

Faculty of Health Sciences

Biennial Research Review 2008/2009



Message from the Dean

This Research Review is the first of its kind for the Wits Faculty of Health Sciences. I am exceptionally proud of the research in which members of the Faculty are engaged and the aim of this report is to share with you some of the research ideas and outputs which have brought distinction to the Faculty, especially in 2008 and 2009.

Contributing both nationally and internationally to health sciences research are individual researchers in the Faculty, as well as the members of the 21 Faculty Research Committee (FRC) - recognised research entities based in the Schools in the Faculty. The range of research in the Faculty is considerable and a sizable proportion of the research undertaken in the Faculty falls within priority health areas identified for the country.

The Review details significant research highlights in 2008 and 2009, as well as activities through which members of the Faculty contribute to increasing public awareness of research in their respective fields, such as public debates and seminars, and awareness days. These activities add richness to the Faculty's research culture.

We would not have had research to report on, were it not for the generosity of our partners in funding research. Here special mention must be made of the South African Medical Research Council which co-recognises eight of our research entities, the National Research Foundation, which sponsors many individual researchers, our Research Chair holders and co-sponsors our Centre of Excellence, the United States National Institutes of Health and the UK Wellcome Trust. The National Health Laboratory Service and Gauteng Department of Health and Social Development provide a platform for some of our research activities. The Wits Health Consortium plays a substantial role in managing and supporting the Faculty's research enterprise, as does the Research Office of the University.

I acknowledge the challenges which our researchers endure, many of whom face the considerable demands of teaching and service provision and still continue to be productive in research. This Review is about their success and the Faculty's contribution to advancing knowledge in important areas of health and disease in South Africa.

Much of the Faculty's current research profile can be attributed to the energy, enthusiasm and leadership of Professor Beverley Kramer who was appointed Assistant Dean: Research and Postgraduate Support early in 2008. Together with a small team, Professor Kramer has re-invigorated a research ethos in the Faculty and has been responsible for many initiatives which are bearing fruit in terms of research outputs, reputation and post-graduate success. I wish to acknowledge her key role in the Faculty, with gratitude.

My thanks to Professor Kramer and particularly Mrs Philippa McKechnie, Strategic Projects Assistant, for their enthusiasm and hard work in putting this publication together.

Helen P. Laburn, BSc (Hons), PhD, FRSSAf
Dean, Faculty of Health Sciences
Wits University



Dean: Professor Helen Laburn



Assistant Dean:
Research and Postgraduate Support
Professor Beverley Kramer

Research Highlights

New species of mosquito discovered

Malaria remains one of the biggest killers in Africa, particularly of children under the age of five years as well as pregnant women. In 2009, researchers and students from the Vector Control Reference Unit (School of Pathology) and the National Institute for Communicable Diseases (NICD), carried out field studies in northern Malawi and discovered a new species of malaria mosquito related to the major African malaria vector *Anopheles funestus*. *An. funestus* belongs to a group of morphologically similar species which are commonly distinguished from one another through the use of chromosomal and molecular techniques. Using the unique mosquito breeding facilities at the NICD, the Wits researchers were able to conduct a range of experiments to demonstrate that the mosquitoes from Malawi were not the same as *An. funestus* and that they were dealing with a species new to science. The results have implications for malaria vector control, particularly any attempt to use genetically modified mosquitoes. They also demonstrate how little we know about the malaria mosquito vectors in Africa despite over 100 years of research on this important disease.

Spillings B, Brooke B, Koekemoer L, Chipchwanya J, Coetzee M and Hunt R (2009). A new species concealed by *Anopheles funestus* Giles, a major malaria vector in Africa. *American Journal of Tropical Medicine and Hygiene*, 81: 510-515.



Larvae of the new mosquito species



Dr Clare Cutland

Chlorhexidine – no more useful than water?

In a large trial involving 8,011 women at Chris Hani-Baragwanath Hospital, **Dr Clare Cutland** and co-workers in the **Respiratory and Meningeal Pathogens Unit** (School of Pathology) tested the efficacy of chlorhexidine wipes, when used during labour, in reducing the early onset of neonatal sepsis and the transmission of group B streptococcus. The investigators found that the chlorhexidine intravaginal and neonatal wipes did not prevent neonatal sepsis or the vertical acquisition of potentially pathogenic bacteria by neonates. Therefore, the intervention did not reduce the mortality rate of infants included in the treatment group. The investigators assert that other interventions are needed to reduce child mortality. The findings of the study were published in the prestigious journal, the *Lancet*.

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.

Health in South Africa

In August 2009, the prestigious medical journal, the *Lancet*, published a series of six papers entitled *Health in South Africa*, the aim of which was to assess the status of health in South Africa as one of the most diverse regions of the world. The series is the result of collaboration between the *Lancet* and various academic centres in South Africa. It highlighted health issues such as the state of the health system, the high number of maternal and infant deaths, and the increase in the occurrence of non-communicable disease. Several Wits researchers from the Faculty of Health Sciences were involved in this landmark series, including Professors Sharon Fonn, Stephen Tollman, Rachel Jewkes and Peter Barron (School of Public Health) and Professor Hoosen Coovadia (Reproductive Health and HIV Research Unit).

The articles in the series can be downloaded from: www.thelancet.com/series/health-in-south-africa

Large grants awarded during 2008 and 2009

Wellcome Trust Programme grant

Professors Stephen Tollman and Kathleen Kahn
Rural Public Health and Health Transitions Research Unit, School of Public Health

Progress in the struggle against malaria in Africa

Professor Martin Grobusch, Head of the Infectious Diseases Unit (School of Pathology), served as a principal investigator for one of six trials on Intermittent Preventive Treatment of infants (IPTi). The trials, funded by the Bill and Melinda Gates Foundation, were conducted by a team of collaborators from around the world. In the series of trials the team investigated the safety and efficacy of Intermittent Preventive Treatment of infants with sulfadoxine-pyrimethamine in the battle against malaria. IPTi is the administration of a full course of an anti-malarial drug at specified time points, whether or not parasites are present. The trials were conducted in Gabon, Ghana, Mozambique and Tanzania. An analysis of the results of the six studies revealed that IPTi with sulfadoxine-pyrimethamine was safe and that the drug had a protective efficacy of 30.3% against clinical malaria.

The findings of the analysis were published in the *Lancet* in 2009.

Aponte J, Schellenberg D, Egan A, Breckenridge A, Carneiro I, Critchley J, Danquah I, Doodoo A, Kobbe R, Lell B, May J, Premji Z, Sanz S, Sevene E, Soulaymani-Becheikh R, Winstanley P, Adjei S, Anemana S, Chandramohan D, Issifou S, Mockenhaupt F, Owusu-Agyei S, Greenwood B, Grobusch M, Kreamsner P, Macete E, Mshinda H, Newman R, Slutsker L, Tanner M, Alonso P, Menendez C (2009). Efficacy and safety of intermittent preventive treatment with sulfadoxine-pyrimethamine for malaria in African infants: a pooled analysis of six randomised, placebo-controlled trials. *Lancet*, 374 (9700): 1533-1542.

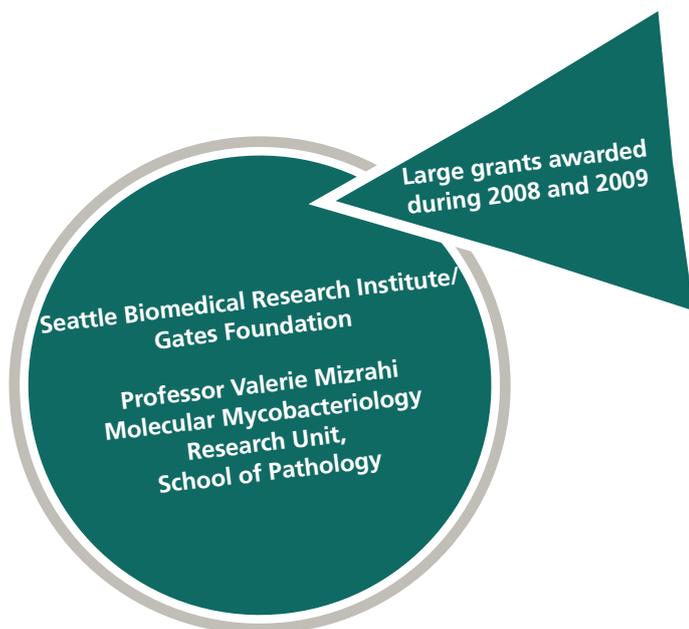


Professor Martin Grobusch

Researchers participate in the largest clinical trial of a microbicide (HIV) gel

The trial of the vaginal microbicide gel, *PRO 2000*, took place between September 2005 and September 2009. The trial was carried out by the Microbicides Development Programme (MDP), a not-for-profit partnership of 16 African and European research institutions. It was funded by the UK Department for International Development (DFID) and the UK Medical Research Council. The trial involved 9,385 women at six research centres in four African countries. The **Reproductive Health and HIV Research Unit (RHRU)** (School of Clinical Medicine) was responsible for 2,508 of the women at their research sites in Soweto and Orange Farm. The RHRU research team was lead by **Professor Helen Rees** and **Dr Sinead Delany-Moretlwe**.

A vaginal microbicide was given to participants together with a package of prevention against HIV infection which included free condoms, counselling for safer sex negotiation and sexual health services throughout the trial. The trial found no evidence that *PRO 2000* reduced the risk of HIV infection in women, ending scientific speculation about the gel's clinical importance.



Research Lectures and Events

Hillel Friedland Lecture

In 2008, the Hillel Friedland Lecture was delivered by **Professor Lenore Manderson** (Monash University, Australia). In her lecture, entitled *Acts of Remembrance: Prisons of memory, the power of memory and the healing of indigenous Australia*, Professor Manderson juxtaposed Australia's policy initiatives and implicit understandings of indigenous identity with post-holocaust and post-apartheid strategies of truth and reconciliation.

Professor Manderson was the recipient of a senior Hillel Friedland Sabbatical Grant in the School of Public Health. She spent much of 2008 at Wits supporting the development of a PhD programme, conducting workshops with postgraduate supervisors as well as co-supervising students.



Professor Lenore Manderson

AJ Orenstein Memorial Lectures

An inaugural lecture held in 1962, at the inception of the Adler Museum of Medicine, was delivered by Major General Orenstein under the auspices of the Adler Museum and the Medical Graduates Association. Since that date, 38 lectures have been held. In 1974 the name of the lecture was changed to the AJ Orenstein Memorial Lecture. This was to perpetuate the memory of the late Major General Orenstein who passed away in 1972, and to commemorate the part he played in the establishment of medical services in the mining industry.

In 2008, the AJ Orenstein Memorial Lecture entitled *Digging for the truth: lessons from my casebook*, was delivered by **Dr Hendrik Scholtz**. Dr Scholtz is the Group General Manager: Professional Development, International SOS. Previously, Dr Scholtz served as Professor and Chief Specialist of Forensic Pathology Services in the Gauteng Department of Health and as Head of the Division of Forensic Medicine in the School of Pathology.

In his lecture Dr Scholtz imparted some of the important lessons he has learnt from the array of cases he has dealt with in 17 years of forensic pathology practice. He drew on his experience of homicidal deaths, ritual murders, accidental deaths (including mine-related deaths) and mass disasters such as the 2004 South East Asian tsunami.



Dr Hendrik Scholtz



Dr Lucille Blumberg

In 2009, **Dr Lucille Blumberg**, Deputy Director, National Institute for Communicable Diseases in the National Health Laboratory Service presented the AJ Orenstein Memorial Lecture entitled *Outbreaks: New threats and old culprits. The work of disease detectives*. The talk focused on recent emerging pathogens, particularly those affecting southern Africa, the work of 'disease detectives' in unravelling the clues and the interaction between people, politics and pathogens.

Emerging infectious diseases and pathogens such as the novel arena and influenza viruses and old culprits such as cholera and meningococcus, have been particularly topical in South Africa in recent years. The emerging new diseases are often serious threats to the life of individuals, uncertain threats to communities and very definite threats to the healthcare workers dealing with infected patients. Dr Blumberg highlighted the extensive experience of South African scientists in pathogen research, from pioneering work done on pneumonia, typhoid and the Plague nearly 100 years ago, to viral haemorrhagic fever research by experts such as Margaretha Isaäcson and Robert Swanepoel.

Prestigious Research Lecture Series

In 2009, the Faculty of Health Sciences held its first two Prestigious Research Lectures. The lectures aim to highlight high-profile research conducted by members of the Faculty and to provide the public with the opportunity to engage with health sciences research. Instituted by Professor Beverley Kramer, the lectures are set to become regular features in the Faculty's calendar.

Cardiovascular disease: Life versus lifestyle

The Prestigious Research Lecture series was formally opened by **Professor Anthony Mbewu**, the President of the South African Medical Research Council. The first lecture, entitled *Cardiovascular disease: Life versus lifestyle*, was delivered by **Professors Karen Sliwa, Gavin Norton** and **Angela Woodiwiss**. In an animated presentation, the Directors of the Faculty's two cardiovascular research units discussed the outcomes of large cardiovascular studies conducted in Soweto, Johannesburg. The potential factors accounting for the burden of cardiovascular disease in urban, developing communities in South Africa were underscored. Professor Sliwa argued for a need to aggressively educate and manage the changes in lifestyle which accompany developing communities in order to prevent the increasing prevalence of cardiovascular disease in South Africa, while Professor Norton suggested that there is an urgent need to identify the mechanisms of obesity-induced cardiovascular damage. Lastly, Professor Woodiwiss presented potential solutions to the problem of managing the epidemic of hypertensive cardiovascular disease in urban, developing communities in South Africa. **Professor Lionel Opie**, a legendary cardiovascular scientist and Director of the Hatter Heart Institute at the University of Cape Town provided insightful and entertaining commentary.



Professor Gavin Norton



Associate Professor Angela Woodiwiss



Professor Karen Sliwa

An end to the AIDS epidemic? – Test and Treat

The second Prestigious Research Lecture interrogated the feasibility of the Test and Treat strategy for reducing the rate of HIV infections in South Africa. Entitled *An end to the AIDS epidemic? – Test and Treat*, the lecture was delivered by **Dr Francesca Conradie** (Deputy Director in the **Clinical HIV Research Unit**, School of Clinical Medicine) and **Dr Guy De Bruyn** (Programme Director for HIV Prevention Studies in the **Perinatal HIV Research Unit**, School of Clinical Medicine). Dr De Bruyn argued in favour of the “test and treat” model, which proposes that the only way to gain significant ground in the fight against HIV/AIDS is to introduce universal, regular testing and to begin ARV treatment as soon as a patient is diagnosed as being HIV positive. Dr Conradie pointed out the very real challenges – financial, logistical and social – which would have to be addressed if the strategy were to be effective. **Professor Gavin Churchyard**, founder and CEO of The Aurum Institute for Health Research, and an internationally respected HIV/TB researcher, provided astute commentary on the points which had been raised.



Dr Guy De Bruyn, Dr Francesca Conradie and Professor Gavin Churchyard

Large grants awarded during 2008 and 2009

Gates Foundation Grant: Human Resources for Health Research in Africa

Professor Sharon Fonn
School of Public Health

Research Day and Postgraduate Expo

Every second year, the Faculty hosts a Research Day and in 2008 the event included a Postgraduate Expo. Approximately 1,000 people attended, making it the largest Research Day to date. The event and prizes were sponsored by Roche Diagnostics, Sanofi Aventis, the Wits Health Consortium and the Faculty Research Office.

Fascinating plenary lectures were delivered by **Professor Lenore Manderson** (Monash University, Australia) who is known for her work in medical anthropology, sociology and public health and **Professor Tim Noakes** (Discovery Health Professor of Exercise and Sports Science at the University of Cape Town and Director of the UCT/MRC Research Unit for Exercise Science and Sports Medicine), and a world leader in sports and exercise science. Six parallel sessions were held, under the themes of: *HIV/AIDS; Infectious Diseases; Healthcare Delivery; Chronic Diseases and Diseases of Lifestyle; Science and Therapeutics and Molecular and Comparative Biosciences*. A total of 108 oral presentations were delivered over the course of the day and 215 posters were on display. Prizes for the best poster, the best presentation and the best presentation by a young researcher were awarded in each theme.

The Postgraduate 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.

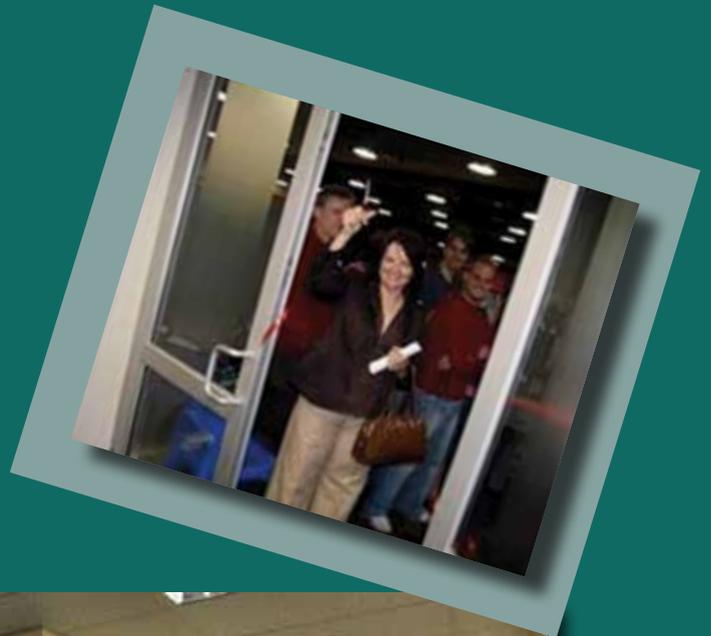


Winners in each of the themes were:

Chronic Diseases and Diseases of Lifestyle	<p>Oral Presentation Gavin Norton</p> <p>Poster Presentation Harold Majane</p> <p>Young Researcher Phikolomzi Mgandela</p>
Infectious Diseases	<p>Oral Presentation Bavesh Kana</p> <p>Poster Presentation Charmaine Mlambo</p> <p>Young Researcher Tristan Scott</p>
Healthcare Delivery	<p>Oral Presentation Heleen van Aswegen</p> <p>Poster Presentation Peter Owen</p> <p>Young Researcher Jacqueline Mendes</p>
Molecular and Comparative Biosciences	<p>Oral Presentation Kubendran Naidoo</p> <p>Poster Presentation Geoffrey Kwenda</p> <p>Young Researcher Sheena Saayman</p>
Science in Therapeutics	<p>Oral Presentation Abdullah Ely</p> <p>Poster Presentation Pule Maleshwane</p> <p>Young Researcher Gina Fanucchi</p>
HIV/AIDS	<p>Oral Presentation Aye Violari</p> <p>Poster Presentation Mhairi Maskew Viness Quan</p> <p>Young Researcher Penny Moore</p>

Opening of the Postgraduate Hub

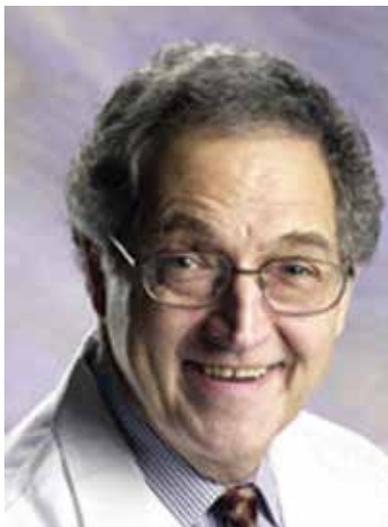
Professor Belinda Bozzoli, Deputy Vice-Chancellor: Research, cut the red ribbon to inaugurate the new Faculty of Health Sciences Postgraduate Hub in 2009. The Hub has four areas: a lounge, a discussion/tutorial room; a computer mini-lab and a small kitchen. The computers in the Hub are equipped with the relevant statistical software needed by postgraduate students and statisticians are at hand to assist students with the analysis of their data.



Notable Research Achievements

Doctor of Science

Professor Michael Jeffrey Maisels (Department of Paediatrics and Child Health, School of Clinical Medicine) received the degree of Doctor of Science in Medicine in 2008 for a thesis entitled *Neonatal hyperbilirubinemia and bilirubin encephalopathy. Investigations into the diagnosis, epidemiology, pathogenesis, management and treatment of the jaundiced newborn*. Professor Maisels graduated from Wits in 1961 and moved to the United States in 1966 where he began his studies on the jaundiced newborn infant. Over the last 40 years, he has published over 100 papers and chapters on this subject and has made major contributions to the understanding of the epidemiology and management of neonatal hyperbilirubinemia. Using innovative research techniques, he measured the rate of bilirubin production, evaluated non-invasive measurements of bilirubin and showed clinicians how to use phototherapy to treat the jaundiced neonate. His seminal studies have had a major impact on how jaundiced newborns are cared for throughout the world.



Professor Jeffrey Maisels



Professor Charles Feldman

Professor Charles Feldman (Head of the Division of Pulmonology, School of Clinical Medicine), received the degree of Doctor of Science in Medicine in 2009 for a thesis entitled *Contributions to an understanding of community-acquired pneumonia*. The thesis explores the important topic of community-acquired pneumonia (CAP) and includes a range of studies spanning more than 20 years. Several of the more recent studies have described the laboratory, clinical and microbiological findings in HIV-infected patients with CAP and have indicated important strategies for the treatment and prevention of these infections. Some of Professor Feldman's clinical research has involved trying to understand the optimal antibiotic management of the infection, while the laboratory-based research has focused on understanding the pathogenesis of pneumonia with the aim of deriving alternative strategies that may be used as an adjunct to antibiotic therapy 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. For his exceptional research efforts, Professor Feldman was also awarded the 2009 **Vice-Chancellor's Research Award**.

Faculty Research Awards

Several of the prizes awarded at the Faculty's annual prize-giving ceremony acknowledge excellence in research. The most prestigious of these awards is the **Faculty Research Prize** which goes to the researcher, usually the first author on the publication, whose paper in an international peer-reviewed journal is considered to have made the greatest impact on the global community of biomedical scientists.

In 2008, **Dr Paul Pronyk** and **Ms Sibongile Sibambo** shared the award. Dr Pronyk (School of Public Health) won the award for the publication of his paper: Effect of a structural intervention of the prevention of intimate partner violence and HIV in rural South Africa. *Lancet*, 368: 1973-1983 (2006); and Ms Sibambo (School of Therapeutic Sciences) for her paper: Elucidation of the physicochemical and *ab initio* quantum energy transitions of a cross linked PLGA scaffold. *Biomaterials*, 28: 3714-3723 (2007).

In 2009, the award was shared by **Dr Hendrick (Manuel) van Deventer** (School of Pathology), for his publication: Estimating glomerular filtration rate in black South Africans by use of the modification of diet in renal disease and Cockcroft-Gault equations. *Clinical Chemistry*, 54: 1197-1202 (2008) and **Dr Marco Weinberg** (School of Pathology), for his publication: An RNA targeted to the HIV1 LRT promoter modulates indiscriminate off-target gene activation. *Nucleic Acids Research*, 35: 7303-12 (2007).

The **Prestigious Postgraduate Degree Awards** introduced in 2009, are presented in recognition of a range of postgraduate degrees. Candidates are nominated by their supervisor(s) and the degrees are assessed on the basis of several criteria. The awards were presented to **June Fabian (MMed)**, **Philip Haycock (MSc)** and **Dr Elin Gray (PhD)**.

National and International Research Awards

2008

Professor John Pettifor received the 32nd Gopalan Oration Award from The Gopalan Oration Trust during the 40th National Conference of the Nutrition Society of India.

Professor Lorna Jacklin won the Shoprite Checkers / SABC 2 Woman of the Year Award for Health.

Dr Tony Bamigboye and **Professor Justus Hofmeyr** received an award from the International Journal of Gynaecology and Obstetrics for the best clinical research paper from a middle or low income country in 2008.

Professor Ian Sanne was awarded the Influential Leaders in Healthcare award by the South African Institute of Healthcare Managers.

2009

Professor Shabir Madhi was awarded the National Science and Technology Forum / National Research Foundation TW Kambule Award for a Senior Black Male Researcher for his intense research into the killer diseases of children.

Professor Maureen Coetzee was second runner-up in the 2009 Department of Science and Technology / L'Oreal Women in Science Awards.

Dr Lizette Koekemoer was awarded the British Association Medal (Silver) by the Southern African Association for the Advancement of Science.

Professor Angela Woodiwiss received the Excellence in Physiology Research award from the Physiological Society of Southern Africa.

Professor Richard Hunt was awarded the Elsdon Dew Medal by the Parasitological Society of Southern Africa.

Professor Stephen Tollman was first author on a paper, published in the *Lancet*, which was awarded the INDEPTH (International Network of field sites with continuous Demographic Evaluation of Populations and Their Health in developing countries) prize for Extraordinary Research in Population and Health at INDEPTH sites.

Professor Viness Pillay was a finalist in the National Science and Technology Forum Awards 2008/2009 for his contribution to the development of innovative drug delivery products.

Mr Phillip Haycock was awarded the Southern African Association for the Advancement of Science Medal (Bronze) for his outstanding Masters dissertation.

Ms Deborah Jones was awarded the South African Dental Association's Young Essayist Award for a paper published in the Association's journal.

National Research Foundation – Rated Researchers

The Faculty has encouraged its researchers to gain ratings from the National Research Foundation and is proud of the steady increase in the number of rated researchers over the last two years. In South Africa approximately 2,100 academics hold NRF ratings.

Rated Researchers in the Faculty of Health Sciences

Researcher	Title	Discipline	Rating
Adrian, P	Dr	Pathology	C
Arbuthnot, PB	Prof.	Pathology	C
Ballot, DE	Prof.	Clinical Medicine	L
Buchmann, EJ	Prof.	Clinical Medicine	C
Cleaton-Jones, PE	Prof.	Oral Health Sciences	B
Coetzee, M	Prof.	Pathology/NICD	B
Coetzer, TL	Prof.	Pathology	B
Coogan, MM	Prof.	Oral Health Sciences	C
Crowther, NJ	Prof.	Pathology	C
du Plessis, M	Dr	Pathology	Y
Erlwanger, KD	Dr	Physiology	C
Feldman, C	Prof.	Clinical Medicine	B
Flanagan, C	Dr	Physiology	C
Fuller, A	Prof.	Physiology	C
Glencross, DK	Prof.	Pathology	B
Gordhan, B	Dr	Pathology	C
Gray, DA	Prof.	Physiology	B
Grobusch, MP	Prof.	Pathology	C
Gulumian, M	Prof.	Pathology	C
Hosie, M	Prof.	Anatomical Sciences	C
Kamerman, P	Prof.	Physiology	Y
Kana, B	Dr	Pathology	C
Kielkowski, D	Dr	Public Health	C
Klipstein-Grobusch, KKG	Prof.	Public Health	C
Klugman, K	Prof.	Pathology	A
Koekemoer, L	Dr	Pathology/NICD	C
Kramer, B	Prof.	Anatomical Sciences	C
Kramvis, A	Prof.	Clinical Medicine	B

Laburn, HP	Prof.	Physiology	B
Libhaber, EN	Dr	Clinical Medicine	C
Madhi, SA	Prof.	Pathology	B
Madziva, MT	Dr	Physiology	Y
Manger, PR	Prof.	Anatomical Sciences	B
Marais, E	Dr	Pathology	Y
Mitchell, D	Prof.	Physiology	A
Mizrahi, V	Prof.	Pathology	A
Moore, PL	Dr	Pathology/NICD	Y
Morris, L	Prof.	Pathology/NICD	B
Naicker, S	Prof.	Clinical Medicine	C
Norris, SA	Prof.	Clinical Medicine	Y
Papathanasopoulos, MA	Dr	Pathology	C
Paweska, JT	Prof.	Pathology/NICD	C
Pettifor, JM	Prof.	Clinical Medicine	A
Phillips, JI	Prof.	Pathology	C
Pillay,V	Prof.	Therapeutic Sciences	C
Potterton, JL	Dr	Therapeutic Sciences	L
Raal, F	Prof.	Clinical Medicine	C
Ramsay, M	Prof.	Pathology	B
Ripamonti, U	Prof.	Clinical Medicine	B
Rogers, G	Prof.	Physiology	C
Sliwa-Hahnle, K	Prof.	Clinical Medicine	B
Smith, AM	Prof.	Pathology/NICD	C
Stewart, AV	Prof.	Therapeutic Sciences	C
Szabo, CP	Prof.	Clinical Medicine	C
Tiemessen, CT	Prof.	Pathology/NICD	C
van Eyk, AD	Dr	Therapeutic Sciences	C
van Vuuren, S	Prof.	Therapeutic Sciences	C
Warner, D	Dr	Pathology	Y
Weinberg, MS	Dr	Pathology	Y
Woodiwiss, AJ	Dr	Physiology	B

Swiss South African Joint Research Programmes grant

Dr Kathleen Kahn
Rural Public Health and Health Transitions Research Unit,
School of Public Health

Large grants awarded during 2008 and 2009

A-rated Researchers

The National Research Foundation first introduced its system of rating researchers by peer review in the early 1980s. Through a rigorous application process, a researcher is assigned a rating, which is valid for five years. Researchers assigned an A-rating are considered to be *'researchers who are unequivocally recognised by their peers as leading international scholars in their field for the high quality and impact of their recent research outputs'*. The Faculty of Health Sciences is proud to have four A-rated scientists.

Since 2000, **Professor Keith Klugman**, the former Director of the South African Institute for Medical Research and former Chair of the School of Pathology at Wits, has kept a 25% appointment at his alma mater and returns at least three times each year to participate in research. He is the Co-Director of the **Respiratory and Meningeal Pathogens Research Unit** (see page 43). Professor Klugman's time overseas is spent as the Foege Professor of Global Health at Emory University in Atlanta, Georgia. He has been able, during the past ten years, to leverage a number of National Institutes of Health, Gates and other funded studies through both Emory and Wits and shares the passion of his South African colleagues to find innovative ways to protect children and adults from pneumonia.



Professor Keith Klugman



Emeritus Professor Duncan Mitchell

Professor Duncan Mitchell is Emeritus Professor of Physiology, Honorary Professorial Research Fellow in the **Brain Function Research Group** and a long-standing A-rated scientist. Before joining the University in 1975, he was on the scientific staff of the National Institute for Medical Research (London) and 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 is currently 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.

Another A-rated researcher of long standing is **Professor John Pettifor** who for many years served as Head of the Department of Paediatrics at the Chris Hani Baragwanath Hospital in Soweto, Johannesburg. He is currently Director of the **Mineral Metabolism Research Unit** and the Birth to Twenty longitudinal study (see page 32). He qualified as a medical doctor from Wits in 1968 and specialised in Paediatrics. In 1978/9, he spent a year as a clinical research fellow in Montreal, Canada, under the guidance of Professor Francis Glorieux studying paediatric bone diseases and on his return he established the Mineral Metabolism Research Unit. Professor Pettifor's major research interests have focused on metabolic bone diseases in children. He is currently involved in a longitudinal study of the ethnic differences in bone mass in children and the factors influencing bone growth and acquisition during puberty.



Professor John Pettifor



Professor Valerie Mizrahi

Professor Valerie Mizrahi is Research Professor, Director of the **Molecular Mycobacteriology Research Unit** and Co-Director of the DST-NRF Centre of Excellence for Biomedical TB Research (see page 19). Professor Mizrahi is an International Research Scholar of the Howard Hughes Medical Institute (HMMI) as well as Fellow of the Royal Society of South Africa, a Member of the Academy of Science of South Africa, an Associate Fellow of the Academy of Sciences of the Developing World and a Fellow of the American Academy of Microbiology. Her research has focused on elucidating aspects of the physiology and metabolism of *Mycobacterium tuberculosis* of particular relevance to TB drug discovery and drug resistance.

Professor Mizrahi said of her "A" rating: 'This rating reflects the hard work and dedication of the outstanding group of people that I have been privileged to work with over the past few years.'

Large grants awarded during 2008 and 2009

Gates Foundation Grand Challenges Exploration Grant

Dr Leonard Damelin
School of Pathology/NICD

Research Focus

South African Research Chairs

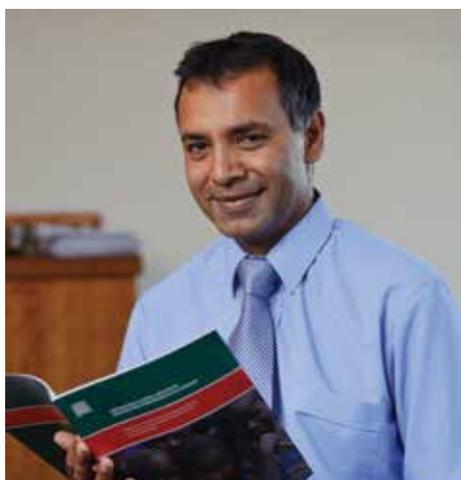
The South African Research Chairs Initiative (SARChI) is a research attraction and retention intervention by the government of South Africa. It is led by the Department of Science and Technology (DST) and the National Research Foundation (NRF) and is designed to significantly expand the scientific research base and supervisory capacity of South Africa in a way that is relevant to national development imperatives and to improve the international competitiveness of the South African science system.

Chair in Vaccine Preventable Diseases

In the **Respiratory and Meningeal Pathogens Research Unit** (RMPRU), a team of researchers work tirelessly to study vaccines which can potentially save the lives of millions of children around the world.

In a first for Africa, the Unit's research has demonstrated that childhood morbidity can be significantly reduced with pneumococcal conjugate and rotavirus vaccines. In addition, their research has contributed to South Africa being the first in Africa to introduce these vaccines into the public immunisation programme. Immunisations are anticipated to reduce childhood mortality in South Africa by 10-15%.

Associate Professor Shabir Madhi, Co-Director of the RMPRU, was awarded a South African Research Chair in Vaccine Preventable Diseases in 2008.



Professor Shabir Madhi

Research focus

The Unit's main research focus is the development and evaluation of vaccines aimed at combating diseases caused by pneumococcal bacteria and the rotavirus. The Unit's work includes basic sciences, epidemiology and clinical research. Basic sciences are geared towards identifying future potential vaccine targets for different bacteria and viruses. The Unit's immunology research focuses on the immune responses to the vaccines by comparing HIV infected children with uninfected children. Their epidemiology research focuses on the effects of the introduction of vaccines on childhood diseases and the subsequent burden of the disease in terms of morbidity and mortality. The aim of their clinical research is to evaluate how well the vaccines work by comparing HIV infected children with those who are uninfected.

Read more about the research on page 43.

The SARChI funding has primarily been used to provide bursaries and sponsor the research activities of postgraduate vaccinology students. The Unit's aim is to increase their postgraduate output substantially over the next five years. Professor Madhi currently supervises or co-supervises six doctoral and five masters students. Three doctoral and three masters students are funded by the SARChI.

Professor Madhi believes that the establishment of the Chair at the University is an acknowledgement that Wits is a leader in the field of vaccinology in Africa.

Chair in Medical Entomology and Vector Control

Between 300 and 500 million malaria cases are reported worldwide every year and an estimated one million people die annually as a result of the disease. According to the World Health Organisation (WHO) more than 90% of malaria-related deaths occur in Africa.

One of the major problems facing researchers is the fact that mosquitoes, as well as the parasites, develop resistance to insecticides and drugs at a very fast rate. This means that new drugs have to be developed every three to five years to combat the parasite, but for the mosquitoes, no new insecticides have been introduced since the eighties.

The **Malaria Entomology Research Unit (MERU)**, under the directorship of **Professor Maureen Coetzee**, made international headlines in 2009 when they announced the discovery of a new species of mosquito in the northern regions of Malawi.

Professor Coetzee, who is also a research professor of medical entomology in the School of Pathology was awarded a South African Research Chair in Medical Entomology and Vector Control in 2007.



Professor Maureen Coetzee

Research focus

The Unit's studies are focused on four very important aspects which include:

- the identification of species and phylogenetic relationships within the *Anopheles funestus* group in southern Africa
- insecticide resistance in malaria vectors in Africa
- entomopathogenic fungi
- parasite-vector interactions

To read more about the team's research, turn to page 42.

The discovery of the new species of mosquito in Malawi can be directly attributed to the funding provided by the SARCHI, says Professor Coetzee. Not only did it enable MERU to purchase state-of-the-art equipment, but they were also able to send staff and students to Malawi to carry out the field work. The SARCHI funding has also supported a number of students to spend time at the Liverpool School of Tropical Medicine in the United Kingdom for training in various molecular techniques associated with research on insecticide resistance in malaria vector mosquitoes.

Professor Coetzee considers the provision of bursaries to students as another substantial perk. "The funding has not only allowed us to recruit more students, but also to retain talented students who would otherwise have left the University after completing their Masters." Within MERU, 12 postgraduate students, working on various projects within the broad malaria umbrella, are being supervised.

Chair in Pharmaceutical Biomaterials and Polymer-Engineered Drug Delivery Technologies

Professor Viness Pillay, Director of the Wits-BioPAD Drug Delivery Platform (WDDP), and his team have successfully developed a number of biocompatible and biodegradable delivery technologies that can improve the efficacy of drugs used to treat diseases and conditions ranging from cancer to tuberculosis, HIV and epilepsy. If these technologies prove to be as effective as initial animal studies have shown, they will offer new hope to patients and will result in a drastic reduction in the cost of medicine.

Professor Pillay was awarded a South African Research Chair in Pharmaceutical Biomaterials and Polymer-Engineered Drug Delivery Technologies in 2007.



Professor Viness Pillay

Research focus

Professor Pillay has been working on a suite of drug delivery technologies for the past 19 years and together with his team, has developed several niche technology development foundations, including: nano-neuropharmaceutics, wafer-technology, chronotherapeutics and gastroretentive systems.

The majority of technologies have already undergone *in vitro* and *ex vivo* testing as well as *in vivo* preclinical studies. The next step is to undertake pilot human bio-studies.

Read more about the research on page 48.

According to Professor Pillay one of his main focuses is human capacity development. Each year he uses a portion of the SARChI funding to send three or four students to international conferences. This allows them to compare their work with their peers in the international arena.

The funding has enabled the team to purchase state-of-the-art equipment which has given them an edge both locally and internationally. According to Professor Pillay – who was a postdoctoral student and lecturer at universities in the United States – his research team currently has better equipment than many of the universities there.

The WDDP has also been able to invest in new offices and laboratories for postgraduate students. Furthermore, the Platform has been able to provide bursaries to a number of students. Professor Pillay currently supervises or co-supervises 30 masters and seven doctoral students as well as two postdoctoral fellows.

Centre of Excellence for Biomedical Tuberculosis Research

One of the key components of government's National Research and Development Strategy is the creation of centres and networks of excellence in science and technology. The aim of these centres is to stimulate sustained distinction in research while simultaneously generating highly qualified human resource capacity in order to impact meaningfully on key national and global areas of knowledge.

There are currently seven Department of Science and Technology / National Research Foundation Centres of Excellence countrywide, of which three are hosted at Wits. One of these three is based in the Faculty of Health Sciences, which hosts one of two nodes making up the Centre of Excellence for Biomedical Tuberculosis Research (CBTBR).

The **Molecular Mycobacteriology Research Unit** (MMRU) was founded in 2000 as a joint research unit of the Medical Research Council of South Africa, the National Health Laboratory Services and Wits. In 2004, the MMRU was established as the Wits node of the CBTBR, in partnership with the University of Stellenbosch. Investigators at the Wits node of the CBTBR, under the directorship of **Professor Valerie Mizrahi**, have received international acclaim for their fundamental research into the metabolism of *Mycobacterium tuberculosis* to identify, characterise and validate new drug targets and vaccine candidates for tuberculosis (TB).



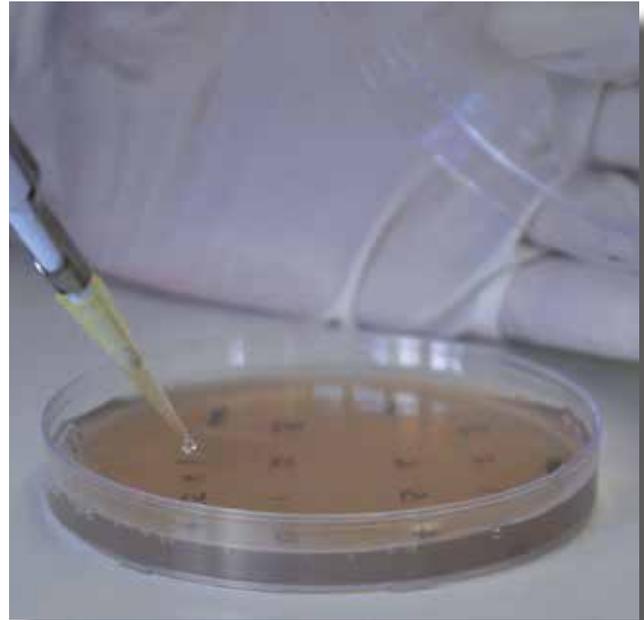
Mycobacterium tuberculosis, the bacterium responsible for causing tuberculosis, is an exquisitely evolved human pathogen and is well-equipped to infect its host and maintain itself throughout the infection cycle. The TB bacterium has the inherent metabolic flexibility to respond to different stages of infections and stressors from drugs or the human immune system. Focusing on the biochemical responses to TB infection, researchers in the CBTBR carry out big-picture analysis of the different components of a metabolic pathway and determine how they interact.

“We investigate metabolic pathways in *M. tuberculosis* which are relevant to TB drug discovery and drug resistance and collaborate with top research groups in the United States, the United Kingdom and South Africa. Our work is slow, technically demanding and requires specialised laboratory facilities. Ours is one of very few laboratories in South Africa undertaking this type of research,” says Professor Mizrahi.

“In a given population, 30% of those exposed to the TB bacillus will become infected; 10% of those will develop active disease while the remaining 90% enter into a state of latent TB infection which can reactivate many years after the initial infection. Nearly two billion people – and the majority of South Africans – have latent TB infection. We are exploring phenomena such as the nature of multi- and extensive drug resistance in *M. tuberculosis* to establish how this organism can acquire mutations that lead to drug resistance while retaining its ability to cause disease,” she explains.

As part of an ongoing study on mechanisms of DNA metabolism in *M. tuberculosis*, researchers in the MMRU have investigated the function of genes encoding subunits of ribonucleotide reductase (RNR), an enzyme which catalyses the first committed step in DNA replication by providing the building blocks required for DNA synthesis. In a paper published in the February 2009 issue of the *Journal of Bacteriology*, doctoral student Betty Mowa, together with Drs Digby Warner and Baves Kana and international collaborator Professor Gilla Kaplan from the Public Health Research Institute in the United States of America, identify a potential vulnerability in mycobacteria. The results of this study offer compelling evidence for a potential target for anti-tubercular drug discovery.

Internationally renowned for her work, Professor Mizrahi is the only South African researcher to be awarded an International Research Scholar’s grant from the prestigious Howard Hughes Medical Institute (HHMI), which she received in 2000 and again in 2005. She has also received the presidential Order of Mapungubwe (Silver), a Gold Medal from the South African Society for Biochemistry and Molecular Biology, and the Unesco-L’Oréal Women in Science Award for the Africa Region. Mizrahi chaired the 2007 Gordon Research Conference on Tuberculosis Drug Development, regarded by peers as the pinnacle of international TB research meetings.



The Centre has received grants from the HHMI, the Seattle Biomedical Research Institute and the Swiss / South Africa Bilateral Research Programme. Major grants from the National Research Foundation and the Medical Research Council ensure ongoing support for the basic research carried out in this laboratory and for the postgraduate students trained in the Centre.

Large grants awarded during 2008 and 2009

Swiss South African Joint Research Programmes grant

Professor Valerie Mizrahi and Dr Digby Warner
Molecular Mycobacteriology Research Unit, School of Pathology

Research Thrusts

The University has supported the formation of several research thrusts across various disciplines. A Research Thrust is a dynamic coalition of researchers, research teams and research entities, working in an area which the University Research Committee has acknowledged as having societal relevance and is multi-disciplinary in nature. A distinguished academic who feels passionately about the forceful advancement of research in the particular area, the 'Champion', draws together a number of senior academics, who work together to achieve a set of research objectives. Research Thrusts are intended to stimulate academic initiative, creative thinking and imaginative ways of addressing, organising and funding research in the broad area identified.

The Faculty of Health Sciences has been actively involved in the establishment of two Research Thrusts which were formally recognised by the University Research Committee and Senate in 2008. Members of the two thrusts work together to secure cross-cutting grants and to develop capacity in several areas of overlapping research activity.

Chronic Diseases of Lifestyle Research Thrust: An emerging African problem

The Chronic Diseases of Lifestyle Research Thrust is championed by **Professor Karen Sliwa (Soweto Cardiovascular Research Unit, School of Clinical Medicine)** and **Associate Professor Nigel Crowther (Department of Chemical Pathology, School of Pathology)**. 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 diseases.

The Thrust includes a number of senior researchers and clinicians, who have experience in a broad field of research areas and techniques, working in the fields of cardiovascular disease, diabetes and obesity. The wide range of expertise is vital to the ability of the Thrust to investigate all aspects of diseases of lifestyle in Africa and to broaden knowledge and provide appropriate research training and resources to new investigators.



The main goals of this Research Thrust are:

- to study the metabolic and genetic aetiology of cardiovascular disease, obesity and related disorders in African subjects;
- to provide efficient health service delivery to subjects with chronic diseases which can only be accomplished if more is known about the epidemiology of these diseases;
- to investigate disease epidemiology and delivery of health services in rural and urban areas;
- to increase public and government awareness of the severe impact of diseases of lifestyle on the health of the nation.

In 2009, Discovery Health and the Faculty of Health Sciences co-hosted a symposium which focused on the work of the Thrust. The symposium brought together 80 clinicians and researchers, providing an opportunity for potential collaborators to discuss current research findings and to develop new research projects. The Thrust then facilitated a hugely successful Chronic Diseases of Lifestyle Awareness Day, held at the Chris Hani Baragwanath Hospital. The purpose of the day was to create awareness amongst the public, patients and health professionals about the causes, treatment and prevention of chronic diseases of lifestyle.

Molecular Biosciences Research Thrust: Health for Africa

This Thrust is championed by **Professor Michèle Ramsay** (Division of Human Genetics / NHLS; Wits Bioinformatics) and **Professor Chrissie Rey** (School of Molecular Cell Biology in the Faculty of Science; Wits Bioinformatics).

The Thrust aims to stimulate research and other academic activities in the broad area of health-related molecular biosciences and to create a vibrant atmosphere in which students and scientists in the Faculties of Science and Health Sciences can realise their full research potential. A seminar series, a combined MSc degree by coursework and research report and research workshops aim to foster interdisciplinary research and collaboration. Groups of researchers and postgraduate students who share common research interests have the opportunity to identify suitable collaborators within the University and partner institutions, a hallmark of effective modern science. The research focus of the Thrust is encapsulated in the molecular understanding of common diseases and the health of sub-Saharan African populations. At present the primary element binding participants of the Thrust is the use of common technologies and equipment to address research questions. The vision of the Thrust is to foster clusters of researchers working on different aspects of the same theme. In this way bigger research questions can be tackled and more research funding can be leveraged for the successful completion of research projects.

Throughout 2008, one of the members of the thrust, **Professor Anna Kramvis**, organised several seminars on key topics in modern molecular bioscience. Notably, the series included a seminar entitled *Forward and Inverse Problems in Biology* presented by Nobel Laureate and Wits Faculty of Health Sciences graduate, **Dr Sydney Brenner**.

In 2009, a joint Wits/Arizona University genomics symposium entitled *Bioinformatics and genomic approaches for functional gene expression in vector-virus-host interactions* was held. The symposium highlighted current genomic, proteomic and bioinformatics approaches used to understand complex biological systems such as host-virus interactions, and served as a platform for the establishment of a number of long term research collaborations between Wits and Arizona scientists.

Sydney Brenner Institute for Molecular Bioscience

In 2009, Wits approved plans to develop the Sydney Brenner Institute for Molecular Bioscience (SBIMB). Dr Sydney Brenner, who started his research career at Wits, won the Nobel Prize for Physiology / Medicine in 2002. 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 Chronic Diseases of Lifestyle and Molecular Biosciences Research Thrusts. The SBIMB initiative has received the support of the Department of Health and the Medical Research Council.



Dr Sydney Brenner and Professor Emeritus Phillip Tobias



A world-class research environment for the study of non-communicable diseases in Africans

Focus on Research Resources

The Witwatersrand Health Sciences Library (WHSL)

Senior Librarian: Dr Glenda Myers

The Witwatersrand Medical Library (WML) was founded in 1926 by Professor Raymond Dart, a renowned anthropologist and onetime Dean of the Faculty, with a collection of 600 books. By 1958, the WML had outgrown its accommodation in the north east corner of the original Medical School building in Hospital Street. The Dean at the time, Professor Francois Daubenton, observed that "the continued growth of the library has been accomplished by a successive process of bursting through to adjacent rooms". In 1964 the library finally moved to new premises in the Esselen Street Medical School building. At that time accommodation was provided for 800,000 print volumes and 800 current print periodicals. The bust of Raymond Dart that now stands in the foyer of the current library, was commissioned originally to stand in the entrance to the library in Esselen Street, and was sculpted by the renowned plastic surgeon, Jack Penn.

The present library in York Road opened its doors in January 1983, when the Medical School moved to Parktown, adjacent to the Charlotte Maxeke Johannesburg Academic Hospital premises. In 1995 the name of the library was formally changed to the Witwatersrand Health Sciences Library (WHSL). The Library's perennial physical space problems were partially resolved by the initiative in 1999/2000 to introduce electronic resources wherever possible. At that time the e-journal collection comprised some thirty-odd titles. Today's e-journal collection for researchers and students stands at roughly 75% of the print collection, in the region of over 1,500 titles, making it the largest electronic journal collection in Africa.

The WHSL is currently staffed by a team of 15, including 8 professionally qualified librarians, who amongst them hold no fewer than 13 post-graduate qualifications from honours through to doctoral level, thus making a wide range of practical and theoretical research experience available to students and researchers in the Faculty. Although now in every sense a modern electronic library, the legacy and the memory of Raymond Dart still lives on through the library he founded over eight decades ago.



A bust of Professor Raymond Dart, which casts its thoughtful gaze across the library he established.



While the WHSL retains a strong sense of history, the commitment to increasing its online resources continues the tradition of it being a core asset to researchers in the Faculty.

Schools and Research Entities

The Faculty of Health Sciences has seven Schools, homes to independent researchers and research entities alike. The table lists the Schools and their respective research entities:

Anatomical Sciences
<ul style="list-style-type: none"> Embryonic Differentiation and Development Research Programme
Clinical Medicine
<ul style="list-style-type: none"> Bone Research Unit Birth to Twenty Research Programme Carbohydrate and Lipid Metabolism Research Unit Clinical HIV Research Unit Effective Care Research Unit Hepatitis Virus Diversity Research Programme Mineral Metabolism Research Unit Perinatal HIV Research Unit Pulmonary and Infectious Diseases Research Unit Reproductive Health and HIV Research Unit Soweto Cardiovascular Research Unit
Oral Health Sciences
<ul style="list-style-type: none"> No FRC/URC entities at present
Pathology
<ul style="list-style-type: none"> Antiviral Gene Therapy Research Unit Human Genomic Diversity and Disease Research Unit Malaria Entomology Research Unit Molecular Mycobacteriology Research Unit Respiratory Meningeal Pathogens Research Unit
Physiology
<ul style="list-style-type: none"> Brain Function Research Group Cardiovascular Pathophysiology and Genomics Research Unit
Public Health
<ul style="list-style-type: none"> Centre for Health Policy Research Unit Rural Public Health and Health Transitions Research Unit
Therapeutic Sciences
<ul style="list-style-type: none"> No FRC/URC entities at present

Research entities recognised by the Faculty and the University Research Committees are referred to as Units, Groups or Programmes.

Key to entity recognition:

FRC Recognised by the Faculty Research Committee

URC Recognised by the University Research Committee

MRC Co-sponsored by the SA Medical Research Council

School of Anatomical Sciences

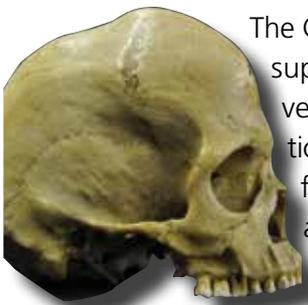
Head of School: Professor Joe Daly

The School of Anatomical Sciences houses three significant skeletal collections which attract researchers working on both human and animal material.

The **Raymond Dart Collection** was started in the early 1920s and houses a very large collection of human skeletons - 2,605 documented in all. The collection includes those ranging from neonates to centenarians, different populations represented by both sexes, as well as skeletons exhibiting a variety of pathologies. Researchers from across the globe draw on this remarkable assortment of individuals.

The **Hunterian Museum** contains an extensive collection of human and comparative anatomical specimens, an annotated and labelled display of X-rays, over 18,000 projection slides, embryological models, casts and specimens of congenital malformations, endocasts, charts and sketches. The **Middleton-Shaw Odontology Collection** and the **Comparative Collection** house over 1,500 recent animal skeletons.

The Comparative Collection specifically supports research in primatology, veterinary science, human evolution studies, comparative anatomy, forensic anthropology and neuro-anthropology.



Embryonic Differentiation and Development Research Programme

FRC

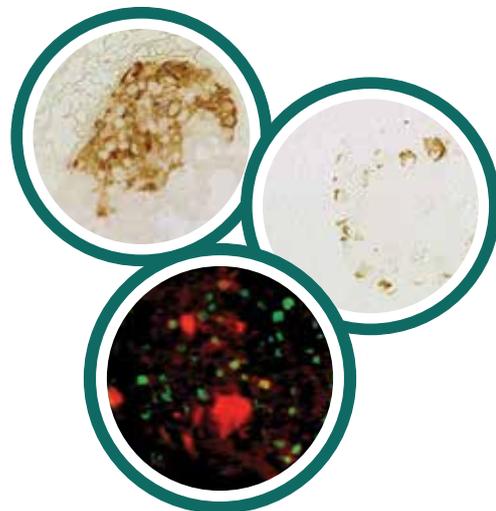
Programme Leader:
Professor Beverley Kramer

www.wits.ac.za/Health/AnatomicalSciences/Research/EDDRP

The aim of the Embryonic Differentiation and Development Research Programme (EDDRP) is to elucidate factors affecting embryonic development and early reproductive events.

Members of the team investigate many aspects relating to embryology. In 2008/2009, research highlights included:

- Results showing that in relation to insulin cells a number of factors affected their proportions. For example, both TGF- β_1 and high levels of glucose decreased the proportions of β -cells in the avian dorsal pancreatic bud *in vitro*.
- In a study on the development of teeth, members of the team generated teeth by combining embryonic stem cells with mouse molar ectomesenchyme, thus demonstrating that the stem cells were able to respond to cues from the ectomesenchyme.
- On the reproductive biology front, the hyperstimulation of pregnant animals with exogenous gonadotropins around the time of implantation effects the expression of vascular endothelial growth factor, cyclooxygenase 2 and transforming growth factors - β_1 and - β_2 . These effects may contribute to the disruption of the endometrial environment required for successful implantation.



References for selected papers:

- Marais A, Goven-Shiba P and Kramer B (2008). TGF- β_1 and high levels of glucose do not increase insulin cell proportions in the avian embryonic pancreas. *In Vitro Cellular and Developmental Biology*, 44: 41-43.
- Jovanovic A and Kramer B (2010). The effect of hyperstimulation on transforming growth factor β_1 and β_2 in the rat uterus: possible consequences for embryo implantation. *Fertility and Sterility*, 93: 1509-1517.

Focus on Individual Researchers

Stripping away the myths of animal behaviour by studying how their brains are wired is all in a day's work for **Associate Professor Paul Manger**, Reader in the School. He specialises in the evolution of the brain by examining the brains of different mammals to answer the question: 'As brains change in size, what changes and what stays the same?'

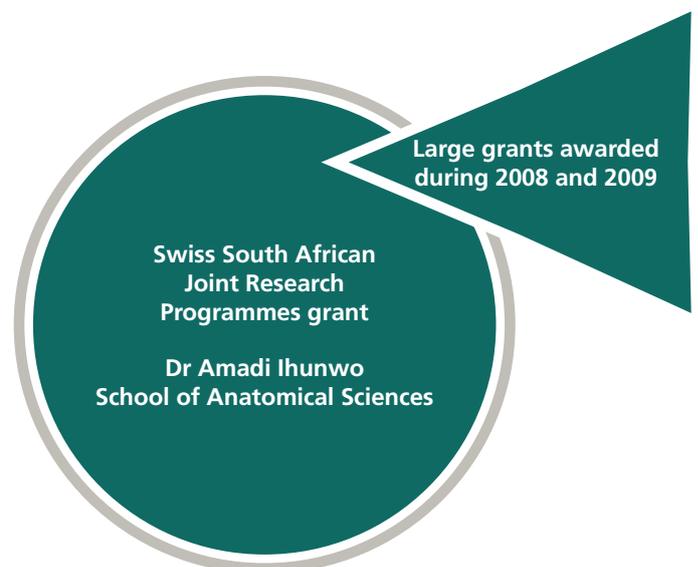
Understanding basic processes in the brains of different animals will lead to a greater understanding of how the human brain evolved. Africa is well placed for this type of research because of the rich diversity of animal species on the continent. South Africa alone has 85 species of rodent, allowing research on brains ranging in size from 100 milligrams to 35 grams to ascertain what changes occur as brain size increases.

The Comparative Adult Neurogenesis Research Group is led by **Dr Amadi Ihunwo**. He is the Principal Investigator under the prestigious Switzerland-South Africa Joint Research Programme, which enjoys research collaboration with researchers in the Division of Neuroanatomy and Brain Behaviour at the Institute of Anatomy, University of Zurich, Switzerland.

The Group's research is aimed at providing a database of active and potential neurogenic sites in adult mammalian brains including humans. The investigation focuses first on South African mammalian species for species-specific proliferation rate and time courses of adult hippocampal neurogenesis over the species' life histories. The ultimate goal of this comparative approach is to find a species in which the characteristics of hippocampal neurogenesis are similar to those observed in humans. Another aim is to describe parametrically the time course of neuronal proliferation and differentiation in the human hippocampus - from childhood to the mid-life stage.

Associate Professor Margot Hosie's interests lie in reproductive biology. Her major project concerns the effects of ovarian hormones and in particular, hormone-analogues (receptor modulators), especially those used in fertility or anti-fertility treatments on the uterus. Professor Hosie has enjoyed much success with both an animal model as well as human biopsy material. An extension of this work includes work on uterine cancer where the same receptor modulators are used in breast cancer treatment.

Another project considers the evolution of viviparity (live birth) and involves examining the uterus of Australian and South African lizards in which viviparity has evolved separately to determine how uterine epithelial cells in particular have altered in structure and function to accommodate the transition from egg-laying to live birth. This project involves detailed ultrastructural examination of uterine epithelial cells from species with differing modes of placentation and then comparison of these cells with those in mammals. Professor Hosie also conducts work on human embryonic stem cells, which so far has meant documenting the structure of the cell lines.



School of Clinical Medicine

Head of School: Professor Merryll Vorster

Bone Research Unit

FRC

URC

MRC

Director: Professor Ugo Ripamonti

www.wits.ac.za/Health/Research/BoneResearchUnit

The Bone Research Unit (BRU) is committed to creatively and scientifically gaining insight into the mechanisms of bone development and morphogenesis for the benefit of the people of South Africa. The Unit researches the design and biological activity of the spontaneous induction of bone formation. It strives to understand how newly-formed bone induction is initiated even if the specially designed, chemically primed matrices are implanted in extraskeletal sites. The role of the osteogenic transforming growth factor beta (TGF- β) supergene family in bone formation continues to be one of the themes explored by the team.

During 2008, in a ground-breaking study, a human growth factor (hTGF- β_3) was combined with a human bone-forming protein (hOP-1) and embedded in a biological scaffold. The scaffolds were then implanted into muscle tissue in baboons (*Papio ursinus*), resulting in the formation of substantial bony structures. These unique studies have paved the way for application in human subjects who have skeletal abnormalities, or who have lost bone. A massive mandibular defect in a juvenile patient was reconstructed using the binary synergistic application of hOP-1 and hTGF- β_3 loaded onto CSIR/MRC macroporous constructs. The procedure was carried out at the Chris Hani Baragwanath Hospital in Soweto (see photographs alongside).

Additional research achievements include periodontal tissue regeneration in *Papio ursinus* in which substantial regeneration of alveolar bone, cementum and periodontal ligament was shown after application of hTGF- β_3 in Matrigel biomatrix to Class II furcation defects.

The Unit will continue to strive to provide new information for the planning of therapeutic strategies



Juvenile patient with a large odontogenic tumour which resulted in a pronounced bony mandibular defect. Pre-op (top image) and post-op (bottom image).

to initiate and accelerate the induction of bone formation; restore local and systemic bone mass and to induce bone growth into prosthetic implants; identify novel bone inducing morphogens; develop synthetic self-inducing biomaterial matrices for bone tissue engineering in clinical contexts; and approach regenerative medicine tissue biology and therapeutic bone tissue engineering in molecular terms.

References for selected papers:

- Teare J, Ramoshebi L and Ripamonti U (2008). Periodontal tissue regeneration by recombinant human transforming growth factor- β_3 in *Papio ursinus*. *Journal of Periodontal Research*, 43: 1-8.
- Heliotis M, Ripamonti U, Ferretti C, Kerawala C, Mantalaris A and Tsiridis E (2009). The basic science of bone induction. *British Journal of Oral and Maxillofacial Surgery*, 47: 511-514.
- Ripamonti U and Petit J-C (2009). Bone morphogenetic proteins, cementogenesis, myoblastic stem cells and the induction of periodontal tissue regeneration. *Cytokine & Growth Factor Reviews*, 20: 489-499.

Carbohydrate and Lipid Metabolism Research Unit

FRC

URC

Director: Professor Derick Raal

www.wits.ac.za/Health/ClinicalMed/InternalMedicine/Research

The focus of the Carbohydrate and Lipid Metabolism Research Unit's research includes 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 and other dyslipidaemias, insulin resistance, diabetes mellitus as well as other related metabolic disorders.

Familial hypercholesterolaemia (FH) is one of the most commonly inherited genetic disorders in the world. A genetic mutation renders patients unable to remove low-density lipoprotein (bad cholesterol) from their bloodstream. As a consequence, cardiovascular disease often manifests at a far earlier age in these people than in individuals who do not have the mutation. The Unit is recognised both nationally and internationally for their work on FH and has one of the largest cohorts of homozygous FH patients in the world. Homozygous FH refers to a double mutation, where both copies of the gene are abnormal. This form of FH is less common than heterozygous FH but the symptoms are generally more severe than in heterozygous cases.

The Unit has contributed and continues to contribute to the management of patients with FH. Statins are one of the treatment options available to patients with FH. Pivotal high dose statin studies with simvastatin, atorvastatin and rosuvastatin performed in the Unit have confirmed the efficacy of high dose statin therapy in patients with familial hypercholesterolaemia. Although ideal low-density lipoprotein (LDL) cholesterol levels are not achieved with the use of high dose statins, evidence shows that cardiovascular morbidity and mortality is reduced and life expectancy prolonged. The Unit continues to conduct studies on novel therapies in this patient group.



The hand of a young girl with familial hypercholesterolaemia. The protrusions on her hand are deposits of cholesterol. Due to a genetic abnormality, her body is unable to remove low density lipoprotein from her bloodstream, leading to early-onset cardiovascular disease.

References for selected papers:

- Marais A, Raal F, Stein E, Radar D, Blasetto J, Palmer M and Wilpshaar W (2008). A dose-titration and comparative study of rosuvastatin and atorvastatin in patients with homozygous familial hypercholesterolaemia. *Atherosclerosis*, 197: 400-406.
- Ntyintyane L, Panz V, Raal F and Gill G (2008). Postprandial lipaemia, metabolic syndrome and LDL particle size in urbanized South African blacks with and without coronary artery disease. *Quarterly Journal of Medicine*, 101: 111-119.
- Raal FJ, Santos RD, Marais AD, Charng MJ, Cromwell W, Lachmann R, Gaudet D, Tan JL, Chasan-Tabar S, Tribble DL, Flaim JD and Crooke ST (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: 998-1006.

Clinical HIV Research Unit

FRC

URC

Director: Associate Professor Ian Sanne

www.chru.co.za

The Clinical HIV Research Unit (CHRU) based at Helen Joseph Hospital is a major contributor to the successful response to the HIV/AIDS pandemic in South Africa, the scale and size of which continues to be overwhelming. The CHRU was initiated in 1998 by Professor Ian Sanne, under the auspices of the Department of Internal Medicine and since its inception, the CHRU has grown to attract over R50 million in research funding per annum, with over 100 permanent staff members. Successful collaborations have been solidified with the National Health Laboratory Service, Boston University, the Wistar Institute and the University of North Carolina.

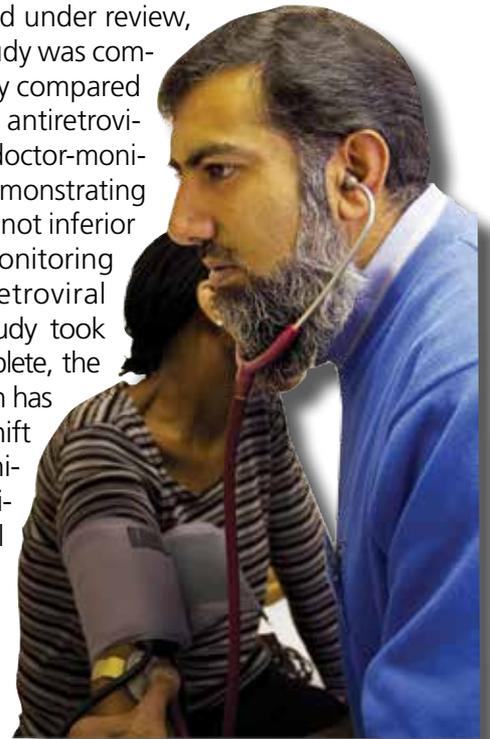
The CHRU provides groundbreaking research in the field of HIV to optimise antiretroviral therapy and treatment of opportunistic infections including tuberculosis (TB). The CHRU remains the leading enrolling site of the International AIDS Clinical Trials Group.

The implementation of TherapyEdge-HIV, a decision support clinical record system, in the Themba Lethu Clinic at Helen Joseph Hospital has been successfully expanded to over 40 sites, with a total of over 120,000 patient records. The database at Helen Joseph Hospital, known as the Themba Lethu Clinic Cohort (TLCC), has grown to over 24,000 patients and forms the basis for a growing research agenda in HIV and TB epidemiology, health systems research and health economics. In collaboration with the National Department of Health, the National Treasury and Finance and Boston University, the CHRU through the Health-Economics and Epidemiology Division conducted a review of the health cost economics of HIV treatment. This information was used to inform the five year budget for national HIV treatment, leading to a substantial increase in the national funding for HIV. In addition, clinical information from the database led to significant changes in the treatment guidelines for South Africa, recently announced by the South African President and the Minister of Health.

During the period under review, the CIPRA-ZA study was completed. This study compared nurse-monitored antiretroviral therapy with doctor-monitored therapy, demonstrating that nurses were not inferior to doctors in monitoring ongoing antiretroviral therapy. The study took five years to complete, the outcome of which has supported the shift towards nurse-initiated and -monitored antiretroviral therapy.

In collaboration with the Faculty's Department of Haematology and Molecular

Medicine, the CHRU has significantly contributed to the understanding of sub-type C HIV drug resistance, research which is considered to be world-leading, with a number of unique publications from the group. The evaluation of the database in the TLCC has also led to significant and original publications to define incident TB in patients on antiretroviral therapy, and related early mortality.



References for selected papers:

- Rosen S, Long L, Fox M, Sanne I (2008). Cost and cost-effectiveness of switching from stavudine to tenofovir in first-line antiretroviral regimens in South Africa. *Journal of Acquired Immune Deficiency Syndrome*, 48(3): 334-44.
- Firnhaber C, Vianna R, Reyneke A, Schultze D, Malope B, Maskew M, Di Bisceglie A, MacPhail P, Sanne I, and Kew M (2009). Occult hepatitis B virus infection in patients with isolated core antibody and HIV co-infection in an urban clinic in Johannesburg, South Africa. *International Journal of Infectious Diseases*, 13(4): 488-492.
- Westreich D, MacPhail P, Van Rie A, Malope-Kgokong B, Ive P, Rubel D, Boulme R, Eron J, and Sanne I (2009). Effect of pulmonary tuberculosis on mortality in patients receiving HAART. *AIDS*, 23(6): 707-715.

Effective Care Research Unit

FRC

URC

Director: Professor Justus Hofmeyr

The Effective Care Research Unit (ECRU), although a research unit within the Wits Faculty of Health Sciences, is located in the East London Hospital complex in the Eastern Cape. The Unit addresses important issues in maternal health in low-resource settings. The ECRU has been accredited as a WHO Collaborating Centre in Reproductive Health Research Synthesis. The Unit conducted the first ever randomised trials of misoprostol, a medication used to prevent and to treat postpartum haemorrhage and described a new technique for overcoming intractable shoulder dystocia (obstructed labour).

Other work includes contributions to global efforts to evaluate calcium supplementation to reduce the risk of pre-eclampsia (a condition in which the mother-to-be experiences high blood pressure and fluid retention). Members of the ECRU are conducting a large randomised trial comparing an intrauterine contraceptive device with depot progestogen contraception, to determine relative effects on unplanned pregnancy and HIV acquisition and progression.

One of the key contributions made by members of the ECRU is the maintenance of more than 50 Cochrane Reviews (a database of reviews and meta-analyses, which summarise and interpret the results of high-quality medical research). Recent Review themes include postpartum haemorrhage and caesarean section.



Professor Justus Hofmeyr

References for selected papers:

- Hofmeyr G and Gülmezoglu A (2008). Misoprostol for the prevention and treatment of postpartum haemorrhage. *Best Practice and Research Clinical Obstetrics and Gynaecology*, 22(6): 1025-41.
- Cluver C and Hofmeyr G (2009). Posterior axilla sling traction: A technique for intractable shoulder dystocia. *Obstetrics and Gynecology*, 113(2): 486-488.

Hepatitis Virus Diversity Research Programme



Programme Leader:
Associate Professor Anna Kramvis

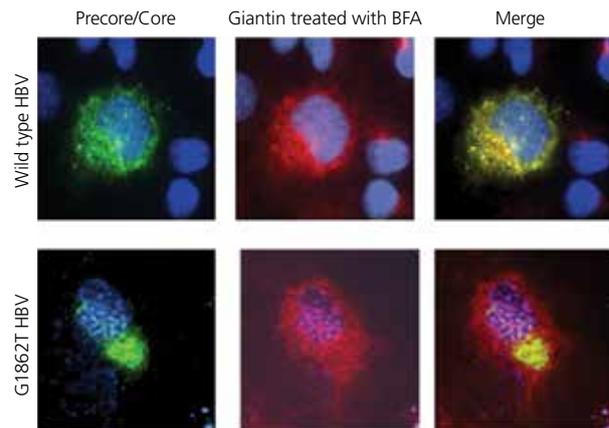
www.wits.ac.za/Health/ClinicalMed/InternationalMedicine/HVDRP

The Hepatitis Virus Diversity Research Programme (HVDRP) established in 2008, is a research entity within the Department of Internal Medicine. The Programme's dictum is, 'a compassionate team, creating knowledge, developing capacity' and its objective is the study of sequence variation of hepatitis viruses, in particular of Hepatitis B Virus (HBV), their functional characterisation, and their role in the clinical manifestation of liver disease.

In South Africa, HBV has a prevalence of 5% to 20%, with a correspondingly high incidence of hepatocellular carcinoma (HCC, commonly known as liver cancer). The predominant strain of HBV which infects South Africans, subgenotype A1, is different to strains found in other hyperendemic regions of the world. Southern African black carriers of the virus infected with this subgenotype are 4.5 times more likely to develop HCC than individuals infected with other genotypes of the virus. Distinctive sequence characteristics of subgenotype A1 which may contribute to the pathogenesis of HBV-induced HCC have been identified. Therefore, it is of paramount importance that this subgenotype, which is of direct relevance to South Africa and its people, is studied in depth.

Important findings made by the team in this area of research include the molecular and functional characterisation of subgenotype A1 and the comparison of the South African subgenotype A1 isolates to those circulating in other regions of the world including India and Brazil. The team has also constructed replication-competent clones of subgenotype A1 necessary for the study of this strain in tissue culture and animal models.

Researchers in the HVDRP have shown that apoptosis can be used as a marker of both HCC and chronic hepatitis independent of ethnicity, viral load and genotype. Using a transgenic animal model they demonstrated that infection with subgenotype A1 strains containing the G1862T (valine to phenylalanine) mutation result in higher apoptotic activity in the animal model, results



A photomicrograph showing that a single mutation (G1862T) in Hepatitis B Virus can change the expression of viral proteins. Compare the bottom and top panels, where liver cells have been exposed to virus with and without the mutation, respectively.

[Chien Yu Chen, PhD student]

which are comparable to what had been shown in tissue culture.

It has become increasingly evident that any discussion of HBV infection in Africa must take into account the HIV pandemic scourging the continent. No comprehensive data are available on the number of individuals infected with both HBV and HIV in South Africa because of the lack of systematic surveillance, underreporting, and the lack of resources. The HVDRP has initiated research into HBV-HIV co-infection in both urban and rural cohorts and has successfully established a rural cohort in Shongwe, Mpumalanga. Three-hundred baseline, treatment-naïve participants have been recruited and are being followed up after the initiation of antiretroviral treatment. A comprehensive database of these participants has been established and 24% have been shown to be co-infected with HBV and HIV.

References for selected papers:

- Kramvis A, Arakawa K, Yu M, Stram D, Kew M (2008). Relationship of subtype, basic core promoter and precore mutations to genotypes/subgenotypes of hepatitis B virus. *Journal of Medical Virology*, 80: 27 – 46.
- Chen C, Crowther C, Kew M, Kramvis A (2008). A valine to phenylalanine mutation in the precore region of hepatitis B virus causes intracellular retention and impaired secretion of HBe-antigen. *Hepatology Research*, 38: 580 – 592.

Mineral Metabolism Research Unit

FRC

URC

MRC

Directors: Professor John Pettifor and Associate Professor Shane Norris

www.wits.ac.za/Health/ClinicalMed/Paediiatrics/Research

The Mineral Metabolism Research Unit was established 25 years ago within the Department of Paediatrics at the Chris Hani Baragwanath Hospital to study metabolic bone diseases of relevance to the population of South Africa and to Africa in general. The areas of interest have been focused in particular on the role of low dietary calcium intakes in the pathogenesis of rickets in developing countries and the factors influencing bone mass accrual and development during adolescence.

In recent years, members of the research team have demonstrated that children with active rickets in Nigeria in whom dietary calcium deficiency is believed to play a major role, have elevated concentrations of the active form of vitamin D, which is an attempt by the body to optimise dietary calcium absorption from the gastrointestinal tract. These results contrast strongly with those found in pure vitamin D deficiency, in which dietary calcium absorption is impaired because of the lack of vitamin D. These results indicate that rickets due to dietary calcium lack can be differentiated from that due to vitamin D deficiency by the ability of the gastrointestinal tract to absorb calcium. The team believes the response to a bolus of vitamin D also suggests that low dietary calcium intakes might increase vitamin D requirements in growing children. Collaborators on these studies include researchers from Jos, Nigeria and the Mayo Clinic.

The team has been involved in the Birth to Twenty longitudinal cohort study since its inception in 1990. Over 3,000 children born during a six-week period in the greater Johannesburg region have been followed up annually and are now in their 20th year. Several findings have emerged from an intensive study of the factors influencing development and bone accretion during adolescence in a sub-cohort of this group (approximately 450 children):

- Bone fracture rates in black children are approximately half those of white children. This finding is in line with previous studies which have reported much lower hip fracture rates in adult South African blacks compared to their white peers. The lower fracture rates in black children occur despite poorer nutrition and growth compared to their white counterparts. Possible reasons for the difference in fracture rates are currently being investigated.
- Mean menarcheal age (onset of first menstruation) has fallen markedly over the past 50 years in black girls and is now similar to that of white girls. This probably reflects general improvements in health and nutrition in South Africa. However, black boys still lag behind their white peers as far as skeletal development during puberty is concerned.
- Physical activity is thought to be important during the peri-pubertal period to optimise bone accretion and therefore peak bone mass, once the children reach young adulthood. Studies conducted in the Unit have documented the lack of formal physical activity in schools in townships and other disadvantaged areas. Despite this and the poorer growth and nutritional status of children from the townships, bone mass at the hip in particular is higher in black than white children. Similar racial differences in bone mass at the hip are found in adult South Africans. These findings suggest that genetic differences may play a role in determining the structure and bone mass of the femoral neck.



The wrist of a child with dietary calcium deficiency rickets. The picture to the left shows the untreated child. The picture to the right shows the same wrist several months later on healing of the bone disease through dietary calcium supplementation.

References for selected papers:

- Jones L, Griffiths P, Norris S, Pettifor J and Cameron N (2009). Age at menarche and the evidence for a positive secular trend in urban South Africa. *American Journal of Human Biology*, 21: 130-132
- McVeigh J, Norris S and Pettifor J (2007). Bone mass accretion rates in pre- and early-pubertal South African black and white children in relation to habitual physical activity and dietary calcium intakes. *Acta Paediatrica*, 96: 874-880
- Micklesfield L, Norris S, van der Merwe L, Lambert E, Beck T and Pettifor J (2009). Comparison of site-specific bone mass indices in South African children of different ethnic groups. *Calcified Tissue International*, 85: 317-325.

Perinatal HIV Research Unit

FRC

URC

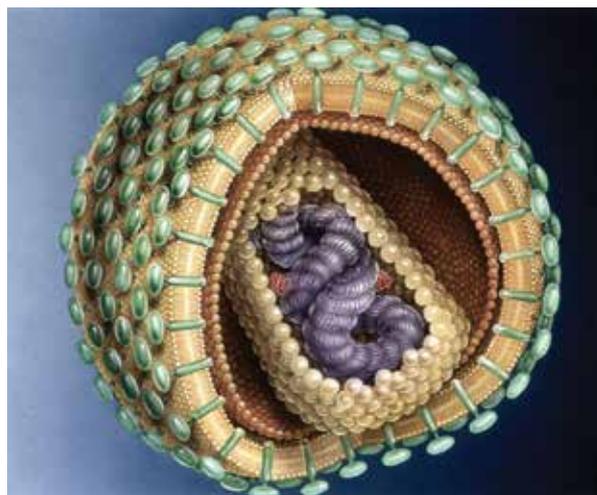
Director: Associate Professor Glenda Gray

www.phru.co.za

The Perinatal HIV Research Unit (PHRU), established in 1996 by Drs Glenda Gray and James McIntyre, is a leading AIDS research centre in Africa. The PHRU is based at the Chris Hani Baragwanath Hospital in Soweto. The Unit focuses on innovative strategies for HIV prevention and for enhancing the care of HIV infected adults and children. Established initially to study interventions to prevent mother to child transmission, the PHRU has expanded its portfolio in response to the evolving HIV epidemic in South Africa and now conducts research into TB, other opportunistic infections and sexually transmitted infections: herpes simplex virus (HSV) and human papillomavirus (HPV). The research of the Unit spans the spectrum of basic science research to socio-behavioural and ethnographic research. Furthermore, members of the Unit aim to be agents of influence with regards to HIV policy in South Africa. The Unit enjoys extensive collaborative partnerships both locally and abroad.

The PHRU has been at the forefront of HIV vaccine research, with Associate Professor Gray leading the first phase IIB vaccine efficacy study in Africa and the clinical development of South Africa's first two HIV vaccine candidates. The results of the interim efficacy analysis were presented in a plenary session at the AIDS Vaccine Conference in Paris in 2009.

The PHRU has also made significant contributions to the management of HIV in children. A study led by Dr Auye Violari, published in the *New England Journal of Medicine*, conclusively showed that HIV-infected infants who received antiretrovirals early in life, were more likely to survive as compared to infants who received standard care. This finding has changed guidelines both nationally and internationally.



The Unit's research in the field of prevention of mother to child transmission (PMTCT) has contributed to preventing HIV resistance and the improved care of women and infants in resource poor settings. Members of the Unit have shown that the addition of a short course of two anti-retroviral agents virtually eradicated HIV resistance after nevirapine. Further studies involve ways of preventing TB in HIV infected individuals and published results on this have impacted on policy both locally and internationally. Moreover, members of the Unit have reported on the deleterious role of smoking and low body mass index on the incidence of TB in HIV-infected adults and a study is underway to investigate the impact of visiting household contacts of TB patients in Klerksdorp, testing for HIV and TB, and rapid onset of anti-retroviral therapy.

References for selected papers:

- Violari A, Cotton M, Gibb D, Babiker A, Steyn J, Madhi S, Jean-Philippe P, McIntyre J and the CHER Study Team (2008). Early antiretroviral therapy and mortality among HIV-infected infants. *New England Journal of Medicine*, 359 (21): 2233-44.
- Martinson N, Morris L, Johnson J, Gray G, Pillay V, Ledwaba J, Dhlamini P, Cohen S, Puren A, Steyn J, Heneine W and McIntyre J (2009). Women exposed to single-dose nevirapine in successive pregnancies: effectiveness and nonnucleoside reverse transcriptase inhibitor resistance. *AIDS*, 23(7): 809-16.
- McIntyre J, Hopley M, Moodley D, Eklund M, Gray G, Hall D, Robinson P, Mayers D and Martinson N (2009). Efficacy of short-course AZT plus 3TC to reduce nevirapine resistance in the prevention of mother-to-child HIV transmission: a randomized clinical trial. *PLoS Medicine*, 6 (10): e1000172.

Pulmonary Infectious Diseases 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, due to a small shift in the Unit's research direction. The Unit's main research interest is in the field of pulmonary infections, and in particular community-acquired pneumonia. In addition to clinical studies, investigations to understand the interaction between bacteria (the pneumococcus in particular), the human host and antibiotics, have been undertaken. Initial studies focused on the interaction of bacteria and antibiotics within the human host, including in human ciliated respiratory epithelium, whereas more recent studies focused on the interaction of antibiotics with the bacteria. The pneumococcus is by far the most common cause of community-acquired pneumonia worldwide and hence it has been the primary target of the Unit's research.

Much of the Unit's research is conducted in collaboration with local and international colleagues. The basic science research studies are undertaken jointly by the Department of Immunology at the University of Pretoria, and the clinical studies together with different groups of investigators throughout the world, coordinated and lead by researchers in the USA.

Among important clinical studies conducted during the past few years have been investigations of the occurrence of community-acquired pneumonia in the setting of HIV infection. Included in this research have been studies investigating the impact of HIV infection on the outcome of patients with community-acquired pneumonia of either all-cause, or specifically pneumococcal in nature. These studies have clearly indicated, in contrast to previous studies, that HIV infection itself is associated with higher mortality in patients with pneumococcal pneumonia. A study in patients

with pneumococcal community-acquired pneumonia was among the first to evaluate the efficacy of severity of illness scores in their ability to determine which patients should be admitted to ICU.

Among the basic science studies have been ongoing investigations into the activity of pneumolysin, considered by many to be the most important virulence factor of the pneumococcus, as well as other virulence factors of the pneumococcus.



References for selected papers:

- Feldman C, Alanee S, Yu V, Richards G, Ortqvist A, Rello J, Chiou C, Chedid M, Wagener M, Klugman K and the International Pneumococcal Study Group (2009). Severity of illness scores in patients with bacteremic pneumococcal pneumonia: implications for ICU care. *Clinical Microbiology and Infection*, 15: 850-857.
- Cockeran R, Mitchell T, Feldman C and Anderson R (2009). Pneumolysin induces release of matrix metalloproteinases -8 and -9 from human neutrophils. *European Respiratory Journal*, 34: 1167-1170.
- Malinis M, Myers J, Bordon J, Peyrani P, Kapoor R, Nakamatzu R, Lopardo G, Torres A, Feldman C, Allen M, Arnold F and Ramirez J (2010). Clinical outcomes of HIV-infected patients hospitalized with bacterial community-acquired pneumonia. *International Journal of Infectious Diseases*, 14(1): e22-7.

Reproductive Health and HIV Research Unit

FRC

URC

Director: Associate Professor Helen Rees

www.rhru.co.za

The Reproductive Health and HIV Research Unit (RHRU) was established in 1994. It has since grown into an organisation that employs more than 400 people in four provinces: Gauteng, Limpopo, KwaZulu-Natal and the North West. The RHRU produces groundbreaking research on a variety of topics related to reproductive health, sexual health and related infectious diseases.

Building on its research foundation, the RHRU is actively involved in community programmes in Hillbrow, Johannesburg, and the roll-out of HIV treatment in public health facilities. The RHRU plays a major role in the Hillbrow Health Precinct – a world first project creating health facilities to stimulate urban regeneration.

The RHRU also plays a part in large multi-centred clinical trials. In 2009, the organisation completed the largest clinical trial to date into a microbicide gel designed to prevent HIV infections. The gel was shown to not have an effect on HIV infection rates. However, the trial leaves a strong legacy. Research centre staff have gained experience and training in conducting clinical trials to the highest international standards. The trial also helped many women to discuss HIV prevention with their partners.

The RHRU has also conducted research on the female condom and contraception. The USA's Food and Drug Administration used the Unit's research to register the FC2 female condom. The researchers also studied the effect on bone mineral density in young women aged 19-24 after 4-5 years of exclusive and mixed hormonal contraception.



HIV/AIDS accounts for more than one-third of non-obstetric maternal and neonatal deaths. The RHRU has studied the impact of HIV treatment on maternal mortality, a result of its goal of working to save the lives of mothers and children. In South Africa, RHRU treats over 80,000 patients living with HIV and the Unit's research has shown that the use of antiretrovirals by women during pregnancy is safe and effective and that immune reconstitution inflammatory syndrome is common, but mortality is low.

References for selected papers:

- Beksinska M, Kleinschmidt I, Smit J, Farley T and Rees H (2009). Bone mineral density in young women aged 19-24 after 4-5 years of exclusive and mixed use of hormonal contraception. *Contraception*, 80(8): 128-32.
- Scorgie, F, Kunene B, Smit J, Manzini N, Chersich M, Preston-Whyte E (2009). In search of sexual pleasure and fidelity: vaginal practices in KwaZulu Natal, South Africa. *Culture, Health and Sexuality*, 11(3): 267-283.

Soweto Cardiovascular Research Unit

FRC

URC

Director: Professor Karen Sliwa

www.socru.org

The Soweto Cardiovascular Research Unit (SOCRU) was established in 2006 in order to coordinate research and promote research collaboration into cardiovascular diseases commonly observed in sub-Saharan Africa. The Unit partners with the Department of Cardiology at Chris Hani Baragwanath Hospital. Key areas of research include peripartum cardiomyopathy, acute coronary syndrome in HIV-positive and HIV-negative patients, idiopathic dilated cardiomyopathy and management of heart failure, and hypertension. The SOCRU researchers have also partnered with researchers at the University of Cape Town, as well as researchers in Canada (McMaster University) and Australia (University of Queensland; Baker Institute), amongst others.

SOCRU has two major research projects at present:

The peripartum cardiomyopathy (PPCM) project is a large, ongoing project investigating the pathogenesis, etiology, epidemiology and management of this condition which is common in African women. This research has resulted in numerous prestigious publications and has included a collaborative effort between the Unit and the University of Hannover (Germany) and Emory University (USA).

The team has found that dysfunctional prolactin causes activation of pro-apoptotic signalling pathways in the heart, leading to left ventricular dilatation and heart failure. In a randomised study of newly-diagnosed patients, the team investigated the effect on PPCM of bromocryptine, which inhibits prolactin.

The Heart of Soweto study is a collaborative project that examines the emergence of heartdisease in Soweto and other African communities in epidemiological transition. Since January 2006, a prospective registry of more than 9,000 men and women from Soweto presenting to the Chris Hani Baragwanath Hospital with heartdisease has been compiled. Information on 8,000 patients have been documented to date. Several intervention trials have been initiated and published.



Large grants awarded during 2008 and 2009

Medtronic Foundation Award

Professor Karen Sliwa
Soweto Cardiovascular
Research Unit,
School of Clinical Medicine

References for selected papers:

- Sliwa K, Wilkinson D, Hansen C, Ntyintyane L, Tibazarwa K, Becker A and Stewart S (2008). Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): a cohort study. *Lancet*, 371(9616): 915 – 922.
- Tibazarwa K, Ntyintyane L, Sliwa K, Gerntholtz T, Carrington M, Wilkinson D and Stewart S (2009). A time bomb of cardiovascular risk factors in South Africa: Results from the Heart of Soweto Study "Heart Awareness Days". *International Journal of Cardiology*, 132(2): 233 – 239.
- Stewart S and Sliwa K (2009). Preventing CVD in resource-poor areas: perspectives from the 'real world'. *Nature Reviews Cardiology*, 6: 489-492.

School of Oral Health Sciences

Head of School: Professor Abdool Essop



The School of Oral Health Sciences is home to a number of Departments. Researchers in the **Department of Prosthodontics** have focused their efforts on developing cost-effective techniques and materials for use in dental and maxillo-facial prosthetics so that patients can receive optimum treatment in the fewest number of visits. One project aimed to reduce the number of visits for the fitting of a complete set of dentures to four, and has involved collaboration with researchers at the University of British Columbia (Canada), and the University of Thammasat (Thailand).

The ultimate goal of making recommendations to the National Health Department on an appropriate maxillo-facial prosthetics service for the country is the driving force behind another project which has aimed to determine how many patients require and receive rehabilitation after the surgical removal of tissue. The team conducted clinical trials on the handling characteristics of new dental materials and recently tested a new formulation for a cost-effective palliative mouth rinse for patients

receiving irradiation therapy, as well as a new slow-release formulation of chlorine dioxide as a disinfectant for impression materials.

The testing of cost-effective implant-supported prostheses is another research focus; the team has worked on a virtual impression technique using digital photography and 3D modelling software to optimise the precision of the fit of maxillo-facial prostheses. Lastly, a firm belief in the need to train the next generation of dentists motivates the team to improve dental education by researching and developing the use of interactive electronic learning materials, as well as tools for assessing students' clinical performance.

Academically, the **Division of Oral Pathology** is located within the School of Pathology but functions as a vital part of both the Schools of Pathology and Oral Health Sciences. The team's research thrust continues to be based on clinico-pathological studies which have led to the description of several new entities, or variants of existing ones, and to the identification of possible aetiological agents. The team has elucidated the pathogenesis of some of these entities, and has proposed or contributed to the development of new classifications of oral diseases, some of which have been adopted internationally.



Regarding odontogenic tumours and cysts, the Division participated in an international collaborative study on "ghost cell odontogenic tumours". The aim of this collaboration was to propose an objective, comprehensive and useful classification based on the 2005 World Health Organisation guidelines. It is hoped that this classification will provide some clarity in an area previously marred by confusion, thus increasing diagnostic accuracy. The team also addressed the question of metaplastic mineralisation versus tissue induction in adenomatoid odontogenic tumours (AOTs).

In 2008 and 2009, the Division also offered a biopsy service. Observing an increasing number of AIDS-defining lesions in the oral cavity of patients, members of the Division initiated an international collaborative study which aims to define the characteristics of oral plasmablastic lymphomas, and to address questions pertaining to the cause and diagnosis of this form of non-Hodgkin's lymphoma.

The **Division of Experimental Odontology** has had a long and illustrious research history and has been synonymous with the Wits Dental Research Institute until the latter's closure in 2008. The Institute was formed in 1954 through a partnership between the University and the Council for Scientific and Industrial Research (CSIR). To date, research output consists of 702 peer-reviewed publications, 31 other publications (books, book chapters and editorials), as well as 116 higher degrees. Joint research and supervision is undertaken in partnership with other university departments locally and abroad.



Professor Elly Grossman

Over the past two years, the Division examined its past training and research output and important insights into postgraduate and research training emerged. During the academic training and careers of 131 dental research postgraduates (1954-2007) there was an 87% throughput rate for the group consisting of 18 PhDs, 55 MScs, and 42 MDents. Seventy five percent of postgraduates published their research (total of 164 publications) while 50% presented their work at conferences. Most (48%) went into exclusive private practice with 30% having academic links. Over the 53 years included in the study the 131 postgraduates published a total of 2,287 peer-reviewed publications. It is mainly the PhD subset who publish, have the longest research careers (29.1 years), and participate in academic teaching. Most of the postgraduates (63%) have remained in South Africa but emigration is high among the PhD and MSc groups.

Selected publications in these areas of focus:

- Grossman E and Cleaton Jones P (2008). What becomes of dental research trainees once they leave the Dental Research Institute? An analysis over 53 years. *European Journal of Dental Education*, 12: 69- 74.
- Osswald M and Owen C (2008). Fracture resistance of acrylic resin and metal-reinforced acrylic resin distal extension cantilevers of fixed implant-supported prostheses. *International Journal of Prosthodontics*, 21: 413 - 414.
- Ledesma-Montes C, Gorlin R J, Shear M, Praetorius F, Taylor A, Altini M, Unni K, Paes de Almeida O, Carlos-Bregni R, de León E, Phillips V, Delgado-Azañero W and Meneses-García A (2008). International collaborative study on ghost cell odontogenic tumours: calcifying cystic odontogenic tumour, dentinogenic ghost cell tumour and ghost cell odontogenic carcinoma. *Journal of Oral Pathology and Medicine*, 37: 302-308.
- Jivan V, Altini M and Meer S (2008). Secretory cells in adenomatoid tumour: tissue induction or metaplastic mineralization? *Oral Diseases*, 14: 445-449.

School of Pathology

Head of School: Professor Ahmed Wadee

Antiviral Gene Therapy Research Unit

FRC

URC

Director: Associate Professor Patrick Arbuthnot

[www.wits.ac.za/Health/Pathology/
Haematology/ResearchAnalytical/AGTRU](http://www.wits.ac.za/Health/Pathology/Haematology/ResearchAnalytical/AGTRU)

Discovery of the RNA interference (RNAi) pathway has led to considerable enthusiasm for advancing gene therapy for viral infections. Importantly, viruses which cause serious human disease in South Africa, e.g. hepatitis B virus (HBV) and human immunodeficiency virus type 1 (HIV-1), have been shown to be susceptible to silencing by activating RNAi. The major focus area of the Antiviral Gene Therapy Research Unit (AGTRU) is to employ gene silencing technology to develop improved treatment of these important viral infections.

Persistent infection with Hepatitis B Virus (HBV) is a major global public health problem. It is estimated that there are 350 million carriers of the virus and the infection is hyperendemic to sub-Saharan Africa and parts of Asia. Available treatment for HBV infection has variable efficacy and there is a need to develop better therapies to prevent life-threatening complications associated with chronic HBV infection. Research from the AGTRU has demonstrated the feasibility of RNA interference-based therapy and research is currently aimed at developing this technology for clinical application.

Several antiretroviral drugs are available for HIV treatment but toxicity and treatment failure makes it important to develop new therapies. As with HBV, harnessing the RNAi pathway to silence HIV gene expression and counter replication of the virus offers exciting new possibilities. To overcome problems of viral escape from gene silencing, research in the AGTRU is aimed at silencing multiple HIV-1 targets simultaneously and also inhibiting host factors that are essential for HIV replication. This therapeutic rationale has been extended



to counter Rift Valley Fever Virus, which is responsible for causing severe hepatitis, encephalitis and associated haemorrhagic fever.

Research highlights in 2008 and 2009 include the publication of several findings which demonstrated 'proof of concept' that RNAi may be harnessed for treatment of HBV and HIV-1 infection. A major component of the research was participation in the research activities of the RNA Interference Technology for Human Treatment (RIGHT) Consortium, which was supported by the European Commission Framework 6 Programme. Participation in this activity enabled the establishment of valuable strategic research partnerships with top European laboratories in the field.

References for selected papers:

- Saayman S, Barichievy S, Capovilla A, Morris K, Arbuthnot P and Weinberg M (2008). The efficacy of generating three independent anti-HIV-1 siRNAs from a single U6 RNA Pol III-expressed long hairpin RNA. *PLOS One*, 3(7): e2602.
- Crowther C, Ely A, Hornby J, Mufamadi S, Salazar F, Marion P and Arbuthnot P (2008). Efficient inhibition of hepatitis B virus replication in vivo using PEG-modified adenovirus vectors. *Human Gene Therapy*, 19: 1325-1331.
- Ely A, Naidoo T and Arbuthnot P (2009). Efficient silencing of gene expression with modular trimeric Pol II expression cassettes comprising micro RNA shuttles. *Nucleic Acids Research*, 37. doi: 10.1093/nar/gkp446.

Human Genomic Diversity and Disease Research Unit

FRC

URC

MRC

Director: Associate Professor Himla Soodyall

www.wits.ac.za/Health/Pathology/HumanGenetics/ResearchGroups/HumanGenomicDiversityAndDiseaseResearchUnit

The Human Genomic Diversity and Disease Research Unit's research activities in the field of human molecular evolutionary genetics/molecular anthropology, coupled with the service it provides to the public for ancestry testing, has shown once again the value of translating science to the public. Professor Soodyall was a sought-after speaker for both local and international meetings to celebrate the 200th birthday of Charles Darwin, where she discussed her research on the peopling of Africa and how genetic studies have contributed to our understanding of human origins.

The Genographic Project, funded by the National Geographic Society, has given the Unit an opportunity to extend the project into remote regions of South Africa as well as other regions of sub-Saharan Africa, with mitochondrial DNA (mtDNA) and Y chromosome DNA genotyping now being completed on over 4,500 individuals. The team has also given back individual results to all subjects who were sampled since 2005, thereby encouraging dialogue with participants about science and heritage. The Unit has successfully introduced new methods for mtDNA and Y chromosome genotyping which are specific for resolving the lineages commonly found in Africa. A comic strip overview of their research and reports for genetic ancestry testing has been produced by the Unit and this has been translated into Afrikaans, isiZulu and isiXhosa in collaboration with JiveMedia.

A recent publication in this area of focus:

- Schlebusch C, Naidoo T and Soodyall H (2009). SNaPshot minisequencing to resolve mitochondrial macro-haplogroups found in Africa. *Electrophoresis*, 30: 3657 – 3664.



Professor Himla Soodyall in the Kalahari, returning to members of the Ashkam San community to convey their genotype results

Molecular Mycobacteriology Research Unit

FRC

URC

MRC

Director: Professor Valerie Mizrahi

The Molecular Mycobacteriology Research Unit constitutes the Wits node of the DST/NRF Centre of Excellence for Biomedical TB Research (see feature on page 19).

Large grants awarded during 2008 and 2009

NRF National Nanotechnology Flagship Programme grant

Professor Patrick Arbuthnot
Antiviral Gene Therapy
Research Unit,
School of Pathology

Malaria Entomology Research Unit

FRC

URC

Director: Professor Maureen Coetzee

Malaria is the major vector-borne disease in Africa, killing close to one million people annually, most of them children under five. Research on the vectors, however, has been limited compared with other fields, prompting the University to support the establishment of the Malaria Entomology Research Unit (MERU). MERU is the synthesis of expertise based in the Vector Control Reference Unit (VCRU), the National Institute for Communicable Diseases (of the National Health Laboratory Service) and the DST/NRF Research Chair in Medical Entomology and Vector Control. The main research focus is on the anopheline mosquitoes responsible for malaria transmission in Africa. The Unit houses a valuable collection of live mosquito colonies of the three most important vector species in Africa, *An. gambiae*, *An. arabiensis* and *An. funestus*. Three colonies of *An. funestus* from Mozambique and Angola continue to provide the team with a unique resource for research into insecticide resistance in this important malaria vector. This, and the Unit's experience in malaria control in many parts of Africa, places MERU in a unique position 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. Research highlights in 2008/2009 included:

- The description of a new species of mosquito from northern Malawi, closely related to the major African malaria vector *Anopheles funestus*. This new species is morphologically identical to the vector but differs from it significantly at the chromosomal and DNA levels. It was found resting inside houses in Malawi but at this stage there is no evidence of it being involved in malaria transmission, nor is the distribution of the species known.
- Demonstration that fungal infection in mosquitoes counteracts insecticide resistance. The Unit's insectaries contain insecticide resistant strains of the three major African malaria vectors mentioned above and these were used



A mosquito infected with entomopathogenic fungi
[J Mouatcho, MERU]

for fungal experiments. The team demonstrated that if insecticide-resistant strains were first exposed to entomopathogenic fungi and then subsequently exposed to the insecticides to which they were resistant, the mortality was dramatically increased.

- Evidence that two duplicated P450 genes were associated with pyrethroid resistance in *Anopheles funestus*. Using positional cloning and quantitative trait loci approaches, single nucleotide polymorphisms were identified that could be used as markers for insecticide resistance in this important vector mosquito. Identification of markers that can be easily used for detecting resistance in wild mosquito populations has obvious advantages for malaria control programmes in Africa.

References for selected papers:

- Spillings B, Brooke B, Koekemoer L, Chipwanya J, Coetzee M and Hunt R (2009). A new species concealed by *Anopheles funestus* Giles, a major malaria vector in Africa. *American Journal of Tropical Medicine & Hygiene*, 81:510–515.
- Farenhorst M, Mouatcho J, Kikankie C, Brooke B, Koekemoer L, Hunt R, Thomas M, Knols B and Coetzee M (2009). Fungal infection counters insecticide resistance in African malaria mosquitoes. *Proceedings of the National Academy of Science*, 106:17443-17447.
- Wondji C, Irving H, Morgan J, Lobo N, Collins F, Hunt R, Coetzee M, Hemingway J and Ranson H (2009). Two duplicated P450 genes are associated with pyrethroid resistance in *Anopheles funestus*, a major malaria vector. *Genome Research*, 19:452-459.

Respiratory Meningeal Pathogens Research Unit

FRC

URC

MRC

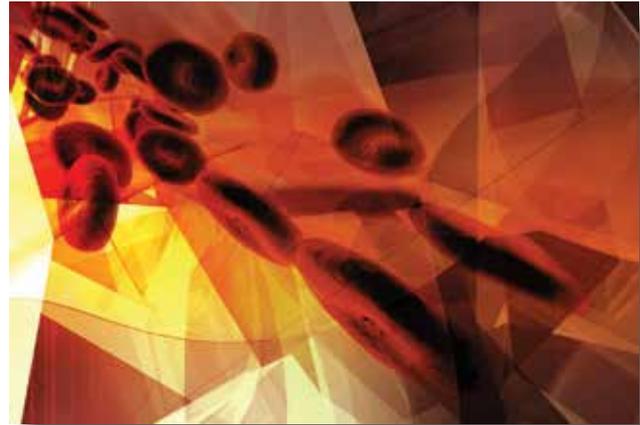
Directors: Professor Keith Klugman and Associate Professor Shabir Madhi

www.mrc.ac.za/pneumococcal

Pneumonia is the leading cause of death preventable by a vaccine. The Respiratory and Meningeal Pathogens Research Unit (RMPRU) is an internationally recognised research Unit involved in basic science and clinical research. Additionally, collaborators in the National Institute for Communicable Diseases conduct national laboratory-based surveillance for invasive disease due to *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. The focus of the Unit's research activities is the prevention and management of diseases caused by respiratory and meningeal pathogens that cause significant morbidity and mortality worldwide. The organisms are also the leading cause of death in children in African countries.

The results of a pivotal trial involving 8,011 women were published in the *Lancet* by members of the research Unit. The results highlighted the high burden of neonatal sepsis in settings with a high prevalence of HIV and which provided insight into the efficacy of intrapartum genital-tract chlorhexidine wipes in reducing the early onset of neonatal sepsis and the transmission of group B streptococcus.

Additional highlights include the publication of results from a phase III rotavirus vaccine efficacy trial which was published in the *New England Journal of Medicine*. This study is the first to demonstrate the efficacy of the rotavirus vaccine in an African setting. The positive findings from this study were instrumental in the World Health Organisation recommendation for the inclusion of the rotavirus vaccine into childhood immunisation programmes. It is anticipated that introduction of the vaccine and will reduce mortalities resulting from diarrhoea, the second leading cause of death in Africa and globally, by 30-40%.



The research efforts of the Unit have influenced the South African government's decision to introduce pneumococcal conjugate vaccine and rotavirus vaccine into its public immunisation programme (a first in Africa). The introduction of these vaccines will be of greatest benefit to those with limited access to curative healthcare services and is predicted to reduce childhood mortality in children under the age of five years by 10-15% in South Africa.

Ongoing active laboratory-based national surveillance for invasive pneumococcal disease performed by the Unit has already documented a decrease in vaccine serotype disease as early as six months after vaccine introduction. In addition, analysis of meningococcal disease surveillance data from 2003 through 2007 has shown that HIV-infected individuals may be at increased risk of meningococcal disease, and increased case-fatality ratios in HIV-infected patients may be explained by their increased odds of bacteremia compared to meningitis.

References for selected papers:

- 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: 1909-1916.
- Madhi S, Cunliffe N, Duncan S, Witte D, Kirsten M, Louw C, Ngwira B, Victor J, Gillard P, Chevart B, Han H and Neuzil K (2010). Impact of human rotavirus vaccine on severe gastroenteritis in African infants. *New England Journal of Medicine*, 362: 289-98.

School of Physiology

Head of School: Professor David Gray

Brain Function Research Group

FRC

URC

Director: Associate Professor Andrea Fuller

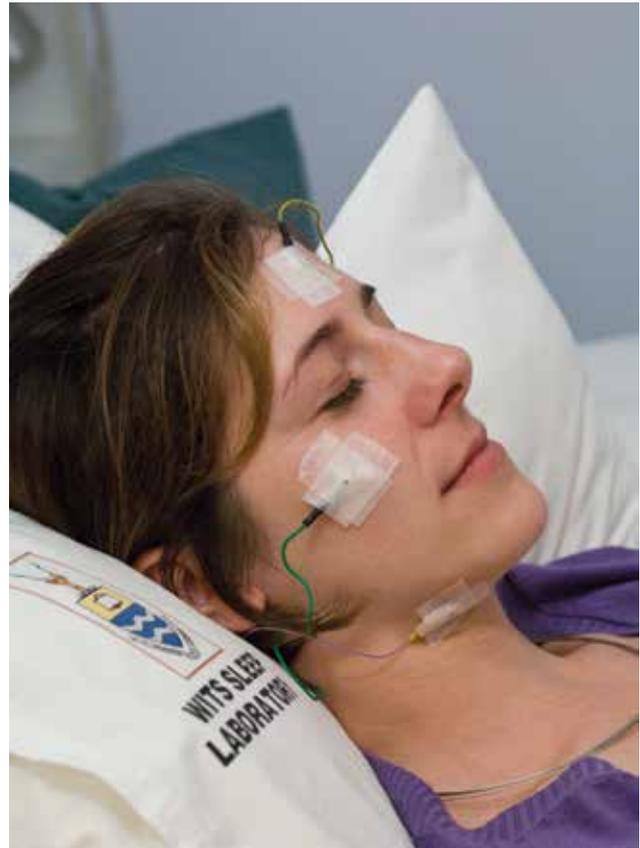
www.ac.za/Health/Physiology/ResearchUnits/BFRG

The mandate of the Brain Function Research Group (BFRG) 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 thermal responses of wild animals to their environment.

Over the past two years, the Group's pain laboratory has validated pain questionnaires for the South African population and investigated the mechanisms leading to enhanced pain sensitivity in patients with HIV infection. Pain is a common symptom of HIV infection, and may result directly from virus-mediated effects, indirectly through secondary infections or from the drugs used to treat HIV infection. The team also investigated the effects of primary dysmenorrhoea, the cramping and often debilitating pain that many women experience at menstruation, on voluntary activity levels and exercise performance.

The Wits Dial.a.Bed Sleep Laboratory conducted studies on the interaction between pain and sleep, an area in which it leads research internationally. The lab published work on the quality of sleep in women, children with Attention Deficit Hyperactivity Disorder (ADHD), South African university students, alcoholics and aging adults. The team further investigated the relationship between sleep and exercise, and aspects of Restless Legs Syndrome.

In the fever laboratory, researchers investigated the mechanisms mediating fever and sickness behaviours and explored the effect of recurrent bacterial infections on learning and the memory of growing animals. These findings are important for managing not only the thermal but also the non-thermal responses to infection, such as anorexia and fatigue, particularly in patients with prolonged illness.



Using its surgical and technological expertise in the remote measurement of physiological variables in animals, the wildlife environmental physiology team published research on the effects of environmental stressors and game management practices on the physiology of free-living mammals. In the face of rapid climate change, the outcomes of the work have important practical implications for veterinarians, game managers and conservationists.

References for selected papers:

- Harden L, du Plessis I, Poole S and Laburn H (2008). Interleukin (IL)-6 and IL-1 β act synergistically within the brain to induce sickness behaviour and fever in rats. *Brain, Behaviour and Immunity*, 22(6): 838 – 849.
- Iacovides S, Avidon I, Bentley A and Baker F (2009). Diclofenac potassium restores objective and subjective measures of sleep quality in women with primary dysmenorrhea. *Sleep*, 32(8): 1019–1026.
- Maloney S, Fuller A, and Mitchell D (2009). Climate change: is the dark Soay sheep endangered? *Biology Letters*, 5: 826 – 829.

Cardiovascular Pathophysiology and Genomics Research Unit



Directors: Professor Gavin Norton and Associate Professor Angela Woodiwiss

www.wits.ac.za/Health/Physiology/ResearchUnits/CPGRU

Members of the Cardiovascular Pathophysiology and Genomics Research Unit (CPGRU) undertake both basic and clinical research to address questions regarding the risks and mechanisms of cardiovascular (CVS) disease. In 2002, the Unit initiated the African Programme on Genes in Hypertension (APOGH). The Programme, the first of its kind to be conducted in Africa, is a large family-based cross-sectional and prospective population study aimed at identifying the factors that determine all conventional and novel CVS risk factors in emerging communities in Africa, by separating genetic from environmental effects on CVS risk. Soweto was selected as the study site as it is a developing urban community with a high prevalence (over 66%) of obesity, and it provides the necessary uniformity of environment to assess familial aggregation and heritability. The APOGH study is one of the few studies worldwide where both 24-hour ambulatory and central blood pressure measurements are being evaluated.

Hypertension is the single-most important determinant of CVS events in sub-Saharan Africa and therefore the Unit's members are interested in studying the genetic determinants of blood pressure (BP), the degree to which environmental, phenotypic and genetic factors determine BP, the modifying effects of genetic variants on environmental and phenotypic determinants of BP, the degree to which hypertension influences target organ damage (cardiac hypertrophy and large artery dysfunction) in hypertension, the impact of cardiac hypertrophy on CVS disease and the importance of specific antihypertensive approaches in subjects of African ancestry.

The team recently showed that pre-hypertension does not predict CVS target organ changes, independent of other CVS risk factors (namely, age, obesity and diabetes mellitus), in young-to-middle-aged persons of African descent. Current guidelines suggest the therapeutic management of patients with pre-hypertension but the team's data encourage an approach to diagnosis and management of hypertension which goes beyond only blood pressure thresholds. The team found also that high-quality nurse-recorded auscultatory blood pressure values obtained at a single visit are as strongly associated with CVS target organ changes as ambulatory blood pressure values, providing the first substantial evidence that high-quality nurse-recorded auscultatory blood pressure values can be used to predict CVS target organ changes instead of costly and time consuming ambulatory BP measurements.

Members of the Unit demonstrated that adiposity-induced increases in left ventricular mass reflect an enhanced effect of blood pressure on left ventricular growth. In other words, uncontrolled hypertension has an impact on the left ventricular mass index in obese, but not lean people, thus highlighting the impact of obesity as a cardiovascular risk factor. Further, the Unit established a dietary-induced animal model of obesity and in this model showed that dietary-induced obesity promotes the progression from compensated cardiac hypertrophy to cardiac dilatation and pump dysfunction in hypertensive rats.

References for selected papers:

- Norton G, Maseko M, Libhaber E, Libhaber C, Majane O, Dessein P, Sareli P and Woodiwiss A (2008). Is pre-hypertension an independent predictor of target organ changes in young-to-middle aged persons of African descent? *Journal of Hypertension*, 26: 2279-87.
- Woodiwiss A, Molebatsi N, Maseko M, Libhaber E, Libhaber C, Majane O, Paiker J, Dessein P, Brooksbank R, Sareli P and Norton G (2009). Nurse-recorded auscultatory blood pressure at a single visit predicts target organ changes as well as ambulatory blood pressure. *Journal of Hypertension*, 27: 287-297.
- Majane O Vengethasamy L, du Toit E, Makaula S, Woodiwiss A and Norton GR (2009). Dietary-induced obesity hastens the progression from concentric cardiac hypertrophy to pump dysfunction in spontaneously hypertensive rats. *Hypertension*, 54: 1376-1383.

School of Public Health

Head of School: Professor Sharon Fonn

Centre for Health Policy Research Unit



Director: Dr Jane Goudge

www.wits.ac.za/Centres/CHP

The Centre for Health Policy Research Unit (CHP) is a multidisciplinary research group which seeks to contribute to excellence in health policy and health economics research and to be a critical participant in health policy processes. Established in 1987, the CHP has more than 21 years of research experience and is recognised by the South African Medical Research Council as the Research Group in Health Policy.

The CHP's mandate is to undertake high quality policy research to support change in the health sector, teach and build capacity, develop collaborative links and advocate for, and promote policies in support of equity and social justice. The Unit has strong links with the London School of Hygiene and Tropical Medicine and has recently conducted collaborative work with the University of MacMaster (Canada), the University of Dublin (Ireland), the University of Queen Margaret (Edinburgh), as well as research units such as the Ifakara Health Institute (Tanzania), the Kemri Wellcome Centre (Kenya), and the International Health Policy Programme (Thailand). The CHP has an international reputation for conducting high quality health policy and systems research.

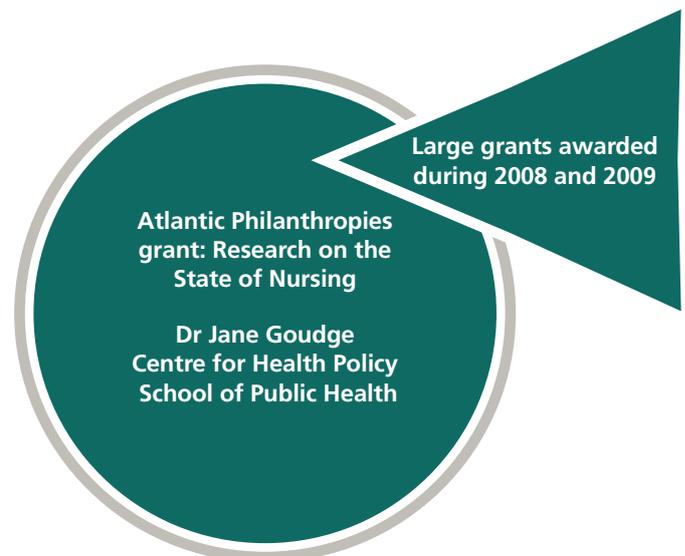
The primary focus of the CHP's research is to support the development and transformation of the South African health system and to influence regional and international health systems developments. Research thrusts include: health systems, policy analysis, health economics and financing, HIV/AIDS, maternal healthcare services, health equity, access to healthcare and household interaction with the health system and human resources for health. Since its inception, the Unit's alumni have gone on to lead transformation initiatives in

diverse organisations, ranging from large government departments, international foundations, parastatals and universities.

The Unit also participated in the Institutional Support Team, established in February 2009 at the initiative of the then Minister of Health, Barbara Hogan. The overall health systems review was prompted by the projected overspending in some of the provinces during the 2008/9 financial year. Its purpose was to examine the underlying factors behind the provincial health overspending, review health service delivery priorities and programmes and to make recommendations to prevent its recurrence.



Dr Jane Goudge



References for selected papers:

- Goudge J, Gilson L, Russel S, Gumede T and Mills A (2009). The household costs of healthcare in rural South Africa with free public primary care and hospital exemptions for the poor. *Tropical Medicine & International Health*, 14(4): 458-467.
- Mbidyo P, Gilson L, Blaauw D and English M (2009). Contextual influences on health worker motivation in district hospitals in Kenya. *Implementation Science*, 4 (43): 1-10.
- McIntyre D, Goudge J, Harris B, Nxumalo L and Nkosi M (2009). Prerequisites for National Health Insurance. *South African Medical Journal*, 99(10): 725 -729.

Rural Public Health and Health Transitions Research Unit (Agincourt)

FRC

URC

MRC

Director: Associate Professor Stephen Tollman

www.wits.ac.za/Health/PublicHealth/Agincourt

Rural southern Africa is in the midst of far-reaching socio-demographic transitions reflected in complex health and social challenges spanning the life course. The Unit aims to make an exceptional scientific contribution to vulnerable communities which addresses critical health and development challenges, enhances the quality of life and productivity of individuals and families and informs public policy, programmes and practice.

A Medical Research Council Unit since 2003, the Unit is an integral part of the Wits School of Public Health with a major field research site in rural northeast South Africa. It serves as a satellite secretariat for the INDEPTH Network (International Network for the Demographic Evaluation of Populations and Their Health) and leads multi-site African and Asian work on Migration and Urbanisation and Adult Health and Aging.

The Unit's research platform is a health and socio-demographic surveillance system (HDSS) which has been running since 1992, thus spanning dramatic socio-political and epidemiological change. This involves long-term follow-up of 84,000 people in 25 rural villages through annual household visits to record all vital events – births, deaths and migrations. Critical to this, are stable and respectful relationships with village communities and public sector departments, particularly health and education.

Based on the HDSS platform is a range of interdisciplinary observational and intervention research projects involving a rich network of national and international scientists, funded by diverse research investors. The Unit's research is organised into five thematic areas: Levels, trends and transitions, Child health and development, Adult health and wellbeing, HIV/AIDS and Chronic care, and Household response to shocks and stresses.



Enhanced surveillance involves linking project datasets to the HDSS, linking HDSS and clinic records, and developing an accessible web-based approach to sharing data. Every project is linked to the HDSS, relies on its data management system during field and analytical phases, and will ultimately contribute new datasets to the research platform, thus extending and enriching it.

The Unit supports a dynamic, interdisciplinary graduate training programme which focuses on doctoral students while maintaining a strong masters pipeline and providing post-doctoral opportunities. Some 20 doctoral students are nested within ongoing research projects.

References for selected papers:

- Tollman S and Kahn K (guest editors). Health, population and social transitions in rural South Africa. *Scandinavian Journal of Public Health* 2007; 35 (supplement 69):1-187 (available at www.tandf.no/sjpublic). This journal supplement, featuring 19 articles spanning 15 years, provides a comprehensive account of the rapid and complex health, population and social transitions underway in rural post-apartheid South Africa.
- Tollman S, Kahn K, Sartorius B, Collinson M, Clark S and Garenne M (2008). Implications of mortality transition for primary healthcare in rural South Africa: a population-based surveillance study. *Lancet*; 372: 893-901. In 2009, the Unit was awarded the INDEPTH prize for extraordinary Research in Population and Health at INDEPTH sites for this paper.

School of Therapeutic Sciences

Head of School: Professor Alan Rothberg

Wits-BioPAD Drug Delivery Platform

The Wits-BioPAD Drug Delivery Platform (WDDP), based within the Department of Pharmacy and Pharmacology, is committed to the innovative design of quality drug delivery products. Under the leadership of Professor Viness Pillay, the WDDP is funded by Biotechnology Partnerships and Development (BioPAD), a Department of Science and Technology (DST) initiative. The WDDP was launched in March 2007 with an initial investment of R11.6 million, for the development of drug delivery technologies. As a result of their dedication to research excellence, the team has become one of the most highly-respected drug delivery research units in South Africa.



The WDDP provides a platform for cutting-edge postgraduate scientific training and facilitates the realisation of innovative drug delivery research of the highest quality. The WDDP aims to maintain and further enhance its position as a leading platform by sustaining globally competitive standards of excellence in drug delivery and pharmaceutical biomaterials research, while taking into account the South African government's biotechnology strategy. Thus far, this goal has been realised through close consultation with key expert clinicians and pharmaceutical industry stakeholders who are able to advise on the application of the technologies under development by the WDDP team. As a result, the pioneering technologies produced by the team do not remain on the bench-top, but are fashioned into pharmaceutical products primed for commercialisation.

Professor Pillay and his team of researchers and business partners have been dedicated in their quest to develop novel drug delivery technologies. The team has generated several new drug delivery solutions that will revolutionise the ways in which people take medication. Research undertaken by the WDDP in recent years has led to an understanding of the control of the rate of drug delivery, an understanding of how to ensure the correct duration of therapy, and of the best means of targeting a specific organ or tissue while maintaining appropriate blood concentrations. Recent research includes:

- Drug delivery to the brain remains a challenging yet essential field of study. To optimise drug delivery to the brain, the numerous protective barriers surrounding the central nervous system must be understood. Investigations of drug delivery to the brain are needed urgently, so that effective treatments for patients living with neurodegenerative disorders such as Parkinson's disease can be devised. In response to this need, the team conducted a study which focused on the design, biometric simulation and optimisation of an intracranial nano-enabled scaffold device. This type of device allows for the site-specific delivery of dopamine - a strategy which aims to minimise the peripheral side-effects of conventional forms of Parkinson's disease therapy. The team demonstrated that the site-specific delivery of DA was indeed enhanced by the Nano-enabled Scaffold Device they designed.

- Advances in biomaterials research have provided solutions for combating many of the challenges posed by various diseases. The amalgamation of polymeric science with the pharmaceutical sciences and medicine has led to the development of novel biomaterials for specific applications. Work undertaken by the team in this field includes a study which focused on the application of computational chemistry as a modelling tool for the design of a neurocompatible biopolymeric membrane system for the delivery of methotrexate (MTX) in the treatment of Primary Central Nervous System Lymphoma (PCNSL). The results of their investigation showed that the composite neurocompatible biopolymeric membrane may be promising for the novel delivery of MTX in the treatment of chronic PCNSL.
- Nanotechnology employs engineered materials or devices that interact with biological systems at a molecular level. The treatment of neurodegenerative disorders (NDs) could be revolutionised by using such materials or devices to stimulate and interact with target sites to induce physiological responses while minimising side-effects. Conventional drug delivery systems do not provide adequate cyto-architecture restoration and connection patterns essential for functional recovery in NDs, due to limitations imposed by the restrictive blood-brain barrier. A review article written by members of the team in 2009 provided a concise discussion of the current and future applications of nano-enabled drug delivery systems for the treatment of NDs, in particular Alzheimer's and Parkinson's diseases. The review also explored the application of nanotechnology in clinical neuroscience to develop innovative therapeutic modalities for the treatment of NDs.

The WDDP currently has over 30 patents at various stages of application. Several have been granted in South Africa, and are now also being pursued in the US, Europe and UK.



Professor Viness Pillay

Large grants awarded during 2008 and 2009

NRF National Nanotechnology Equipment Programme award

Professor Pillay
Wits-BioPAD
Drug Delivery Platform,
School of Therapeutic Sciences

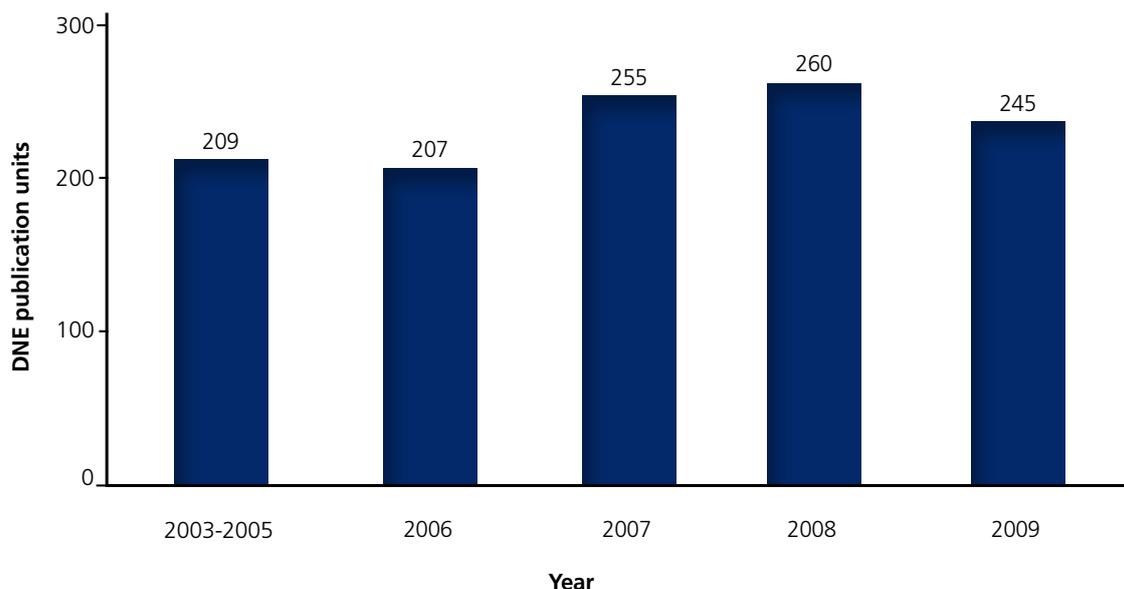
Selected publications in these areas of focus:

- Pillay S, Pillay V, Choonara Y, Naidoo D, Khan R, du Toit L, Ndesendo V, Modi G, Danckwerts M and Iyuke S (2009). Design, biometric simulation and optimisation of a nano-enabled scaffold device for enhanced delivery of dopamine to the brain. *International Journal of Pharmaceutics*, 382: 277-290.
- Sibeko B, Pillay V, Choonara Y, Khan R, Modi G, Iyuke S, Naidoo D and Danckwerts M (2009). Computational molecular modeling and structural rationalisation for the design of a drug-loaded PLLA/PVA biopolymeric membrane. *Journal of Biomedical Materials*, 4: 1-11.
- Modi G, Pillay V, Choonara Y, Ndesendo V, du Toit L and Naidoo D (2009). Nanotechnological applications for the treatment of neurodegenerative disorders. *Progress in Neurobiology*, 88: 272-285.

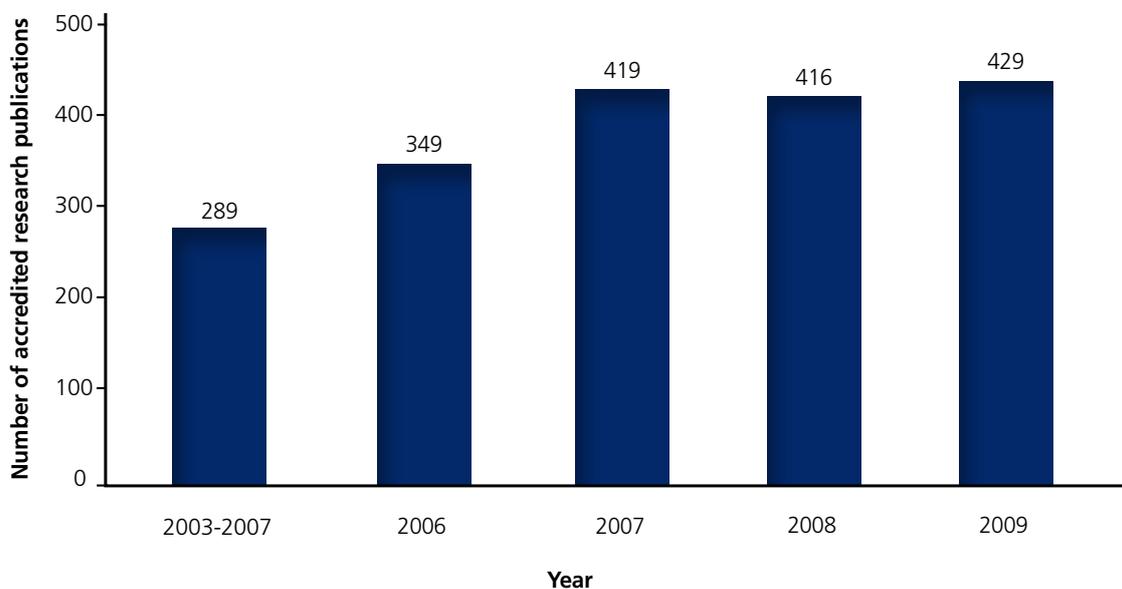
Research Outputs

Research Publications

The Faculty is proud of its publication record and continues to strive for an increase in the number of scholarly publications in reputable journals and books. The following graphs demonstrate the publication units, confirmed by the Department of National Education and Training (now known as the Department of Higher Education and Training), awarded to the Faculty for accredited publications produced between 2003 and 2009, and the total number of research articles published in accredited journals.



Department of National Education (DNE) Units awarded for accredited publications produced by Faculty researchers (the value given for 2003-2005 is the mean across the three years; the 2009 value is an estimate).



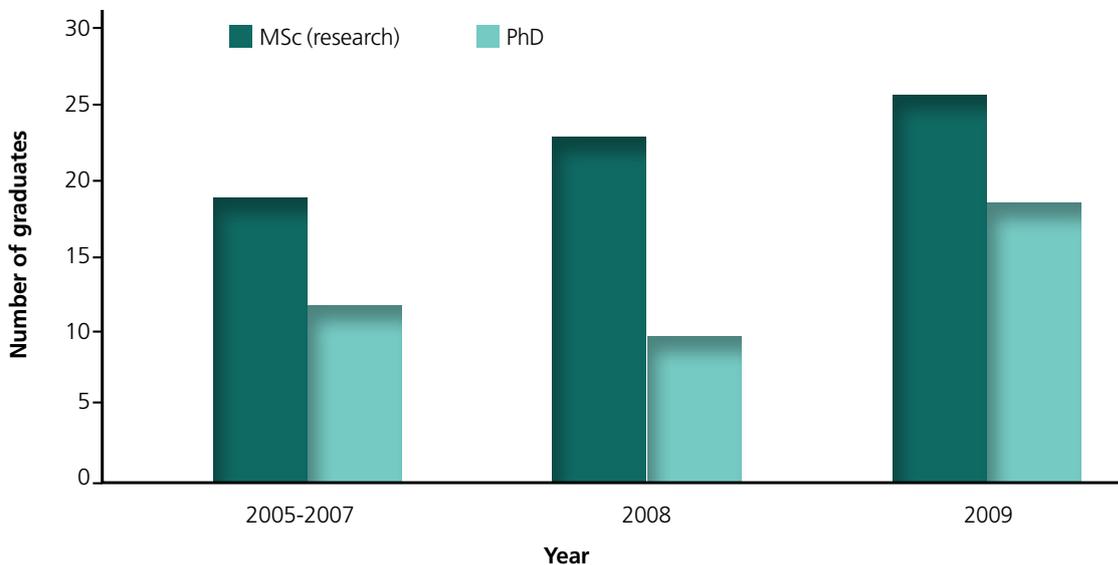
The total number of accredited research articles published in accredited journals or books by Faculty researchers (the value given for 2003-2005 is the mean across the three years; the 2009 value is an estimate).

Note:

Each year, the Faculty submits a list of all its publications to the University Research Office, which in turn submits a report to the Department of Higher Education and Training (DHET). For journal articles and books or chapters in books, the DHET awards 'units' if the contributions are published in journals and books accredited by the Department. In return for units generated, the DHET awards funding to the University. The number of units given to the Faculty for a submission depends also on the number of authors based within the Faculty. This means that a publication for which there is a co-author at another institution will produce fewer units for the Faculty than a publication for which all authors are based within the Faculty. The Faculty is, however, committed to partnering with researchers at other higher education institutions. Please note that the units for 2009 have not yet been confirmed.

Research Postgraduates

The Faculty produces research masters (MSc) and doctoral (PhD) graduates in all health sciences disciplines. The figure below illustrates the mean number of graduates for 2005-2007 and shows the number of postgraduate students who graduated with these degrees in 2008 and 2009.



Research Funding

The Faculty receives funding for research from a variety of sources. The University Council allocates funds to the Faculty Research Committee, the national research agencies (South African Medical Research Council and the National Research Foundation) support research through grants to individual researchers and groups, while the Wits Health Consortium (WHC) is responsible for managing several grants from other external funding agencies. A dividend declared by the Wits Health Consortium was used in 2008 and 2009 to support research activities in the Faculty.

The table illustrates, in Rand, the funding available for research in the Faculty in 2008 and 2009.

FHS Research Funding - (R'000)		
	2008	2009
Funds allocated by the University Council	7,839	8,985
Funds administrated by the Wits Health Consortium		
Total funds	552,814	614,567
Research funds	299,600	305,407
Dividend	2,175	3,738
Funds awarded by external funding bodies		
Total funds	43,547	48,292
South African Medical Research Council	11,412	9,495
National Research Foundation	12,289	9,804
Other grants and contracts (not administrated by WHC)	19,846	28,993
Total	905,975	980,989

The Wits Health Consortium

The Wits Health Consortium was established in 1997 as a private company, the main business of which was to provide commercial and administrative support for income-generating activities which are ancillary to the main objectives of the Faculty of Health Sciences, namely teaching and research and the provision of medical services. In the ensuing 13 years, many Faculty members have used the Consortium to manage their research and clinical services grants. Some 70 syndicates exist within the Consortium. Several of the large research groups in the Consortium have made important contributions to our knowledge about HIV and AIDS and have furthered understanding of diagnosis and treatment. In addition, the WHC's Clinical Research Group encompasses trial sites for the conducting of Faculty-based clinical trials. The Consortium has been essential in assisting Faculty researchers to attract and manage large grants, mainly from the United States. Currently, annual funds under management within the WHC are well in excess of R500 million.

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FACULTY OF HEALTH SCIENCES

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Heads of School

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