES



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## MESSAGE FROM THE DEAN



The Wits Faculty of Health Sciences continues to produce research of relevance and significance as is evidenced by the reports in our Biennial Review of 2010 and 2011. I am extremely proud of all the research being undertaken in the Faculty and hope that you will enjoy reading about the various research projects as much as I have.

Sustained funding sources for research are of the utmost importance if the University and the country are to succeed in producing research of local and international relevance. Thus, I would like to acknowledge and thank funders such as the South African Medical Research Council and the National Research Foundation for their continued generosity and support. Acknowledgement should also be made to funding from international

sources, such as the UK Wellcome Trust, the US National Institute of Health and the Bill and Melinda Gates Foundation. The Wits Health Consortium plays a huge role in supporting and managing part of the Faculty's research endeavours. Additional partners are the Department of Health and the National Health Services Laboratories who provide platforms for some of our research activities, while the Research Office of the University plays a role in providing support and management in this arena.

The range of research in the Faculty is considerable. However, in this Review we have focused on the research being undertaken by the 18 entities recognised by the Faculty Research Committee, as well as our DST Chairs, Centres of Excellence, Platforms and Thrusts. The Review also highlights significant research achievements by many of our staff and students during 2010 and 2011. These awards and recognition of achievements have been bestowed by both national and international bodies bringing great distinction and pride to our Faculty.

As part of its drive to engage with the community and to increase public awareness of research, the Faculty holds public lectures, research days and contributes to media awareness campaigns which are also highlighted in this Review. All these events and activities add lustre to the Faculty's research culture.

The continued intense research activities and productivity in the Faculty bear testimony to the ongoing energy of our Assistant Dean for Research and Postgraduate Support, Professor Beverley Kramer. In particular, the Faculty and I wish to pay tribute to her sterling work. Her personal involvement in the affairs of the Research Office shows in the many ways that our researchers have benefitted. Beverley and her team of staff continue to provide support, initiate activities and present a platform on which research can generate and grow. I wish to acknowledge the boundless support which Bev and the team provide for our researchers. My thanks too, to Professor Kramer, Mrs Philippa Mckechnie and Ms Greer van Zyl for their enthusiasm in putting this publication together.

The period under review has not been an easy one for our researchers. They have had to face new challenges and demands over this period. Despite this, they continue to succeed in their research. This Review is thus a tribute to the many researchers in the Faculty for their ongoing contributions to science, to health and to the University.

**Ahmed A. Wadee Ph.D**  
**Dean, Faculty of Health Sciences**  
**University of the Witwatersrand**

# RESEARCH ENTITIES

- Antiviral Gene Therapy Research Unit
- Bone Research Unit
- Brain Function Research Group
- Carbohydrate and Lipid Metabolism Research Unit
- Cardiovascular Pathophysiology and Genomics Research Unit
- Centre for Health Policy
- Clinical HIV Research Unit
- Developmental Pathways for Health Research Unit
- Effective Care Research Unit
- Hepatitis Virus Diversity Research Programme
- Human Genomic Diversity and Disease Research Unit
- Malaria Entomology Research Unit
- Perinatal HIV Research Unit
- Pulmonary Infections Research Unit
- Respiratory and Meningeal Pathogens Research Unit
- Rural Public Health and Health Transitions Research Unit (Agincourt)
- Soweto Cardiovascular Research Unit
- Wits Reproductive Health and HIV Institute



## ANTIVIRAL GENE THERAPY RESEARCH UNIT

**Director: Professor Patrick Arbuthnot**

Research conducted by the Antiviral Gene Therapy Research Unit (AGTRU) is focused on countering viral infections that cause serious health problems in South Africa. The team works mainly on advancing strategies to inhibit replication in the hepatitis B virus (HBV), HCV, HIV-1 and rift valley fever (RVF) virus. Specifically, RNA interference (RNAi) and engineered DNA-digesting enzymes are being developed to disable gene expression of these viruses and thereby achieve a therapeutic effect.

Elucidation of the molecular machinery of the RNAi pathway, particularly microRNA biogenesis, has enabled the design of artificial antiviral sequences that are capable of efficiently reprogramming the silencing pathway to inactivate viral gene expression. Work from the AGTRU has led to development of a variety of antiviral RNAi expression cassettes that generate mimics of primary microRNAs (pri-miRs). These substrates of microRNA biogenesis are capable of highly efficient silencing of targets, they are compatible with production from tissue-specific regulatory elements, and they may also be combined to generate multimeric RNAi activators. Tissue-specific regulation enables improved dose control and multimerisation of the cassettes is important to prevent emergence of viral escape mutants. Chemically modified synthetic antiviral sequences have also been developed in collaboration with German research partners in Frankfurt. These viral silencers are effective against HBV, and although shorter acting than artificial pri-miRs, they may be conveniently produced on a large scale.

Despite achieving potent inhibition of virus replication in models of human infections, efficient delivery of the DNA and RNA silencing molecules to target cells in a clinically relevant setting remains the main obstacle to their use for treating viral infections in humans. Importantly, DNA and RNA molecules are large and highly negatively charged, which distinguishes them from conventional small molecule drugs. Entry of DNA or RNA silencers into target tissues therefore requires that they be carried across lipid-rich cell membranes by vectors. To advance use of antiviral sequences to a stage where they may be applied clinically, research emphasis of the AGTRU has recently shifted to developing technology for delivering antiviral sequences to target infected tissues. The team is advancing use of several types of engineered viral and non-viral vectors. Included are 'gutless' helper dependent adenoviral vectors. By engineering viruses to serve as vectors, researchers are able to exploit the mechanisms of traversing the cell membrane barrier that these organisms have evolved over many years. Sterile helper dependent adenovirus carriers have all of the viral protein coding sequences stripped from them, which makes them less immunostimulatory and safer to use. Preliminary results have been promising and sustained inhibition of HBV replication has been achieved in transgenic mice when using engineered helper dependent adenoviruses to deliver antiviral sequences. Recombinant lentiviral vectors, which express anti-HBV and HIV-1 sequences, have also been developed. These engineered viruses are capable of stably integrating into host cell genomes



to effect sustained silencing of target viral genes. This particular feature may be useful to make liver or haematopoietic progenitor cells resistant to HBV or HIV-1 infection, and is being explored in partnership with French collaborators.

In addition to the recombinant viral vectors, members of the AGTRU are developing the use of chemically synthesised lipoplexes and modified capsid nanoparticles as nucleic acid carriers. These vectors have the advantages of being amenable to modification to confer intended biological properties (e.g. specific tissue targeting) and they can also be prepared conveniently on a large scale using recombinant or chemical synthesis techniques.

During 2011, the AGTRU was recognised as one of **32 African Network for Drugs and Diagnostics Innovation (ANDI) Centres of Excellence**. The programme is being run under the aegis of the World Health Organization and the European Commission for Africa. It is aimed at advancing the creation of solutions to African health problems through research carried out by African research institutions. The Centre of Excellence for Viral Gene Therapy will be an extension of the work already

being done by the AGTRU. Another highlight during 2010/11 was the acquisition of an IVIS Kinetic in vivo imaging system. This instrument enables real time tracking of nucleic acid vector formulations in live animals. Highly sensitive cameras are capable of detecting bioluminescent and fluorescent signals within organs of anaesthetised mice. This powerful instrument will be particularly important for development of antiviral vectors.

**Website: [www.wits.ac.za/agtru](http://www.wits.ac.za/agtru)**





## BONE RESEARCH UNIT

Director: Professor Ugo Ripamonti



The restoration of normal anatomy and function of cranio-mandibulo-facial defects is a grand challenge. Only a decade ago, many basic scientists were confidently (but prematurely) stating that the mystery of bone regeneration in humans had been solved. Novel methods and procedures dramatically shown to regenerate bone in pre-clinical animal models have, however, not yet been routinely translated into clinical contexts.

Physical trauma or pathology, such as cancer, may result in partial or complete bone loss. Currently, the bulk of craniofacial skeletal reconstruction is accomplished by harvesting bone from the patient. Whilst the results are often good, this procedure is accompanied by considerable pain and disfigurement associated with the removal of a body part. Moreover, in very large defects the lack of sufficient “donor” bone is a substantial obstacle. This challenge is particularly acute in children where reconstructive attempts are hamstrung by the small volume of available autologous bone. In response to these hurdles, the Bone Research Unit in “world firsts” experiments has identified novel bone-inducing morphogens other than the previously known bone morphogenetic proteins (BMPs), delivered by novel sintered self-inducing biomimetic biomaterial matrices to engineer the induction of bone formation.

The Unit has made several significant contributions to the field of bone induction. A great discovery has been the mechanistic understanding of the spontaneous induction of bone formation by macroporous constructs when implanted in extraskelatal heterotopic intramuscular sites. Importantly, the Unit has shown the unique capacity of the three mammalian transforming growth factor  $\beta$  (TGF- $\beta$ )

isoforms to induce bone formation in non-human primates. The hTGF- $\beta_3$  isoform has been shown to be the most powerful inducer in pre-clinical contexts. The team has also found that Noggin protein, a bone morphogenetic inhibitor competing for the type II BMP receptors, resulted in reduced bone formation in macroporous constructs, indicating that the spontaneous induction of bone formation by macroporous constructs when implanted intramuscularly is initiated by specific BMPs.

Following more than a decade of pre-clinical trials in a non-human primate, *Papio ursinus*, the Bone Research Unit is now translating research results from the bench to the bed side. Doses of hTGF- $\beta_3$  have been implanted in pediatric patients affected by massive craniomandibulofacial defects. The Unit is now seeking to systematically identify the molecular and cellular basis for the significant differences in regenerative potential between non-human and human primates. Pediatric patients have been implanted with hTGF- $\beta_3$  to restore massive mandibular defects. The patients are thriving with the induction of bone formation within the implanted defects.

The images above illustrate the reconstruction of large mandibular segmental defects (A) with hTGF- $\beta_3$  in the non-human primate (*Papio ursinus*) (A,B). (B) Complete restoration of the mandibular defect as early as 30 days post implantation. This is an unprecedented digital image showing *restitutio ad integrum* just 30 days post-op. (C) Massive mandibular defect in human patient implanted with 250 $\mu$ g hTGF- $\beta_3$  per gram of demineralized bone matrix showing tissue morphogenesis and mineralization as early as 15 days post-implantation.



## BRAIN FUNCTION RESEARCH UNIT

**Director: Associate Professor Andrea Fuller**

The mandate of the Brain Function Research Group is to research selected functions of the brain, and physiological and biochemical processes in which the central nervous system plays a key regulatory role. The selected focus areas include research on pain, sleep and thermal physiology. Research in the field of thermal physiology includes fever and sickness behaviour and the physiological responses of wild animals to their environment.

The Pain Lab (the Group's pain section), which has a main focus on HIV-associated neuropathic pain, started investigating the genetic basis of HIV-associated sensory neuropathy through the use of medium throughput genotyping technology during 2010/11. It also continued to assess the treatment of HIV-related pain. On behalf of the Neuropathic Pain Special Interest Group (NeuPSIG) of the International Association for the Study of Pain, the section organised and ran two large-scale international online surveys on the availability and administration of drugs used for the treatment of neuropathic pain. The information from the surveys will be used to tailor treatment guidelines developed by NeuPSIG to local and regional conditions. One of the section's 2011 papers, on HIV neuropathy risk factors, was featured on the cover of the *Journal of Pain and Symptom Management*. Working with members of the Group's sleep section, the section also investigated several aspects of the relationship between pain and sleep.

The interaction between pain and sleep is a field in which the Wits Dial.a.Bed Sleep Laboratory (the Group's sleep section) leads research internationally. The pain and sleep researchers started working together to understand the impact of HIV infection, HIV treatment, and HIV-related pain on sleep and circadian rhythms. The Group's sleep section also published work on the relationship between adolescent brain development and sleep, and further

investigated the relationship between sleep and exercise. Restless Legs Syndrome – its characterisation and diagnosis – was another topic of research pursued by members of the section. A sleep and circadian rhythms study also was initiated during the period under review.



In the Fever Lab of the Group's thermal section, researchers continued to investigate the mechanisms mediating fever and sickness behaviours. Having previously focused on mycoplasma infection, the Lab has shifted its focus to the study of fever and sickness behaviours, including potential learning and memory deficits, during *mycobacterium* infection (simulated TB).

Also a part of the Group's thermal section, the Wildlife Environmental Physiology team investigates how large mammals can adapt physiologically to the consequences of climate change. Using its surgical and technological expertise in remote measurement of physiological variables in animals, the team assessed the thermal physiology of several species of free-living mammal, including wildebeest, elephant and vervet monkeys. In the face of rapid climate change, understanding the ways in which animals cope with environmental stressors is of great importance to conservationists. Members of the team also collaborated with researchers at the Max Planck Institute for Ornithology on an investigation of sleep and brain temperatures in free-living ostriches, with the sleep results published in *PLoS One*. The team also published research on the effects of game management practices on the physiology of animals being captured. The outcomes of this work have important practical implications for veterinarians and game managers, in particular.

[www.wits.ac.za/bfrg/9015/bfrg](http://www.wits.ac.za/bfrg/9015/bfrg)



## A-RATED RESEARCHER

**Professor Duncan Mitchell** is Professor Emeritus of Physiology and an Honorary Professorial Research Fellow in the Brain Function Research Group and has held an NRF A-rating since 1984.

Before joining Wits in 1975, he was on the scientific staff of the National Institute for Medical Research (London) and of the Research Organisation of the Chamber of Mines of South Africa. His research started in the field of applied physiology of deep-level mining, and he has added research in somatosensory neurophysiology, fever physiology, and thermal ecophysiology to a lifelong career in thermal physiology. His interest in somatosensory neurophysiology led to a parallel research programme in pain pathophysiology and pharmacology. He now is pursuing research in conservation physiology related

to climate change, in the pathophysiology of pain resulting from HIV and its treatment, the interaction between pain and sleep, and in sickness behaviour.

Professor Mitchell is an expert on the pharmacological mechanisms of action of pain medication. He is a highly sought-after speaker internationally and often is invited by pharmaceutical companies to present seminars to specialists.

Following the award of the prestigious Harry Oppenheimer Fellowship in 2011, with funding for research aimed at understanding how South Africa's mammals will cope with climate change, Professor Mitchell was interviewed by Rohit Kachroo and extracts from the interview were broadcast on ITV's "News at Ten" in the UK on the 28<sup>th</sup> of November, as part of their coverage of COP 17.



Professor Emeritus Duncan Mitchell with research team members, Dr Leith Meyer, Professor Andrea Fuller and Dr Robyn Hetem, after the ceremony at which Duncan was honoured with the Harry Oppenheimer Fellowship.

Photo: Elaine Banister

## CARBOHYDRATE AND LIPID METABOLISM RESEARCH UNIT

**Director: Associate Professor Derick Raal**

The Unit focuses on the epidemiological, clinical and biochemical aspects of common diseases affecting lipid and glucose metabolism in the different ethnic groups of Southern Africa. These include familial hypercholesterolaemia (FH) and other dyslipidaemias, insulin resistance, the metabolic syndrome, diabetes mellitus as well as other related metabolic disorders.

**Professor Raal** and co-workers are well recognised both nationally and internationally for their work on familial hypercholesterolaemia, one of the commonest inherited disorders worldwide caused by a defect on chromosome 19 which renders the body unable to remove low density lipoprotein (LDL) cholesterol from the blood. High levels of LDL cholesterol are a risk factor for atherosclerosis at an early age.

The Unit has one of the largest cohorts of homozygous FH patients in the world, and undertakes research which contributes to the management of these patients. Pivotal high dose statin studies with simvastatin, atorvastatin and rosuvastatin performed in the Unit confirmed the efficacy of high dose statin therapy in these patients. Although ideal LDL cholesterol levels are not achieved with the use of high dose statins, cardiovascular morbidity and mortality has definitely been reduced and life expectancy has been prolonged.

Studies with novel therapies such as anti-sense apo B-100 in this patient group are ongoing. The results of one such study were published in 2010 as a lead article accompanied by an editorial in *The Lancet*. In 2011, the Unit completed a review of the records of all patients with homozygous familial hypercholesterolaemia (HoFH) seen by the Unit over the past 30 years. They reported on the reduction in mortality associated with advances in lipid-lowering therapy in one of the largest cohort of subjects with HoFH described worldwide. This was published in *Circulation*, the leading cardiovascular journal with the highest impact factor.

Although the Unit continues to conduct studies in subjects with FH and has been integrally involved in the research and development of novel lipid-modifying

therapy in this patient group, the Unit has also studied risk factors for, and metabolic aspects of, atherosclerosis within the South African Black population. Dr Lucas Ntyintyane obtained his PhD dissertation for this work and published a total of nine papers.

Professor Raal was elected as an active member of the Endocrine Society in recognition of achievements in clinical practice, research and education in the field of Endocrinology in 2010. Dr Ntyintyane was awarded the prestigious Fogarty International Clinical Research Fellowship for 2009-2010, while Dr. Nazeer Mohamed was awarded a Discovery Health Fellowship Award enabling him to initiate his MMED project entitled "Alterations in vitamin D status in the Intensive Care Unit and its impact on mortality and morbidity in patients with and without sepsis". Dr Daksha Jivan was awarded a prize for the best oral presentation at the 2011 Society of Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) Congress held in April 2011, while Andrew Immelman was awarded the best poster prize at the South African Association of Clinical Biochemistry Meeting held in Sandton in September 2011.

[www.wits.ac.za/academic/health/clinicalmed/internalmedicine/research/9454/research.html](http://www.wits.ac.za/academic/health/clinicalmed/internalmedicine/research/9454/research.html)



Xanthomas (cholesterol deposits) on the elbows of a young patient with homozygous familial hypercholesterolaemia



## CARDIOVASCULAR PATHOPHYSIOLOGY AND GENOMICS RESEARCH UNIT

**Directors: Professor Gavin Norton  
and Associate Professor Angela Woodiwiss**

Hypertension is the single most important determinant of cardiovascular events in sub-Saharan Africa. In 2003, the Cardiovascular Pathophysiology and Genomics Research Unit (CPGRU) initiated a large cross-sectional study, the first of its kind in sub-Saharan Africa, to investigate cardiovascular risk factors in an urban developing community of African ancestry. The Unit has published a number of important publications in pre-eminent international journals from the data collected in this study.

A highlight of 2010/11 was the publication of four manuscripts in the prestigious journal *Hypertension*. While a number of studies indicate that salt intake contributes to the variability of blood pressure (BP), most have shown only modest effects on BP. However, members of the CPGRU hypothesized that salt intake may determine central dynamic (pulsatile) BP rather than peripheral steady state BP. Pulse pressure (PP) is reported to predict cardiovascular outcomes beyond measures of mean arterial pressure (MAP), and central PP may be more closely associated with cardiovascular outcomes than peripheral PP. Their research showed strong independent relationships (after adjustments for confounders including MAP) between salt intake and the dynamic component of central BP (central PP), the component reflective and forward pressure waves of central PP, and 24-hour PP. In contrast, independent relationships between salt intake and steady-state BP or pulse wave velocity (PWV, an index of arterial stiffness) were not observed. They concluded that modifying salt intake could influence cardiovascular risk through effects on 24-hour and central PP, as well as on reflective and forward pressure waves independent of steady state pressure (MAP or diastolic BP) or PWV. The importance of these data was highlighted in an editorial review in *Hypertension*.

Central aortic BP (indexed by central PP) has also been shown to be more closely associated with cardiovascular outcomes than PP or steady-state pressures (indexed by MAP) measured at the brachial artery. One of the concerns regarding the measurement of central aortic haemodynamics is the use of non-invasive devices which use complex transformations to obtain measures of central aortic BP. In another study published in *Hypertension*, members of the CPGRU showed that using the SphygmoCor device, P2-derived central BP, which does not require complex transformations using a generalised transfer function (GTF), is associated with target organ changes independent of brachial BP. They demonstrated further that these relationships are as strong as brachial BP-independent GTF-derived central BP-target organ changes, and that P2-derived central BP-target organ relations survive adjustments for nurse-derived brachial BP measurement, whilst "gold-standard" 24-hour, day or night brachial BP-target organ relations do not. These data therefore suggest that P2-derived central BP may be employed as a potential complementary brachial BP-independent risk predictor in future outcome studies in circumstances where the use of a GTF may be questioned.

In a further collaborative study published in *Hypertension*, members of CPGRU provided strong evidence to suggest that populations of African descent have higher central BP and augmentation indices than many other population groups around the world.

Continuing with the question of the impact of salt intake on BP, members of the CPGRU showed in another *Hypertension* publication that in the presence of a high Na<sup>+</sup>/low K<sup>+</sup> diet, which suppresses renin release, circulating angiotensinogen



concentrations are more closely related to aldosterone and BP than in participants receiving a low Na<sup>+</sup>/high K<sup>+</sup> diet. These data may explain why renin-angiotensin-aldosterone system (RAAS) blockers produce a synergistic effect on BP when used in conjunction with strategies that enhance Na<sup>+</sup> excretion, and suggest that a combination of these strategies may be the most appropriate method of treating salt-sensitive hypertension. This is particularly important considering that only 4.3% of the participants in their population-based study were receiving an angiotensin-converting enzyme (ACE) inhibitor-diuretic combination and that left ventricular hypertrophy is more prevalent in salt-sensitive groups such as those of African ancestry, where considerable benefits may accrue from RAAS blockers.

**[www.wits.ac.za/physiology/cpgru/academic/health/physiology/cpgru/9001/cpgru.html](http://www.wits.ac.za/physiology/cpgru/academic/health/physiology/cpgru/9001/cpgru.html)**





## CENTRE FOR HEALTH POLICY

**Director: Dr Jane Goudge**

The Centre for Health Policy (CHP) is a multi-disciplinary research group based in the School of Public Health which strives to promote excellence in health policy and systems research. This emerging field seeks to understand how societies organise themselves to achieve collective health goals to improve health systems and outcomes. Since 1987, CHP has contributed to high quality policy research to support change and propose strategies in the health sector based on theoretical insights and empirical evidence. While mandated to teach and build capacity, the emphasis in the Centre is on conceptual and methodological development in health systems and policy research, often using a combination of qualitative and quantitative methods. Capacity development is central to CHP which is currently hosting four PhD students and two National Research Foundation (NRF) interns.

The Centre is sought after by local and international entities to conduct collaborative research for health policies which promote equity and social justice. Over the past two years, CHP supported the transformation of the South African health system through its active engagement with the Department of Health to revitalise the primary health care system, South Africa's nursing profession and improve quality surveillance for the new Office of Health Standards Compliance ahead of the introduction of National Health Insurance.

On the international front, CHP signed new international research agreements worth in excess of R16-million. It currently collaborates with 23 countries, 13 of which are developing countries (loosely, the 'South') and 10 developed (the 'North'). All are multi-country collaborative projects of between three to seven years, with strong capacity building and/or knowledge translation-dissemination components. These include studies on health policy and system analysis in Africa (CHEPSAA), researching equitable access to health care services (REACH), exploring universal coverage in Tanzania and South Africa (UNITAS) and researching strategies for health insurance mechanisms to address inequities in Ghana, South Africa and

Tanzania (SHIELD). A new six-year project initiated in 2011 focuses on research to encourage policy changes that enhance health system resilience and responsiveness in low and middle income countries to promote health and health equity and reduce poverty (RESYST). Several international projects focus on child, adolescent and women's health, and CHP was awarded a grant with a new research funder, the Netherlands Organisation for Scientific Research (NWO-WOTRO) to compare maternal health within the health systems of South Africa, Rwanda and the Netherlands.

The Rockefeller Foundation awarded CHP a highly competitive grant to organise a workshop on "Social Inclusion and the Right to Health" in Bellagio, Italy in December 2011 which led to research collaboration between Monash University in Australia and Wits. Locally, CHP works with universities, science councils, government at national, provincial and local levels, and non-governmental and professional associations such as the Public Health Association of South Africa (PHASA) and the Democratic Nurses Organisation of South Africa.

The period under review was exceptionally productive, with 12 articles published in peer reviewed journals in 2010 and 26 articles in 2011. In addition, staff published chapters in books, editorials, technical reports and presented oral papers and posters at local and international conferences. A highlight in 2011 was the launch of the special edition of the international *Journal of Public Health Policy (JPHP)* entitled **Public Health, health sector reforms, and policy implementation in South Africa: Studies and perspectives on the 24th anniversary of the Centre for Health Policy**. CHP staff contributed to nine out of the 15 articles in this journal which are all open access (Volume 32 Supplement 1, 2011). Three of these staff members were first-time lead authors. CHP is committed to research translation and disseminates research findings to key stakeholders through mini-symposia, conferences, policy briefs and its website.

[www.wits.ac.za/chp](http://www.wits.ac.za/chp)







## CLINICAL HIV RESEARCH UNIT

**Director: Associate Professor Ian Sanne**

The Clinical HIV Research Unit (CHRU) has focused on the optimisation of the diagnosis and treatment of HIV, TB and the complication of AIDS since 2001. The research agenda targets “game changing” (guideline changing) interventions, with the results of research used to provide technical assistance to the South African Department of Health and the World Health Organization.

Based at the Helen Joseph Hospital in Johannesburg, with sites at Witkoppen and Sizwe Hospital, the CHRU is an internationally acclaimed HIV/AIDS research unit, contributing to prospective new drugs through investigation and biotechnology clinical trials. Helen Joseph has the largest HIV and tuberculosis clinic in South Africa with a well-established clinical database (TherapyEdge™). This provides a rich study population for observational and clinical trials linked to pathogenesis, immunology research, epidemiologic and health economics research.

The AIDS Clinical Trials Group (ACTG) clinical trials agenda has been an important focus of the CHRU. Professor Ian Sanne was appointed the International Vice-Chair of this network in 2010, and the Helen Joseph Hospital under Dr Prudence Ive has become one of the most successful sites internationally. The site participated in the “Prevention of HIV-1 infection with early antiretroviral therapy” study, demonstrating a 96% reduction in HIV transmission in discordant couples. This study was considered by *Journal of Science* as the most influential scientific breakthrough in 2011.

The CHRU team were centrally involved in the design and publication of the definitive study “Timing of antiretroviral therapy for HIV-1 infection and tuberculosis” published in the *New England Journal of Medicine* in 2011, which led to a change in the WHO guidelines for TB and HIV treatment. The provision of antiretroviral therapy for HIV treatment in women exposed to single-dose Nevirapine prophylaxis for mother-to-child transmission was completed and published in 2011, demonstrating the long-term impact of Nevirapine resistance. Multiple studies conducted demonstrated the safety and efficacy of influenza vaccine and human papilloma vaccine in HIV infected patients. The Unit has investigated and published on cancer, tuberculosis, hepatitis, neurologic and renal complications of HIV and AIDS in multiple publications. Professor Cynthia Firnhaber successfully established research in cervical dysplasia, human papilloma virus and cancer in both men and women.

The Health Economics and Epidemiological Research Office (HE<sup>2</sup>RO), representing a collaboration between the University of the Witwatersrand and Boston University, is a unique combination of epidemiology, health economics utilizing the high-quality dataset from TherapyEdge™ for data driven research. HE<sup>2</sup>RO is widely recognised for the development of the “National ART Costing Model” in collaboration with the Departments of Health and National Treasury. The results were used to plan the South African medium and long-term budgets for HIV treatment, led to significant increases in funding, reductions in cost through ART procurement, “task-shifting” to nurse initiated antiretroviral therapy and increased access to treatment.

Major research collaborations with international funding include the ACTG, a Division of AIDS in the National Institute of Allergy and Infectious Diseases at the National Institute for Health; the Global Tuberculosis Alliance; the European EDCTP and Panacea Consortium; the AIDS Malignancy Consortium; and the INSITE, HIV Prevention Trials, Microbicide Trials and IMPAACT networks. The Unit also collaborates with the University of North Carolina, Boston University, the Wistar Institute and University College London.

In 2011, the Unit signed 13 new research contracts to complement the 51 research projects already underway. Professors Sanne and Firnhaber received Faculty Research Awards in 2011, while Dr Denise Evans was awarded the OWSD/TWAS/Elsevier Young Woman Scientist in Biology for the Africa Region for 2011, and received the Claude Leon Foundation post doctoral fellowship for 2011 and 2012. Fourteen Masters and PhD candidates are currently completing their degrees in the Unit.

**[www.chru.co.za](http://www.chru.co.za)**





## DEVELOPMENTAL PATHWAYS FOR HEALTH RESEARCH UNIT

**Director: Associate Professor Shane Norris**

A new WITS and MRC research unit was born when the Mineral Metabolism Research Unit and the Birth to Twenty Programme merged in December 2010. The Developmental Pathways for Health Research Unit (DPHRU) is based in the Department of Paediatrics in the School of Clinical Medicine. Its research spans the developmental stages of the life-course, from pregnancy to ageing adults. Focusing chiefly on non-communicable disease in South Africa, the Unit applies this life-course approach to explore how biological and environmental exposures, particularly in early life (fetal, infancy and childhood), subvert physiological and other developmental systems resulting in latent vulnerabilities. The studies draw upon genetics, cross-sectional and longitudinal population cohorts, and formative intervention work to test key hypotheses.

One of the flagship projects is the Birth to Twenty cohort (Bt20), a cohort of 3273 mothers and their newborns who are now over 22 years old, with over 70% still in contact with the study. The Unit found that of the full-term, normal birth weight babies recruited, a quarter were stunted by age two years. Furthermore, the data also suggest that the variation in adult attained height is largely due to the degree of growth failure in the first two years of life, and that being stunted by the age of two years is associated with poorer educational attainment by 18 years of age. Between the ages of 13 and 17 years in the Bt20 cohort, the combined prevalence of overweight and obesity remained static at 10% across the years for boys. However, for girls, the prevalence was double that of boys and increased from 20-28% by the end of adolescence. Findings indicate that poor eating habits and practices are well established by the age of 13 and these poor habits track with increasing age.

Moving home can result in improved living conditions and well-being, but may also reinforce inequalities and conditions of vulnerability, and moving may pose particular risks for children. However, little is known about the frequency and reasons for residential mobility amongst South Africa's urban children, and the

consequences of movement have not been explored. Data from Bt20 revealed that two-thirds (64%) of the children had moved home at least once by the time they reached 15 years of age, while a third had never moved. Mobility was found to be more likely amongst children whose mothers or caregivers had no formal education and who lived in poorer households, suggesting that residential movement within this group of children was more common in the context of disadvantage. However, the consequences of such movement were somewhat unexpected. The results showed no evidence that residential mobility impacted negatively on children's progression through school. On the contrary, children who had moved home appeared to achieve higher scores in a numeracy and literacy evaluation. The study concludes that residential mobility may be associated with opportunities for some children and challenges for others. However, such movement, even where it was connected to disadvantage, did not appear to prejudice children's educational progression or potential for achievement. The findings point to children's resilience and adaptability in the face of change and highlight the potential for residential mobility to influence children's lives positively.

DPHRU researchers pooled data from five low- or middle-income country birth cohorts (Brazil, Guatemala, India, the Philippines and South Africa), and found that lower birth weight was consistently associated with higher adult glucose concentrations and an increased risk of glucose intolerance (impaired fasting glucose or type-2-diabetes). Weight in early life and mid-childhood and weight gain at these ages were unrelated to glucose concentrations and diabetes risk. In contrast, weight gain between mid-childhood and adulthood was strongly positively related to these outcomes. These findings are important in defining policy around weight gain in early childhood.

DPHRU is home to two A-rated researchers – Professor Emeritus John Pettifor and Honorary Professor Linda Richter (2012).

## A-RATED RESEARCHER

**Professor John Pettifor** is an A-rated researcher of long standing who for 23 years was Head of the Department of Paediatrics at Chris Hani Baragwanath Hospital in Soweto, Johannesburg. Although recently retired, he remains active in research and postgraduate student supervision as an honorary Professorial Researcher in the newly established MRC/Wits Developmental Pathways for Health Research Unit and as Director of the Carnegie Clinical Scientist Fellowship programme of the Faculty of Health Sciences.

Over the years, Professor Pettifor has had major research interests in metabolic bone diseases in children and in calcium and vitamin D physiology. He continues to be active in both these fields, and his research in the vitamin D field was recently recognised internationally when he received a Career Award at the 15<sup>th</sup> Workshop on Vitamin D for his longstanding contributions to vitamin D research. His contributions to Children's Bone Health were also recognized some 10 years ago when he received the Dr Charles Slemenda Award from the International Conference on Children's Bone Health.

Professor Pettifor is currently leading research into establishing factors (both environmental and genetic) which influence bone mass and accretion in a longitudinal cohort of adolescent children who are part of the Bt20 cohort. The data obtained from



this cohort annually over more than 12 years form a unique collection of information on the changes in bone mass that occur during pubertal growth and development. Studies in this area have already resulted in a number of international publications on the influences of genetics, ethnicity and gender on bone development. They have also highlighted the striking differences in fracture rates between the ethnic groups during childhood with black children fracturing less than half as frequently as white children. Now that the children have reached their final adult heights, data collection will occur less frequently but will continue to monitor changes in bone mass as an adult.

## EFFECTIVE CARE RESEARCH UNIT

**Director: Professor Justus Hofmeyr**

The Effective Care Research Unit is located in the East London Hospital complex in the Eastern Cape, although it is a WITS Faculty of Health Sciences Research Unit. The focus of the Unit's work is to undertake primary research, research synthesis, implementation research, training and dissemination of research findings which address important issues in maternal, child and women's health in low income settings. The Unit is accredited as a WHO Collaborating Centre in Reproductive Health research synthesis and is on the WHO guideline development panels on calcium supplementation for pre-eclampsia, and task-shifting for improving maternal health.

The emphasis of ECRU's primary research is on randomised clinical trials relevant to the major obstetric and reproductive problems of resource-poor countries. A Cochrane systematic review showed that calcium supplementation in the second half of pregnancy reduces pre-eclampsia and severe morbidity. The Unit hypothesised that for calcium supplementation to have a more complete effect on the development of pre-eclampsia, it would need to be commenced before conception. In 2010 they developed the protocol for a randomised, placebo-controlled trial to test this hypothesis in collaboration with colleagues at WHO and in Argentina. The trial of calcium supplementation in women with previous pre-eclampsia who are planning another pregnancy is being conducted in three centres in SA (East London, Chris Hani Baragwanath Hospital and Cape Town) and one in Zimbabwe, co-ordinated by ECRU. The Unit was awarded a sub-grant of USD 1 100 000 to conduct this trial from the University of British Columbia, a grantee of the Bill & Melinda Gates Foundation. If shown to be effective, the next step would be a food fortification study, with a view to developing a population-based approach to calcium supplementation to reduce pre-eclampsia.

The Unit completed a randomised, multicentre trial of misoprostol to prevent postpartum haemorrhage to determine whether using misoprostol in addition to oxytocin improves outcomes. Candidates were recruited from sites in South Africa and Nigeria in 2006. The trial results were consistent with at best modest benefits of misoprostol over and above the effect of oxytocin. Two papers reporting these findings were published in the *International Journal of Gynaecology & Obstetrics* in 2011 and were awarded the John J Sciarra IJGO prize paper award for "Best clinical research article from a low/middle income country" for 2011.

The Unit collaborated with the World Health Organization on the completion of the Active Management of 3<sup>rd</sup> Stage of Labour (AMTSL) trial. Active management of this phase of labour reduces the occurrence of severe postpartum haemorrhage by approximately 60-70%. The relative contribution of the components of AMTSL to the overall reduction in blood loss is not clearly known. Understanding the contribution of the components of AMTSL to the overall effect in reducing the incidence of haemorrhage could have major programmatic significance since some components require training while others require an efficient drug procurement and utilisation system.

The primary objective of this hospital-based, multi-centre, randomised controlled trial was to determine whether the effectiveness of a simplified package of oxytocin 10 IU IM/IV and uterine massage is comparable to the full AMTSL package. The main outcome measures were the incidence of severe post partum haemorrhage ( $\geq 1000$  mls) and the use of additional uterotonics comparing women allocated to receive the full package versus the limited package. Blood loss measurements were made using the calibrated drape BRASSS-V® and measured from delivery to

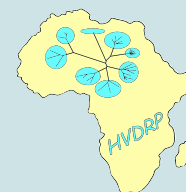


one hour following delivery. The trial found that the contribution of controlled cord traction to prevention of severe postpartum haemorrhage was minimal and the results will be published in the *Lancet* in 2012.

The unit produced 12 articles for publication in the Cochrane Library, the WHO Reproductive Health Library (RHL) and other journals in the 2010/2011 period. The team is responsible for updating more than 50 Cochrane reviews, making a substantial contribution to the Cochrane Library and the RHL. Prof Hofmeyr is an Editor of the Cochrane Pregnancy and Childbirth Group and the regional editor for the WHO Reproductive Health Library. In 2010 the unit filmed another teaching video on Kangaroo Mother Care, bringing to seven the number of its teaching videos included in the RHL.



The calcium and pre-eclampsia study team at the trial meeting in East London in 2011



## HEPATITIS VIRUS DIVERSITY RESEARCH PROGRAMME

**Director: Associate Professor Anna Kramvis**



Housed in the Department of Internal Medicine, the Hepatitis Virus Diversity Research Programme (HVD RP) was established in 2008 to study the sequence variation of hepatitis viruses, in particular of hepadnaviruses, their functional characterization and their role in the clinical manifestation of liver disease.

Of particular interest is hepatitis B virus (HBV), a very sophisticated virus with nine genotypes and at least 32 sub-genotypes. South Africa has a HBV prevalence of 5% to 20%, with a correspondingly high incidence of liver cancer. Southern African Black carriers of the virus infected with the subgenotype A1, which is different to strains found elsewhere in the world, have a 4.5 increased risk of developing liver cancer than individuals infected with other genotypes of the virus.

Since there is very little data on the number of patients infected with both HBV and HIV in South Africa, we have also initiated research into this co-infection in urban and rural cohorts. A study of 300 HIV-infected rural patients found that 72 were co-infected with HBV, 9% had an overt infection, while 15% had a hidden (occult) infection detected through expensive DNA testing, as opposed to the usual HBs antigen test. The vast majority were infected with sub-genotype A1. In a parallel study, researchers have explored the prevalence and clinical course of occult HBV infection in HIV patients in a clinic at the Helen Joseph Hospital in Johannesburg. The aim of this study was to determine the prevalence of HBV DNA in HIV-positive patients, negative for all HBV serological markers and to retrospectively evaluate the clinical course in mono- and co-infected patients. Our research found that 5.4% of the HBV serologically-negative HIV-positive patients had low levels of HBV DNA. There were no significant differences in clinical outcome between the mono- and co-infected groups. A total of 35 patients were

followed for up to 18 months after ART treatment was initiated. The Unit believes this was one of the first longitudinal studies to trace the molecular evolution of HBV belonging to sub-genotype A1. This is a milestone since sub-genotype A1 has unique characteristics that differentiate this genotype from other genotypes and/or sub-genotypes of HBV. Eight of the 35 patients experienced viral breakthrough and reactivation following the initiation of ART. The researchers conducted molecular characterisation of the surface overlapping polymerase region of HBV of two of the eight patients, and found unique mutations.

In 2010 the Unit completed the characterisation of HBV isolates from Zimbabwean blood donors, which was the first publication on HBV genotypes in Zimbabwe. In a similar study in 2011, the programme genotyped HBV isolated from Kenyan carriers with liver disease, providing the first comprehensive HBV genotyping data from Kenya. They found that genotypes A and D predominate. A PhD study has examined HBV isolates from Kerala, India, most of which belong to sub-genotype A1 with a similar prevalence to that of South Africa. This study successfully amplified the complete genome of nine HBV isolates and the complete S region of another 51 isolates. This is an important achievement as complete genome amplification is generally difficult in liver cancer patients because of the low HBV viral loads in these patients. The complete genome analyses of the Indian isolates will enable comparison with South African isolates to determine similarities and/or differences that can account for the hepatocarcinogenic potential of this sub-genotype.

In a collaborative and complementary study, a PhD student has developed a number of bioinformatic tools to facilitate the study of HBV genotypes. These programmes aim to analyse the sequences the team is working on to automate the processing of sequences and so speed up the process considerably.

[www.wits.ac.za/health/hvdrp](http://www.wits.ac.za/health/hvdrp)

## HUMAN GENOMIC DIVERSITY AND DISEASE RESEARCH UNIT

**Director: Associate Professor Himla Soodyall**

Established in 2001 by the Medical Research Council in partnership with the National Health Laboratory Service (NHLS) and Wits University, this Unit is located at the Central Branch of the NHLS in Braamfontein. Its mandate is to incorporate population history in mapping and modelling human genetic variation in Africa in health and disease, and provide a public service through genetic ancestry testing.

Using a molecular genetics approach to reconstruct population history, the Unit has been able to demonstrate patterns of variation in susceptibility to disease in South African and other sub-Saharan African and Malagasy populations. It sheds light on which factors and to what extent they have contributed to changing the human gene pool in health and disease. This work has shown that living Khoi and San populations have retained some of the most ancestral DNA signatures found in modern humans.



The Unit participated in the international Genographic project spearheaded by the National Geographic Society in partnership with IBM and the Waitt Family Foundation which

aims to map the history of the world. They have collected samples from the Central African Republic, Democratic Republic of Congo, Uganda, Zambia, Zanzibar and from various regions in South Africa and used mitochondrial DNA (mtDNA) and Y chromosome DNA variation to examine genomic variation in sub-Saharan Africa. The research highlight was the unique distribution of the mtDNA branch L0 among southern African populations. This study emphasized the antiquity of the Khoe-San gene pool among living people such as the Karretjie people in the vicinity of Colesberg.

Haplogroup A is the oldest of the Y chromosome haplogroups and is restricted almost entirely to the African continent, with subclades A1 found in Central and

West Africa, A3b2 in East Africa, while A2 and A3b1 are usually found in Southern Africa. This research provided population data on haplogroups A2 and A3b1, defined by bi-allelic and microsatellite markers. After screening almost 5000 male, primarily sub-Saharan African individuals, and an extensive literature survey, the Unit identified 155 A3b1 Y chromosomes and 64 A2 chromosomes. The highest frequencies of haplogroup A3b1 were found among the Khoe-San populations of Angola, Namibia and South Africa, and in low to moderate frequencies among Southeastern Bantu-speakers and South African Coloureds, with one chromosome found as far as Mozambique. This distribution indicates the origin of haplogroup A3b1 in the Khoe-San population of Southern Africa before it developed a presence in other neighbouring populations through gene flow.

Most of the subclade chromosomes of haplogroup A2 were found among the Northern Khoe-San populations of Angola and Namibia, and a Khoe-San/Bantu-speaker population in Botswana. However, an ancestral clade of haplogroup A2 was found at low frequencies among the Pygmy and Ubangian populations of Central Africa, and in the Malagasy of Madagascar. This occurrence of an ancestral A2 has extended the range of haplogroup A2 and raised the possibility that it did not originate in the Khoe-San.

Using science to corroborate oral history is another focus of this Unit's work. Since Y chromosome DNA is inherited from the paternal line, the Unit used Y chromosome DNA markers to test the oral history of the Mlungu clan of the Eastern Cape that they are descended from "two brothers" of European origin. If their claim is correct, then the scientists 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, the Unit has found a high proportion of non-African Y chromosomes among men tested, but the female gene pool examined using mtDNA is very sub-Saharan African.

## MALARIA ENTOMOLOGY RESEARCH UNIT

**Director: Professor Maureen Coetzee**

The Malaria Entomology Research Unit (MERU) was established in 2009. It is the synthesis of expertise based in the Vector Control Reference Unit (VCRU) of the National Institute for Communicable Diseases and the **DST/NRF South African Research Chair** in Medical Entomology and Vector Control (Wits). The main focus of research continues to be on insecticide resistance in the major African malaria vectors *Anopheles funestus* and the *Anopheles gambiae* complex with over 50% of their publications addressing various aspects of this field. Other topics include the use of novel mosquito control methods, distribution mapping of vectors and information systems for malaria control programmes, amongst others.

The Unit houses a unique collection of live mosquito colonies of the three most important vector species in Africa, *Anopheles gambiae*, *An. arabiensis* and *An. funestus*, as well as the minor vector *An. merus*, and the non-vector species *An. quadriannulatus*. Three colonies of *An. funestus* from Mozambique and Angola continue to provide a unique resource for research into insecticide resistance in this important malaria vector. This, and the team's experience in controlling malaria mosquitoes in many parts of Africa, makes MERU well-placed to offer collaboration with international institutions investigating similar problems and to play a role in influencing policy decisions on vector control strategies in the region.

MERU insectaries contain insecticide resistant strains of the three major African malaria vectors mentioned earlier and these were used to assess the mosquitoes' susceptibility to a specific fungus. In collaboration with researchers at Penn State University, the team successfully demonstrated that if insecticide-resistant strains were first exposed to this entomopathogenic fungus and then subsequently exposed to the insecticides to which they

were resistant, the mortality rate was dramatically increased.

MERU has also initiated a project to evaluate the potential of the Sterile Insect Technique (SIT) for use by the South African provincial malaria control programmes. SIT is a species-specific and environmentally-friendly method of suppressing insect pest populations. The method relies on the mass release of sterile laboratory-reared males into target populations and is based on the premise that the sterile males will successfully compete against wild males for mates. The study forms part of a larger project involving the Nuclear Technologies in Medicine and the Biosciences Initiative (NTEMBI), a national technology platform developed and managed by the South African Nuclear Energy Corporation (Necsa) and supported by the Department of Science and Technology (DST). The project has also attracted the support of the Technical Cooperation Programme of the International Atomic Energy Agency (IAEA).

Insecticide formulations were evaluated for collaborators at the University of Pretoria through a project grant from the Gates Foundation Grand Challenges Exploration initiative. Possible causes of insecticide degradation (temperature, humidity, pH and UV light) were tested on the four different classes of insecticides approved by the World Health Organization for use in malaria vector control.

In 2010, the Malaria Institute of Johns Hopkins School of Public Health, Baltimore, USA, in collaboration with MERU, was awarded a NIH International Centre of Excellence in Malaria Research grant (ICEMR, southern Africa). MERU's role in this Centre of Excellence is to study insecticide resistance in the malaria vector populations in Zambia and Zimbabwe. The seven-year grant includes capacity building for local students.

**[www.wits.ac.za/academic/health/pathology/9313/meru.html](http://www.wits.ac.za/academic/health/pathology/9313/meru.html)**

## DST/NRF RESEARCH CHAIR

**Professor Maureen Coetzee** holds the **Department of Science and Technology (DST)/ National Research Foundation (NRF) Chair** in Medical Entomology and Vector Control. Starting research on African malaria mosquitoes in 1977, Professor Coetzee is today internationally recognised as one of the leading malaria entomologists in Africa. In 2010, Dr Yiau-Min Huang and colleagues at the Smithsonian Institution characterised a new subgenus of the genus *Aedes*, and named it *Coetzeemyia* in recognition of Professor Coetzee's "many contributions to our knowledge of the mosquito fauna of Africa."



Professor Maureen Coetzee and team



## PERINATAL HIV RESEARCH UNIT

**Director: Associate Professor Glenda Gray**

The Perinatal HIV Research Unit (PHRU) is situated at the Chris Hani Baragwanath Hospital in Soweto and conducts research on adult, paediatric and adolescent HIV treatment, HIV prevention and HIV co-infections. In addition to clinical trials, the Unit also undertakes behavioural and social science research on HIV. In 2010/2011 the PHRU published more than 100 articles in peer-review journals, including six articles in the *New England Journal of Medicine* and two in *The Lancet*.

In 2010 the Unit completed the Infant, Maternal, Paediatric, Adolescent Clinical Trials (IMPAACT) study funded by the National Institutes of Health which compared the responses to initiation of non-nucleoside reverse transcriptase inhibitor (NNRTI)-based versus protease inhibitors (PI)-based antiretroviral therapy (ART) in HIV infected infants who have and have not previously received a single dose of nevirapine for prevention of mother-to-child transmission (MTCT). The results changed the infant treatment perspective globally by demonstrating the superiority of the PI-based regimen for children who had been exposed to nevirapine. An adult clinical trial evaluated the superiority of PI-based ART over NNRTI-based ART in women with a prior single dose of nevirapine prophylaxis for MTCT of HIV. The findings showed that in women with prior exposure to peripartum single-dose nevirapine, the PI-based ART was superior to the NNRTI-based ART. The results of these studies were published in the *New England Journal of Medicine* in 2010.

Since co-infection of HIV and tuberculosis (TB) are among the leading causes of death among women of reproductive age worldwide, the Unit undertook a study to screen for active TB during MTCT prevention at antenatal clinics in Soweto. All pregnant women aged 18 years or older presenting for routine care to these public clinics were screened for symptoms of active TB, cough for two weeks or longer, sputum

production, fevers, night sweats, or weight loss, regardless of their HIV status. Participants with any symptom of active TB were asked to provide a sputum specimen for smear microscopy,

mycobacterial culture and drug-susceptibility testing. A total of 3963 pregnant women were enrolled and screened for TB, of whom 1454 (36.7%) were HIV-seropositive. Active pulmonary TB was diagnosed in 10 of 1454 HIV-seropositive women (688 per 100 000) and 5 of 2483 HIV-seronegative women (201 per 100 000). The study found there was a high burden of active TB among HIV-seropositive pregnant women. The researchers recommend that TB screening and provision of isoniazid preventive therapy and antiretroviral therapy should be integrated with prevention of mother-to-child transmission services. This study was published in the *Journal of Acquired Immune Deficiency Syndrome* in 2011.

New research initiatives include the neuropsychological assessment of HIV infected and exposed children and controls and active case finding in contacts of children with TB. A trial is underway to assess the safety and effectiveness of the vaginal microbicide 1% Tenofovir Gel in the prevention of HIV type 1 infection in young women and to examine the effects of the microbicide on the incidence of Herpes Simplex Virus type 2. The PHRU had a weekly slot on Jozi FM from January to September 2011, dealing with HIV/AIDS issues, including the promotion of microbicide trial. Medical male circumcision (MMC) is found to be up to 60% effective at preventing HIV in men, and the Unit offered free MMC to over 15 000 patients in 2010/11. Through its Treatment Access Programme, the Unit provides over 2000 people with ARVs.



[www.phru.co.za/index.php](http://www.phru.co.za/index.php)

## PULMONARY INFECTIONS RESEARCH UNIT

**Director: Professor Charles Feldman**

The Unit was established as the “Human Ciliated Epithelium Research Unit” in 2001 and a name change to the “Pulmonary Infectious Diseases Research Unit” was approved in 2006 when the Unit’s research direction shifted away from pure studies on ciliated respiratory epithelium and investigations of the host regarding the pathogenesis of pulmonary infections, to focus more on the bacteria.

Work has progressed on studying the effects of the more recently introduced antibiotics, linezolid and tigecycline, on human neutrophils *in vitro* in order to determine whether these agents, similar to those of the macrolide class of antibiotics, reduce inflammation and/or influence the immune response. Tigecycline, a recently approved, intravenously administered glycylcycline class of antibiotics was developed to counteract the increasing problem of antibiotic resistance in Gram-positive bacteria, especially *Staphylococcus aureus*, as well as Gram-negative bacteria and anaerobes. Relatively little is known about the immunomodulatory potential of tigecycline, specifically its interactions with human neutrophils. One aspect of the study investigated the effects of tigecycline at therapeutically relevant concentrations and greater, on alterations in cytosolic  $\text{Ca}^{2+}$  concentrations and generation of antimicrobial reactive oxygen species (ROS) among other things. Cytosolic  $\text{Ca}^{2+}$  concentrations were measured using spectrofluorimetry and radiometric procedures, and generation of ROS by oxygen consumption. The study found that by functioning as a Calcium ionophore-like agent - independent of its antimicrobial activity and unlike that of the macrolides - tigecycline actually increased the pro-inflammatory functions of human neutrophils *in vitro*. The exact significance of this is uncertain, but could possibly account for some of the effects, including some side effects, seen with use of tygecycline in clinical practice.

A similar study investigating the same interactions was undertaken for the fluoroquinolone antibiotic, moxifloxacin, with human neutrophils. Moxifloxacin is used to treat respiratory infections including community-acquired pneumonia, and is also a promising antibiotic for treating tuberculosis which requires extended drug therapy. Relatively little is known about the effects of this agent on the antimicrobial and proliferative activities of human neutrophils and T-lymphocytes. This study found that extended use of this agent is unlikely to compromise the protective functions of neutrophils and T-lymphocytes and may even reinforce neutrophil-mediated antimicrobial activity by increasing the release of elastase.

The Unit is involved in a number of multi-centred clinical collaborative studies, one of which has been underway for nearly five years investigating pneumococcal bacteraemia. Another study focuses on community-acquired all-cause pneumonia, as part of the Community-Acquired Pneumonia Organization (CAPO) Collaboration. A further collaborative study is exploring genetic factors which may predispose patients to community-acquired pneumonia and/or be associated with severity and outcome of this infection. The data collection for the South African component has been completed and the specimens have been shipped to the collaborating centre in the USA.

Other recent local research has focused on the effects of cigarette smoke condensate on the pneumococcus. Cigarette smoking has been found to be one of the most important risk factors for pneumococcal infection. Smoking increases the risk of invasive pneumococcal disease and both the severity of this infection and the mortality are greater in smokers. The aim of this study is to investigate the effects of tobacco condensate on the microbiological characteristics of appropriate clinical isolates of the pneumococcus *in vitro*.

## A-RATED RESEARCHER

**Professor Charles Feldman** is a Chief Specialist and the Head of the Division of Pulmonology in the School of Clinical Medicine, whose research into community acquired pneumonia has brought great distinction to the School of Clinical Medicine, the Faculty and the University.

In 2010, Professor Feldman was appointed to the Board of the South African Medical Research Council, and in 2011, he was made an Honorary Life Member of the Federation of Infectious Diseases Societies of Southern Africa (FIDSSA) for his "outstanding contribution to Infectious diseases in South Africa, for your tireless work as Editor of the *Southern African Journal of Epidemiology and Infection*, and to FIDSSA itself." He also received an Honorary Fellowship of the South African Thoracic Society (SATS) for his contributions to pulmonology in South Africa.

His research in the field of community acquired pneumonia includes both clinical and translational research. Some of the clinical research has been involved in understanding the optimal antibiotic management of the infection. The laboratory-based research has focused on understanding the



pathogenesis of pneumonia to derive alternative strategies as an adjunct to antibiotic therapy in order to improve the prognosis of patients with pneumonia. Much of this research has informed both local and international guideline recommendations for the optimal management of pneumonia. In 2010/11, Professor Feldman published 14 papers and co-authored five book chapters. He has over 300 publications in books, book chapters, and in both indexed and Department of Education (DE) accredited peer reviewed journals.



## RESPIRATORY AND MENINGEAL PATHOGENS RESEARCH UNIT

**Directors: Professor Shabir Madhi and Professor Keith Klugman**

Acute respiratory infections are the leading cause of death in children in developing countries and the leading infectious cause of death in all ages. The Respiratory and Meningeal Pathogens Research Unit (RMPRU) is at the forefront of clinical and basic research into the treatment and prevention of respiratory and meningitis infections.

The Unit's work had major global impact in providing the research basis for progress towards introduction of conjugate pneumococcal vaccine in developing countries. The outcome of a 5-year vaccine trial conducted in Soweto with 39 876 children showed that the 9-valent pneumococcal conjugate vaccine (PCV) reduced the burden of invasive disease due to vaccine serotypes by 85% and was also shown to be effective in HIV-infected children. The 7-valent PCV was licensed for use in South Africa in 2005, and was introduced into the national Expanded Programme on Immunisation (EPI) in April 2009. The 13 valent vaccine was introduced into the EPI during 2011 and South Africa is the only country in Africa self funding PCV vaccine for its children. The scientific basis for the vaccine introduction was largely provided by this research Unit, which remains at the forefront of evaluating the effectiveness of PCV in reducing childhood morbidity and mortality in South Africa.

These initiatives include two large multi-centred case-control studies in major urban centres which are evaluating the effectiveness of the vaccine against invasive pneumococcal disease and pneumonia in HIV-infected and HIV-uninfected children. In addition, the Unit is undertaking studies to evaluate the "indirect effect" which childhood PCV immunization may have on protecting adults against developing pneumococcal disease. Professors Klugman and Madhi contributed to the WHO guidelines for the treatment of pneumonia in HIV-infected children.

The Unit was also involved during 2010 in studying the efficacy of rotavirus vaccine in preventing severe diarrhoea in African children. The findings were published in the *New England Journal of Medicine*, and

confirmed that rotavirus vaccine prevented severe diarrheal disease in African settings of diverse socioeconomic backgrounds. This research contributed to WHO's recommendation for its global use, including African countries, and was instrumental in advocating for the inclusion of rotavirus vaccine into the childhood immunization programme in South Africa since August 2009. The Unit remains involved in further studies on rotavirus in evaluating its effectiveness in reducing under-5 childhood morbidity and mortality in South African children.

Despite initial success of the Hib conjugate vaccine (HibCV) introduced in 1999 to combat Hib disease, surveillance led by the Unit showed that Hib disease in fully vaccinated children doubled from 2003 through 2009. These findings contributed to South African children receiving a booster dose of HibCV from November 2010 as part of a pentavalent vaccine.

The Unit collaborated with the Wellcome Trust's genome research entity, the Sanger Institute, to conduct pneumococcal whole-genome sequencing. An analysis of over 250 global strains of the Pneumococcal Molecular Epidemiology Network Clone 1 provided insight into both vaccine and antibiotic mediated evolution of the organism in a paper co-authored by Drs von Gottberg and Prof Klugman among others in Science in 2011.

The results of earlier work by the Unit showed that trivalent influenza vaccine (TIV) was associated with a 75% reduction in confirmed influenza illness. Following this, in 2011 the RMPRU initiated two Gates-funded trials evaluating seasonal influenza vaccine in pregnant women and their infants. The outcomes to be measured include protection from influenza in both the mothers and their newborns through six months of age. The researchers will also evaluate the impact of influenza prevention on the acquisition of pneumococcal colonization by newborn infants.

The Unit produced 70 articles and a book chapter during the period under review.



## DST/NRF RESEARCH CHAIR A-RATED RESEARCHERS

**Professor Keith Klugman** is the co-director of the Respiratory and Meningeal Pathogens Research Unit of the MRC, Wits and the National Institute for Communicable Diseases (NICD), and the William H Foege Professor of Global Health at Emory University in Atlanta, USA.



An outstanding scientist, Professor Klugman has made major contributions to the field of pneumococcal disease. His work has led to interventions that have the potential to save countless lives especially in Africa. He is the President of the International Society for Infectious Diseases which has more than 50 000 members and is an author or co-author of more than 450 scientific papers to date.

Most of the burden of pneumococcal disease in South Africa today is placed on HIV infected children and adults. The Unit conducted the first efficacy trial of pneumococcal conjugate vaccine in Africa and pioneered a surveillance programme for the disease in South Africa which led to South Africa becoming the first country in Africa to introduce the vaccine as part of its EPI program. Professor Klugman has leveraged a number of NIH, Gates and other funded studies over the past decade through both Emory and Wits, and is passionate about finding innovative ways to protect children and adults from pneumonia. He looks forward to building further collaborative partnerships with the Wits Medical School to promote public health research at Wits in the future.

**Professor Shabir Madhi** is both an A-rated scientist and holds a **Department of Science and Technology (DST)/National Research Foundation (NRF) Chair** on Vaccine Preventable Disease. An international leader in his field of vaccinology, Professor



Madhi is the co-director of the Respiratory and Meningeal Pathogens Research Unit of the MRC, and Executive Director of the National Institute for Communicable Diseases (NICD) at NHLS. He qualified as a paediatrician at Wits in 1996 and is currently a Professor of Vaccinology in the Wits Faculty of Health Sciences. Prof Madhi is also the President of the World Society for Infectious Diseases (2010-2014), which is the umbrella Society of the various continental Pediatric Infectious Disease Societies.

Prof Madhi has over 135 publications to his name, and his research has focused primarily on reducing morbidity and mortality from infectious diseases through vaccination. His work is of critical importance to African children, and concentrates on newly developed vaccines in preventing the two leading causes of death in children, namely pneumonia and diarrheal disease. This research was the first to demonstrate in Africa that childhood morbidity can be significantly reduced with pneumococcal-conjugate and rotavirus vaccines. These findings were published in the highest ranking medical journals, including *New England Journal of Medicine* and *Nature Medicine*, and helped to inform WHO recommendations on the issue of these vaccines in Africa and globally. The research has also contributed to South Africa being the first in Africa to introduce these vaccines into the public immunisation programme, which is anticipated to reduce childhood mortality in South Africa by 10-15%.





## RURAL PUBLIC HEALTH AND HEALTH TRANSITIONS RESEARCH UNIT (AGINCOURT)

**Director: Associate Professor Stephen Tollman**

This interdisciplinary MRC/WITS research unit is based in the School of Public Health, with a rural field research centre at Agincourt in Mpumalanga. Based on a well-established, longitudinal health and socio-demographic surveillance platform, the centre also serves as a satellite secretariat for the INDEPTH<sup>1</sup> Network, leading work in adult health and aging, and migration and health.

The Agincourt Unit's goal is to understand the dynamics of health, population and social transitions in rural Southern Africa to mount a more effective public health, public sector and social response. The Unit provides a critical research platform for research to highlight causal pathways and test interventions, and strives to translate research findings into relevant policy and programmes.

In an intervention research project known as the Kulani Child Health and Resilience Project, researchers undertook a cluster-randomised trial to evaluate a school-based intervention including both Soul Buddy Clubs and 'Schools as Nodes of Care', developed by Soul City and introduced by the Mpumalanga Department of Education. This intervention sought to provide emotional/social support to pupils aged 10-12 years and enhance their ability to cope and learn in an environment of chronic adversity. The baseline is complete and analysis of trial data is underway. Five control schools received the intervention in 2011.

The Unit is collaborating with the University of North Carolina, Chapel Hill, the University of California, San Francisco, and the Wits Reproductive Health and HIV Institute (WRHI) in a randomised control trial on conditional cash transfer and community mobilisation. The trial, known as Swa Koteka, seeks to determine effects of a multi-level HIV prevention intervention to jointly address structural and social factors contributing to young women's increased vulnerability to HIV. Interventions provide cash

transfers to families of young women conditional on their attending school. In 2011 detailed planning for the intervention to shift gender norms took place, including development of the community mobilisation survey instrument, recruitment of community mobilisers, development of their training programme and materials, and development of the intervention based on the 'One Man Can' campaign led by Sonke Gender Justice. The community mobilisation survey commenced in 2012.

Understanding the health and well-being of ageing populations in low- and middle income countries is vital for policy and planning, yet insufficient attention is given to this while the spotlight focuses on achieving the Millennium Development Goals. In a multi-country study, the Unit is leading eight INDEPTH sites in Africa and Asia in the World Health Organization's (WHO) Study on Global Ageing and Adult Health (SAGE). The first round of data collection in 2006/07 aimed to assess baseline measures of physical and cognitive function and establish cohorts of older adults in Africa and Asia. In 2010, a second round took place which included a module on health care utilisation of people 50 years and older. Analysis and international comparisons are underway.

The PRICELESS (Priority Cost Effective Lessons for Systems Strengthening) initiative focuses on generating and supporting evidence-based information and tools to help determine how best to use existing scarce resources so that health systems work more effectively and efficiently to deliver better population health. Current work focused on cost-effectiveness of measles campaigns, a screening programme for diabetic retinopathy, and strengthening delivery platforms. PRICELESS provided a modelled analysis of the number of lives that would be saved – from stroke especially – by reducing the sodium content of bread, margarine, soup mixes and flavourings, which contributed to Department of Health policy regarding the salt content of foods.

<sup>1</sup>INDEPTH: International Network for the Demographic Evaluation of Populations and Their Health.  
[www.indepth-network.org](http://www.indepth-network.org). Primary secretariat is in Accra, Ghana.



The Unit produced 46 peer-reviewed articles and research reviews and six book chapters in 2010/11 and several research journal editorials, commentaries and letters.

**[www.wits.ac.za/academic/health/publichealth/10394/agincourt.html](http://www.wits.ac.za/academic/health/publichealth/10394/agincourt.html).**

A 1-in-10 sample dataset, data dictionary and directions on how to request data are freely available at **[www.agincourt.co.za/DataSection/](http://www.agincourt.co.za/DataSection/)**





## SOWETO CARDIOVASCULAR RESEARCH UNIT

**Director: Professor Karen Sliwa**

The Soweto Cardiovascular Research Unit (SOCRU) was established in 2006 at Chris Hani Baragwanath Hospital to co-ordinate research into cardiovascular disease and promote research collaboration on cardiovascular diseases common in Southern Africa.

The Heart of Soweto Study (HOS) is a collaborative project that examined the emergence of heart disease in Soweto and other African communities in epidemiological transition. In January 2006, a prospective registry of more than 9000 men and women from Soweto presenting to the Baragwanath Hospital with heart disease was initiated. In conjunction with the Baker Cardiovascular Research Institute and the University of Queensland, the Unit was involved in creating the very large 'Heart of Soweto Study Registry'. Over 20 papers have been published from this cohort study since its inception, including data related to hypertension, rheumatic heart disease, pericardial disease and right heart failure.

A paper published in the *European Heart Journal* in 2011 described the effects of migration and socio-economic factors in the HOS study based on an analysis of data captured between 2006 and 2008. Of 5238 cases, 19% presented with uncomplicated hypertension or diabetes, 35% were found to have 'new' heart disease including hypertensive heart failure and coronary artery disease, while 39% of cases had historically prevalent heart disease. The results showed that level of education and non-communicable risk factors were important correlates of advanced disease. The rate of historically prevalent cases was higher in those aged 20-49 years and higher for 'new' heart disease in those aged over 50 years. Historically prevalent heart disease cases were more likely to be African, female and less likely to originate from Soweto. The researchers concluded that socio-economic and lifestyle factors typical of epidemiological transition have placed the urban, mainly African community of Soweto at the crossroads between historically prevalent and 'new' forms of heart disease. In the same year, the researchers published a paper in the *International Journal of Cardiology* which extended these findings to primary care in Soweto, highlighting the key role of enhanced primary prevention.

Another study explored the dietary habits and potential nutritional deficiencies in black African patients diagnosed with heart failure. From food intake data collected as part of the HOS, they found damaging food choices and potential nutritional deficiencies in a subgroup of urban black African patients diagnosed with congestive heart failure living in Soweto. The authors recommend that the nutritional status of black African patients with heart failure could be improved through healthier food choices and by reducing the intake of sweet drinks and excess salt. This work was published in the *Cardiovascular Journal of Africa* in 2011.

The HOS Outreach Project was launched in April 2011 and the chairperson of BHP Billiton South Africa, Dr Xolani Mkhwanazi, presented a cheque of R1.625 000 to Professor Sliwa at Michael Maponya Primary Health Clinic in Soweto. The event coincided with a cardiovascular health awareness day where residents were screened for heart disease, diabetes and high cholesterol. During 2011, over 1000 patients and 3000 learners at schools were screened during community awareness days. In a novel public health approach, the Unit conducted Healthy Eating Cooking Demonstrations at four primary health care clinics in Soweto for nurses and patients, and reached over 400 people in 2011. The Unit published 20 articles and commentaries during 2010/11.

[www.socru.org](http://www.socru.org)





WITS REPRODUCTIVE HEALTH &amp; HIV INSTITUTE

## WITS REPRODUCTIVE HEALTH AND HIV INSTITUTE

**Director: Professor Helen Rees**

In 2010, the Reproductive Health and HIV Research Unit (RHRU) was awarded Institute status by Wits in recognition of its outstanding range of research. The newly named Wits Reproductive Health and HIV Institute (WRHI) merged with Enhancing Children's HIV Outcomes (ECHO), adding significant paediatric HIV expertise to the Institute's portfolio. Based in the Hillbrow Health Precinct, WRHI has a national impact and works in five provinces, funded by a wide range of national and international donors. In 2010/11, WRHI had over 60 active research protocols and contributed to 82 peer-reviewed publications.

All WRHI trials are supported by a social science programme that focuses on the social context of trial participants and their communities. In 2010, with funding from the Dutch government, the WRHI established a dedicated specialised research site, the WRHI Research Centre in Hillbrow. This site has the capacity to recruit and retain hundreds of study participants on a monthly basis.

Amongst its many projects, Follow-on African Consortium for Tenofovir Studies (FACTS) is a newly-created South African-led consortium established to develop and conduct a Phase 3 clinical trial to establish the safety and effectiveness of 1% tenofovir gel used before and after sex in protecting women against HIV and genital herpes. The consortium comprises eight South African research institutions and is led by Professor Helen Rees as the Protocol Chair and co-ordinated by WRHI.

WRHI is participating in three studies of the Microbicide Trials Network (MTN), a worldwide collaborative clinical trials network funded by the US National Institutes of Health. One involves taking an ARV tablet once a day (Pre-Exposure Prophylaxis - PrEP), or applying an ARV-based vaginal microbicide daily. The Vaginal and Oral Interventions to Control the Epidemic Study (VOICE) involves trial sites across Africa. It is evaluating the safety and effectiveness of different approaches for preventing sexual transmission of HIV in women, and determining which approach women are more likely to follow.

The Characterisation of Novel Microbicide Safety Biomarkers study aims to characterise the vaginal environment with respect to the vaginal microbial flora, biomarkers of epithelial integrity and soluble and cellular biomarkers of immune activation, including target cells for HIV in HIV-negative adult women in good health at low risk for HIV. The study focuses on four different groups including low-risk HIV negative women, pregnant women, adolescents and women who engage in vaginal practices considered to be high-risk. This is a collaborative study between WRHI and other partners in Africa and Europe.

Another long-term, observational MTN study is underway to understand the nature of HIV progression and treatment response in HIV-positive women who become infected incidental to their participation in an HIV prevention trial of either a topical microbicide or oral PrEP. WRHI is also partnering with the MTN on an evaluation of Maternal Baby Registry Outcomes after Chemoprophylactic Exposure. This is the first registry of its kind of women who become pregnant while participating in an HIV prevention trial of either a microbicide or an oral antiretroviral drug.

WRHI is also participating in six studies of the International Maternal Pediatric Adolescent AIDS Clinical Trials Group (IMPAACT). Current IMPAACT studies include a wide range of studies including phase I/II safety and dose finding studies for new antiretroviral agents and large strategy trials such as the PROMISE prevention of mother-to-child transmission study.

WRHI has been involved in several studies investigating new technologies to prevent HPV-related diseases, including cervical cancer. The HPV in Africa Research Partnership (HARP) study is being conducted by a consortium of several academic institutions across the globe. HARP is the first study of the simultaneous evaluation of currently existing cervical cancer screening strategies against histological endpoints conducted among HIV-positive African women. This is also the first rigorous evaluation of CareHPV in an African setting.

[www.wrhi.ac.za](http://www.wrhi.ac.za)

# RESEARCH CENTRE OF EXCELLENCE, PLATFORMS AND RESEARCH THRUSTS

## - Research Centre of Excellence

DST/NRF Centre of Excellence for Biomedical TB Research (CBTBR) - School of Pathology

## - Platforms

Wits Advanced Drug Delivery Platform - School of Therapeutic Sciences

## - Research Thrusts

Molecular Biosciences Research Thrust: Health for Africa

## - Other Research Endeavours

Building Research Capacity in Africa

Sydney Brenner Institute for Molecular Bioscience

Wits Bioinformatics



# RESEARCH CENTRE OF EXCELLENCE

## DST/NRF CENTRE OF EXCELLENCE FOR BIOMEDICAL TB RESEARCH (CBTBR)

**Director: Dr Bavesh Kana**  
**School of Pathology**

**The DST/NRF Centre of Excellence** for Biomedical TB Research (CBTBR) was established by the Department of Science and Technology (DST) and the National Research Foundation (NRF) to facilitate biomedical research on tuberculosis (TB). The CBTBR is made up of three distinct nodes: Wits, Stellenbosch University (SU) and the University of Cape Town (UCT). The success of the CBTBR has been a result of the concerted efforts of the three nodes, which strive to excel in their respective areas of expertise and to serve as outstanding platforms for the training and development of postgraduate students and Postdoctoral Fellows.

A key feature of the Wits node is that it is co-hosted with the National Health Laboratory Service (NHLS); its laboratories are housed within the central complex of the NHLS in Braamfontein. The Wits node has two Biosafety Level II (BSLII) and three Biosafety Level III (BSLIII) laboratories, the latter for research on human pathogens under containment conditions. The largest of the three BSLIII laboratories, which conforms to international Centre for Disease Control (CDC) standards, was refurbished during 2010/11 and will serve as the primary platform for pathogen work at the Wits node. The research conducted at the Wits node aims primarily to understand aspects of the basic biology of *Mycobacterium tuberculosis* with

the ultimate aims of identifying and validating new drug targets for TB.

In January 2011, **Dr Bavesh Kana** was appointed as the new Head of the Wits node. Under his leadership, researchers at the Wits node work to identify, characterise and validate new drug targets and vaccine candidates by investigating the metabolic pathways utilised by *M. tuberculosis*, the causative agent of TB. Recently, their work has focused on characterising enzymes which are associated with remodelling the cell wall of the tubercle bacillus during infection. The team also studies the biosynthesis of molybdopterin cofactor and several components of the mycobacterial electron transport chain. They hope to identify new molecular determinants which are important for essential disease processes. The team (which included seven Masters, one Doctoral student and two Postdoctoral Fellows in 2011) has received international acclaim for its research, which has been published in leading international research journals.

Apart from partnering with researchers at the SU and UCT nodes on various projects, members of the Wits node have several other exciting research collaborations underway:

### **1. Detection of Rpf-dependent populations in sputum in TB patients**

Recent studies demonstrate that sputa from TB patients are characterised by a heterogeneous population of cells carrying different amounts of lipid inclusion bodies and a significant proportion of non-culturable cells. These non-culturable bacteria can be stimulated to grow by supplementation with resuscitation promoting factors (Rpfs), a group of peptidoglycan (PG) degrading enzymes that have the ability to enhance bacterial culturability, when added at picomolar concentrations to dormant bacteria, and furthermore also allow for bacterial growth under otherwise non-permissive conditions. These data suggest that PG degradation and the resulting breakdown products, termed muropeptides, may be critical in controlling the ratio of non-culturable bacilli present in sputum. This raises some interesting biological questions: How is disease outcome related to the ratios of bacterial populations in differential states of culturability? Are Rpfs and other PG degrading enzymes important in the chain of transmission? Is there a greater level of genotypic and phenotypic heterogeneity in sputum samples that cannot be detected by conventional TB diagnostics? With regards to the latter, it is noteworthy that the Rpf-dependent population identified in sputum samples appears to be tolerant to rifampicin. Hence, the prediction is that these non-culturable bacteria would effectively constitute

a population of persisting bacteria which would have important implications for disease relapse in treated patients. CBTBR researchers propose to study the presence of non-culturable bacterial populations in sputa isolated from TB patients with varying degrees of disease and associated treatment.

## 2. South African TB Research and Innovation Initiative

**Dr Bhavna Gordhan** from the Wits node, together with Professor Valerie Mizrahi and Dr Digby Warner from the UCT node of the CBTBR, were awarded grants from the South African TB Research and Innovation Initiative (SATRII), a new TB drug discovery project funded by the Technology Innovation Agency (TIA). The biological components of the research will be carried out in the CBTBR and forms part of a larger collaborative venture which involves Professor Kelly Chibale (H-3D Drug Discovery Centre, UCT), Dr Chris Edlin (iThemba Pharmaceuticals, Gauteng) and leading TB drug discovery experts from the US National Institutes of Health, including Wits graduate, Dr Helena Boshoff.

The Wits node continues to explore joint research efforts in TB drug discovery, as well as research and training partnerships with institutions in the United States of America.

The primary source of funding has been a large grant awarded to the node by the DST/NRF under the auspices of the national Centre of Excellence programme rolled out in 2004/5, while smaller grants from the NHLS, MRC and Wits have also supported the programme. In 2011, two additional large grants from the US National Institutes of Health and the Technology Innovation Agency were awarded to the Wits node. Funding has also been secured through an award made to Dr Bवेश Kana by the Howard Hughes Medical Institute, USA.

### High-impact articles in 2010/2011:

1. Warner D, Ndwandwe D, Abrahams G, Kana B, Machowski E, Venclovas and Mizrahi V (2010). Essential roles for *imuA'*- and *imuB*-encoded accessory factors in DnaE2-dependent

mutagenesis in *Mycobacterium tuberculosis*. *Proceedings of the National Academy of Sciences, USA*, **107**: 13093-8.

2. Kana B, Mizrahi V, Gordhan B (2010). Depletion of resuscitation-promoting factors has limited impact on the drug susceptibility of *Mycobacterium tuberculosis*. *Journal of Antimicrobial Chemotherapy*, **65**: 1583-5.
3. Scott L, Gous N, Cunningham B, Kana B, Perovic O, Erasmus L, Coetzee G, Koornhof H and Stevens W (2011). Dried Culture Spots for Xpert MTB/RIF External Quality Assessment: Results of phase 1 pilot study from South Africa. *Journal of Clinical Microbiology*, **49**(12): 4356 – 60.
4. Williams M, Kana B and Mizrahi V (2011). Functional analysis of molybdopterin biosynthesis in mycobacteria identifies a fused molybdopterin synthase in *Mycobacterium tuberculosis*. *Journal of Bacteriology*, **193**: 98-106.

[www.tuberculosis.org.za](http://www.tuberculosis.org.za)

# PLATFORMS



## WITS ADVANCED DRUG DELIVERY PLATFORM

**Director: Professor Viness Pillay**  
**School of Therapeutic Sciences**

The team at the Wits Advanced Drug Delivery Platform (WADDP) is engaged in the prototyping of advanced drug delivery technologies. Their research is focused on intelligent solutions for drug delivery technology and they aim to design active/passive programmable innovative and commercialisable polymeric devices which will positively impact the global pharmaceutical industry in every therapeutic category.

Their molecular target-based therapies, which utilise pseudo-peptides to stabilise large active protein molecules, provide novel treatment options for diseases such as cancer, infectious diseases, as well as metabolic and neurodegenerative disorders. The team aims specifically to provide new delivery systems for existing drugs, as well as systems for new molecules which are difficult or impossible to use in conjunction with conventional drug delivery systems.

One of their nanotechnology projects is a groundbreaking initiative which involves the novel treatment of Spinal Cord Injury (SCI). SCI results in inflammation of the spinal cord with either temporary or permanent loss of sensory, motor or autonomic function. Immediate and effective treatment is required to prevent further tissue damage. The progression of secondary degenerative processes provides a therapeutic window of about an hour after a SCI, for the

administration of a glucocorticoid drug such as methylprednisolone. However, high systemic doses of methylprednisolone impose serious side-effects and toxicity. The relatively modest gain in terms of repair resulting from this conventional therapy reflects the inefficient dosing of the drug at the actual injury site. The team in the WADDP is working to design an injectable, biodegradable Polymer-Engineered Spino-mimetic Neural Device (PEND) which will provide site-specific delivery of a model steroidal drug at a dose 100 times less than systemic methylprednisolone for improved SCI therapy.

The team also recognised that newer drugs and molecules which have many attractive properties, although continuously under development, sometimes are associated with disadvantages such as short *in vivo* half-lives, poor physicochemical stability and low bio-availability. These result in frequent administration which may limit the drugs' clinical use, as it becomes costly, painful, and inconvenient to treat patients. These challenges may lead to poor patient compliance and erratic drug concentrations in the blood but they can be overcome by improving the ways in which they are delivered to the tissues which need them. The team employs futuristic techniques which range from macroscopic monolithic devices for oral drug delivery in the form of multilayered

tablets with customised release kinetics, chronotherapeutic delivery, gastroretentive systems with adhesive as well as floating abilities, through microscopic and nanoscopic devices for implantation into the eye, brain, spinal cord and vagina, nasal drug delivery, to targeted drug delivery such as that needed for the treatment of cancer. The technologies are developed using custom-synthesised novel polymers, co-polymers, and interpolymeric electrolyte complexes which are stimuli responsive. The team also uses electrospun nanofibres, memblets, cryogels, nanobubbles, hydraulic delivery systems and biosensors.

### Networking and collaboration

During 2011/12, the WADDP established several new research collaborations, such as the partnership with the University of Twente (Enschede, The Netherlands) and the spin-off biotech company MyLife Technologies (The Netherlands). Advances in nanotechnology made by Dr Regina Luttge and her team at the MESA+ Institute for Nanotechnology at University of Twente allowed for the production of microneedle patches specifically suited for use on human skin. A drug delivery patch which combines novel, patented electroconductive hydrogel technology developed by the WADDP is envisaged, the concept being that the electroconductive hydrogel will allow controlled release of drugs by electrical stimulation of the array.

## DST/NRF RESEARCH CHAIR

Collaboration was also established with Professor Riaz Khan in the Department of Medicinal Chemistry at Qassim University (Qassim, Saudi Arabia). He works with the WADDP on projects involving aspects of in silico modeling theories for polymeric device conceptualisation employing molecular mechanics. The focus is on ensuring the biodegradable scaffold devices are biocompatible for clinical application.

A key step in establishing an effective network in drug innovation and delivery research in South Africa was the establishment of the National Medical Device Innovation Platform (NMDIP) by the South African Medical Research Council (MRC) in 2010. The WADDP is engaged with the MRC on this initiative that focuses on creating innovative medical devices to ensure superior clinical outcomes, reduce the costs of disease diagnosis and treatment, provide greater patient comfort for chronic disease management and provide solutions for unmet health needs in underserved communities.

### A Centre of Excellence

In 2011, the WADDP was recognised as an **African Network for Drugs and Diagnostics Innovation (ANDI) Centre of Excellence (CoE)**, to be known

as the CoE in Advanced Drug Delivery Technology. ANDI, based at the United Nations Economic Commission for Africa in Addis Ababa (Ethiopia), aims to increase research and development collaboration among African institutions and countries; support and promote public-private partnerships and new firms within Africa; and leverage existing capacity to support south-south and north-south collaboration.

### DST/NRF South African Research Chair Initiative

Professor Viness Pillay holds the **DST/NRF South African Research Chair in Pharmaceutical Biomaterials and Polymer-engineered Drug Delivery Technologies**. Passionate about the research conducted by the team he leads, and committed to the development of research capacity, he supervises and/or mentors over 30 postgraduate students and members of research staff.

### High-impact articles in 2010/2011:

A total of 25 papers were published by the WADDP during 2010/11. All publications appeared in ISI-accredited international scientific journals with the highest impact factors in the pharmaceutical

sciences. A selection of the highest-impact factors papers include:

1. Wadee A, Pillay V, Choonara Y, du Toit L, Penny C, Ndesendo V and Murphy C (2011). Recent advances in the design of drug-loaded polymeric implants for the enhanced treatment of solid tumors. *Expert Opinion on Drug Delivery*, **8**(10): 1323 - 1340.
2. du Toit L, Govender T, Pillay V, Choonara Y and Kodama T (2011). Investigating the effect of polymeric approaches on circulation time and physical properties of nanobubbles. *Pharmaceutical Research*, **28**(3): 494 - 504.

In 2011 alone, staff and postgraduate students of the WADDP presented 27 papers at various conferences. A particular highlight for the WADDP in 2011 was the 6<sup>th</sup> International Conference on Pharmaceutical and Pharmacological Sciences (ICPPS) Award for Best Research Publication in Pharmaceutics for a paper authored by several members of the team: Ndesendo N, Pillay V, Choonara Y, Meyer L, Buchmann E, du Toit L, Khan R and Rosin U (2010). Investigation of the physicochemical and physicomachanical properties of a novel intravaginal bioadhesive polymeric device in the pig model. *AAPS PharmSciTech*, **11**(2): 793-808.

[www.wits.ac.za/waddp](http://www.wits.ac.za/waddp)





# RESEARCH THRUSTS

## CHRONIC DISEASES OF LIFESTYLE



A Research Thrust is a dynamic coalition of researchers, research teams and research entities working across various disciplines. Thrusts are intended

to stimulate academic initiative, creative thinking and imaginative ways of addressing, organising and funding research in the broad area identified. They aim to create an awareness of existing research capacity and technical platforms which can be shared among researchers.

Collaboration between research groups at Wits and partner institutions is facilitated through cross-disciplinary seminars and symposia, which enable researchers to identify synergies and to formulate collaborative projects which draw on each group's unique strengths. Members of the Thrusts work together to secure cross-cutting grants and to develop capacity in several areas of overlapping research activity. These collaborations encourage researchers to tackle larger and more focused research questions with multidisciplinary input.

The Faculty of Health Sciences was involved in the establishment of two Research Thrusts: *Diseases of Lifestyle: An Emerging African Problem* and *Molecular Biosciences: Health for Africa*. These Thrusts were formally recognised by the University Research Committee and Senate in 2008 and have gone from

strength to strength. These Thrusts bring together the many clinicians and researchers across Wits who are interested in understanding the aetiology of diseases of lifestyle in our communities and those who are interested in the molecular exploration of biological questions.

### Chronic Diseases of Lifestyle Research Thrust: An emerging African problem

The Chronic Diseases of Lifestyle Research Thrust is championed by **Professor Karen Sliwa** and Associate **Professor Nigel Crowther**. Diseases of lifestyle (such as diabetes, hypertension and heart disease) are increasing in prevalence in developing countries. This worldwide epidemic has received much public and scientific interrogation in the developed world but has been largely ignored in the developing world where communicable diseases such as HIV and TB have taken centre stage. However, in low and middle income countries over half of the prevailing disease burden is due to non-communicable disease.

#### Key Thrust objectives:

1. To study the metabolic and genetic causes and epidemiology of obesity, cardiovascular disease and related chronic diseases among the indigenous population groups of South Africa;
2. To analyse and improve the delivery of healthcare services for

these chronic diseases in both urban and rural areas;

3. To facilitate the implementation of innovative intervention strategies with specific focus on African societies in transition, both in underserved rural and urban communities.

Members of the Thrust are active in local communities. In 2010/11 they hosted several Awareness Days at primary health care clinics in Soweto, which aim to raise consciousness of diseases of lifestyle amongst nurses as well as patients. The Thrust also seeks to equip members of the community to avoid or overcome diseases of lifestyle and so hold Healthy Eating Cooking demonstrations to provide practical advice on what to eat and how to prepare food in a healthy manner. To reach younger members of the community in Soweto, members of the Thrust visited several secondary schools, teaching the learners about chronic diseases of lifestyle and how to avoid these through a healthy diet and lifestyle, providing screening of diseases of lifestyle risk factors.



## MOLECULAR BIOSCIENCES RESEARCH THRUST: HEALTH FOR AFRICA

This Thrust is championed by **Professor Michèle Ramsay** (Faculty of Health Sciences) and **Professor Chrissie Rey** (Faculty of Science). Molecular bioscience encompasses a range of research fields in both the natural and health-related sciences, with a focus on exploring the genetic and biochemical foundation of life. The Thrust's research focuses on understanding the molecular basis of scientific research questions which are of particular concern in Africa and developing nations.

Partnerships embrace diverse groups ranging from:

- the clinicians who see patients at the University teaching hospitals to
- the research scientists who perform experiments in the broad fields of genomics, proteomics and structural biology to
- computer scientists, statisticians and bioinformaticists who mine and analyse data to
- molecular biologists, physical chemists and pharmacists who develop drugs and
- clinical trials. This multidisciplinary research approach includes collaboration with the clinical research thrust 'Diseases of Lifestyle - an emerging African problem'.

The Molecular Biosciences Research Thrust (MBRT) is an active community, regularly hosting visitors and arranging or participating in meetings to facilitate the exchange of ideas. In 2010, the Thrust held a student retreat, providing a platform for its young research students to meet and to discuss their projects. The invited speaker, Dr Musa Mhlanga (Head: Synthetic Biology Group, CSIR Bioscience), shared aspects of his science philosophy and groundbreaking imaging work.

In 2011, the Molecular Biosciences Research Thrust held a Research Day to bring students of the Faculties of Health Sciences and Science together to present and discuss "hot topics" in their fields. Twelve oral presentations and 25 posters were presented by postgraduate students and Postdoctoral Fellows, covering areas such as cancer, Alzheimer's disease, malaria, HIV, tuberculosis, hepatitis, rift valley fever virus

infections, cassava mosaic virus infections and avocado fruit infections. The guest speaker, Dr Sharon Prince (University of Cape Town), gave a fascinating presentation on T-box factors as targets for cancer treatment.

During 2010/2011, the Thrust hosted several researchers:

Dr David Landsman (US National Center for Biotechnology Information), Professor Chris Mathew (Guy's Hospital/King's College London), Professor Janet Kelso (Head: Bioinformatics Group, Max Planck Institute, Germany), Professor George Davey-Smith (University of Bristol, UK), Dr Caroline Relton (University of Newcastle, UK), Professor Ruth Gabizon (Department of Neurology, Hadassah University Hospital, Jerusalem Israel) and Dr Abdelkrim Rachedi (European Bioinformatics Institute prior to joining Wits Bioinformatics).

**[www.wits.ac.za/Research/MBRT](http://www.wits.ac.za/Research/MBRT)**



Members of the Molecular Biosciences Research Thrust who participated in the Thrust's 2011 Research Day. The day provided a wonderful opportunity for interaction between the Faculties of Science and Health Sciences

## BUILDING RESEARCH CAPACITY IN AFRICA

### The NIH-Fogarty Non-communicable Diseases Research Leadership Training Programme

is part of the Millennium Promise Awards: Non-communicable Chronic Diseases Research Training. The Programme aims to develop a group of well-trained researchers at the Masters, PhD and Postdoctoral levels, building capacity to perform integrated research spanning many disciplines. The research focuses on chronic, non-communicable diseases in southern Africa, particularly among disadvantaged groups. The Programme also seeks to find ways of incorporating the research findings into community practice aimed at prevention and treatment.

The training is facilitated by collaboration across several established

research programmes in the Faculty, including the Soweto Heart Study, the Agincourt Rural Facility and the Birth to Twenty Study. Principle investigators include Professors Karen Sliwa, Nigel Crowther, Michèle Ramsay and Kerstin Klipstein-Grobush. Each year, supervisors from different fields of expertise offer projects related to non-communicable diseases in African populations. Interested post-graduate students and Postdoctoral Fellows from all over Africa can apply for these projects.

Two Masters and two PhD students signed up to the Programme during 2011 (two from South Africa, one from Kenya and one from Nigeria). At a retreat held at the Vredefort Dome World Heritage Site in 2011, the students had the opportunity to present aspects of their research.

[www.wits.ac.za/health/research/NIH](http://www.wits.ac.za/health/research/NIH)



**From left:** Professor Nigel Crowther, Alex Kasembeli (MSc student), Sandra Pretorius (PhD student), Professor Karen Sliwa, Professor Michèle Ramsay, Thandiswa Ngcungcu (MSc student) and Ameh Soter (PhD student) at the Programme retreat held in October 2011

### Southern African Human Genome Programme

**Professor Michèle Ramsay** and **Associate Professor Himla Soodyall** are part of a team which in 2011 secured seed-funding from the Department of Science and Technology (DST) to initiate the groundbreaking national Southern African Human Genome Programme (SAHGP). It involves collaboration between scientists at education institutions, science councils, government and industry.

The Programme aims to make a significant contribution to the understanding of DNA variation among southern Africans and how this impacts on the health of the people of our country. The vision of the SAHGP is to improve the quality of life through understanding human genetic diversity, and the mission is to develop capacity for genomic research in South Africa, to establish a sustainable resource for genomic research (including a national database) and to translate the information into improvements in human health. Another critical objective of the SAHGP is to develop the required bioinformatics skills and capacity which will be needed to analyse the vast amount of data which will be generated. This national initiative will focus specifically on southern African genomes and will also have a public awareness component. In its first phase, the programme is jointly coordinated by Professor Michael Pepper from the University of Pretoria and Professor Ramsay.



## GEOCODE

As researchers start to understand the complexity of many diseases, it is becoming clear that joint investigations are needed to find solutions. The **Genomic and Epigenomic Complex Disease Epidemiology (GEOCODE)** initiative is a joint exchange programme which seeks to bring together great research minds in this rapidly evolving field, to stimulate areas of synergy and to support research. The overall aims of the programme are to:

- establish a multilateral network of researchers active in genetic and epigenetic epidemiology;
- strengthen research capacity through exchange of knowledge and expertise in both areas;
- develop integrated approaches to investigate both genetic and epigenetic aspects of complex disease.

While the 28 consortium partners include institutions across Europe, Australia, Brazil, Canada, China, India, New Zealand, South Africa and the USA, the programme will be co-ordinated by University of Bristol, UK. The partners plan to investigate a wide variety of



complex diseases including cancer, type 2 diabetes, obesity, cardiovascular disease and perinatal health problems. A focus on translational aspects of genetic and epigenetic epidemiology will be actively maintained. A series of short and long term periods of staff exchanges are envisaged, as well as annual workshops at which all participating partners will be represented.

Wits is one of the institutional partners, and **Associate Professor Shane Norris** (Director: MRC/Wits Developmental Pathways for Health Research Unit) is a

member of the managing committee. Several researchers from Wits have attended training workshops on genetics and epigenetics. During the period under review, colleagues from the Universities of Bristol and Newcastle visited Wits, presented seminars, and engaged researchers and postgraduate students in discussions of study ideas and collaborations.



## SYDNEY BRENNER INSTITUTE FOR MOLECULAR BIOSCIENCE

**Dr Sydney Brenner**, who started his research career at Wits, won the Nobel Prize for Physiology/Medicine in 2002. Plans for the Sydney Brenner Institute for Molecular Bioscience (SBIMB) began in 2009, when Dr Brenner agreed to lend his name to an institute to be established at Wits. The initiative is led by the Office of the Vice-Chancellor and has received the support of the Department of Health and the Medical Research Council.

The SBIMB vision is to become a leader in biomedical research on the African continent, conducting world-class, innovative and relevant research, which will benefit the southern African community, and to excel as a centre for learning. The SBIMB will focus its research activities on understanding the molecular

and genomic basis of non-communicable diseases prevalent in South African populations and will foster collaborative biomedical and molecular research between the Thrusts.

Steadily making progress, a site for the SBIMB on the Wits Education Campus was approved in 2010. With the proximity to the new Public Health Building, Medical School and one of the Wits teaching Hospitals, it will form part of a medical precinct in the area, ideal for the purpose of stimulating health-related research. It will be immediately adjacent to the Nelson Mandela Children's Hospital, which will facilitate collaboration across areas of synergy.

During 2010 and 2011, the Institute's Interim Director, **Professor Michèle Ramsay**,

together with the Institute's Project Manager (Dr Kurt Lightfoot in 2010 and Ms Caryn McNamara in 2011) networked extensively, both with local stakeholders as well as experts and interested parties across the globe. In 2010 they engaged with scientists based at various centres and institutes in the UK, including the Wellcome Trust Sanger Centre, the London School of Hygiene and Tropical Medicine, Imperial College-London, and King's College-London. In 2011 they met with potential funders in the US and Switzerland.

In 2011, Dr Brenner hosted a meeting at the Stellenbosch Institute for Advanced Study (STIAS) in the Western Cape. The Wits delegation to the meeting consisted of seven young scientists, the two staff of the SBIMB, and the Senior Advisor to the Vice-Chancellor, Professor Belinda Bozzoli. Apart from discussing various research projects, Dr Brenner sought to inspire young upcoming scientists in their respective research fields. Projects discussed ranged from basic evolutionary biology, gene therapy, high-throughput genomic science, and the molecular and immunological aspects of HIV and TB infections. The second aim of the meeting was to discuss the way forward for the SBIMB.

**[www.wits.ac.za/Research/SBIMB](http://www.wits.ac.za/Research/SBIMB)**



**Back (standing left to right):** Dr Natalya Nikitina (School of Molecular and Cell Biology), Dr Penny Moore (National Institute for Communicable Disease), Dr Baves Kana (DST/NRF Centre of Excellence for Biomedical TB Research, NHLS), Ms Lee-Ann Wood (Wits Bioinformatics), Dr Abdullah Ely (Antiviral Gene Therapy Research Unit, Department of Molecular Medicine and Haematology), Dr Pierre Durand (Evolutionary Medicine Unit, Dept of Molecular Medicine and Haematology), Dr Samantha Barichievy (Sydney Brenner Postdoctoral Fellow, Gene Expression & Biophysics Group, CSIR Biosciences), Ms Caryn McNamara (SBIMB Project Manager) **Front (seated left to right):** Prof Michèle Ramsay (SBIMB Interim Director), Dr Sydney Brenner, Prof Belinda Bozzoli (Senior Advisor to the Vice-Chancellor)



## WITS BIOINFORMATICS

Wits Bioinformatics is a cross-faculty initiative with research projects in both the Faculties of Science and Health Sciences. The team is responsible for teaching and training, research and service provision in the field of bioinformatics. Its members work with colleagues across the University with interests in bioinformatics and computational biology. Projects in the following areas are carried out by people in Wits Bioinformatics, most of them in collaboration with other researchers or elsewhere:

- Bioinformatics of viral diversity
- Evolutionary biology
- Experimental algorithms and high-performance computing
- Assembly of second generation sequence data
- Functional annotation of novel data
- Genome-wide Association Studies
- Human Diversity Studies

Wits Bioinformatics provides a number of services for the Wits and broader bioinformatics community, including:

- Consulting
- Tools
- High-Performance Computing
- Databases
- Structural Targets Databases

In March 2011, scientists gathered from across the globe, but most importantly from different parts of Africa, to attend the joint Congress of The International Society for Computational Biology and The African Society for Bioinformatics and Computational Biology in Cape Town. The topics under discussion included database and tool development, functional and comparative genomics, molecular epidemiology and evolution, and their application to host and pathogen systems as well as drug and vaccine development. Dr Sydney Brenner gave the welcome address, urging an emphasis on questions

of biological relevance and not just manipulation of large data sets for broad hypothesis generation. **Associate Professor Scott Hazelhurst**, Director of Wits Bioinformatics, spoke about a novel algorithm for clustering expressed cDNA sequences.

[www.bioinf.wits.ac.za](http://www.bioinf.wits.ac.za)





## RESEARCH HIGHLIGHTS AND HIGH IMPACT PAPERS

- Rotavirus vaccine saves lives
- New-generation treatment offers hope for inherited high cholesterol
- Hitting back at bacteria
- A new combination to combat pain
- Cancer of the mouth: Reviewing what we know
- Growing older in Africa and Asia
- Unicellular suicide
- Increased cancer risk for HIV-infected women
- Johannesburg: One in three male teens likely to use a performance-enhancing substance
- Ostriches sleep like Platypuses: Uncovering the evolution of REM sleep
- High-tech drug delivery for HIV prevention
- HIV infection during lactation increases infant's risk
- Two Wits publications in same issue of *New England Journal of Medicine*
- *Journal of Public Health Policy*: Special issue celebrates Wits research unit
- Greater awareness of dietary intolerance will save lives
- HIV vaccine trial highlights particular need to protect women
- Can reducing viral load lower the risk of transmission of HIV?
- A superior test to detect TB in HIV-infected adults
- Description of additional features of rare skin cancer to improve diagnosis
- Biopesticide may solve challenge of mosquito resistance
- When delayed antiretroviral treatment costs lives
- Human violence - evidence from ages past

## Rotavirus vaccine saves lives

Rotavirus is the leading cause of severe diarrhoea worldwide. This virus takes the lives of more than 500 000 children under the age of five every year. Almost half of these deaths occur in Africa. Research published in the *New England Journal of Medicine* in 2010 demonstrated the importance of vaccination in achieving the significant reduction of severe rotavirus infections amongst children in the developing world, where disease impact has been the greatest.

Trials were conducted in Mexico and in Africa (Malawi and South Africa). The African clinical trial specifically focused on the vaccine's performance amongst infants in high mortality, low-income settings. In South Africa and Malawi, more than 4 900 infants were enrolled in the clinical trial, which examined the efficacy of the Rotarix™ vaccine. The results showed that the vaccine reduced severe rotavirus infection by 61.2% in African infants during the first year of life.

These studies informed the World Health Organization's (WHO) recommendation that rotavirus vaccines be included in every nation's immunisation programme. The recommendation was especially important for Africa, which is hard hit by the disease. It placed rotavirus vaccines amongst a comprehensive set of other interventions key to stopping diarrhoeal deaths. These interventions include access to clean water, proper sanitation and oral rehydration therapies, breastfeeding, vitamin A and zinc supplementation.

The lead author on the African study paper was **Professor Shabir Madhi (Respiratory and Meningeal Pathogens Research Unit)**.

**Madhi S**, Cunliffe N (joint first authors), Steele D, Witte D, Kirsten M, Louw C, Ngwira B, Victor J, Gillard P, Cheuvart B, Han H and Neuzil K (2010). Effect of human rotavirus vaccine on severe diarrhea in African infants. *New England Journal of Medicine*, **362**(4): 289 – 298.

## New-generation treatment offers hope for inherited high cholesterol

Homozygous FH is a rare genetic disorder affecting one in every million people. Patients have severely elevated low-density lipoprotein (LDL or "bad" cholesterol), a high risk of early cardiovascular disease and, if untreated, rarely live beyond the age of 30. Because LDL receptors do not function in people with homozygous FH, they have a poor response to standard lipid-lowering drugs such as statins. Thus new therapies to reduce LDL levels are needed. Mipomersen, a second-generation antisense therapy, acts by inhibiting apolipoprotein B synthesis, a building block of LDL, thereby reducing concentrations of LDL cholesterol.

**Professor Derick Raal (Carbohydrate and Lipid Metabolism Research Unit)** and international colleagues conducted a randomised phase 3 trial to examine the safety, tolerability, and effects of Mipomersen on LDL cholesterol levels in patients with homozygous FH who were already receiving

lipid-lowering drugs, including high-dose statins. Fifty one patients worldwide were randomly assigned Mipomersen 200mg or placebo, to be taken every week for 26 weeks.

After 26 weeks of treatment, Mipomersen reduced mean LDL cholesterol levels compared with placebo by about 25%. Although most patients did not achieve therapeutic targets for LDL cholesterol concentration, the additional 25% mean reduction, and the more than 2.5 mmol/L absolute reduction, brought about by Mipomersen should benefit patients with homozygous FH. If such effects are maintained, they would be expected to reduce the risk of atherosclerotic cardiovascular complications and improve survival. In the study published in the *Lancet* in 2010, the authors concluded that Mipomersen could be a valuable addition to the drugs used in the management of homozygous FH and should prove useful in the management of other forms of severe refractory hypercholesterolaemia.

**Raal F**, Santos R, Blom D, Marais D, Charng M, Cromwell W, Lachmann R, Gaudet D, Tan J, Chasan-Taber S, Tribble D, Flaim J and Crooke S (2010). Mipomersen, an apolipoprotein B synthesis inhibitor, for lowering of LDL cholesterol concentrations in patients with homozygous familial hypercholesterolaemia: a randomised, double-blind, placebo-controlled trial. *Lancet*, **375**(9719): 998 – 1006.



Xanthomas (subcutaneous cholesterol deposits) in a young patient with homozygous familial hypercholesterolaemia

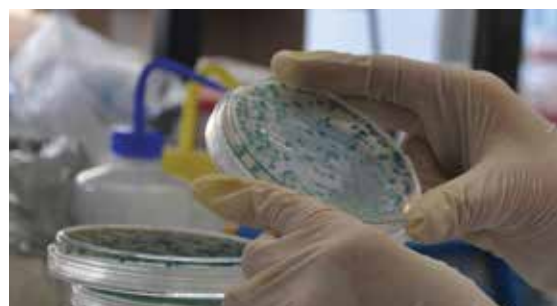
## Hitting back at bacteria

The war against TB has raged on, as the pathogen responsible for the disease has continued to outsmart conventional treatments. However, in July 2010, researchers in the WITS node of the **DST/NRF Centre of Excellence for Biomedical TB Research (CBTBR)** took a significant stride forward in understanding the infection's *modus operandi*. In a paper published in the *Proceedings of the National Academy of Sciences*, the team described one mechanism that *Mycobacterium tuberculosis*, the species of bacterium which causes TB, might employ to subvert current antibiotic therapies. Their research suggests a compelling alternative strategy to thwart the development of drug resistance.

Previously, team member Dr Helena Boshoff (now at the National Institute of Allergy and Infectious Diseases, USA) identified a major player in the evolution of drug resistance in *M. tuberculosis*. The 2010 study, led by **Dr Digby Warner**, followed up on Dr Boshoff's earlier observations. The team added crucial molecular details to a novel system comprising multiple components whose combined action is required for DNA damage-induced mutagenesis in mycobacteria. Their results have opened up the possibility of targeting separate components of this pathway as part of a novel antibacterial strategy aimed at "inhibiting evolution".

Dr Warner's study involved vital contributions from doctoral student, **Duduzile Ndwandwe**, and was the result of collaboration with the internationally-renowned computational biologist, Professor Česlovas Venclovas from the Institute of Biotechnology in Lithuania. Both Professor Venclovas and the paper's senior author, Professor Valerie Mizrahi, are International Research Scholars of the Howard Hughes Medical Institute.

**Warner D, Ndwandwe D, Abrahams G, Kana B, Machowski E, Venclovas C and Mizrahi V** (2010). Essential roles for *imuA'* – and *imuB*-encoded accessory factors in DNAE2-dependent mutagenesis in *Mycobacterium tuberculosis*. *Proceedings of the National Academy of Sciences USA*, **107**: 13093 – 13098.



## A new combination to combat pain

The top-selling prescription pain medications in South Africa all are combination products, typically containing two or three agents, usually a weak opioid (for example, codeine, dextropropoxyphene, tramadol), a nonsteroidal anti-inflammatory drug (such as ibuprofen) or a non-opioid analgesic (paracetamol for example). Numerous studies in rodents and humans have shown that combining two pain-relieving agents with different mechanisms of action potentiates the potency of the agents, allowing the use of lower doses of each component agent, which reduces side-effects, while maintaining or enhancing pain relief.

The use of combinations containing three different classes of pain medication is unique to South Africa. Although these three-agent combinations, especially those containing codeine, ibuprofen and paracetamol, are well known to prescribers and patients alike, and their efficacy supported anecdotally, there was no direct evidence of positive therapeutic interaction when three agents are combined.

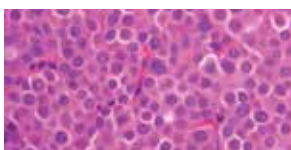
This was, however, prior to a study published in the *European Journal of Pharmacology* by **Professor Emeritus Duncan Mitchell** and colleagues in the **Brain Function Research Group** in 2010. Using a rat model of pain, the researchers showed for the first time that combining codeine, ibuprofen and paracetamol significantly enhances the analgesic potency of the agents, even more so than when the agents are administered in pairs. At the time, Professor Mitchell reported, "The three-agent combination completely abolished pain-like responses in the rats, even when using doses that had absolutely no pain-relieving effect when the agents were administered alone or in pairs. Our study provides the first evidence to support combining sub-therapeutic doses of codeine, ibuprofen and paracetamol for pain control".

**Mitchell D, Gelgor L, Weber J and Kamerman P** (2010). Antihypernociceptive synergy between ibuprofen, paracetamol and codeine in rats. *European Journal of Pharmacology*, **642**: 86-82.

## Cancer of the mouth: Reviewing what we know

Within the **Division of Oral Pathology**, is a young researcher determined to lay a solid foundation for her research into oral health. **Dr Farzana Mahomed** says of her 2010 review, "Neuroendocrine cells and associated malignancies of the oral mucosa":

"With the advent of molecular laboratory diagnostic techniques and investigations into the molecular biology of malignancies of the oral cavity, new tools have become available to aid the oral pathologist in the diagnosis of a vast array of tumours that can arise primarily within the oral cavity. This review aims firstly to provide the reader with an up-to-date



Photomicrograph of a neuroendocrine tumour

exposition of the biological role of neuroendocrine (NEC) cells in the oral cavity, and secondly to detail recent advances in the classifications of NEC tumours and their application to oral NEC tumours. These classifications incorporate features pertaining to the tumour tissue architecture as well as the expression of specific immunohistochemical markers by the tumour cells. The biological behavior of oral NEC tumours appears to be more aggressive than their extraoral counterparts. It is therefore hoped that this review will prove to be of value in the often difficult distinction of oral NEC tumours from their histological mimics."

**Mahomed F** (2010). Neuroendocrine cells and associated malignancies of the oral mucosa: a review. *Journal of Oral Pathology and Medicine*, **39**(2): 121 – 127.

## Growing older in Africa and Asia

Health and social services will need to be restructured to provide effective care for older people living in rural South Africa with impaired functionality and chronic health problems. This was according to a study in an INDEPTH-WHO supplement published in the international peer-reviewed journal *Global Health Action* in September 2010.

"The growth in the world population aged 50 and over is expected to increase from 21% in 2011 to 34% in 2050. This increase will affect not only developed countries but also developing countries," commented **Associate Professor Kathleen Kahn (MRC/Wits Rural Public Health and Health Transitions Research Unit)**. "In particular, in developing countries demographers have predicted an increase of 140% between 2006 and 2030, from 35 to more than 69 million. The health effects of this global demographic change are, as yet, not fully known but estimations predict that the change in age structure in coming years will produce an increase in mortality due to non-communicable diseases, changing the pattern of the most common causes of death in the poorer regions of the world. This becomes more complicated in sub-Saharan Africa, where we are also faced with a crippling HIV epidemic."

The high HIV prevalence, together with an ageing population and the emerging epidemic of non-communicable diseases, will put immense pressure on already weak health services as well as on society



Photo by Paul Weinberg

as a whole. Important changes in household structure and in the roles and responsibilities of older people are likely to result. In South Africa, the proportion of the population aged 50 and over slightly increased from 14.8% in 2006 to 15% in 2009, and is predicted to be 19% in 2030. According to the

study, changes in the social structure and roles and responsibilities of older people, particularly women, have already occurred.

The supplement was co-edited by Professor Kahn and **Associate Professor Stephen Tollman** (also **MRC/Wits Rural Public Health and Health Transitions Research Unit**) in conjunction with partners from the INDEPTH Network, the World Health Organization Study on Global AGEing and adult health, the Umeå Centre for Global Health Research in Sweden, and research sites in Ghana, South Africa, Tanzania, India, Indonesia and Viet Nam.

**Gómez-Olivé X, Thorogood M, Clark D, Kahn K and Tollman S** (2010). Assessing health and well-being among older people in rural South Africa. In: Growing Older in Africa and Asia: Multicentre study on ageing, health and well-being, *Global Health Action* Supplement 2, pp 23-35. Eds: Suzman R, Tollman S, Kahn K and Ng N.



## Unicellular suicide

Investigating why organisms die may seem rather macabre to most people. However, **Dr Pierre Durand** from the **Evolutionary Medicine Unit** (School of Pathology), together with his co-workers Armin Rashidi and Rick Michod from the University of Arizona made an unexpected discovery which has helped to unravel a perplexing phenomenon. They found that programmed cell death in a single-celled green alga can benefit other cells in the population, but dying passively can be harmful to other cells.

In multi-cellular organisms cells cooperate for the good of the organism; in unicells, the cell is the organism. "This raises several questions," commented Dr Durand, joint lead author of a paper which appeared in the *American Naturalist*. "Why under some circumstances would an organism actively kill itself? Why and how did this suicide-like behaviour evolve? Is programmed cell death simply an evolutionary accident?"

Explaining the evolution of programmed death in unicellular organisms is difficult by Darwinian principles

as death could hardly provide a fitness advantage to the dying individual. "Following several experiments, using *Chlamydomonas reinhardtii* (a unicellular green alga) as a model organism, we discovered that single cells can actively destroy themselves as an altruistic behaviour to benefit other cells (presumably relatives) in the population," explained Dr Durand. "When they die, these unicells release materials into the environment which enhance the growth of other *Chlamydomonas reinhardtii* cells. In contrast, dying in a way that excludes the active death programme is in fact harmful to the other cells. We have thus concluded that programmed death may have evolved in environmentally stressful conditions because it provides a group level advantage." The work suggests that programmed death could have facilitated the evolution of social groups and multicellular forms in these and other organisms.

**Durand P**, Rashidi A (joint first authors) and Michod R (2011). How an organism dies affects the fitness of its neighbours. *The American Naturalist*, **177**(2): 224-232.

## Increased cancer risk for HIV-infected women

HIV-positive women are at increased risk of developing pre-invasive and invasive cancers of the cervix, according to **Dr Pamela Michelow**, Principle Medical Officer in the **Cytology Unit** (School of Pathology). "These lesions are usually related to infection with the Human Papillomavirus (HPV), reflecting the high rate of co-infection of these two sexually transmitted viruses (HIV and HPV). A review of the literature pertaining to HIV and squamous lesions of the cervix revealed that HIV-positive women exhibit higher rates of infection with multiple oncogenic HPV types. They also show more abnormal pap smears and increased rates of invasive squamous carcinoma which tend to present a decade earlier than HIV-negative women."

There is conflicting data related to the effect of antiretroviral therapy on cervical cancer and its precursor lesions. Some studies have shown a reduction in cervical abnormalities, whereas others demonstrate no change with antiretroviral therapy. Current cervical screening recommendations for HIV-positive women pertain largely to developed nations. The best strategy to screen HIV-positive women in low-resource countries remains uncertain.

Pantanowitz L and **Michelow P** (2011). Review of Human Immunodeficiency Virus (HIV) and squamous lesions of the uterine cervix. *Diagnostic Cytopathology*, **39**(1): 65-72.



## Johannesburg: One in three male teens likely to use a performance-enhancing substance

A study conducted by **Philippe Gradidge (Centre for Exercise and Sports Medicine)**, which described the prevalence of use of performance-enhancing substance (PES) by Johannesburg male adolescents involved in competitive high school sports, found that substance use in this sample was reasonably low (30%). The majority used legitimate substances for performance enhancement, namely: creatine (32%), vitamins (61%), protein (61%), caffeine (57%) and carbohydrates (54%).

However, a number of banned substances were used by individuals including growth hormone

(5%), anabolic androgenic steroids (4%), and adrenaline/ephedrine (4%). The findings highlighted the need for education on doping and for effective interventions to reduce the use of banned substances in adolescent sport.

**Gradidge P, Coopoo Y and Constantinou D** (2011). Prevalence of performance-enhancing substance used by Johannesburg male adolescents involved in competitive high school sports. *Archives of Exercise in Health and Disease*, **2**(2): 114-119.

## Ostriches sleep like Platypuses: Uncovering the evolution of REM sleep

Birds and most mammals engage in two types of sleep: slow wave sleep (SWS) is characterised by large, slow waves, measured by electroencephalogram (EEG), and rapid eye movement (REM) sleep as small, fast waves. But how did these states come to be? That is the question researchers **Associate Professor Andrea Fuller, Dr Leith Meyer, and Professor Shane Maloney** (a Wits Honorary Research Fellow based at the University of Western Australia) in the **Brain Function Research Group**, sought to answer in collaboration with leading sleep investigators, Niels Rattenborg and John Lesku of the Sleep and Flight Group at the Max Planck Institute for Ornithology, Seewiesen, Germany.

Understanding how SWS and REM sleep evolved might provide insight into their function. Unfortunately for the research team, the brain activity that defines these states does not fossilise, so in order to study how these states evolved one must study living animals as

representatives for extinct forms. For instance, while marsupial and placental mammals, including ourselves, engage in SWS and REM sleep, echidnas and platypuses – members of the most “ancient” group of living mammals – exhibit only SWS. However, concurrent with SWS, signs of “classical” REM sleep have been observed in monotremes, suggesting that monotremes do experience a form of REM sleep.

Like mammals, birds also engage in SWS and REM sleep, but until now it has been unknown if birds share a similar pattern of sleep evolution to the one inferred for mammals. In this collaborative study, the teams conducted the first study of sleep in an “early” bird, by studying ostriches in South Africa. Remarkably, the brain activity of sleeping ostriches was reminiscent of that observed in sleeping monotremes. That is, ostriches periodically entered a REM sleep state characterised by rapid eye movements and reduced muscle tone. However, instead of an EEG consisting only of REM sleep-related activation, the EEG flipped between activation and SWS-like slow waves. Because ostriches have some activation during REM sleep, such ancient birds may be further along the sequence of evolutionary steps towards “classical” REM sleep than are monotremes.

Lesku J, **Meyer L, Fuller A, Maloney S**, Dell’Omo G, Vyssotski A and Rattenborg N (2011). Ostriches sleep like platypuses. *PLoS ONE*, **6**(8): e23203.



## High-tech drug delivery for HIV prevention

In 2011, researchers in the **Wits Advanced Drug Delivery Platform** reported on the efficacy of a unique medical device designed to protect women against HIV infection (that is, a microbicide-ARV delivery system). Economic and social conditions are key factors which must be considered during the design and development of any drug delivery system, as acceptability depends on affordability, ease of use and the reduction of side-effects.

Using a suitable animal model, the study focused on determining the concentration of zidovudine (AZT) and polystyrene sulfonate (PSS) in plasma and vaginal tissue, following the insertion of an intravaginal bioadhesive polymeric device (IBPD) containing the two compounds. The IBPD was designed and developed in such a way that the formulation would initially swell in order to facilitate bioadhesion, and thereafter erode gradually to release the selected compounds in a controlled manner, to finally permeate laterally into the vaginal tissue and provide a preventive effect against HIV and sexually transmitted infections (STIs).

The results of the team's evaluation showed that the matrix hardness, matrix integrity, thermal stability

and friability of the IBPD were good. Importantly, the highly-controlled release pattern, the permeation dynamics and the satisfactory adhesion meant that the IBPD maintained a steady-state concentration of the bioactives within the vaginal tissue. Apart from providing encouraging results for the delivery of PSS and AZT specifically, the study provides a novel systematic approach for the development of delivery systems for other microbicide-ARVs.

**Ndesendo V, Pillay V, Choonara Y, Toit L, Meyer L, Buchmann E, Kumar P and Khan R (2011).** *In vivo* evaluation of the release of zidovudine and polystyrene sulfonate from a dual intravaginal bioadhesive polymeric device in the pig model. *Journal of Pharmaceutical Sciences*, **100**(4):1416-1435.



The intravaginal bioadhesive polymeric device showing typical dimensions in relation to a USA quarter dollar coin

## HIV infection during lactation increases infant's risk

HIV studies at the **DST/NRF South African Centre for Epidemiological Modelling and Analysis** (SACEMA) have led to theoretical work on important questions such as: "Can the early and aggressive use of antiretroviral therapy lead to reductions in HIV incidence?" **Dr Edmore Marinda** (Senior Statistician, School of Public Health), was part of the team which found that postnatal HIV seroconversion of breastfeeding mothers substantially increases the risk of vertical transmission to their babies.

The ZVITAMBO study in Zimbabwe found that women who became HIV infected in the post-partum period were up to 4.6 times more likely to transmit HIV to their breastfed babies than women who had tested HIV positive at the time of delivery (1). This is presumed to be linked to the fact that viral loads in recently-infected mothers are much higher than in women who have been infected for a long time.

To design effective intervention programmes, it is important to ascertain if the risk of mother-to-child transmission for these recently-infected women is similar during the three main transmission periods: pregnancy (in-utero), delivery (intra-partum) and breastfeeding (post-natal). In the team's analysis of the existing ZVITAMBO data they classified women who had just given birth into six distinct groups according

to their likelihood of being recently infected based on their CD4 cell count. The team also used the BED capture enzyme-immunoassay to measure plasma concentration of HIV-specific antibodies (IgG), which increase with time following primary infection.

Women classified as likely to have been recently infected were 50% more likely than women with established infections to transmit HIV to their baby. By contrast there was no evidence of increased risk of infection during delivery among recently infected women (2). In order to effectively inform intervention programs, investigations of the issues around maternal acute infection and its associated risk with child infection are ongoing.

1. Humphrey JH, **Marinda E**, Mutasa K *et al* (2010). Mother to child transmission of HIV among Zimbabwean women who seroconverted postnatally: prospective cohort study. *British Medical Journal*, **341**:c6580.

2. **Marinda E**, Moulton L, Humphrey J Hargrove J, Ntozini R, Mutasa K and **Levin J** (2011). *In utero and intra-partum* HIV-1 transmission and acute HIV-1 infection during pregnancy: using the BED capture enzyme-immunoassay as a surrogate marker for acute infection. *International Journal of Epidemiology*, **40**(4): 945-954.

## Two Wits publications in *New England Journal of Medicine*

Two original research papers produced by Wits Health Sciences researchers were published in the July 2011 issue of the prestigious international medical journal, the *New England Journal of Medicine*. **Professor Shabir Madhi (Respiratory and Meningeal Pathogens Research Unit)** and **Dr Neil Martinson (Perinatal HIV Research Unit)** were the senior authors on the papers. It is very unusual for two investigators from the same institution to have separate articles as lead authors in the highest ranking medical journal globally. Both papers investigated the prevention of tuberculosis in HIV-infected individuals.

### Four effective regimens to prevent HIV-related TB

Previous studies have demonstrated that prevention of tuberculosis (TB) in HIV-infected individuals is feasible. There are, however, two key issues which stop people from prescribing TB preventive treatment: a concern about poor-compliance with long term regimens; and the short-lasting effect of treatment in HIV-infected patients (about two years).

Led by **Dr Neil Martinson**, a team of investigators evaluated three new treatment regimens for latent tuberculosis, which previous evidence had shown may be more potent and durable than standard isoniazid treatment, and compared them to the WHO standard of daily isoniazid for six months.

Over 1000 South African adults living in Soweto, with HIV infection and a positive tuberculin skin test, and who were not taking antiretroviral therapy, were randomly assigned one of the following regimens:

- rifapentine (900 mg) plus isoniazid (900 mg) weekly for 12 weeks,
- rifampin (600 mg) plus isoniazid (900 mg) twice weekly for 12 weeks,
- isoniazid (300 mg) daily for up to 6 years (continuous isoniazid),
- isoniazid (300 mg) daily for 6 months (control group).

The median age of patients was 30 years and the median CD4 cell count 484 per cubic millimetre. Incidence rates of active tuberculosis or death were 3.1 per 100 person-years in the rifapentine–isoniazid group, 2.9 per 100 person-years in the rifampin–isoniazid group, and 2.7 per 100 person-years in the continuous-isoniazid group, as compared with 3.6 per 100 person-years in the control group. The statistical comparisons between the groups all showed non-significant differences.

The data, interpreted within the context of this high-prevalence setting, showed that all four prophylactic regimens are effective against tuberculosis infection in HIV-infected patients. Therefore, the use of any of

these regimens in clinical practice could substantially increase the number of patients who receive and complete preventative therapy, which is essential if we are to see a decrease in the prevalence of HIV-related tuberculosis across the continent.

**Martinson N**, Barnes G, Moulton L, **Msandiwa R**, **Hausler H**, Ram M, **McIntyre J**, **Gray G** and Chaisson R (2011). New regimens to prevent tuberculosis in adults with HIV infection. *New England Journal of Medicine*, **365**(1): 11 – 20.

### Anti-TB drug shown to be ineffective in HIV-infected infants

HIV-infected African children contribute 40 to 60% of the high burden of childhood tuberculosis (TB) disease in sub-Saharan Africa. An IMPAACT study, led by **Professor Shabir Madhi**, aimed to assess whether TB infection and disease could be prevented in both HIV-exposed uninfected and HIV-infected infants by giving them the prophylactic medication isoniazid (INH).

Starting at three months of age, 504 children with HIV infection and without prior exposure to TB took either INH or a placebo once a day for two years. All infants received oral co-trimoxazole to prevent bacterial and other infections and most had access to anti-retroviral therapy to treat HIV infection. Infants were enrolled into the study at three sites in South Africa between December 2004 and June 2008, with an average follow-up of 74 weeks. Overall, 98.9% participants were started on antiretroviral treatment during the course of the study. The median time to antiretroviral initiation was 11 weeks post-randomisation and did not differ by treatment arm.

Final analysis of the data showed that INH prophylaxis did not improve TB-free survival. Protocol-defined TB or death occurred in 19.0% of the INH group and 19.3% of the placebo group. The overall mortality rates were 9.9% in the INH group and 6.2% in the placebo group. Therefore, the investigators concluded that giving INH to HIV-infected South African infants, who had access to antiretrovirals, did not protect them against tuberculosis or death. The incidence of tuberculosis amongst this group remains high (21% by 96 weeks), despite these children having access to antiretroviral treatment. Finding an effective means of TB prevention for this group must continue to be a priority.

**Madhi S**, Nachman S, **Violari A**, Kim S, Cotton M, Bobat R, Jean-Philippe P, McSherry G and Mitchell C for the P1041 Study Team (2011). Primary Isoniazid Prophylaxis against Tuberculosis in HIV-Exposed Children. *New England Journal of Medicine*, **365**(1): 21 – 31.

## *Journal of Public Health Policy:* Special issue celebrates Wits research unit

The launch of the special edition of the international *Journal of Public Health Policy* dedicated to the **Centre for Health Policy** (CHP) highlighted the stature and relevance of the Centre which celebrated its 24<sup>th</sup> anniversary on 26 July 2011. Gathered at the celebration were founders, and old and new generation researchers who reflected on the Centre's achievements since its establishment in 1987 during the final years of the anti-apartheid struggle.

The Special Issue of the journal (Volume 32, Supplement 1) analyses different aspects of South African health sector reform designed to improve population health outcomes. The edition brings together eight scholarly articles and six commentaries which explore themes that have captured global attention in recent years: improving population health; reducing health inequities; enhancing the influence and impact of research on health policy; and optimising

health systems performance. In the guest editorial, the Centre's **Professor Laetitia Rispel** notes the value of an independent health policy and systems research unit, such as the CHP, which is able to contribute to the transformation of health systems through long-term research, training of researchers, collaborative networks, and peer-reviewed publications.



## Greater awareness of dietary intolerance will save lives

Coeliac disease is an auto-immune disorder of the small intestine. It is caused by a genetically pre-disposed reaction to gliadin, a gluten protein found in wheat, and similar proteins found in other grains such as barley and rye. Generally, the disease is well-managed by avoiding gluten, but in poorer settings, particularly where other diarrhoeal diseases are common, gluten intolerance may not be suspected and children may die. Coeliac disease has emerged as an increasingly-recognised public health problem over the last half-century, and is now seen as a global phenomenon, despite a profound lack of globally representative epidemiological data. **Associate Professor Kathleen Kahn (MRC/Wits Rural Public Health and Health Transitions Research Unit)**, together with researchers at Umeå University, Sweden, compiled the first global estimates of coeliac disease and associated mortality.

Building a model of childhood coeliac disease, Professor Kahn and colleagues took into account estimates of population prevalence, probability of

non-diagnosis, and likelihood of mortality among the undiagnosed from 1970 to 2010, based on the scant data available. According to the model, in 2010 there were around 2.2 million children under five years of age living with coeliac disease. Among these children there could be 42 000 deaths related to coeliac disease annually, mostly on the African and Asian continents. In 2008, deaths related to coeliac disease probably accounted for approximately 4% of all childhood diarrhoeal mortality. These deaths are not preventable by applying normal diarrhoea treatment guidelines, which may even involve gluten-based food supplements. As other causes of diarrhoeal mortality decline, coeliac disease will become a proportionately increasing problem unless consideration is given to providing gluten-free diets for children with chronic diarrhoea and malnutrition.

Byass P, **Kahn K**, Ivarsson A (2011). The global burden of childhood coeliac disease: a neglected component of diarrhoeal mortality? *PLoS One*, **6**(7): e22774.



## HIV vaccine trial highlights particular need to protect women

HIV vaccine trials were started in the United States as far back as 1987 but positive results are yet to be seen. In 2004, a phase IIb test-of-concept trial, funded by the HIV Vaccine Trials Network (HVTN), was initiated in North and South America, the Caribbean and Australia, known as the HVTN 503/STEP study. The study aimed to test the efficacy of Merck's MRKAd5 vaccine in either preventing HIV infection or reducing the viral load of volunteers who became infected despite vaccination. A South African leg of the STEP study, dubbed HVTN 503/Phambili, was launched in January 2007 by the **Perinatal HIV Research Unit**, directed by **Associate Professor Glenda Gray**. This sub-study was designed to assess efficacy in a clade C region of the world in populations with high levels of pre-existing immunity to Ad5, the most commonly used adenovirus vector used to deliver genetic material into cells.

A two-arm, double-blind, placebo-controlled randomised clinical trial was launched at five sites, which included Soweto, Cape Town, Klerksdorp-Orkney-Stilfontein-Hartbeesfontein (North West Province), eThekwinini (KwaZulu-Natal) and Medunsa (Tshwane). A total of 801 participants were assigned to either vaccine or placebo, which was administered by intramuscular injection on a zero, one and six month schedule. Nine months into the trials, the HVTN called

the study to a halt, following initial findings which indicated that the vaccine did not protect against HIV-1 infection, and no further participants were drafted.

Although the study could not be completed, Professor Gray and colleagues analysed the data they had collected and published their observations in *Lancet Infectious Diseases* (July 2011). The majority of vaccine recipients developed an HIV-1-specific T-cell response to both clade B and clade C antigens, but this response was unfortunately not sufficient to produce protection against infection. The team also observed that existing herpes simplex virus type 2 infection was a risk factor for HIV-1 infection in heterosexual men but not women. A particularly important finding was that the incidence of HIV-1 was greater in women than in men, in both the vaccine and placebo groups. This highlights the vulnerability of women to infection and the need to find effective ways of protecting them.

**Gray G**, Allen M, Moodie Z, **Churchyard G**, Bekker L-G, ... Metch B, **de Bruyn G**, ... on behalf of the HVTN 503/Phambili study team (2011). Safety and efficacy of the HVTN 503/Phambili Study of a clade-b-based HIV-1 vaccine in South Africa: A double-blind, randomised, placebo controlled test-of-concept phase 2b study. *Lancet Infectious Diseases*, **11**:507–515.

## Can reducing viral load lower the risk of transmission of HIV?

According to a study published in the *New England Journal of Medicine* in 2011, reducing viral load can lower the risk of HIV transmission. In a study conducted across nine countries, the HIV-positive partner in each of 1763 serodiscordant couples was placed on antiretroviral treatment. Treatment was either initiated immediately (early-therapy) or was started only after a decline in CD4 count or after the onset of HIV-1-related symptoms (delayed-therapy).

The HIV-infected subjects all had CD4 counts of between 350 and 550 cells per cubic millimeter at the point of entry into the study. Most of the participants were disciplined in taking their antiretroviral treatment, with 79% in the early therapy group and 74% in the delayed therapy group demonstrating adherence of at least 95%. Although several combinations of antiretroviral medications were used, 72% received a combination of zidovudine, lamivudine and efavirenz.

Over the course of the study, 39 HIV-1 transmissions were observed, 28 of which were virologically linked to the infected partner. Of these 28 cases, only one occurred in the early therapy group. Furthermore, all linked transmissions in the delayed-therapy group occurred while the infected partner was not receiving antiretroviral therapy. The team believes that the most likely explanation is the sustained suppression of HIV-1 in genital secretions by the antiretroviral medications. This paper, co-authored by **Associate Professor Ian Sanne (Clinical HIV Research Unit)** and **Dr Guy de Bruyn (Perinatal HIV Research Unit)** with researchers from around the world, demonstrates that the reduction of the risk of transmission by the early initiation of treatment could be the answer to the global scourge of HIV.

Cohen M, Chen Y, **de Bruyn G**, **Sanne I**, Eron J, and Fleming T, for the HPTN 052 Study Team (2011). Prevention of HIV-1 infection with early antiretroviral therapy. *New England Journal of Medicine*, **365**:493-505.



## A superior test to detect TB in HIV-infected adults

The rapid diagnosis of tuberculosis (TB) enables faster initiation of treatment, greatly increasing an individual's chances of overcoming the infection, especially in HIV-positive patients and in those who have contracted drug-resistant TB. The most reliable technique used to diagnose TB is mycobacterial culture, but this technique requires time. Tools which can provide an accurate diagnosis quickly will prevent backlog in laboratories and enable rapid initiation of treatment.

In a study published in *PLoS Medicine*, **Associate Professor Lesley Scott (Department of Molecular Medicine and Haematology)** and colleagues evaluated the performance of the WHO-endorsed nucleic acid amplification technology test Xpert MTB/RIF in a South African community. Using liquid culture as the “gold standard”, the team compared the sensitivity and specificity of Xpert MTB/RIF with smear microscopy and two other nucleic acid amplification technology tests (MTBDRplus and LightCycler Mycobacterium Detection).

In 177 samples tested for TB, smear microscopy, MTBDRplus, LightCycler Mycobacterium Detection, and Xpert MTB/RIF exhibited sensitivities of 59%, 76%, 76%, and 86%, respectively. The specificity of all the tests compared to liquid culture was greater than 97%, indicating a low false-positive rate. In HIV-positive participants, Xpert MTB/RIF exhibited a greater sensitivity than the two other nucleic acid amplification technology tests (84% compared with 70%). Importantly, the study supports the WHO in its recommendation that Xpert MTB/RIF be the first test used to detect TB in HIV-infected individuals, rather than smear microscopy.

**Scott L, McCarthy K, Gous N, Nduna M, Van Rie A, Sanne I, Venter WF, Duse A and Stevens W** (2011). Comparison of Xpert MTB/RIF with other nucleic acid technologies for diagnosing pulmonary tuberculosis in a high HIV prevalence setting: a prospective study. *PLoS Medicine*, **8**(7): e1001061.

## Description of additional features of rare skin cancer to improve diagnosis

“Carcinomas of the eccrine sweat gland represent a rare group of tumors with potential for local destruction and metastasis. The specific classification of eccrine carcinomas is both complex and nebulous, in large part because of the paucity of reported cases but also because many of these tumors show little histologic resemblance to mature eccrine glands; the histogenetic association is based primarily on histochemical, immunochemical, or ultrastructural features.”<sup>1</sup>

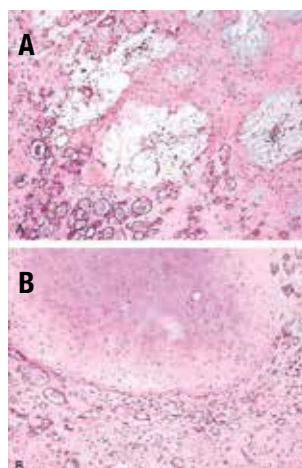
Mixed tumour, eccrine type, is a rare cutaneous adnexal neoplasm, mostly reported as isolated case reports. A systematic analysis of its histopathologic and immunohistochemical features has not previously been performed on a large series.

**Professor Wayne Grayson** in the **Department of Anatomical Pathology** teamed up with collaborators to assess a large number of cutaneous eccrine mixed tumours. Their aim was to fully characterise the entire spectrum of changes in the epithelial and stromal components, with an emphasis on unusual histopathologic features that may represent a diagnostic pitfall. After the light microscopic and immunohistochemical study of 50 cases of eccrine mixed tumour, the team identified some unusual histopathologic features, extending the morphologic spectrum of this neoplasm (literally meaning “new growth”). These features included prominent cribriform areas, clear cell change, pseudorosette

structures, prominent osseous metaplasia, and physaliphorous-like cells. Most of these features have not been previously recorded in eccrine mixed tumours and may represent challenges to diagnosis.

<sup>1</sup>Source: <http://emedicine.medscape.com/article/1101796-overview>

Kasakov DV, Kacerovska D, Hantschke M, Zelger B, Kutzner H, Requena L, **Grayson W**, Bisceglia M, Schaller J, Kempf W, Denisjuk N and Michal M (2011). Cutaneous mixed tumour, eccrine variant: A clinicopathologic and immunohistochemical study of 50 cases, with emphasis on unusual histopathologic features. *American Journal of Dermatopathology*, **33**(6): 557-567.



Myxohyaline and cartilaginous stroma in eccrine mixed tumor. Note the well-demarcated myxoid “pools” and gradual transition of epithelial elements to cartilaginous areas. (A), Abrupt transition of epithelial elements to cartilaginous areas (B)

## Biopesticide may solve challenge of mosquito resistance

Mosquitoes are fast becoming resistant to conventional pesticides, threatening the human enterprise against the parasite which continues to claim the lives of millions, not only in Africa. Biopesticides based on the spores of entomopathogenic fungi have shown considerable promise by causing substantial mortality within 7–14 days of exposure. This mortality will provide excellent malaria control if there is a high likelihood that mosquitoes contact fungi early in their adult lives. However, where contact rates are lower, as might result from poor pesticide coverage, some mosquitoes will contact fungi in one or more feeding cycles after they acquire malaria, and so risk transmitting malaria before the fungus kills them. Critics have argued that 'slow acting' fungal biopesticides are, therefore, incapable of delivering malaria control in real-world contexts.

Members of the **Malaria Entomology Research Unit** worked alongside researchers at Pennsylvania State University (USA), China Agricultural University (China) and the Fogarty International Center (USA) to demonstrate the effective action of a biopesticide faster than previously reported. Utilising standard WHO laboratory protocols, the cross-continental team showed that transient exposure to clay tiles sprayed with a candidate biopesticide comprising spores of a natural isolate of *Beauveria bassiana*,

could reduce malaria transmission potential to zero within a feeding cycle. The effect resulted from a combination of high mortality and rapid fungal-induced reduction in feeding and flight capacity. Additionally, multiple insecticide-resistant lines from three key African malaria vector species were completely susceptible to the fungus. Thus, fungal biopesticides can block transmission on a par with chemical insecticides, and can achieve this where chemical insecticides have little impact. These results support broadening the current vector control paradigm beyond fast-acting chemical toxins.

Blanford S, Shi W, **Christian R**, Marden J, **Koekemoer L**, **Brooke B**, **Coetzee M**, Read A and **Thomas M** (2011). Lethal and pre-lethal effects of a fungal biopesticide contribute to substantial and rapid control of malaria vectors. *PLoS ONE*, 6(8): e23591.



## When delayed antiretroviral treatment costs lives

In South Africa, co-infection with tuberculosis (TB) and HIV is common. Both require specific and aggressive treatment, as well as strict adherence to treatment regimens. Of great concern is the pill burden, potential drug toxicity and the risk of Immune Reconstitution Inflammatory Syndrome (IRIS) if a patient started on TB therapy begins antiretroviral therapy (ART) soon after. However, if ART is not started promptly there could be consequences for the immune-compromised patient, apart from the progression of the TB infection.

An AIDS Clinical Trial Group (ACTG) team, including Wits researchers **Associate Professor Ian Sanne (Clinical HIV Research Unit)**, **Dr Prudence Ive (Clinical HIV Research Unit)** and **Dr Lerato Mohapi**, decided to take the debate in hand. Over nearly three years, the team enrolled 809 patients at 26 clinical research sites across four continents in a study designed to assess whether those patients started on ART within two weeks of TB therapy experienced better health outcomes than those initiated on ART between 8 and 12 weeks after TB therapy had begun.

When the entire group was included in the analysis, earlier initiation of ART appeared to make little difference to health outcomes (in the earlier-ART group, 12.9% of patients had a new AIDS-defining illness or had died by 48 weeks, as compared with 16.1% in the later-ART group;  $p=0.45$ ). However, when the team assessed just those patients whose HIV infection was advanced (patients with screening CD4 T-cell counts of less than 50 per cubic millimetre), the relatively short delay in the start of ART increased the percentage of patients who had a new AIDS-defining illness (or had died) from 15.5% to 26.6% ( $p=0.02$ ).

Tuberculosis-associated IRIS was more common with earlier ART than with later ART (11% vs. 5%,  $p=0.002$ ). However, in this study, patients were treated with prednisone to alleviate symptoms and IRIS was not associated with worse overall outcomes. There were no significant differences in drug toxicity and laboratory abnormalities between the study groups.

Starting ART within two weeks of the initiation of tuberculosis treatment appears to be quite safe. For patients with CD4 T-cell counts of less than 50 per cubic millimeter, it is not only safe, it is vital for their long-term well-being, and indeed their survival. For this finding to be of consequence to such patients, the authors stressed how the synergy between HIV and TB programmes will need to improve. Focused coordination of programmes

is needed for rapid diagnosis as well as the efficient dispensing of medication.

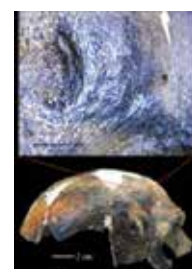
Havir D, Kendall M, **Ive P**, Kumwenda J, Swindells S, **Mohapi L**, Andersen J, and **Sanne I**, for the AIDS Clinical Trials Group Study A5221 (2011). Timing of antiretroviral therapy for HIV-1 infection and tuberculosis. *New England Journal of Medicine*, **365**: 1482-1491.

## Human violence – evidence from ages past

The study of a cranium of an East Asian human from the late Middle Pleistocene age from Maba, China, brings to the fore evidence that interhuman aggression and human induced trauma may have occurred as far back as 126 000 years ago. The report suggests that a 14mm ridged, healed lesion with bone depressed inward to the brain resulted from localised blunt force trauma due to an accident or, more probably, interhuman aggression.

“This wound is very similar to what is observed today when someone is struck forcibly with a heavy blunt object. As such it joins a small sample of Ice Age humans with probable evidence of humanly-induced trauma, and could possibly be the oldest example of interhuman aggression and human induced trauma documented. Its remodeled, healed condition also indicates the survival of a serious brain injury, a circumstance that is increasingly documented for archaic and modern *Homo* through the Pleistocene,” commented **Professor Lynne Schepartz** (School of Anatomical Sciences), one of the co-authors of the paper. “It is not possible to assess whether the incident was accidental or intentional, or whether it resulted from a short-term disagreement, or pre-meditated aggression. The identification of traumatic lesions in human fossils helps us to identify

and understand some the earliest forms of interhuman aggression, and the abilities of Pleistocene humans to survive serious injury and post-traumatic disabilities. This particular individual would have needed social support and help in terms of care and feeding to recover from this wound.”



The Maba cranium was discovered with the remains of other mammals in June 1958, in a cave at Lion Rock in Guangdong province, China. Housed in the Institute of Vertebrate Paleontology and Paleoanthropology at the Chinese Academy of Sciences, the cranium was analysed visually using stereomicroscopy and a high-resolution industrial CT scanner. This state-of-the-art imaging technology enabled the researchers to investigate the inner structure of the bone to verify that healing had occurred.

Wu X, **Schepartz L**, Liu W and Trinkaus E (2011). Antemortem trauma and survival in the late Middle Pleistocene human cranium from Maba, South China. *Proceedings of the National Academy of Sciences*, **108**(49): 19558-19562.

# RESEARCH RECOGNITION

## FACULTY AWARDS

### Faculty Research Prize

The Faculty Research Prize is the Faculty's most prestigious annual prize and is awarded for research excellence in publication. Any full-time or part-time member of staff/postgraduate student who has not reached the age of 40 years may be nominated. A dedicated committee reviews the nominations and selects a winner based on the integrity of the science and the impact of the journal in which the work is published.

**2010: Dr Clare Cutland** (Respiratory Meningeal Pathogens Research Unit, School of Pathology) for her publication:

**Cutland C**, Madhi S, Zell E, Kuwanda L, Laque M, Groome M, Gorwitz R, Thigpen M, Patel R, Velaphi S, Adrian P, Klugman K, Schuchat A, Schrag S, and the PoPS Trial Team (2009). Chlorhexidine maternal-vaginal and neonate body wipes in sepsis and vertical transmission of pathogenic bacteria in South Africa: a randomised, controlled trial. *Lancet*, 374(9705)1909-1916.



Dr Clare Cutland (middle) with the late Professor Emeritus Jack Allen and the Assistant Dean: Research and Postgraduate Support, Professor Beverley Kramer

**2011: Dr Alexio Capovilla** (Department of Molecular Medicine and Haematology, School of Pathology) for his publication:

Cerutti N, Mendelow B, Napier G, Papathanasopoulos, Killick M, Khati M, Stevens W and **Capovilla A** (2010). Stabilization of HIV-1 gp120-CD4 receptor complex through targeted interchain disulfide exchange. *Journal of Biological Chemistry*, **285**: 25743-25752.



Dr Alexio Capovilla with the Assistant Dean: Research and Postgraduate Support, Professor Beverley Kramer

## MOST PRESTIGIOUS POSTGRADUATE DEGREE AWARDS

The Most Prestigious Postgraduate Degree Awards were instituted by the Faculty in 2009 to recognise the efforts of outstanding emerging researchers. Any Faculty of Health Sciences student who has graduated with a Masters or Doctoral degree may be nominated by his/her supervisors if they believe that the dissertation or thesis was of outstanding quality.

### 2010:

#### **Most Prestigious Doctoral degree** (shared)

- **Dr Ely Abdullah.** Optimisation of expressed RNA interference effectors for the inhibition of Hepatitis B virus replication. Supervisors: Professors Wendy Stevens and Patrick Arbuthnot.
- **Dr Harold Majane.** Impact of excess adiposity on blood pressure and cardiovascular target organ damage. Supervisors: Professors Gavin Norton, Angela Woodiwiss and David Gray

#### **Most Prestigious Masters (by dissertation)**

- **Ms Samantha Pillay.** Design and development of an implantable drug delivery polymeric scaffold for the treatment of Parkinson's disease. Supervisor: Professor Viness Pillay.

#### **Most Prestigious Masters (by coursework/research report)**

- No award made

### 2011:

#### **Most Prestigious Doctoral degree**

- **Dr Elizabeth Kimani.** Exploring the Paradox: double burden of malnutrition in South Africa. Supervisors: Associate Professors Kathleen Kahn and Shane Norris.

#### **Most Prestigious Masters (by dissertation)**

- **Mr David Sacks.** Development of a real-time PCR incorporating high resolution melting analysis to screen HIV-1 samples for resistance-related codons. Supervisor: **Dr Gillian Hunt.**

#### **Most Prestigious Masters (by coursework/research report)**

- No award made



## UNIVERSITY AWARDS

### Vice-Chancellor's Research Award

This is the University's most prestigious award for research. The purpose of the Vice-Chancellor's Research Award is to stimulate research and research-related scholarly activities by acknowledging and rewarding an exceptional member of the University who has been engaged not only in research but also in more general scholarly activities. The Faculty was elated to see a member of its academic staff win this award in both 2010 and 2011.

**2010: Professor Shabir Madhi**

**2011: Professor Maureen Coetzee**

### Vice-Chancellor's Academic Citizenship Team Award

The purpose of this award is to acknowledge and reward academic staff who have made substantial and innovative contributions to one or more of the communities within which they are involved. This could be the Division/Faculty/University community or a national/international community relevant to their discipline. Faculty staff won this award in both 2010 and 2011.

**2010:** The **MRC/Wits Rural Public and Health Transitions Research Unit (Agincourt)** under the leadership of **Associate Professor Steve Tollman**

**2011: Professor Sharon Fonn** and **Associate Professor Kathy Kahn**. Professors Fonn and Kahn, recognising that individual African universities and countries lack the requisite human, financial and infrastructural capacity to single-handedly develop globally-competitive doctoral programmes, worked together with colleagues in Africa to set up the Consortium for Advanced Research Training in Africa (CARTA).

### Friedel Sellschop Award

This award recognises and encourages exceptional young researchers and takes the form of a special research grant given to worthy researchers under the age of 35. An applicant must have completed a PhD, or be able to demonstrate comparable achievement, and must have produced a substantial body of research work which has received international recognition, such that the applicant has established, or seems certain to establish shortly, an international reputation as a leader in the field.

**2010: Dr Bavesh Kana, Dr Penny Moore** and **Associate Professor Marco Weinberg**

**2011: Associate Professor Yahya Choonara, Associate Professor Marco Weinberg, Dr Penny Moore** and **Dr Bavesh Kana**

## NATIONAL AND INTERNATIONAL AWARDS 2010

**Associate Professor Francois Venter** was awarded the 2010 **Merle A. Sande Health Leadership Award** by the **Accordia Global Health Foundation**.

**Professor Maureen Coetzee** received a **National Science and Technology Forum Award** for her research and outputs over the preceding five to ten years. This award recognised her substantial contribution to the understanding and control of malaria in Africa.



**Professor Karen Sliwa** was named the **second runner-up** in the **2010 South African Women in Science Awards**, made annually by the Department of Science and Technology. Professor Sliwa was honoured for her “substantial contribution to the understanding of the causes and treatment of unexplained heart failure of pregnancy”, and for her involvement in the Heart of Soweto Study which aims to improve the lives of South Africans by addressing the underlying causes of diseases of lifestyle. **Professor Sliwa** also was awarded the 2010 **International Society of Hypertension (ISH) Boehringer Ingelheim Developing World Award** for her outstanding work in South Africa.

**Professor Emeritus Phillip Tobias** was awarded a **National Research Foundation President’s Award for “Lifetime Achievement”** for his extraordinary contribution to the development of science in and for South Africa, which is deemed to be of international standard and impact.



NRF President Dr Albert van Jaarsveld, the late Professor Emeritus Phillip Tobias, and the Honourable Dr Eugene Ngcobo (Chairman of the Science and Technology portfolio committee in the South African National Legislature). Photo courtesy of the NRF

**Professor Shabir Madhi** received a **National Research Foundation President’s Award for “Transformation of the Science Cohort”** for his outstanding role in addressing the challenges of getting more women and black scientists to advance to world-class research performance.



Professor Madhi with NRF President, Dr Albert van Jaarsveld. Photo courtesy of the NRF

## NATIONAL AND INTERNATIONAL AWARDS 2011

In 2011, **Professor Emeritus Duncan Mitchell** was awarded the prestigious **Harry Oppenheimer Fellowship Award** for 2010. The award is granted to scholars of the highest calibre who are engaged in cutting-edge, internationally significant work that has particular application to the advancement of knowledge, teaching, research and development in South Africa. It is considered the top award for research on the African continent.



Professor Emeritus Duncan Mitchell receiving the Harry Oppenheimer Fellowship Award for 2010, from Mrs Mary Slack, Chair of the Oppenheimer Memorial Trust, and the daughter of the late Harry Oppenheimer. Photo: Elaine Banister

**Professor Laetitia Rispel** was inducted into the **Nurse Researcher Hall of Fame** by the **Forum of University Nursing Deans of South Africa** in recognition of her invaluable research contribution in health policy and health systems.



Professor Laetitia Rispel with Professor Karen Morin (College of Nursing, University of Milwaukee, Wisconsin, USA)



Professor Keith Klugman with Dr Margaret Avery FRSSAf, Editor of the Transactions of the Royal Society and a long-standing Council member of the Royal Society

**Professor Keith Klugman** was awarded the **Royal Society of South Africa John F.W. Herschel Medal** for 2011. The award recognises Professor Klugman's multidisciplinary contribution to science in South Africa and his contribution to the reduction of childhood mortality through the development of conjugate pneumococcal vaccination in developing countries.



**Professor Helen Rees** was awarded the 2011 **Science-for-Society Gold Medal** by the **Academy of Science of South Africa**. This award is made for outstanding scientific thinking in the service of society.



Three women in the Faculty were selected as finalists for the 2011 **DST/L'Oreal SA Women in Science Awards**. **Professor Aimee Stewart** was the winner in the **Distinguished Woman Scientist: Social Sciences and Humanities** category. **Professor Maureen Coetzee** was the first runner-up in the **Distinguished Woman Scientist: Life, Natural and Engineering Sciences**, and **Professor Lizette Koekemoer** was the second runner-up in the **Distinguished Young Woman Scientist: Life, Natural and Engineering Sciences** category.

**Professor Maureen Coetzee** was given the wonderful accolade of having a mosquito subgenus named after her. Colleagues at the Smithsonian Institution, who described the new subgenus, wished to honour Professor Coetzee for her many contributions to our knowledge of the mosquito fauna of Africa. Further to this, Professor Coetzee was awarded a **Women Scientist Regional Award**, under the **African Union Kwame Nkrumah Scientific Award Programme 2011**. The award honours Professor Coetzee for her "great scientific achievement and contribution through science for the socio-economic development of Africa".



Professor Andrea Fuller with Deputy Minister of Science and Technology Derek Hanekom and Head of ASSAF, Robin Crewe

**Associate Professor Andrea Fuller**, **Associate Professor Yahya Choonara** and **Dr Penny Moore** were chosen as three of a very limited number of founding members of the **South African Young Academy of Science (SAYAS)**, backed by the Academy of Science of South Africa. This is a significant statement regarding the esteem in which these researchers are held, and their capacity to contribute to the new body's ability to fulfil its mandate.

**Dr Harold Majane** was awarded a **Canadian Institutes of Health Research Canada-Hope Scholarship**. The application process is a rigorous system of peer-review and to be selected is an excellent achievement.



## APPOINTMENTS AND FELLOWSHIPS 2010

**Professor Maeve Coogan** was awarded an **Honorary Fellowship** of the **British Society for Oral Medicine** in recognition of her enormous contribution to the discipline over many years. Her special focus has been on the oral effects of HIV.

**Honorary Adjunct Professor Rosemary Crouch** was awarded an **Honorary Fellowship** of the **World Federation of Occupational Therapists** in recognition of her service to the profession for the development of training in occupational therapy in Africa, and for her contribution to the development of the profession in South Africa.

**Professor Sharon Fonn** was elected **Deputy President** of the **Association of Schools of Public Health in Africa** (ASPHA).

**Associate Professor Andrea Fuller** was elected **Vice-Chair** of the committee of the **Northern Branch** of the **Royal Society of South Africa**.

**Associate Professor Glenda Gray** was appointed **Director of the HIV Vaccine Trial Network (HVTN) Africa Programs**.

**Associate Professor Amadi Ihunwo** was elected to the **Council** of the **International Society for Neurochemistry** (ISN) to represent Africa from 2011 – 2015. He was also elected as a member of the Society's **Committee for Aid and Education in Neurochemistry** (CAEN).

**Associate Professor Peter Kamerman** was appointed as a member of the management committee of the **Special Interested Group on Neuropathic Pain** (NeuPSIG) of the **International Association for the Study of Pain**, and the secretary of the Developing Countries Subcommittee of NeuPSIG. He was also elected **Vice-Chair** of NeuPSIG's Education Committee.

**Professor Shabir Madhi** was elected as the **President** of the **World Society of Paediatric Infectious Diseases** (WSPID). Professor Madhi is the first African to hold the position.

**Dr Siyanda Makaula** was elected **Chairperson** of the **South African National Committee** of the **International Union of Physiological Sciences (IUPS)** for 2010.

**Professor Gavin Norton** was elected **President** of the **Southern African Hypertension Society** for 2010.

**Professor Helen Rees** took over as the **Chair** of WHO's leading advisory group on immunisation, the **Strategic Advisory Group of Experts** (SAGE).



## APPOINTMENTS AND FELLOWSHIPS 2011

**Dr Carol Benn** was invited to be on the **Board of Directors** of the **International Breast Disease Centers** (Paris) and was appointed **Editor** of the *Breast Disease Centers Journal*.

**Mr Brendon Billings** was elected to the **Council** of the **Royal Society of South Africa**.

**Professor Ken Boffard** was appointed as an **Honorary Fellow of the American College of Surgeons** and elected **Patron of the Imperial College School of Medicine Medical Students Society** in both 2010 and 2011.

**Dr Basil Brooke** was elected a **Fellow** of the **Royal Entomological Society**, London.

**Professor Maureen Coetzee** and **Professor Hoosen Coovadia** were elected to **Fellowship** of the **Royal Society of South Africa**.

In 2010, **Professor Peter Cooper** was elected to the **Standing Committee** of the **International Pediatric Association**, which represents over 160 National Paediatric Societies and special interest groups. In 2011, he was elected to the Association's **Executive Committee**.

**Professor Elias Degiannis** was awarded **Honorary Membership** of the **Greek Trauma Society**.

**Professor Bill Evans** was appointed **Editor** of the *Journal of the South African Dental Association*.

**Professor Charles Feldman** and **Professor Lynn Morris** were appointed to the **Board** of the **South African Medical Research Council**. **Professor Feldman** was also made an **Honorary Life Member** of the **Federation of Infectious Diseases Societies of Southern Africa** (FIDSSA).

**Associate Professor Andrea Fuller** was elected to the **Executive Committee** of the **Section on Thermal Physiology, International Commission of Comparative Physiology, International Union of Physiological Sciences (IUPS)**.

**Associate Professor Glenda Gray** was elected to membership of the **Institute of Medicine (IOM) of the National Academies**, USA. Professor Gray was also appointed **Co-Principal Investigator** of the **NIH HIV Vaccine Clinical Trials Network** (HVTN). In this role, she will lead the international programmes of the HVTN and will oversee all the HIV vaccine efficacy trials in sub-Saharan Africa.

The **Rotary Foundation** (of Rotary International) named **Professor Lorna Jacklin** a **Paul Harris Fellow**, in appreciation of tangible and significant assistance given for the furtherance of better understanding and friendly relations among peoples of the world.

**Dr Bavesh Kana** was appointed to the **Columbia University-Southern African Fogarty AIDS Training Programme Advisory Board**.

**Dr Elizabeth Mayne** and **Dr Melinda Suchard** were appointed to the **Executive Committee** of the **South African Immunology Society** and were appointed to the **National Health Laboratory Service Expert Committee for Immunology**.

**Dr Leith Meyer** was elected **President** of the **South African Association for Laboratory Animal Science**.

**Adjunct Professor Shan Naidoo** was elected to **Fellowship** of the **Faculty of Public Health of the Royal Colleges of Physicians of the UK**.

**Associate Professor Shane Norris** was elected as the developing country representative on the **Council** of the **International Society of Developmental Origins of Health and Disease**.

**Professor Peter Owen** was elected a **Vice-President** of the **International College of Prosthodontists**.

**Professor Helen Laburn** and **Professor Viness Pillay** were inaugurated as members of the **Academy of Science of South Africa** (ASSAf).

**Professor Helen Rees** was awarded the prestigious **Heath Clark Fellowship** for 2011 at the **London School of Hygiene and Tropical Medicine**.

**Professor Laetitia Rispel** was elected to the **executive board** of the **World Federation of Public Health Associations** (Geneva) and is one of only two members representing the African Public Health Association.

**Associate Professor Ian Sanne** was appointed the **International Vice-Chair** of the **Aids Clinical Trials Group ACTG** (the largest international therapeutic network in AIDS and TB research funded by the National Institutes of Health).

**Associate Professor Veerasamy Yengopal** was appointed **President-elect** of the **International Association for Dental Research, South Africa Division**.

## NATIONAL RESEARCH FOUNDATION RATINGS

The National Research Foundation (NRF) is an independent government agency which aims to promote and support research in all fields of scientific endeavour. The NRF provides services to the research community especially at Higher Education Institutions (HEIs) and Science Councils with a view to promote high-level human capital development. The NRF uses a peer-evaluation and rating system as a mechanism to nurture scholarship and grow the country's research capacity. Ratings are awarded based on researcher's recent research outputs and impact as perceived by international peer reviewers. A researcher must re-apply for a rating every five years.

### A-ratings

#### awarded in 2010

Professor Charles Feldman (first rating)

Honorary Professor Rachel Jewkes (first rating)

#### awarded in 2011

Associate Professor Glenda Gray (first rating)

Professor Shabir Madhi (first rating)

Professor John Pettifor (renewed rating)

Professor Linda Richter (first rating) awarded in 2012

Associate Professor Elena Libhaber (first rating)

Dr Michael Madziva (first rating)

Professor Sarala Naicker (renewed rating)

Associate Professor Maria Papathanasopoulos (first rating)

Dr Joanne Potterton (first rating)

Professor Frederick Raal (first rating)

Professor Karen Sliwa (renewed rating)

Professor Angela Woodiwiss (renewed rating)

### New/renewed ratings

#### awarded in 2010

Professor Daynia Ballot (first rating)

Associate Professor Kennedy Erlwanger (renewed rating)

Associate Professor Andrea Fuller (renewed rating)

Dr Bवेश Kana (first rating)

#### awarded in 2011

Associate Professor Geoff Candy (first rating)

Dr Patrick Dessein (first rating)

Associate Professor Deborah Glencross (renewed rating)

Associate Professor Margot Hosie (renewed rating)

Professor Ugo Ripamonti (renewed rating)

Associate Professor Lesley Scott (first rating)

## STUDENT RESEARCH ACHIEVEMENTS

### Pfizer-UKZN National Young Health Scientists Research Symposium

2010

**Mr Wesley Aitchison** (who was in his third year of an MBChB at the time) won best presentation in the clinical research category for his presentation at the **3<sup>rd</sup> Pfizer-University of KwaZulu-Natal (UKZN) National Young Health Scientists Research Symposium**. Wesley's presentation was titled *"The Value of Surveillance of Healthcare Associated Infections in a Trauma ICU Setting"*. He is pictured with the two other students who represented the Faculty at the Symposium, Nadia Joyce and Deshnee Naidoo.



2011

**Ms Thandiswa Ngcungcu** (an MSc student in the Department of Human Genetics) was the winner in the laboratory-based research category for her presentation at the **4<sup>th</sup> Pfizer-University of KwaZulu-Natal (UKZN) National Young Health Scientists Research Symposium**. Her presentation, *"FTO variation at intron 8 and its Association with Body Mass Index in Black South African Females"*, was based on research conducted during her Honours year, under the supervision of Professor Michèle Ramsay and Ms Matshane Masemola. Thandiswa is pictured with Professor Tahir Pillay, Deputy Vice-Chancellor and Head of the College of Health Sciences at UKZN.



Photo courtesy of Albert Hirasen/UKZN

## International Genetically Engineered Machine competition (iGEM)

The **International Genetically Engineered Machine competition**, or 'iGEM', run by the Massachusetts Institute of Technology (MIT), is considered to be the premier synthetic biology competition worldwide. It encourages multi-disciplinary teams of undergraduate students from universities worldwide to design and build biological machines with a novel function. Teams can seek guidance and feedback from graduate student advisors and faculty supervisors but ultimately, the project is entirely student-driven.

### 2010: A new tool to detect cervical cancer

In 2010, a team of students from Wits University represented South Africa and the continent as the first African team ever to participate in iGEM. The Wits team attempted to modify lactic acid bacteria, which live naturally in the female body, to detect cervical cancer. They combined a gene from a jellyfish which produces a purple colour, and the genetic material which enables bacterial cells to communicate, to test if bacteria could change colour in response to a stimulus. The aim was to get the bacteria to change colour in the presence of Human Papilloma Virus, which causes cervical cancer. The team received a bronze medal for their efforts.

The Wits multidisciplinary team comprising students from philosophy, molecular biology, computational and applied mathematics, health sciences and engineering, was backed by the Council for Scientific and Industrial Research (CSIR). Two Health Sciences students in the team, **Michelle Robinson** and **Gregory Meyer**, were Honours students under the supervision of **Associate Professor Marco Weinberg** in the School of Pathology at the time of the competition.



The Wits-South Africa 2010 iGEM team: Liam Wilson (School of Social Sciences), Byron Jacobs (School of Computational and Applied Mathematics), Gregory Meyer (School of Pathology), Michelle Robinson (School of Pathology), Shaun Burd (School of Chemical and Metallurgical Engineering), Langelihle Ntloko (School of Molecular and Cell Biology)



## 2011: Tweeting bacteria

In 2011, a Wits-CSIR team was again formed to build on the experiences of the previous year in the iGEM competition. The format changed, with teams being given the opportunity to present their projects at three regional Jamborees: Europe and Africa; North and South America; and Asia and Australia. Top teams from each regional were then selected to compete in a final World Championship Jamboree at MIT.

The Wits-CSIR team formulated a project inspired by the phenomenon of social networking, which they dubbed 'Biotweet'. The concept was to develop tools which could be used by a bacterial communication network. Bacteria could respond to environmental stimuli and 'tweet' this information to other bacteria in the network. At the European Jamboree, the Wits-CSIR team was named one of three finalists out of 17 teams.

At the World Championship Jamboree, the team was commended for their excellent work, and was selected as one of the 'Sweet Sixteen', iGEM judges' selection of the best sixteen teams of the competition. Over 180 teams competed in iGEM 2011, including teams from Yale, Harvard, MIT, Cambridge, Caltech and Stanford.

The 2011

iGEM team members:

Alexandra Reznichenko, Ezio

Fok, Natasia Kruger, Gloria

Hlongwane and Bradley

Marques with their supervisor,

Associate Professor Marco

Weinberg



### Discovery Foundation Academic Fellowships

The Discovery Foundation was set up in 2006 with the specific goal of providing support for the training of 300 medical specialists for South Africa's public sector over a 10-year period. The Foundation's vision is to address specific areas of need through a series of awards for fellowships, research grants and further training. The Academic Fellowship Awards aim to address shortfalls in medical training and research in the field of Academic Medicine.

#### 2010

Dr Mosa Moshabela

Dr Survana Buldeo

Dr Nazeer Mohamed

#### 2011

Dr Keir McCutcheon

Dr Melinda Suchard

Dr Nirvarthi Maharaj

### Tata Africa Scholarships

Started in 2006, the scholarships awarded by Tata Africa aim to build research capacity by providing financial assistance to students wishing to pursue a Masters or Doctorate in key science fields. Of the almost 2000 applications made by students across the country in 2010, only 40 were successful. A total of six students in the Faculty were awarded these prestigious scholarships:



Four of the Tata Africa Scholarship awardees: Aameena Wadee, Rubina Shaik, Kovanya Moodley and Deshika Reddy

**Zinhle Gasa** (Masters, School of Physiology)

**Jeffrey Sibiya** (Masters, School of Physiology)

**Kovanya Moodley** (Masters, School of Therapeutic Sciences)

**Rubina Shaik** (Masters, School of Therapeutic Sciences)

**Deshika Reddy** (Masters, School of Therapeutic Sciences)

**Aameena Wadee** (Masters, School of Therapeutic Sciences)

## Novartis Internship

From July to September 2011, two Wits students were granted the opportunity to participate in the prestigious **Novartis Internship in Drug Discovery and Clinical Research** in Basel, Switzerland. Through the internship programme, Novartis aims to help build scientific capacity in developing countries. In 2011, just 15 postgraduate students were given the opportunity to each work on a scientific project, using state-of-the-art facilities, whilst under the expert mentorship of Novartis professionals. The interns also received training designed to hone a set of professional and personal skills that would serve them well in their careers. Selected interns hailed from Russia, Ukraine, Tanzania, Ethiopia, Kenya, Zimbabwe and South Africa. Exposed to the fast-moving world of international pharma, the interns had the chance to mix with scientists from across the world.

Justin Hean (PhD student, Department of Molecular Medicine and Haematology) and Andrew May (MSc student, Division of Human Genetics) were placed within the departments of “Novartis Biologics Centre - RNAi therapeutics” and “Genome Technologies” respectively. Justin worked on “Characterisation of RNAi enhancing compounds in cell line SK-Hep1-Luc”. Andrew’s research project was entitled “Patterns of genetic variation in a black South African population as a prelude to the Southern African Human Genome Programme (SAHGP)”.



Justin Hean, Dr Harlem Gongxeka (South African diagnostic radiology resident), Andrew May and Ntokozo Dambuza (PhD student, UCT)

# RESEARCH EVENTS AND INITIATIVES

## BIENNIAL FACULTY RESEARCH DAY AND POSTGRADUATE EXPO 2010

Every two years, the Faculty hosts a Research Day and Postgraduate Expo. Almost 1000 delegates attended the 2010 event which took place on 22 September. The Research Day covered an impressive diversity of topics within the five themes of the meeting, with a total of 91 oral and 213 poster presentations. The event provided the staff and students of the Faculty the opportunity to present their research to their colleagues and to interact with each other in a way not possible during their regular routines. Members of Faculty competed for substantial travel grants, presenting entertaining talks and outstanding posters.

The day started with an excellent plenary lecture on the "Challenges of the new genetics" by Professor Aubrey Milunsky from the Boston University School of Medicine. Professor Milunsky is a world-renowned medical geneticist and an alumnus of our Medical School. The second plenary lecture of the day was delivered by Dr Nandi Siegfried of the MRC South African Cochrane Centre, who gave an outstanding overview of the systematic review process.

The Postgraduate Expo complemented the activities of the Research Day, showcasing the Faculty's research programmes and presenting students with the opportunity to find out more about possible research projects. The Expo was a huge success, with contributions from the South African Medical Research Council, the National Research Foundation, the Faculty of Health Sciences Postgraduate and Research Offices, the Wits Health Sciences Library, the University's International Office and the Financial Aid and Scholarships Office.

Events like this are possible only through the hard work of the organising committees of the Research Day and Postgraduate Expo and the session chairs and prize adjudicators, the generosity of the Faculty Research Committee and Wits Health Consortium for prizes, the support of the numerous sponsors and exhibitors, and the delegates who engage with the ethos and spirit of the event.

### Research Day Prize Winners

#### *Chronic diseases and diseases of lifestyle*

**Best oral:** Nitien Naran

**Best poster:** Le Roux Booysen

**Best student oral:** Gareth Tarr

**Best student poster:** Marketa Toman

#### *HIV/AIDS*

**Best oral:** Denise Evans

**Best poster:** Carole Wallis

**Best student oral:** Jinal Bhiman

**Best student poster:** David Sacks

#### *Molecular and comparative biosciences*

**Best oral:** Victoria Green

**Best poster:** Trevor Bell

**Best student oral:** Nicole Cerutti

**Best student poster:** Graeme Hofmeyr

#### *Health care delivery, education and management*

**Best oral:** Lilo du Toit

**Best poster:** Tshepo Mareme

**Best student oral:** Nisha Naicker

**Best student poster:** Owen Terreblanche

#### *Infectious diseases*

**Best oral:** Clare Cutland

**Best poster:** Atica Moosa

**Best student oral:** Bintou Ahmadou Ahidjo

**Best student poster:** Karen Koetsie





Dr Nandi Siegfried, MRC Cochrane Centre, gave the second plenary lecture of the day



A researcher explaining the contents of his poster to colleagues



## WITS POSTGRADUATE CROSS FACULTY SYMPOSIUM



Fiona van den Berg receiving her award from  
Professor Belinda Bozzoli



Trevor Bell receiving his award from Professor Belinda Bozzoli

The Wits Cross Faculty Postgraduate Symposium aims to bring together the University's postgraduate community. The 3<sup>rd</sup> Symposium was held from 26-29 October 2010, and awards were presented to the following students in our Faculty:

### **Best Oral Presentation (by Faculty)**

#### **First place: Fiona van den Berg**

*The development of effective Pri-miRNA mimics against HIV*

#### **Second place: Trevor Bell**

*Occult hepatitis B virus infection in a rural cohort of antiretroviral treatment-naïve human immunodeficiency virus-infected patients*

### **Best free-standing posters (by Faculty)**

#### **First place: Lushen Pillay**

*Progressive Nodular Histiocytosis - an exceedingly rare variant of the Non-Langerhans cell histiocytosis*

#### **Second place: Roxanne Naidoo**

*Dodonaea viscosa var. angustifolia an indigenous South African medicinal plant and oral pathogens*

### **Best presented posters (across all five Faculties)**

#### **First place: Faculty of Health Sciences - Charles Carapinha**

*Determining factors of clinical outcomes in paediatric intussusception: the Johannesburg experience*

#### **Second place: Faculty of Health Sciences - Anita Marais**

*Tooth development induced by mouse embryonic stem cells and oral ectomesenchyme*

## PRESTIGIOUS RESEARCH LECTURE SERIES

In 2010 and 2011, the Health Sciences Research Office continued the Prestigious Research Lecture Series. The Faculty is privileged to be home to many researchers who are respected internationally for their work. The purpose of the Series is to showcase these scientists, and to provide an opportunity for them to share cutting-edge health research in their fields with members of the public. It is also a means to engage the wider healthcare community on issues pertaining to health. Open debate is encouraged after each lecture and usually is facilitated by an academic from outside of the Faculty or a member of government.

### Lecture III: 1<sup>st</sup> June 2010

#### Mandela's Children: Securing the health and well-being of future generations

**Associate Professor Stephen Tollman** (Director: MRC/Wits Rural Public Health and Health Transitions Research Unit) painted a picture of the "tough neighbourhood" in which our children grow up, the home environment, livelihood strategies, and the impact of HIV/AIDS. **Associate Professor Kathy Kahn** (MRC/Wits Rural Public Health and Health Transitions Research Unit) then described some of the key challenges with regards to the health of South Africa's infants and children, as well as some of the positive advances which have been made in the last decade. Nutrition has important effects on cognitive development and consequently on participation in society. The environmental stressors to which our children are being exposed are producing marked psychosocial effects, and we need to find effective interventions for this phase of development.

**Associate Professor Shane Norris** (Director: MRC/Wits Developmental Pathways for Health Research



Professors Helen Laburn (Dean), Shane Norris, John Pettifor, Kathy Kahn, Stephen Tollman, Bev Kramer (Assistant Dean: Research & Postgraduate Support) and Haroon Saloojee

Unit) went on to explain how adolescence is a bumpy ride during which it is critical that we provide support for our young people. He highlighted the increasing trend for obesity and the implications for metabolic disease in adulthood, and showed the convergence of urban and rural trends. **Professor John Pettifor** (A-rated researcher) wrapped up the presentation with an assessment of the importance of bone health in children. Calcium intake and exercise during adolescence are vitally important, especially as inadequate amounts of either have serious implications not only for bone health in the youngsters, but for bone health in old age.

**Professor Haroon Saloojee**, Head of the Division of Community Paediatrics at Wits, provided humorous yet challenging commentary, drawing attention to the fact that tough questions remain. We need to ask ourselves what more we should be doing, especially at a policy and health programme level.

## Lecture IV: 25<sup>th</sup> November 2010

### Should we be giving antiretroviral drugs to HIV-negative people?

This lecture took the form of a debate, led by **Professor Helen Rees** (Director: Wits Reproductive Health and HIV Institute) and **Professor Lynn Morris** (Head: AIDS Unit, National Institute for Communicable Diseases, and Research Professor in the Wits School of Pathology). The aim of the debate was to stimulate discussion of the issues surrounding the use of antiretroviral drugs as pre-exposure prophylaxis, such as resistance, side-effects, and which communities should be given priority.

**Dr Yogan Pillay** (Deputy Director: Strategic Health Programmes, National Department of Health) acted as commentator, providing valuable insight from the Department's perspective and encouraging public engagement with the issues.

The speakers had suggested that views of the "man on the street" be included in their presentation. Community Advisory Board members from the Hillbrow Health Precinct, women participating in trials of microbicide gels and members of the Alexandra Township community were asked for their opinion on the debate. Their comments were combined to create a short documentary produced by the Wits School of Arts. The Global HIV Vaccine Enterprise, as part of its *"Let's Talk Prevention"* series in 2010, sponsored the making of the film. Only ten events across the globe were sponsored by the Enterprise.



Professors Lynn Morris and Helen Laburn (former Dean), Dr Yogan Pillay, Professors Helen Rees and Beverley Kramer (Assistant Dean: Research and Postgraduate Support)



Professor Shabir Madhi, Professor Robin Green (University of Pretoria) and Professor Charles Feldman

## Lecture V: 28<sup>th</sup> May 2011

### Fighting the shadow: Pneumococcus and respiratory disease in the 21<sup>st</sup> century

In the first lecture of 2011, National Research Foundation A-rated researchers **Professor Shabir Madhi** and **Professor Charles Feldman** presented a selection of the cutting-edge clinical research in which they are engaged. Professor Madhi (Head: National Institute for Communicable Diseases, National Health Laboratory Service; Co-director: MRC/Wits Respiratory and Meningeal Pathogens Research Unit) described how in Africa, pneumococcal disease is one of the leading causes of death in children under five years. He then showed how the recent introduction of pneumococcal conjugate vaccines in South African immunisation programmes had already produced good results. Professor Feldman, Professor of Pulmonology and Director of the Pulmonary Infections Research Unit, explained how combination antibiotic therapy is vital in the treatment of pneumococcal infections. He further shared how his investigations of antibiotic treatment could lead to breakthroughs in the development of new vaccines. **Professor Robin Green** (Head: Department of Paediatrics and Child Health, School of Medicine, University of Pretoria) acted as the commentator, providing a thoughtful summary together with his own insight with regards to the way forward in this field.

## Lecture VI: 9<sup>th</sup> November 2011

### Target discovery and novel treatment for HIV-1

The sixth lecture in the Series was presented by **Professor Patrick Arbuthnot** (Director: Antiviral Gene Therapy Research Unit) and **Associate Professor Caroline Tiemessen** (Centre for HIV and STIs, National Institute for Communicable Diseases, National Health Laboratory Service, and Wits School of Pathology).

Professor Tiemessen explained how amongst those who become infected with HIV, the ability to control the course of the infection varies. Understanding what constitutes protection from disease progression in individuals with good control of the disease holds the key to providing targets for novel interventions. She has observed how, in patients who are able to suppress the virus, natural killer cells have the ability to be activated in a similar fashion to CD4 or CD8 T-cells. Additionally, it seems that in individuals with a natural ability to control their infection, there is a lack of either one or both alleles responsible for the production of the CCR5 protein, often required by the HI virus to enter host cells.

Professor Arbuthnot presented the case of the "Berlin patient" who saw complete remission of his HIV infection after receiving a bone marrow transplant from a donor who lacked the CCR5 genes. Then, with brilliant simplicity, Professor Arbuthnot illustrated the complex technology being used to replicate this transplant effect without the need for



Professor Ahmed Wadee (Dean), Dr Makobetsa Khati (CSIR), Associate Professor Caroline Tiemessen, Professor Patrick Arbuthnot and Professor Bev Kramer (Assistant Dean: Research and Postgraduate Support)

a donor and the very risky transplant procedure. The process entails the use of engineered enzymes, known as 'Zinc finger nucleases', which cut specific DNA sequences of the CCR5 gene to render it inactive. The methodology has advanced rapidly and preclinical studies show that the approach may be used to modify bone marrow stem cells.

The commentator, **Dr Makobetsa Khati** (Senior Manager and Head of the Emerging Health Technologies Department at the Council for Scientific and Industrial Research) echoed the presenters' enthusiasm, and praised the integrity and relevance of their work. He also encouraged greater collaboration between disciplines, to draw together the efforts of immunologists, gene therapist, engineers, and sociologists.



## MALARIA AWARENESS CAMPAIGN



Late Dr Ivan May (CEO of Radio Today), Associate Professor Robyn van Zyl, Yvonne Chaka Chaka and Professor Theresa Coetzer

Malaria kills nearly one million people a year – most of them children under five in Africa. However, malaria is entirely curable if a patient is given appropriate medication soon after symptoms appear. The Faculty of Health Sciences is home to three teams of malaria researchers, all of which make vital contributions to the global fight against malaria. The malaria research teams include the **Malaria Entomology Research Unit** (directed by **Professor Maureen Coetzee**); the **Head of the Plasmodium Molecular Research Unit** (led by **Professor Thérèse Coetzer**); the **Anti-malarial Drug Discovery research team** (led by **Associate Professor Robyn van Zyl**).

Hearing of **Yvonne Chaka Chaka's** role as UNICEF Goodwill ambassador for malaria and as an ambassador for the Rollback Malaria partnership, the

Health Sciences Research Office approached her regarding a public awareness initiative. After several meetings between the three malaria research team leaders and the "Princess of Africa", a plan for a malaria awareness campaign started to take shape.

Community radio station, Radio Today (1485AM) was approached and its CEO (Wits alumnus, **Dr Ivan May**) responded to the proposed partnership with much enthusiasm. It was decided that an awareness campaign during the month of November 2010 would be appropriate as this would coincide with the SADC Malaria Awareness Week. Short information snippets were recorded by the researchers and Yvonne, and these were aired on Radio Today throughout November. Dr May also interviewed Yvonne on her role as a malaria ambassador, and he spoke to each of the three researchers about their specific research activities. The interviews were aired Dr May's Monday evening programme, *In Town Tonight*.

It was felt that the snippets (ten in total) contained important messages which should not be distributed only in English and so the snippets were translated into Zulu, Xhosa, Afrikaans, Shangaan, and Sotho. These were then engineered by Wits campus radio station manager, Mike Smurthwaite. In 2011, the snippets were offered to community radio stations across the country, and were aired by stations such as Radio Today, Barberton Community Radio, Ka-Nyamazane Radio, Radio Makhado, Khwezi FM, Radio Sunny South and Kangala during the 2011 SADC Malaria Awareness Week.

## ALUMNI DIASPORA PROGRAMME

The Wits Faculty of Health Sciences has a long history of training clinicians and researchers, and has produced many successful and distinguished graduates. Some of these graduates have remained at Wits or in South Africa, while others have set sail for foreign shores over the years, adding immense value in America, Canada, the United Kingdom, Australia and elsewhere. In conversing with many of our graduates in other countries, a general theme of gratitude for the excellent training received at Wits emerged, and a sincere desire to contribute to research endeavours in the Faculty in return.

In 2009, a discussion with a visiting Wits alumnus was the final prompt needed for the Health Sciences Research Office to set up a programme which could facilitate visits by alumni. With start-up funds from the University Strategic Planning and Resources Committee, the Wits Health Sciences Alumni Diaspora Programme was initiated in 2010. Eleven alumni participated in the Programme in 2010 and 2011. Each spent one to two weeks in the Faculty, presenting seminars and meeting with staff and postgraduate students. The following are brief reports of some of the visits:



Professor Rhian Touyz

The first of the Faculty's alumni to take part in the Programme was **Professor Rhian Touyz**, a clinician-scientist with a particular interest in hypertension. After completing a BSc (Hons), she studied medicine and then completed an MSc (Med) and a PhD – all at Wits. Shortly thereafter, Professor Touyz moved to Canada to take up a Postdoctoral Fellowship at the Institut de recherches cliniques de Montréal (IRCM).

Professor Touyz has served as a Senior Scientist at the Kidney Research Centre - Ottawa Health Research Institute (OHRI), as Canada Research Chair in Hypertension, Scientific Chair of Cardiovascular Committee A (Canadian Institutes of Health Research), and Vice-Chair of the Leadership Committee of the Council for High Blood Pressure (American Heart Association). Professor Touyz has authored, or co-authored, more than 220 peer-reviewed publications. She is the Director of the Institute of Cardiovascular & Medical Sciences, University of Glasgow, United Kingdom. As a result of her guidance and assistance, a member of Faculty was awarded a Canadian Institutes of Health Research Canada-Hope Scholarship for 2012.

**Professor Denis Daneman** graduated from Wits Medical School in 1973, moving to Canada after he had completed his internship and senior house officer position in Paediatrics. Professor Daneman is Paediatrician-in-Chief and R.S. McLaughlin Foundation Chair in Paediatrics at The Hospital for Sick Children, and is Chair of Paediatrics at the University of Toronto, Canada. He is past Chair of the Clinical and Scientific Section of the Canadian Diabetes Association, and President of the International Society for Paediatric and Adolescent Diabetes. He has written over 180 publications and has served on multiple expert panels in the field of endocrinology.

His clinical research relates to the care and outcomes of children with diabetes and other endocrine disorders of childhood. He has focused on factors affecting metabolic control and the early onset of complications in children and teens with type-1 diabetes. Professor Daneman met extensively with members of Faculty during his visit, extending his network of relationships with clinician researchers at Wits.



Professor Denis Daneman reminisced about his student days with the late Professor Emeritus Phillip Tobias (who even remembered the details of an assignment he had handed in as an undergraduate student) and the late Professor Emeritus Jack Allan



Professor Roy Zent (front centre) and Professor Ambra Pozzi (back centre) with two of the Hillel Friedland Postdoctoral Fellows (Dr Kwang-Shik Choi and Dr Ranjit Chauhan) during their visit in 2010. Back row, from left: Dr Tembile Kulati, Professors Maureen Coetzee, Anna Kramvis and Beverley Kramer

**Professor Roy Zent** graduated from Wits as a medical doctor in 1984 and is now based at Vanderbilt University, USA, where he is an Associate Professor in the Department of Medicine. Professor Zent conducts predominantly basic research but has a clinical interest in glomerular disease. His research team at Vanderbilt uses biochemical techniques as well as cell biology and whole organ culture to understand the basic mechanisms whereby integrin-ECM interactions modify epithelial cell function.

Professor Zent was accompanied by his wife, Professor Ambra Pozzi, who is a graduate of the Universities of Milan and Florence, Italy. She is also an

Associate Professor in the Department of Medicine at Vanderbilt. The dynamic couple first visited in 2010, meeting with members of the Department of Internal Medicine and the Department of Molecular Medicine and Haematology. They visited again in 2011 presenting a series of talks on grant application and scientific paper writing. Both have served as reviewers for large funding bodies such as the National Institutes of Health (USA) and have been very successful at securing their own grant funding. Professors Zent and Pozzi also serve on the editorial boards of internationally-respected journals and review articles for several journals including *Nature Medicine* and the *Journal of Biological Chemistry*. Smaller workshop sessions provided the opportunity for members of staff who were working on papers or grant applications to present their drafts and receive focused feedback.

Professor Zent is the nephew of Mr Hillel Friedland, who created a Trust in support of Postdoctoral Fellows at Wits. During his first visit, Professor Zent met with Health Sciences Postdoctoral Fellows who were beneficiaries of the Hillel Friedland Trust in that year.

Several collaborative research projects have been initiated as a result of these visits, with plans also to submit joint grant applications. Especially exciting is the collaboration growing between our Faculty and Professor Zent's new home institution, Vanderbilt University.

**Professor Aubrey Milunsky** was born and educated in Johannesburg, but completed his medical specialist training in London. After thirteen years as a medical geneticist at Harvard Medical School and the Massachusetts General Hospital, he was appointed Professor of Paediatrics and Obstetrics and Gynaecology at Boston University School of Medicine, and became the Founding Director of their Centre for Human Genetics. His laboratories are a major International Reference Centre for molecular diagnostics and for prenatal genetic diagnosis. He led the team which first located the gene for X-linked lymphoproliferative disease, first cloned the PAX3 gene for Waardenburg syndrome, and first demonstrated the 70% avoidance of spina bifida afforded by folic acid supplementation taken in the three months prior to pregnancy and the three months after conception. In 1982, Wits conferred on him the degree of Doctor of Science, for his work on the prenatal detection of genetic disorders. Professor Milunsky continues to be research-active, and continues to revise and update his world-renowned text books, such as *"Genetic Disorders and the Fetus"*.

Visiting the Faculty in September 2010, Professor Milunsky delivered a plenary lecture at the Faculty Research Day. He also visited the Department of Paediatrics at Chris Hani Baragwanath Hospital, and a spent a day with the Division of Human Genetics.



Professor Aubrey Milunsky addressing Research Day delegates in the Linder Auditorium





Professor Seth Love, Dr Lynne Hirschowitz (Birmingham Women's Hospital) and Professor Martin Hale (Head of the Department of Anatomical Pathology)

**Professor Seth Love**, who graduated MBBCh cum laude from Wits in 1978, completed internships in Medicine and Surgery before joining the Department of Neuropathology at Queen Square, London, in 1980. He completed his PhD in 1984 and MRCPATH in neuropathology in 1985. He then spent two years as a Fogarty Fellow at the University of California in San Diego before returning to the United Kingdom, to a consultant post at Frenchay Hospital in Bristol. In 1995, he was awarded a personal Chair in Neuropathology at the University of Bristol. He is Director of the South West Dementia Brain Bank and Director of the Institute of Clinical Neurosciences at the University of Bristol. He serves on several editorial boards and scientific committees. Most of his research focuses on Alzheimer's disease and concerns the metabolism and clearance of A $\beta$ , alterations in A $\beta$ -degrading enzymes, impairment of TGF- $\beta$  signal transduction, cerebral amyloid angiopathy, and vascular dysfunction in dementia.

In November 2010, Professor Love spent a week in the Department of Anatomical Pathology, accompanied by his wife, Dr Lynne Hirschowitz, who also gave a lecture to members of the Department.



Professor Jules Kieser with the late Professor Emeritus Jack Allan and Professor Peter Cleaton-Jones

In July 2011, **Professor Jules Kieser** met extensively with members of the Schools of Anatomical Sciences, Oral Health Sciences, and Pathology. Professor Kieser graduated from Wits with a BSc in 1971, going on to pursue a dental qualification. He received his PhD in 1989 and was appointed Reader in Craniofacial Biology and an Honorary Professor of Anatomy at Wits. Professor Kieser then moved to New Zealand and in 1996 was appointed Head of the Department of Oral Sciences at the University of Otago, Dunedin. In 2009, he was appointed the inaugural Director of the University's Sir Jon Walsh Institute.

Professor Kieser is passionate about research, especially in the areas of dental and forensic biology (some of his team's work has even been incorporated into an episode of the TV show, CSI) but also conducts education research. He gave several fascinating lectures including one in honour of his mentor, the late Professor Emeritus Jack Allan. His engagement with Wits has resulted in several visits by Wits staff to the University of Otago, as well as the co-supervision of postgraduate students.



Professor Leigh Hale with Dr Hellen Myezwa (Head: Department of Physiotherapy), Professor Aimee Stewart, and Professor Bev Kramer (Assistant Dean: Research & Postgraduate Support)

In November 2011, alumnus **Professor Leigh Hale** spent a week visiting the Faculty hosted by the Department of Physiotherapy. Professor Hale graduated from Wits with an MSc (Neurorehabilitation) and later a PhD. After doing clinical work in both the public and private sector, she started teaching neurorehabilitation at Wits. In 2000, Professor Hale moved to New Zealand and took up a lecturing post in the School of Physiotherapy at the University of Otago (Dunedin). Her passion for the physiotherapeutic rehabilitation of people with neurological dysfunction has led her into a research career focused on conducting clinically-applicable research in this field.

During her visit, Professor Hale spent much time interacting with members of the Physiotherapy Department, providing feedback on draft manuscripts and grant applications. She also inspired supervisors and lecturers to review the way in which they discuss research with both undergraduate and postgraduate students. In her lecture to Faculty, she described

ways of engaging a community or study group, from the conceptualisation stage of an investigation, to ensure that the study ultimately adds value to the lives of those the research team seeks to help.



**Professor Adrian Di Bisceglie** graduated from Wits with an MBChB in 1977 and a Master of Medicine in 1986. He is Chief of Hepatology in the Division of Gastroenterology and Hepatology at the Saint Louis University School of Medicine, and is Co-Director of the Saint Louis University Liver Centre. His research interests lie in viral hepatitis, particularly aspects of its treatment and natural history, as well as hepatocellular carcinoma, specifically its relationship to chronic viral hepatitis.

In September 2011, Professor Di Bisceglie gave the opening lecture of the 2nd International Symposium on Hepatitis B Virus Genotypes - global diversity & evolution. The symposium was the closing event of the bilateral scientific collaboration between Professor Anna Kramvis, director of the Wits Hepatitis Virus Diversity Research Programme, and Professor Yasuhito Tanaka of Nagoya City University, Japan.

## POSTDOCTORAL FORUM AND SYMPOSIUM

Postdoctoral Fellows play a pivotal role in building an institution's research culture. The Faculty greatly values the contributions of its Postdoctoral Fellows, not only in the form of research papers but also their mentorship of postgraduate students, and the sharing of their knowledge and enthusiasm with all members of the Faculty. In 2010 and 2011, the Faculty was proud to be home to 16 and 22 Postdoctoral Fellows respectively. In 2010, the Faculty initiated a Postdoctoral Forum, with the aim of providing Postdoctoral Fellows the opportunity to raise concerns, share experiences, and suggest new ways of engaging with the Faculty community. By supporting our Postdoctoral Fellows, we look to expand the number in the Faculty significantly in the years to come.

In celebration of its Postdoctoral Fellows, the first Wits Health Sciences Postdoctoral Symposium was held in September 2011. Ten of the Fellows presented aspects of their current or proposed research, while **Julia Wilson** from UK-based charity *Sense About Science* and **Dr Thandi Mgwebi**, Programme Director of the Human Capacity Programme at the National Research Foundation, gave invited talks. Roche generously sponsored the event.



Pictured here are the Postdoctoral Fellows who attended. From front left: Dr Ranjit Chauhan, Dr Ananyo Choudhury, Dr Betty Mowa, Dr Zena Kimaro, Dr Nina Patzke, Dr Valence Ndesendo and Dr Hilary Lease. From back left: Dr Deepak Gopalakrishnan, Dr Sonja Lauterbach, Dr Benjamin Rey and Dr Zané Lombard

## STANDING UP FOR SCIENCE



Workshop participants discuss what concerns hold them back from engaging with the media

On 1 September 2011, **Julia Wilson**, Programme Coordinator at UK charity *Sense About Science*, facilitated a workshop for emergent researchers in the Faculty. Wits Health Sciences researchers **Professor Glenda Gray**, **Professor Stephen Tollman** and **Dr Baves Kana** shared some of their positive (and poor) experiences with journalists, and offered tips on how to communicate one's research to the public, working with the media.

Two journalists were also invited to participate, **Sarah Wild** from the *Business Day* and **Harriet McLea** from *The Times*. The journalists responded to the researchers' criticism and the concerns they had expressed about interactions with journalists, and shared "insider" tips on how print news rooms work. Participants in the workshop had the opportunity to discuss the challenges associated with sharing research in an interesting and informative way with the public. Julia also spoke about the Voice of Young Science network, a global network of early-career researchers who work together to combat "dodgy science", debunking science myths and pointing out weak (or false) "scientific" claims made by unscrupulous companies to market their products.

## CARNEGIE ACADEMIC MEDICINE FELLOWSHIP PROGRAMME

Major concerns have been expressed both from within the University and nationally about the decline in clinical research within South Africa and the associated lack of clinical researchers within the clinical academic environment. Furthermore, the Academy of Science of South Africa has highlighted the paucity of clinicians who have PhDs.

With these concerns in mind, Professors Helen Laburn and Yosuf Veriava approached the Carnegie Foundation for funding to support Fellowships in Clinical Medicine so that recently-trained specialists could spend time out of clinical practice to obtain their PhDs. Carnegie has provided funding to allow the Faculty to appoint two groups of four fellows each, to achieve their PhDs within two years.

The programme falls under the jurisdiction of the Faculty Research Office and is overseen by Professor John Pettifor who is the Director of the programme. During the two years of fellowship, the fellows are expected to not only complete their PHD theses, but also to have attended and participated in courses in statistics, research methodology, scientific writing, curriculum design, student assessment, and medical ethics among other topics.

The first four fellows, appointed in 2011 were:

- **Dr Susan Williams** (Supervisor: **Professor Trevor Carmichael**)
- **Dr Nimmisha Govind** (Supervisors: **Professors Mohammed Tikly** and **Michèle Ramsay**)
- **Dr Martin Brand** (Supervisors: **Professor Martin Veller** and **Professor Gavin Norton**)
- **Dr Nirvarthi Maharaj** (Supervisor: **Associate Professors Elena Libhaber** and **Mohammed Essop** and **Dr Ferande Peters**)

The next four fellows will likely be appointed during the course of 2012.

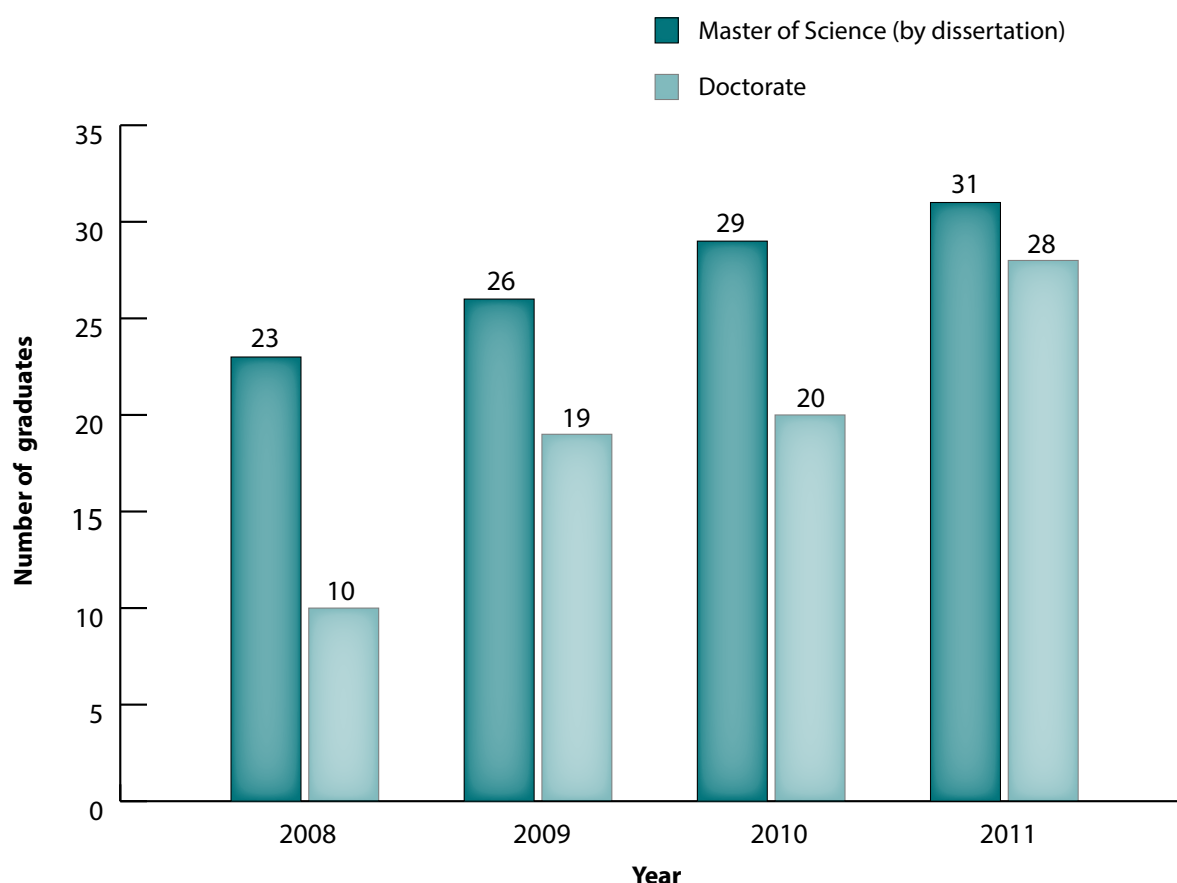
It is hoped that these eight postgraduate students will form the vanguard of a progression of young specialist clinicians who will become equipped through the Academic Medicine Fellowship Programme to lead clinical research into the future in South Africa. Committed to making lasting contributions to the promotion of clinical research in South Africa, the Faculty is looking at ways to make this programme sustainable through diversifying its funding.



# RESEARCH OUTPUTS

## RESEARCH POSTGRADUATES

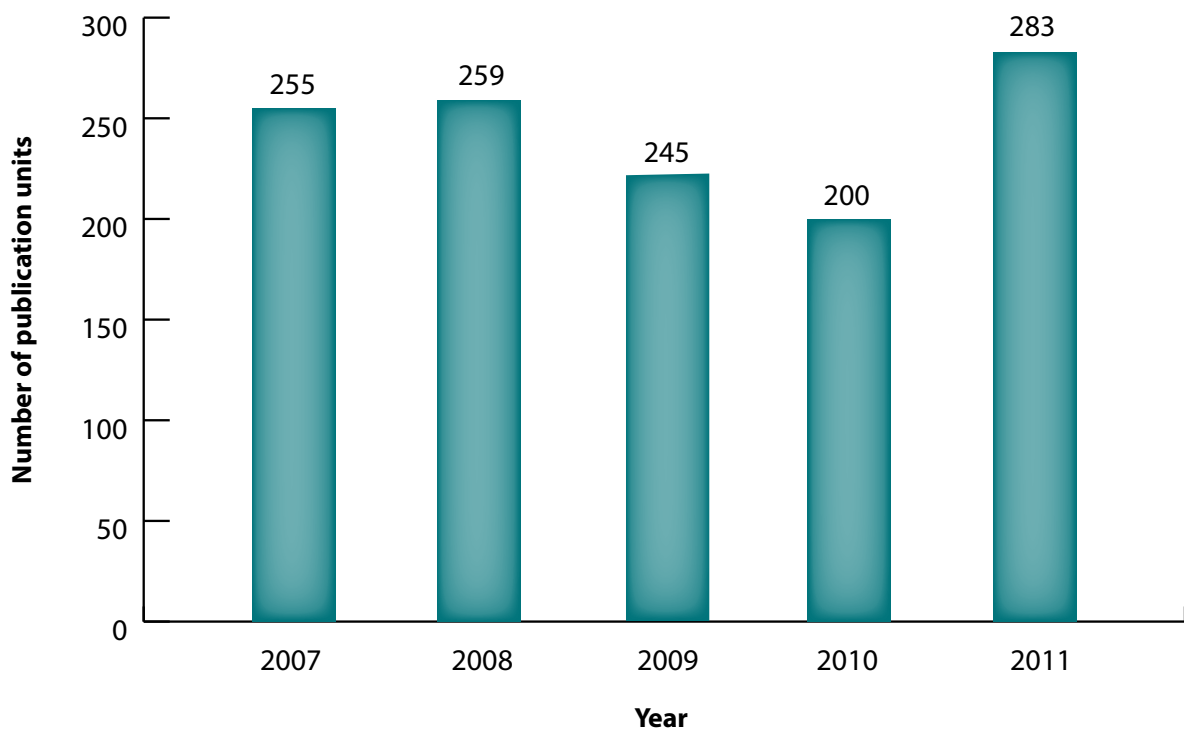
The Faculty graduates Master of Science graduates by dissertation (MSc), and Doctoral (PhD) graduates in all health sciences disciplines. The following figure illustrates the number of Master of Science (by dissertation) and Doctoral graduates in the Faculty of Health Sciences between 2008 and 2011.



## RESEARCH PUBLICATIONS

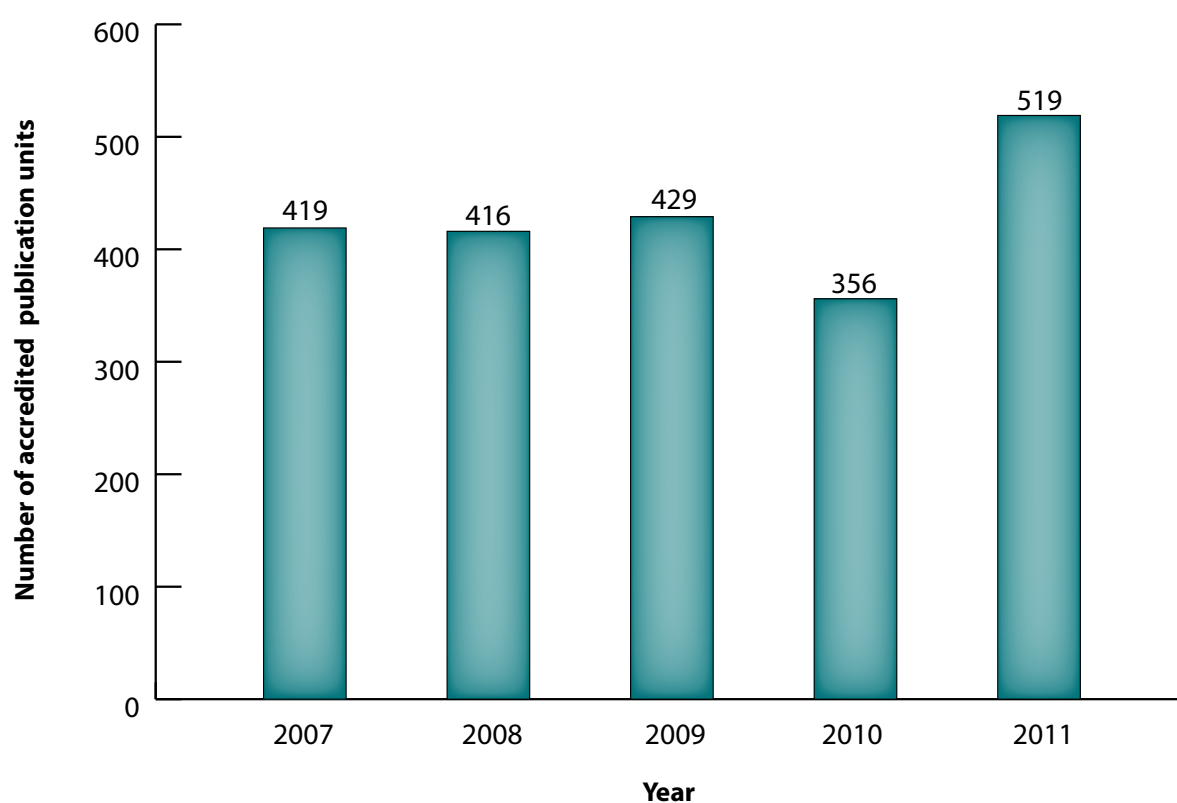
The Faculty is proud of its publication history and continues to strive for an increase in the number of scholarly publications in reputable journals and books. Figure A shows the number of publication units, assigned by the Department of Higher Education and Training (DoHET), awarded to the Faculty for accredited publications (research articles in journals, books, or chapters in books recognised by the Department) between 2007 and 2011.

Figure B illustrates the total number of research articles published in accredited journals (journals recognised by the Institute for Scientific Information or included on the list of accredited South African journals, compiled by the Department) produced between 2007 and 2011.



**Figure A.** The total number of publication units awarded by the Department of Higher Education and Training to the Faculty of Health Sciences between 2007 and 2011. The 2011 value is an estimate yet to be confirmed by the Department of Higher Education and Training.

## RESEARCH PUBLICATIONS



**Figure B.** The total number of research articles published in accredited journals or books by FHS researchers between 2007 and 2010.

## RESEARCH FUNDING

The Faculty receives funding for research from a variety of sources such as the University Council, National Research Foundation, Medical Research Council, Wits Health Consortium, amongst others. The national research agencies (SA Medical Research Council and National Research Foundation) support research through grants to individual researchers and groups, while the Wits Health Consortium is responsible for managing grants from several other external funding agencies. A dividend declared by the Wits Health Consortium was used in 2010 and 2011 to support research activities in the Faculty. The table illustrates, in Rand, the funding available for research in the Faculty in 2010 and 2011.

### **FHS Research Funding - (R'000)**

	<b>2010</b>	<b>2011</b>
<b>Funds allocated by the University Research Council</b>	7 928	8 639
<b>Faculty-specific grants awarded by the University Research Council</b>	1 247	470
<b>Research Funds administrated by the Wits Health Consortium:</b>	353 467	507 761
<b>Wits Health Consortium dividend</b>	3 900	4 199
<b>Funds awarded by external funding bodies:</b>		
- South African Medical Research Council	8 794	6 068
- National Research Foundation	17 814	17 904
- Other grants and contracts	18 245	60 670
<b>Total</b>	<b>411 395</b>	

# CREDITS

**Appreciation is expressed to the following people for their valuable assistance:**

## **Faculty of Health Sciences**

- Heads of School
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- Greer van Zyl
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