September 2011

UNIVERSITY OF JOHANNESBURG

Faculty of Science NEWSLETTER

Innovatively creating **new knowledge** and **leading scientists**

News from Biochemistry at University of Johannesburg

Internationally competitive research, growing international collaboration and excellent teaching have become hallmarks of UJ's Biochemistry Department.

The Department of Biochemistry became an independent academic Department following the merger of RAU and TWR to form the new UJ in 2005, after having been integrated with the Department of Chemistry for a number of years. Following the independence, several new appointments were made, and to date, the Department boasts a 65% staff complement with PhD degrees, with the remaining members registered for PhDs and at various stages of completion. The staff of the Department of Biochemistry at UJ consists of Prof Ian Dubery (Research Professor), Prof Liza Bornman (Associate Professor), senior lecturers Dr Marianne Cronjé (Head of Department) and Dr Lizelle Piater (Deputy Head of Department), lecturers Dr Gerrit Koorsen, Dr Emmanuel Mukwevho, Dr Godfrey Tlou, Ms Lindy Esterhuizen, technical lecturer Ms Jacinda James and instrumental scientists Mrs Heather-Anne Byth-Illing and Mr Mosotho George. In addition two of our postgraduate students, Ntakadzeni Madala and Londiwe McGina are recipients of UJ's *New Generation Scholarships* and will join the staff after completion of their studies. There are also two postdoctoral fellows in the Department, Dr Ju-Chi Huang and Dr Natasha Sanabria. The academic staff members are supported by the very capable Mrs Lynette de Kooker with all administrative and secretarial matters and Bradley Khoza provides technical support.

THIS ISSUE **FOCUSES ON THE DEPARTMENT OF BIOCHEMISTRY.**

Dr Marianne Cronjé

News from Biochemistry

(from page 1)

Teaching Biochemistry to undergraduate students continues to be a major component of the Department's activities. On first year level, an integrated Biology 1A course consisting of fundamental aspects of Biochemistry precludes the second semester course - Principles of Biochemistry - are offered to approximately 170 students. The first years, 60 second year, 40 third year and 18 honours students are the result of a steady growth over the last few years.

In striving for academic excellence, top achievers in Biochemistry are annually awarded prizes at a formal ceremony hosted by the Dean of the Faculty of Science, Prof Kinta Burger. Honours for 2010 went to David Rose (best 2nd year student sponsored by Becton-Dickenson), Siobhan Jenkins (best 3rd year student sponsored by Merck SA) and Furaha Asani (best Honours student sponsored by Labhouse). Eloise Ferreira was awarded best departmental MSc (*cum laude*) sponsored by Inqaba Biotec.

The academic staff members regularly attend international meetings and visit overseas laboratories to present their research results. Prof Ian Dubery was fortunate to attend the International Conference on Plant Pathogenic Bacteria in tropical Reunion Island in June 2010 where he presented a talk on molecular pattern motifs found within bacterial lipopolysaccharides. In 2009, the Department was the official host of the International Cell Death Society meeting with Dr Marianne Cronje acting as organizer. She also organized the first SA Cell Death Society symposium that was held in Cape Town on the 10th – 12th January 2011. Official collaborations exist with several overseas universities and this has contributed to exchange visits of staff and students. Collaboration with the Centre for Plant Molecular Biology has resulted in an exchange agreement and two of our Masters students are conducting their research in Germany. The strong research focus has also contributed to an excellent record of postgraduate student training, with 26 Masters and Doctoral students registered for 2011.

The quality of the BSc Hons and MSc graduates is excellent and several have moved on to international PhD studies in Europe. The students boast with numerous awards and scholarships, including NRF free standing scholarships (Scarce Skill, Innovation), and all the students working on cancer have been awarded UJ-CANSA bursaries (see details in the individual sections).

The Department is located in C2 Laboratory building on the Auckland Park Campus of UJ.

Contact details:
Dr Marianne J Cronjé,
Department of Biochemistry,
University of Johannesburg,
PO Box 524, Auckland Park,
2006.
Tel. +27-11-559-2370 / 2404,
Fax: +27-11-559-2605

Prize winners: From left to right: Furaha Asani (top BSc (Hons) student), Prof Kinta Burger (Dean), Dr Marianne Cronje (HOD), Eloise Ferreira (top MSc student), Siobhan Jenkins (top 3rd year student), David Rose (top 2nd year student)

RESEARCH OVERVIEW

The research activities of the Department are varied and include aspects of plant -, mammalian - and microbial biochemistry. The students are thus exposed to a wide range of topics and different approaches in modern Life Sciences research. The research activities of individual research groups as well as recent achievements are summarized below.

Human Genetics and Infectious Disease

Group Leader: Prof Liza Bornman

Prof Liza Bornman (PhD, Human Genetics, UP) is investigating the combined role of genetics, epigenetics and environment on the vitamin D signaling pathway in susceptibility to tuberculosis (TB) in African populations. According to Statistics South Africa, non-HIV TB is the leading natural cause of death in South Africa. More than one-third of the world's population is infected with *Mycobacterium tuberculosis*, yet only one in ten infected individuals will develop TB in their lifetime. TB is a multifactorial disease and genetically complex, influenced by polymorphisms in several host genes, including the vitamin-D receptor gene (*VDR*). Besides host genetics, TB is influenced by a number of environmental factors including socioeconomic conditions, nutrition, the virulence of the pathogen and HIV infection. In addition to host genetic sequence polymorphisms, such as single nucleotide polymorphisms (SNPs), environmental factors may impose variation on the DNA through epigenetic mechanisms. The epigenome is the combined variation in DNA methylation, histone modification and RNA regulation, influencing gene expression of a cell without changing the DNA sequence. Association between *VDR* sequence variants and TB is inconsistent between studies and populations and epigenetics may contribute an additional layer of variation influencing TB susceptibility. Preliminary results from Prof Bornman's research published in Human Immunology (*Andraos et al.*, 2010) suggest that methylation variable positions (MVPs) in the 3' end of the *VDR* distinguish population, while a complex interaction between SNPs and MVPs may underlie TB predisposition. Collaborators in this project include Dr Gerrit Koorsen and Dr Julian Knight, Wellcome Trust Centre for Human Genetics, University of Oxford.

Students currently enrolled for MSc studies under the supervision of Prof Bornman include, from left to right, Vanessa O'Neill, Donovan Saccone, Ntando Mnisi, Tamsyn Jeffery and Furaha Asani.

Molecular Plant:Microbe Interactions Research Group. (From Left to Right) : Ntakadzeni Edwin Madala; Sherrie-Ann New; John Sherwood; Peggy Maake; Fidele Tugizimana; Maureen Baloyi; Mosotho George; Phumzile Mnisi; Robyn Klemptner; Nicole Petersen; Londiwe Mgcina. Front (From Left to Right) : Dr Natasha Sanabria; Dr Lizelle Piater; Jacinda James; Professor Ian Dubery; Dr Carol Huang.

Molecular Plant:Microbe Interactions

Group leaders: Prof Ian Dubery and Dr Lizelle Piater

The primary objective of this research group is to investigate the biochemical basis of inducible defense responses in crop plants towards pathogenic organisms so as to be able to manipulate the process for enhanced natural disease resistance, and to induce crop protection through measures that are benign to the environment. The focus of the research is on plant and microbial biochemistry, especially with regard to the complex plant: microbe interactions between plants and their pathogens that might lead to either disease or resistance, depending on the perception capacity of the plant. The induction of defense-related genes, proteins and metabolites, and the immunization of plants against diseases that result in induced or acquired resistance are investigated using new *omic* technologies (transcriptomics, proteomics, metabolomics) to further research in this field. The aim is to develop novel strategies for crop protection, to complement traditional plant breeding efforts and to reduce the expense and environmental costs of reliance on conventional pesticide treatments.

Recent conference awards which have been received by students in the group include: (1) Mr Fidele Tugizimana won the award for the 2nd best presentation at the ChromSA Gauteng branch student symposium held at WITS, 18th August 2010. His presentation was entitled: *Application of Chromatography in Metabolite Profiling of Defence-related Secondary Metabolites in Tobacco Cells.* This presentation was based on the project conducted under the supervision of Mr MJ George and Prof Dubery. (2) Ms N Maureen Baloyi won the award for the best BSc Honours poster presentation at the Biotechnology Research Open-day held at UWC, 30-31st August 2010. Her poster was entitled *Investigation of drought or salt-stress related proteins in different sorghum varieties.* This poster was based on the project conducted under the supervision of Bongani Ndimba and Rudo Ngara.

Projects within the research group are supported by both national and international funding bodies including:

South-Africa – Germany Bilateral Agreement Research Award for Collaborative Research between the Department of Biochemistry, University of Johannesburg and the Centre for Plant Molecular Biology, University of Tübingen (Prof Dubery).

NRF Grant for 2010-2012: KFD – Competitive Support for Unrated Researchers (CSUR) – Transcriptomic and proteomic analyses of PAMP/MAMP perception and defence responses in *Arabidopsis thaliana* (Dr Piater). Within this grant, the following bursaries have been awarded in 2010: 8 undergraduate assistants (R64 000); 1 Hons (R20 000), 1 MSc (R40 000) and 2011: 3 undergraduate assistants (R24 000), 1 Hons (R20 000), 2 MSc (R80 000).

Cancer Research Group

Group Leader: Dr Marianne Cronjé

Typically, cell death is thought of as a pathological phenomenon, but considering the adult human body produces and eradicates approximately 60 billion cells per day, the control between self-renewal and elimination of cells is vital for survival of multi-cellular organisms. Physiological or programmed cell death generally occurs by apoptosis, a programmed cell-suicide mechanism. Disorders in the regulation of apoptosis contribute to many disease pathogeneses or progression and involves either impaired cell eradication or turnover (eg cancer) or uncontrolled cell loss (eg Alzheimer's disease). In fact, uncontrolled cell proliferation and eventual tumour development is considered one of the hallmarks of oncogenic cell transformation. Studies have focused on the understanding of the regulatory pathways governing apoptosis, and armed with this knowledge, have led to many studies to induce apoptosis in cancer cells by triggering core components of the cell death machinery. Understanding these molecular events that regulate apoptosis in response to anticancer therapy and how cancer cells evade apoptotic cell death provides novel opportunities for the development of molecular therapeutics that target cell death pathways.

The cancer research group is currently focusing their attention on a number of compounds able to induce apoptosis in cancer cells, including those present in indigenous medicinal plants and a series of novel metal compounds synthesised in-house by Prof Reinout Meijboom from the Department of Chemistry. These so-called metallo-drugs are currently being patented.

Dr Cronjé is a member of the Board of Directors of the International Cell Death Society (ICDS) and recently established and hosted the inaugural meeting of the SA Cell Death Society, a chapter of the ICDS, in Cape Town in January 2011. Aspects of the cell death work have been presented at several ICDS meetings, including: Invited speaker; ICDS satellite meeting (Cancer in Cell Death), Nice, France, 5-7 June 2007. Invited chair; 7th ICDS meeting, Shanghai, China, 3-7 June 2008. Invited speaker; ICDS satellite meeting (Molecular Therapeutics by Scientists without Borders), Tehran, Iran, May 2009. Organized and hosted the 8th ICDS meeting in Johannesburg, South Africa, 5-8 June 2009. Invited speaker; 9th ICDS meeting: *Multidisciplinary Approaches in cell Death Research from yeast to man*, Antalya, Turkey, 28-31 May 2010. Invited chair; 10th ICDS meeting, Sao Paulo, Brazil, 10-13 June 2011.

Many of the students in this research group are NRF Innovation or Prestigious grant holders, while one student holds a UJ-CSIR scholarship. All of the students currently active on the cancer projects were awarded UJ-CANSA bursaries. The recipients of the 2010 UJ-CANSA bursaries had the opportunity to present their work at CANSA's biennial research conference entitled *Awareness, Coping and Beyond, A Women's Health Cancer Conference for our Time*, that was held on 8-10 September 2010 at the Southern Sun Hotel OR Tambo International Airport Johannesburg. Eloise Ferreira received first prize for the best poster presentations. Nicola Skerman was the co-recipient of the SASBMB prize for the best Honours student in 2008. Nicola also recently returned from a visit to the labs of Prof Zahra Zakeri of College University of NY, where she tested one of the medicinal plant's ability to induce apoptosis in several cancerous cells. One of Dr Cronjé's students, Stephan Mumm, is currently undertaking his MSc research project at a German university made possible by the MoU with Tuebingen University and another student, Kailen Boodhia, is conducting his research at the NIOH under the co-supervision of Prof Mary Gulumian.

Back (From Left to Right) : John Walters; Colette Orsmond; Dr Marianne Cronjé; Eloise Ferreira; Tamarisk Horne.
Front (From Left to Right) : Nicola Skerman; Xolani Sikhakhane; Zelinda Human


Dr Mukwevho

Diabetes Therapeutics Research Group

Group leader: Dr Emmanuel Mukwevho

The group aims to study the chronic lifestyle disease Type II diabetes, which contributes ~ 90% of all diabetes cases. A whopping 150% rise in type II diabetes is projected by 2030 in sub-Saharan Africa alone. Exercise has been shown to alleviate the effects of type II diabetes by increasing glucose transport and also enhanced fat oxidation resulting in improved insulin sensitivity. Type II diabetes leads to retinopathy, neuropathy, blindness, leg amputations, high blood pressure, kidney failure, stroke etc.

The diabetes research group focuses on exercise induced gene expressions that provide protective mechanism and delayed onset of type II diabetes and how these genes are regulated. As such mitochondrial and glucose transport genes are being investigated. With regard to mitochondrial genes, Nuclear respiratory factor (NRF)-1, Tfam, Alas and related genes are being investigated. With regard to glucose transport, glucose transporter genes such as Glut4 and Mef2 are being studied in response to exercise. Furthermore, a kinase called calcium/calmodulin dependent protein kinase (CaMK) II which upregulates both mitochondrial and glucose transport genes is also being investigated with a focus on how it influences chromatin structure. An understanding of these mechanisms is vital in that it may provide novel targets for therapeutic drugs required for the treatment and management of type II diabetes. The research is funded by an NRF Thuthuka grant awarded to D. Mukwevho. Currently, one PhD student is involved in the research and collaborating institutions involve the University of Cape Town and the University of Cambridge.

Chromatin Structure and Function Research Group

Group Leader: Dr Gerrit Koorsen

DNA in the eukaryotic cell nucleus is densely packaged within extensive nucleoprotein complexes known as chromatin. This assembly not only facilitates the greater than 10,000-fold lengthwise compaction of DNA in order to accommodate large genomes (of which the extended length is approximately 2 m per cell) within a nucleus with a comparatively small diameter (~ 10 mm), but also forms the substrate for all nuclear processes. However, the compact state of a eukaryotic genome imposes a considerable barrier to DNA access. The histones, a class of highly conserved, basic proteins, constitute the main protein component of chromatin and directly establish and stabilize the structures that are responsible for the compaction of DNA through a hierarchical series of folding steps. Unusual compaction of DNA is associated with a series of epigenetic abnormalities, including cancer. This research group aims to elucidate the role of the linker histones H1/H5 in the establishment of higher-order chromatin structures and well as to uncover epigenetic processes dependent on this histone class.


Chromatin Group (From Left to Right):
Ronél Ferreira; Dr Gerrit Koorsen; Rozanné Schnetler

Besides chromatin research, Dr Koorsen and two of his Masters students are involved in the following interdisciplinary research initiatives:

Identification of Vibrio cholera serotypes/biotypes by MALDI-TOF/MS (In collaboration with Dr TG Barnard, UJ Water and Health research group)

Cholera, the highly epidemic diarrhoeal disease caused by *Vibrio cholerae* infection, continues to devastate many developing countries.

Due to the time-consuming methods for confirming *Vibrio* species, there is a definite need to improve detection methods for more rapid and sensitive detection. Matrix-assisted Laser Desorption Ionization – Time-of-Flight (MALDI-TOF) mass spectrometry biotyping has recently emerged as a rapid and sensitive tool to identify cultured microorganisms. Novel ways are investigating to adapt current MALDI-TOF/MS platforms for subspecies identification of South African *Vibrio cholerae* isolates.

Tear fluid composition of patients affected with dry eye disease and keratoconus (In collaboration with Prof Wayne Gillan, UJ Department of Optometry)

Dry eye disease (DED) and keratoconus continue to affect the quality of life of many South Africans (and patients elsewhere) and in the case of keratoconus often leads to blindness. However, details of the etiology of these diseases, their biochemical fingerprint as well as disease interactions remain uncertain. We are taking a metabolomic approach to addressing these issues, and are specifically focusing our investigations on the lipid and immunological components of the precornial tear film.

Microbial Enzymes and Plant Disease Research Group

Group Leader: Dr Godfrey Tlou

All plants are subject to continuous attack by a wide variety of microorganisms, including phytopathogenic bacteria, fungi, viruses and nematodes found within their environment which annually leads to alarming economic crops losses. During the initial association with plants, pathogens encounter barriers (epicuticular lipids, plant cell walls etc) which need to be penetrated in order to infect the host. Some phytopathogenic bacterial species are amongst some of the best studied lipolytic enzyme producers (potential to degrade the lipid barriers). A few phytopathogenic bacterial species have been shown to produce enzymes that degrade cuticular lipids *in vitro*. However, the identity of the enzymes (true cutinases or *moonlighting* lipases) and the physiology of enzyme production *in planta/in vitro*, remains unknown. On the other hand, some studies have reported on esterases from phytopathogenic bacteria that play a role in the hydrolysis of pectin (plant cell wall component) and that therefore influence phytopathogenecity. However, in all the reported cases, the extent to which these enzymes contribute to phytopathogenicity is underexplored.

The group focuses on *Pseudomonas syringae*, a phytopathogen that can infect a wide variety of plant species and is subdivided into over 50 pathovars. The genome of this bacterium has been sequenced and the annotation has revealed several genes encoding lipolytic enzymes on the genome (no cutinase encoding genes). It makes physiological sense that the numerous lipolytic enzymes encoded on the genome play various roles in the bacterium. However, the group's main focus is to unearth from the bacterium epicuticular/plant cell wall degrading lipolytic enzymes and to investigate the physiological regulation of the genes relative to the pathogenesis.

Dr Tlou

Molecular Plant Pathology
Research Group

Group Leader:
Mrs Lindy Esterhuizen

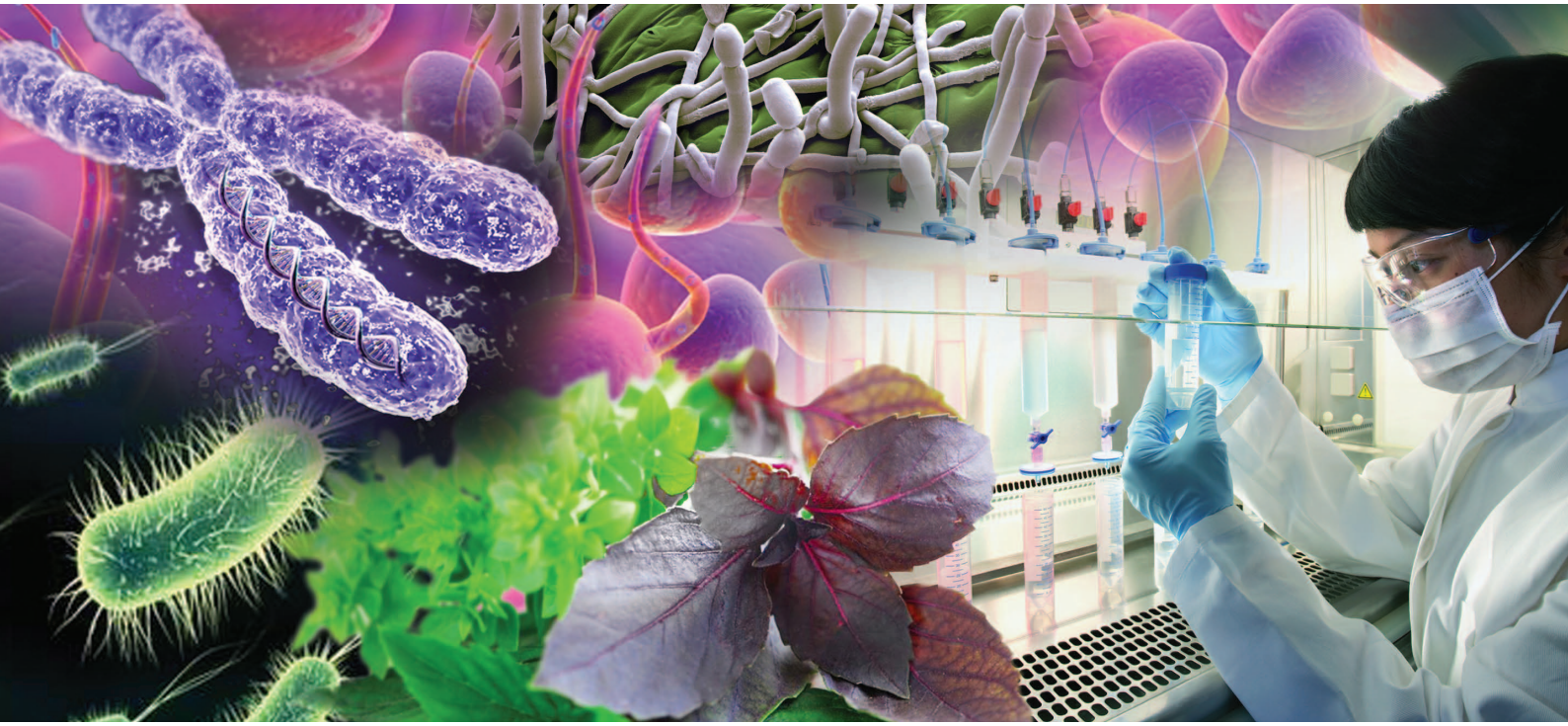
Geminiviruses constitute an important group of insect-transmitted plant pathogens characterized by circular single strand DNA genomes. Geminiviruses in general, but specially those belonging to the genus *Begomovirus*, are considered to be emerging plant viruses, due to their increasing incidence and the severity of the diseases they cause in a number of economically important crops. The genus *Begomovirus* consists of viruses that are whitefly transmitted (*Bemisia tabaci*) and comprises more than 100 member species. Begomoviruses are often the limiting factor in the production of tomato, pepper, squash, melon, and cotton and periodic begomovirus epidemics in staple crops, such as cassava, have caused widespread famines in the developing world. *Tomato curly stunt virus* (ToCSV) transmitted in a persistent manner by a non-indigenous whitefly, *Bemisia tabaci* B-type is among the most important limiting factors that affect tomato production in South Africa. The whitefly *Bemisia tabaci* (Hemiptera) is a cryptic species complex containing some of the most destructive invasive pests of vegetable, ornamental, and field crops worldwide. Some members of this species complex have a global distribution and cause damage directly through feeding and indirectly through the transmission of plant pathogenic viruses, primarily begomoviruses.

The plant pathology research group currently focuses on characterising the genetic diversity of begomoviruses infecting a number of crop plants, including tomato, pepper and sweet potato as well as viruses infecting indigenous plants (weeds) located in vegetable production areas that are transmitted by the four *B. tabaci* cryptic species present in South Africa. Knowing the genotypic range of viruses causing disease and which *B. tabaci* species transmit them are relevant to developing knowledge-based disease management practices.

The group focuses on:

- Diversity and evolutionary history of the genus *Begomovirus*.
- Molecular determinants of pathogenicity and host range of *Tomato curly stunt virus* variants.
- Screening for begomovirus resistant tomato and sweet potato cultivars.
- The diversity and ecology of South African *Bemisia tabaci* species.
- Biological characterisation of indigenous and introduced Bemisia tabaci species in South Africa.
- Virus-vector biology

Collaborating institutions include the University of the Witwatersrand and Sakata Vegenetics Pty (Ltd), South Africa.



The FACULTY OF SCIENCE is a vibrant, dynamic and diverse scientific community that is a premier centre for the generation, dissemination and application of knowledge in the natural sciences and technology.