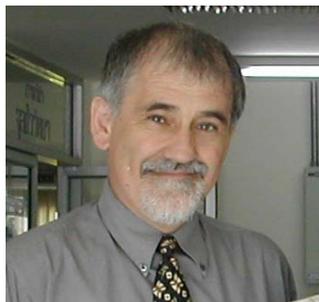


## FROM THE DIRECTOR



My first pleasant duty in this Newsletter is to express my most sincere thanks to retiring CIs Phillip Nagley and John Davies. As outlined below, both were foundation Centre CIs and played major roles in the original establishment of the

Centre. Phillip served as Deputy Director until 2008 and I am especially grateful for his untiring administrative assistance in the early days when we had no administrative support. John's collaboration with Paul Hertzog was in no small way responsible for Paul's subsequent recruitment to the Centre. At the same time it is a pleasure to welcome Paul and also Els Meeusen as Centre CIs. The Centre's research program will benefit from their extensive expertise and experience in veterinary immunology and innate immunity. Thank you Phillip and John, and welcome Els and Paul!

2010 sees a major enhancement of the Centre's international profile, with new or augmented collaborations with institutions in Norway, UK and New Caledonia. Undoubtedly the international highlight of the year is the Centre's first conference on bacterial pathogens of animals (details below). During the course of this year so far I have met with many scientists from around the world who will be participating in the conference. All have indicated to me that there is a clear need for this kind of gathering of researchers in the veterinary field. Significantly, the Elsevier Journal *Veterinary Microbiology* will publish the conference proceedings as a Special Issue. We look forward to a stimulating, exciting and informative meeting.

Ben Adler  
Director

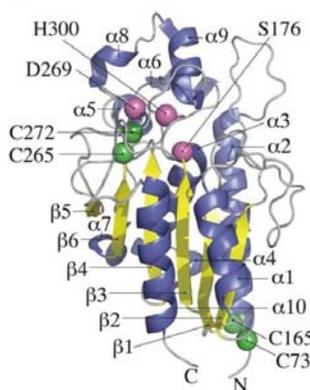
## RESEARCH HIGHLIGHTS

### Natural Selection *In Vivo* Identifies Essential Kinase Residues for Phosphorylation of *Pasteurella multocida* Lipopolysaccharide

This research paper submitted by Centre Research Fellow, Dr Marina Harper was recently highlighted by the Editors in *Infection and Immunity*, September 2010, Vol 78, Issue 9. Full paper can be found (p. 3669-3677).

*Pasteurella multocida* is very unusual in producing two full-length lipopolysaccharide (LPS) glycoforms (A and B) during *in vivo* growth in chickens. A mutant that expresses truncated glycoform A and full-length glycoform B is avirulent. However, Harper et al. show that chickens inoculated with high doses of this mutant become infected with *P. multocida* that no longer expresses any truncated LPS. These *in vivo*-derived mutants all harbor compensatory suppressor mutations within KdkA, a kinase essential for the assembly of glycoform A LPS. Analysis of these *in vivo*-derived LPS mutants allowed the identification of four amino acid residues essential for KdkA function.

### Tetrahydrolipstatin Inhibition, Functional Analyses and Three Dimensional Structure of a Lipase Essential for Mycobacterial Viability



Crystal structure of MSMEG\_6394, catalytic triad shown in magenta spheres.

A recent paper submitted by Centre Research Fellow, Dr Paul Crellin has revealed more about an essential mycobacterial enzyme, Rv3802c from *M. tuberculosis*. This enzyme is a partially characterised phospholipase/thioesterase encoded within a genetic cluster dedicated to the synthesis of core structures of the mycobacterial cell wall, including mycolic acids and arabinogalactan.

Enzymatic assays performed with purified recombinant proteins Rv3802c, and its close homologues from *M. smegmatis* (MSMEG\_6394) and *Corynebacterium glutamicum* (NCgl2775) show that they all have significant lipase activities that are inhibited by tetrahydrolipstatin, an anti-obesity drug that coincidentally inhibits mycobacterial cell wall biosynthesis. The crystal structure of MSMEG\_6394, solved to 2.9Å resolution, revealed an  $\alpha/\beta$  hydrolase fold and a catalytic triad typically present in esterases and lipases. Further, the work demonstrates direct evidence of gene essentiality in *M. smegmatis* and shows the structural consequences of loss of MSMEG\_6394 function on the cellular integrity of the organism. These findings, combined with the predicted essentiality of Rv3802c in *M. tuberculosis*, indicate that the Rv3802c family performs a fundamental and indispensable lipase-associated function in mycobacteria.

Full paper is in press at time of this newsletter in the Journal of Biological Chemistry.

DOI: 10.1074/jbc.M110.150094

## OTHER NEWS

### Centre Director appointed to the Scientific Council of Pasteur Institute in Noumea

Centre Director Prof Ben Adler has accepted an appointment to the Scientific Council of the Pasteur Institute in Noumea, New Caledonia. His role will be to advise on research and other scientific issues related to bacteriology work carried out by the Institute.

### Footrot Research Goes to Europe



Prof Julian Rood and Dr Ruth Kennan with the Norwegian footrot research team

Centre CI Prof Julian Rood and Centre Research Fellows Dr Ruth Kenann and Dr Xiaoyan Han recently attended two important footrot research meetings in Europe. The first meeting held at the end of May in Oslo, Norway, and attended by Rood and Kennan, was the initial research meeting of a new research team that includes the ARC CoE's footrot group. This collaborative team recently obtained funds from the Norwegian Research Council to investigate a major footrot outbreak in Norway. In 2011, a PhD student based at the Norwegian National Veterinary Institute will spend six months in the CoE carrying out genomic analysis of Norwegian isolates of *Dichelobacter nodosus*, the causative agent of footrot. The second

meeting, which was attended by all three members of the CoE, was held in early June at Warwick University as part of a Monash-Warwick Strategic Grant awarded to Prof Rood. The meeting provided an excellent overview of the current footrot disease status in the United Kingdom and Europe. The Monash team gave major presentations at both meetings and several interesting collaborative opportunities have arisen as a result.

### Invited Plenary Speaker at GIM2010

Prof Julian Rood was recently invited to speak at the 11<sup>th</sup> International Symposium on the Genetics of Industrial Microorganisms (GIM2010) held at the Melbourne Convention & Exhibition Centre from 28 Jun – 1 Jul. His talk was entitled '*Dichelobacter nodosus*, the causative agent of ovine footrot: Pathogenesis, genomics and vaccine development'.

### Invited Speaker at Awaji Forum, Japan

Centre Director Prof Ben Adler continued his long term association with Japanese science through an invitation to speak at the Awaji International Forum on Infection and Immunity in September, where he presented the Centre's recent work on pathogenesis of fowl cholera.

### Goodbye and Welcome of CIs

This year we say goodbye to Prof John Davies and Prof Phillip Nagley who are retiring as Chief Investigators of the Centre. We thank them for their tremendous work and contributions towards the Centre since its inception. They will however remain affiliated with the Centre as Associates. We also welcome Prof Els Meeusen and Prof Paul Hertzog who took up the role of Centre CIs from July 2010.



Prof Els Meeusen heads the Biotechnology Research Laboratories (BRL) within the School of Biomedical Sciences at Monash University. She is an international expert in large animal immunology with particular emphasis on parasite immunobiology and vaccine development. Her lab works in close collaboration with commercial companies and industry groups to translate basic research finding into practical applications for animal and human health.



Prof Paul Hertzog is the Director of the Centre for Innate Immunity and Infectious Diseases at the Monash Institute of Medical Research (MIMR) and a Senior Principal Research Fellow of the National Health and Medical Research Council of Australia. Professor Hertzog has an international reputation in

cytokine signaling, innate immunity and the generation and characterisation of mouse models of infectious and inflammatory diseases. Paul is and the Co-convenor of the Monash and Victorian Infection and Immunity Network.

You will be able to hear more about Profs Meeusen's and Hertzog's research at the coming Annual Scientific Meeting in November (details are in the Upcoming Events section).

## STAFF PROFILE

### Mark Edmunds



Mark Edmunds is a Centre Technical Officer and works on *Dichelobacter nodosus* and *Pasteurella multocida* reverse vaccinology projects with Prof Ben Adler, Prof Julian Rood and Dr John Boyce. Mark's scientific interest lies in the interactions occurring between bacterial and host cells leading to infection.

Whilst working towards his undergraduate Biotechnology Degree at Victoria University Mark obtained a place in the Undergraduate Research Opportunities Scheme (UROP) run through BIO21 and Melbourne University. During his time with UROP, Mark studied Hepatitis C viral glycoproteins and their interactions with cellular receptors in the Fusion laboratory at the MacFarlane Burnet Institute. He completed his Honours year in the Fusion Laboratory in 2008 through Monash University, where he first met Ben Adler and John Boyce.

In his spare time, Mark likes to find a quiet reef around Mornington or on the Great Ocean Road to surf.

## STUDENT PROFILE

### Tanya D'Cruze



Tanya is completing her PhD research under the supervision of Prof. Rod Devenish and Dr. Mark Prescott, in collaboration with Prof. Ben Adler and Dr. John Boyce. As a researcher on the *Burkholderia pseudomallei* project, her aim is to identify potential virulence factors which

contribute to bacterial infection and the evasion of host cell autophagy. In the course of her research, she has generated deletion mutants of four potential effector molecules encoded in the *B. pseudomallei* genome; one of the mutants is fully attenuated when tested using *in vivo* mouse disease models.

Previous to Monash, she completed her under-graduate and Honours degrees at Victoria University. Her Honours research focused on apoptosis in P19 embryonal carcinoma cells when induced by bone morphogenetic protein 4 (BMP-4).

Tanya comes from a mixed background of Indian and Portuguese heritage. She is passionate about chocolate,

music, dancing and travelling. And, she hopes to one day crown her travels with a journey to Antarctica.

## UPCOMING EVENTS

### VIIN Post-Doctoral Symposium

The Victorian Infection and Immunity Network (VIIN) will be holding its Post-doc Symposium on 30 September at the South 1 Lecture Theatre, Monash University Clayton Campus.

Keynote speakers include Prof Stephen Locarnini from the Victorian Infectious Disease Reference Laboratory and Prof Fabienne Mackay from Department of Immunology, Monash University

Details of the Symposium can be found on: <http://www.viin.monash.org/pd-symp-2010.html>

Registration is free, open to all (not only post-docs!) and includes food and drink on the day. To register please email the following details to [info@viin.org.au](mailto:info@viin.org.au) by the **24th September**.

### Prato Conference on Pathogenesis of Bacterial Diseases of Animals

The Centre is organising the above-mentioned conference which will take place from 6-9 October 2010 at the Monash Prato Centre, Italy.

This conference will focus on veterinary pathogens and will involve an integrated examination of the latest exciting data on disease epidemiology, bacterial adhesion, intracellular pathogens, extracellular pathogens and toxins, host-pathogen interactions, innate and acquired immunity, and vaccines, all as they apply to bacterial pathogens of animals.

More details can be found on the website: [www.vetpath2010.org](http://www.vetpath2010.org)

### ARC Centre Annual Scientific Meeting

This year, the Centre's Annual Scientific Meeting will be held on 29 November from 9.30am – 5pm at the Monash University Caulfield Campus.

The meeting will focus on the research projects currently taking place within the Centre. The keynote speaker is Prof Charles Mackay who is a recipient of an NHMRC Australia fellowship. More details will be released soon.

## CONTACT

Suggestions for articles are welcomed, as well as requests to be placed on the mailing list, and should be sent to:

[Desmond.Gul@monash.edu](mailto:Desmond.Gul@monash.edu)

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.

Contact or visit us at:

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The Centre works in partnership with the following organisations:

