

From the director



The ambitious human microbiome project aims to map the entire complement of microorganisms associated with the human body, in the process determining the sequences of over 1000 microbial species; many of these organisms have never been cultured in the laboratory. The result will be a greatly improved understanding of the role of these species in health and disease. Similar work on animal species will flow from this research.

I am delighted to inform Centre staff and students that research in the Centre was viewed as being highly internationally competitive and up there with the best in the field. It is an exciting time to be a genomics researcher!

I was honoured to be invited as a speaker at Genomes 2008: Functional Genomics of Microorganisms, which was held in April at the Institut Pasteur in Paris and attended by over 400 international experts and workers in the field of microbial genomics. The amazing recent advances in sequencing technology and capacity are astounding when one recalls that it is only 13 years ago that we gasped in awe at the then ground breaking achievement of the determination of the complete genome sequence of a bacterial species, the 1.8Mb genome of *Haemophilus influenzae*.

There are now many hundreds of publicly available genome sequences of microbes as well as higher eukaryotic organisms, including of course the human genome and many of the animal species on which the centre has research projects. Analysis of these genomes has informed research into vaccine development, new therapies, epidemiology, pathogenesis of disease and a range of other biological mechanisms. Nowhere is this more apparent than in the field of metagenomics.



Professor Adler during his Genomics 2008 talk in Paris

Ben Adler
Director

Highlights

Renowned CI receives the 2008 Health Minister's Award and a Federation Fellowship



Professor James Whisstock with award medal and Professor David de Krester (left) and Sir Gustav Nossal (right) at the award dinner ceremony. Photograph courtesy of the Australian Society for Medical Research.

Centre Chief Investigator Professor James Whisstock has recently been awarded the Health Minister's Award for Excellence in Health and Medical Research.

The award, worth \$50,000, was presented to James at the annual Australian Medical Research Week dinner in recognition of his work in the field of protease biology and pore forming proteins as well as his mentorship skills.

In late 2007 James and his team, in the Department of Biochemistry and Molecular Biology at Monash University, discovered a surprising link between bacterial pore forming toxins and mammalian immune proteins when they solved the 3D structure of the perforin-like protein Plu-MACPF. Structural analysis of Plu-MACPF revealed that this family is structurally and evolutionarily related to a family of bacterial toxins known as cholesterol-dependent cytolysins or CDCs. The structural similarity provided key insight into the molecular mechanism of perforin-like proteins, and suggests how these proteins can punch holes in bacterial membranes and virally infected cells. Further, the discovery presents an intriguing distant evolutionary link between bacterial toxins and mammalian immune proteins. The results were published in the highly prestigious journal, *Science*.



Professor Whisstock with his Federation Fellow lapel and (from left to right) Professor Margaret Shiel (CEO, Australian Research Council), Senator Kim Carr, Minister for Innovation, Industry, Science and Research and Professor Tanya Monro, The University of Adelaide. Photograph by Arthur Mostead courtesy of the Australian Research Council.



Professor Whisstock and his team

Prior to the ceremony, Health Minister Nicola Roxon commented, "Because of (James') work, we now have a better understanding of the causes of diseases such as viral infections, emphysema, liver cirrhosis and thrombosis as well as the causes and treatment of cancer."

The Commonwealth Health Minister's Award for Excellence in Health and Medical Research recognises outstanding achievement and potential for future achievement by an Australian researcher who has received their PhD or MD within the last 12 years.

This award follows hot-on-the-heels of James' receipt of an ARC Federation Fellowship in April awarded to him at a ceremony in Canberra on April 22, 2008 by Prime Minister Kevin Rudd.

This high-status fellowship worth more than \$250,000 a year for five years is usually only awarded to approximately 25 researchers a year. This year James was one of 14 recipients.

James will use the Fellowship to continue his research on perforin-like proteins. "It will allow me to develop new research directions in the field, looking at the role of pore-forming proteins."

James is already recognised as a world-leading expert on bioinformatics and structural biology and another protein family known as serpins and has published more than 110 papers in leading peer reviewed journals. In 2006, James was the recipient of the Science Minister's Prize for Life Scientist of the Year.

"It (the fellowship) is a fantastic opportunity, a great honour, privilege and responsibility. Thank you to my team and I would also like to pay tribute to my great collaborators."

The Centre is now exceptionally privileged to have two Federation Fellows in its chief investigator line-up. Professor Jamie Rosjohn also of the Department of Biochemistry and Molecular biology was awarded a Federation Fellowship in 2006. Jamie's team continues to provide insight on host and microbial aspects of infection and immunity.

Professor Whisstock's lab:
<http://research.med.monash.edu.au/whisstock>

AWI funds footrot vaccine trials

australian wool
innovation
• limited

AWI funds Centre sheep footrot vaccine trials

The Centre is delighted to announce that it will receive \$663,560 funding from the Australian Wool Innovation (AWI) for research on its footrot vaccine development project. The Centre, which has been working on the flagship project for the last five years, with AWI's support, is now able to take its research to the costly yet critical clinical trial phase. Footrot is a highly contagious disease of the feet of sheep which causes severe lameness and loss of body condition. In Australia, the financial impact of the disease on the wool and livestock industry is estimated at \$100 million a year.

Australian Wool Innovation's Program Manager Animal Health, Productivity and Welfare, Dr Johann Schröder said "Footrot has long been the bane of Australian woolgrowers and prime lamb producers. While many improvements have been made over the years in its control, and we have a very good understanding of measures to limit its impact on production, this avenue of research holds great promise."

The vaccine trial work, already commenced at the Centre's project partner institution, the University of Sydney (Camden), continues the recent work of ARC Centre scientists which was published in the prestigious journal *Nature Biotechnology* in 2007.

The findings were the culmination of eight years of collaborative work between scientists at Monash University and The Institute for Genomic Research (TIGR), Maryland, USA, on the pathogenic bacterium that causes footrot, *Dichelobacter nodosus*. The research involved the determination of the bacterium's complete DNA sequence, which was then analysed to identify proteins that are potentially exposed on the surface of the bacterium and therefore more likely to elicit an immune response. Such proteins, if they can be expressed and purified *in vitro*, are suitable candidates for the development of a recombinant protein footrot vaccine.

The AWI grant, funded for a period of three years, will allow the project team to test at least 90 proteins in animal trials, which involve vaccinating sheep with purified surface expressed proteins to assess whether they produce an immune response and protect against footrot.

Centre Chief Investigator Professor Julian Rood and Monash University project leader, who has been researching footrot for over 25 years, said "Our approach has really made significant inroads in the development of a novel vaccine for footrot. However, the AWI funding means the development of a marketable vaccine is likely to happen a lot sooner. This is very good news for sheep producers".

The ARC Centre's reverse vaccinology or genomic approach has been made possible by the Centre's microbial gene expression and protein purification pipeline, an assembly of specialised infrastructure at



A sheep inflicted with footrot

Monash University in proteomics, production production and X-ray crystallography.

The animal vaccine trials are led by Centre Associate Professor Richard Whittington, of the Veterinary Science Faculty of the University of Sydney, New South Wales.

Necrotitis enteritis unravelled



Left to right: Dr Rob Moore (CSIRO Livestock Industries), Dr Anthony Keyburn and Professor Julian Rood.

The Centre's collaborative avian necrotic enteritis vaccine development project with the Australian Poultry CRC and CSIRO Livestock continues to 're-write the book' on the devastating disease.

In a second landmark paper published on 8 February, 2008 in the international journal *PLoS Pathogens* former Centre PhD student Dr Anthony Keyburn has identified that a novel toxin, NetB, is the likely key virulence determinant of necrotic enteritis.

Avian necrotic enteritis is one of the world's most common and financially crippling poultry diseases. It is caused by *Clostridium perfringens* a bacterium found in soil, litter, dust and in small quantities in the intestines of healthy chickens. The bacterium causes disease when it proliferates to high numbers producing extracellular toxins that attack the bird's intestines, causing lesions.

For the last 30 years researchers have believed that the disease's causative factor was an alpha toxin, although this was never proven, and unfortunately has meant that most disease control research work associated with necrotic enteritis to date, has focused on essentially the wrong area. Anthony's work under the supervision of Centre Chief Investigator Julian Rood and Centre Associate Dr Rob Moore of CSIRO Livestock Industries has recently been able to show that the alpha toxin is not the causative factor of the disease and also identified an alternative causative agent, another toxin now referred to as NetB.



In addition, because NetB is an extracellular toxin it also makes for an ideal vaccine candidate. Anthony's work will now be continuing in this direction in a new project led by Professor Rood and Dr Moore with further support from the Australian Poultry CRC.

Anthony is very happy with the new project development and would like to continue to work on a NetB necrotic enteritis vaccine eventually moving into the industry sector to concentrate on other vaccine development projects.

Indeed Dr Moore claims "Around the world, poultry producers are waiting for vaccines against necrotic enteritis. Thanks to Anthony's discoveries, scientists should now be able to develop the vaccines within a couple of years."

The latest developments in Anthony's work have also made him the Centre's most recent media star appearing not only in the *Tamworth Country Leader* and the *Geelong Advertiser* but in a feature article in *The Australian*, on March 31 this year.

Dr Keyburn was awarded his PhD in June.

MIIN Young Investigators

The latest Monash Infection and Immunity Network (MIIN) Young Investigators Symposium, held on 3 July at Monash University, was hailed as another great success. The Symposium talks included presenters from the Monash University faculties of Medicine, Science and Pharmacy, the Monash Institute for Medical Research (MIMR) and the Burnet Institute. Professor Adler summed up the meeting in the closing session by commenting, "Each year the Young Investigators' talks always exceed expectations." He also made special mention to the Symposium's sponsors, Dow AgroSciences, Pacific Laboratory Products, Applied Biosystems and Millennium Science in grateful acknowledgement of their support, as well as, Ms Morag Milton who organised the event.

The Best Poster prize, which is sponsored by the Centre, was awarded to Amelia Vom from the Pharmacy College and the Best Presentation prize was awarded to Johanna Dean from the Burnet Institute.

Centre Director Professor Ben Adler is co-convenor of the network, together with Centre Associate Professor Paul Hertzog.

MIIN homepage:
www.miin.monash.org/index.html

Other news

The Centre would like to congratulate Dr Corrine Porter and Dr Julian Vivian on their successful 2007 Fellowship applications.

Both Corinne and Julian are now NHMRC Peter Doherty Fellows.

Student profile

Radhika Bantwal



Radhika Bantwal is a Centre PhD student who works with Professor Julian Rood and Research fellow Dr Trudi Bannam in the Department Microbiology, Monash University. Her research project is part of a large on-going study which aims to investigate the transfer mechanism of toxin and resistance plasmids in the gram positive anaerobic pathogen, *Clostridium perfringens*.

Radhika completed both her undergraduate and post-

graduate studies in India specialising in clinical microbiology immigrating with her family to Australia in 2004. She has previously worked in areas related to food borne pathogens and opportunistic infections associated with AIDS and cancer. In early 2006 Radhika was the successful recipient of an Australian postgraduate scholarship and commenced her PhD. Radhika has found her experience of studying in Australia to be wonderful and is proud to be part the ARC centre. She likes to dedicate her spare time to her young daughter Deepali, and husband Dinesh. Radhika also enjoys music.

Acknowledgements

The ARC Centre of Excellence in Structural and Functional Microbial Genomics newsletter is compiled and edited by Marianne Johnston. Suggestions for articles are welcome, as well as requests to be placed on the newsletter mailing list, and should be sent to: marianne.johnston@med.monash.edu.au or fax: 9905 9328.

Marianne is now located in Bld 13C, Room G17, phone number: 9905 8610.

The ARC Centre of Excellence in Structural and Functional Microbial Genomics is an Australian Research Council (ARC) funded institute through the Centre of Excellence program. It aims to elucidate key aspects of microbial pathogens and the hosts they infect. The ARC Centres of Excellence are an Australian Government initiative designed to create prestigious hubs of expertise where high-quality researchers can maintain and develop Australia's international standing in research areas of national priority.

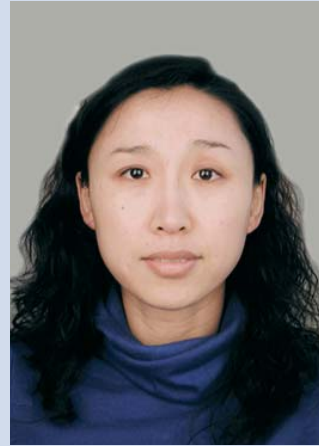
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Staff profile

Xiaoyan Han



One of the Centre's newest Research Fellows is Dr Xiaoyan Han. Xiaoyan works on the pathogenesis of the ovine footrot pathogen, *Dichelobacter nodosus* in Chief Investigator's Professor Julian Rood's laboratory. In 2002 she joined Professor Rood's lab as a PhD student and successfully completed her studies in 2007. Over this period she has already published three significant papers on *D. nodosus*.

The objectives of Xiaoyan's work are to identify genes involved in type IV fimbrial biogenesis and function in *D. nodosus*, to develop an understanding of the molecular mechanisms by which type IV fimbrial biogenesis, natural transformation, and protease secretion are linked, and to investigate the role of carboxyl-terminal extensions of proteases in secretion and function. Two major approaches, genetic analysis and protein complex studies, are being applied to elucidate these issues.

Xiaoyan is originally from China and received her masters and bachelor degrees from Inner Mongolia University, China. After completing her masters degree, she worked for five years as a lecturer in the same institution teaching Biochemistry. Before starting her PhD she worked for 12 months as a visiting scientist at the Centre for Animal Biotechnology in the Veterinary School of the University of Melbourne.

Whilst Xiaoyan misses her home town in China she is very happy working with all the members of the Rood lab and raising her young daughter, Hattie, in Australia.

The Centre works in partnership with the following organisations:



The University of Sydney



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