

FROM THE DIRECTOR



Science without communication is dead. This rather dogmatic and harsh statement emphasises the point that as scientists we have a duty to communicate the results of our research to the wider scientific community and to interact with the public at large. After all, the taxpayers are the major supporters, either directly or indirectly, of our research. I have long been a big fan of science communicators such as Carl

Sagan and Richard Dawkins. I have just finished reading a book by another superb science communicator, Brian Cox. His lay language treatise on *The Quantum Universe* is superb and shows very elegantly that it is possible to explain the most complex issues in an understandable manner and to emphasise its relevance for our everyday lives. For the non-physicist I can think of nothing more complex than quantum theory.

It is therefore very pleasing that the previous year has seen a range of Centre outreach activities. As described in this Newsletter, these activities have ranged from a public lecture on the massive problem of antibiotic resistance, to an expert workshop on diagnostics at the National Institute of Animal Health in Bangkok, through to the supervision of students from the John Monash Science School in Centre laboratories. Indeed, it was my pleasure in October to attend the Science Fair at the John Monash Science School and I was deeply impressed by the level of science achieved by the students and their genuine passion for science and learning. My faith in the future of science and science communication was reinforced!

Ben Adler
Director

RESEARCH HIGHLIGHTS

Role of *bpscN* gene in virulence of *Burkholderia pseudomallei*

B. pseudomallei, the causal agent of melioidosis, employs a number of virulence factors during its infection of mammalian cells. One such factor is the type three secretion system (TTSS), which is proposed to mediate the transport and secretion of bacterial effector molecules directly into host cells. The *B. pseudomallei* genome contains three TTSS gene clusters (designated TTSS1, TTSS2, and TTSS3). Previous research has indicated that neither TTSS1 nor TTSS2 is involved in *B. pseudomallei* virulence in a hamster infection model. We have characterized a *B. pseudomallei* mutant lacking expression of the predicted TTSS1 ATPase encoded by *bpscN*. This mutant was significantly attenuated for virulence in a respiratory melioidosis mouse model of infection. In addition, analyses in vitro showed diminished survival and replication in macrophages and an increased level of colocalization with the autophagy marker protein LC3 but an unhindered ability to escape from phagosomes. Taken together, these data provide evidence that the TTSS1 *bpscN* gene product plays an important role in the intracellular survival of *B. pseudomallei* and the pathogenesis of infection. (D'Cruze T, Gong L, Treerat P, Ramm G, Boyce JD, Prescott M, Adler B, Devenish RJ. 2011. Role for the *Burkholderia pseudomallei* type three secretion system cluster 1 *bpscN* gene in virulence. *Infection and Immunity*, 79, 3659-3664.)

CENTRE STUDENT OVERSEAS LAB VISITS

Three Centre students have recently applied for travel funds from the Centre to visit labs overseas. Below are the reports on their trips and their experiences.

Sarah Preston is a PhD student working under the supervision of Prof Els Meeusen and Dr David Piedrafita.

Due to the generous funding provided by the ARC Centre of Excellence in Structural and Functional Microbial Genomics and Monash University, I was able to attend the 23rd World Association for the Advancement of Veterinary Parasitology conference in Argentina this August. I was also fortunate enough to visit leading scientists in Parasitology and Immunology from the University of Nebraska, the Moredun Institute in Scotland and the National University of Singapore.

I first visited Professor Scott Gardner at the University of Nebraska who is the curator of the extensive collection of parasite specimens at the Harold W. Manter Laboratory -something that only a parasitologist would be excited about! However, I was thrilled to discover that at the same time I was there, the Rocky Mountain society of Parasitologists was holding their annual conference and I was able to attend. The conference went for three days with one of the most interesting talk given by Professor Janice Moore from Colorado State University who talked about the history of parasitology and how the study became fashionable. After the conference I had a chance to tour Professor Gardner's laboratory which is home to the extensive collection of parasite specimen and literature. The parasite collection was elaborate - everywhere you looked there were collection jars full of parasites! I even got to sit at the original desk of Harold W Manter, a famous parasitologist from the 1950's, whom the lab was named after. Professor Scott Gardiner is a very enthusiastic man and I appreciated the time he put in to my visit despite being busy with the FBI trying to locate some missing specimen samples from his recent trip to Mongolia!

My next laboratory visit was to the prestigious Moredun Institute in Edinburgh that specialises in infectious diseases affecting livestock. Here I was fortunate enough to meet with Professor David Knox who kindly showed me around the facilities and organised meetings with other scientists working in my field of interest. It was great to informally discuss my project ideas with people in my field and put faces to people's papers you have read. It turned out that one scientist I met, Dr Tom McNeilly, will soon be receiving samples to analyse the expression of the same protein that I have been working on. It was great to share and exchange knowledge on galectin-11 with him. The institute overall was amazing (people and facilities) and it would be a dream to one day end up there.

Lastly, I visited Professor Ling at the National University of Singapore who specialises in innate immunity. Prior to showing me around the laboratory, Professor Ling gave me some invaluable advice on applying for postdoctoral positions and particularly what most researchers are looking for.

I would like to extend a sincere thank you to all the researchers that took time out of their busy work schedule to show me around and provide excellent advice and guidance for my career ahead. I would especially like to thank my supervisors, Professor Meeusen and Dr Piedrafitra who have been exceptional in assisting me with my research and have provided me with endless opportunities to develop my experimental and professional skills. I would also like to acknowledge the ARC CoE, Monash University, The Biotechnology Research Centre and SheepCRC for providing funding to allow this trip to happen and providing me with the opportunity to undertake research in a field that I am passionate about.

Lakmini Weeramantri is a PhD student working under the supervision of Prof Julian Rood and Dr Trudi Bannam.

My Ph.D. project titled "The Role of Conjugative Plasmids of *Clostridium perfringens* in Toxin Production and Virulence" is supported by a National Institute of Health (NIH) grant (AI056177) entitled, "Virulence plasmids of *Clostridium perfringens* type B-D strains". My research project involves analysis of the pathogenicity of certain strains of *Clostridium perfringens*, which is the primary causative agent of several enterotoxaemic diseases in domestic livestock and humans due to its ability to produce various toxins. Specifically, work on this project includes a detailed characterization of the toxin-encoding plasmids carried by Type B-D strains of *C. perfringens* to better understand their role in disease process and develop new vaccines/antitoxin therapeutics against *C. perfringens* virulence.

My Ph.D. supervisor, Prof. Julian Rood and Prof. Bruce McClane are Principal Investigator's on this NIH grant and to facilitate NIH research collaboration, I completed my field at Prof. McClane's laboratory located at University of Pittsburgh, School of Medicine. This field study allowed me to learn an important molecular biology technique (pulsed-field gel electrophoresis) for characterizing *C. perfringens* toxin plasmids.

Pulsed-field gel electrophoresis (PFGE) technique is used to separate large DNA fragments by periodically switching the direction of voltage applied. PFGE technique has been optimized by Prof. McClane's laboratory to examine the genetic diversity in *C. perfringens* toxin plasmids to provide an

accurate characterization of Type B-D plasmids, which have obvious molecular epidemiology value and direct impact on understanding of *C. perfringens* host specificity and pathogenesis.

During my field study at Pittsburgh, I have learned how to perform PFGE technique, optimize conditions for *C. perfringens* Type B-E strains containing multiple toxin-encoding plasmids and McClane transformation method. The knowledge I have gained through my field study has already assisted me to characterize some of *C. perfringens* Type C strains and mutant strains in the Rood lab. Also, I have tried using McClane transformation method to make mutants in *C. perfringens* Type C strains. Furthermore, I have shared the knowledge of PFGE with an honours student who had experienced difficulties performing this technique. I will be using PFGE technique throughout my research project to characterize Type B-D strains, which lead to a better understanding of the genetic diversity of *C. perfringens* strains and the determination of the role of each toxin in disease. So, the knowledge I gained through this field study will greatly assist my Ph.D. thesis and will also support to obtain maximal progress for an important NIH grant.

Hamish McWilliam is a PhD student working under the supervision of Prof Els Meeusen and Dr David Piedrafitra.

Recently, with the help of a student travel grant from the ARC CoE in Structural & Functional Microbial Genomics, I was able to travel to China to undertake important research towards my PhD at the Hunan Institute for Parasitic Diseases, in Hunan province. This was a great opportunity for the research I am undertaking, and also for me personally.

Over the past two years of my PhD, I have been studying a parasitic disease called schistosomiasis, which is a major problem in many parts of the tropical developing world, including the marsh and flood plains of central-southern China. Here this worm infects humans and other mammals, such as the water buffalo which is responsible for high levels of human transmission. My aim is to discover new parasite molecules which could make an effective vaccine against this disease, which for the buffalo and/or humans.

The travel to China enabled me to conduct an experiment to study the parasite in its natural animal host, the buffalo. Most of the vaccine research to date occurs initially in laboratory models, such as rodents, so this experiment was a unique opportunity to have access to animals naturally exposed to the disease. This may enable us to find a more relevant and effective vaccine, since there can be problems in the translation of discoveries in the lab to real-world situations. In a nut shell, my main aim was to collect antibody samples from the buffalo using a novel method, which isolates the immune response occurring just against the larvae as they migrate through the buffalo. These migrating larvae are the susceptible targets for vaccination. I also wanted to collect various tissue samples in order to characterise other aspects of the immune response, since this has not been done before in buffalo.

The experiment was a success, and we were able to complete what we set out to do. I brought back hundreds of samples that I'm beginning to analyse now, and the results are positive. However there were a few 'hairy' moments where things looked as if they wouldn't go to plan, but we found ways around them. At one point it seemed that we wouldn't find enough of the elusive parasites for the experiments, because of the time of year and that the numbers were down. The parasites live inside an intermediate host, a fresh water snail, and so we went out on a snail-hunting expedition, where we collected thousands of the snails from the marshlands. Down on our hands and knees in the mud, picking up pea-sized snails with tweezers, was strangely therapeutic. Out of the bucketfuls of snails however, only 7 were found that were infected - but luckily these turned out to contain enough parasites for our purpose.

The experimental conditions were different to what I'm used to here in Australia, and it was quite eye-opening when we came to the buffalo dissections. Up at 4:30am, we met the butchers near a market before dawn, who deftly carved the carcasses. In a matter of minutes they had the entire intact skin off, and I had to be quick to get the samples I needed before the animal was taken off to market. When the sun finally came up, the setting I was working in was revealed - chickens running along the street, women cooking food for the market, rubbish being incinerated in a pile along the street. Normally I'm obsessed with cleanliness in the lab, so collecting and processing samples in this environment was a novel experience.

It was valuable to go to an endemic site for schistosomiasis, something I had previously only read about - to see the people and animals at risk of infection, and see the need for a solution. We were also able to cement strong collaborations with the researchers at the institute, who were very hard-working, and extremely kind and accommodating to us. They have access to facilities and opportunities which we lack, and it's likely that these collaborations and friendships will continue into the future.

Centre students are reminded that these travel grants (max. \$1000) are still available. They are not for the sole purpose of attending conferences but to visit overseas labs for exchange and seminar presentations. More details can be obtained from Desmond Gul.

OTHER NEWS

National Science Week Public Lecture

Among the public outreach programs for 2011, the Centre organised an evening public lecture on 16 August, in conjunction with National Science Week. The lecture entitled "The End of Antibiotics" was delivered by guest speaker, Prof Paul Johnson, Deputy Director of the Infectious Diseases Unit at Austin Health, who is also an affiliate of the Department of Microbiology at Monash University. He has collaborated with Centre Director Prof Ben Adler and with former Centre CI Prof John Davies.

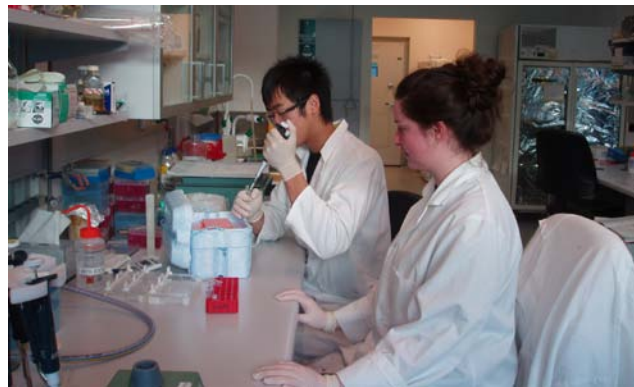
Held at the BMW Edge Theatre at Federation Square, the lecture attracted an impressive audience and received favourable feedback from the public.

The topic has been of great interest recently, especially given the rise of antibiotic resistant bacteria in the last few years. Combating antimicrobial resistance is also the theme for the 2011 World Health Day as selected by the World Health Organisation.

The lecture was followed by questions from the audience and an expert panel discussion comprising staff members from the Centre and the Monash Department of Microbiology.

Supporting future scientists from John Monash Science School

The year 2011 has seen a number of activities developing between the Centre and John Monash Science School (JMSS), a specialised high school which sits within a stone's throw away from the Centre. As part of its drive to nurture these budding science students, JMSS students were given the opportunity to undertake a 1-week attachment (27 June – 1 July) in a science lab. Our Centre students Amy King and Sarah Preston each supervised a Year-10 student, David Daon and Elissa Xu respectively, during this period. JMSS students enjoyed the experience as it gave them the opportunity to take in the experience of working in a proper science lab and learning lab techniques and research approaches which they would not have encountered at their high school.



PhD student Amy King supervising JMSS student David Daon

On October 25, JMSS held a science fair showcasing the projects of their students. Centre Director Prof Ben Adler was part of the adjudicating panel for this event. With over 300 displays and student presenters, the school was packed. Besides judging the various displays and exhibits, Ben also engaged with JMSS students about their exhibit and science.



Centre Director Ben Adler talking with JMSS students at the Science Fair

INTERNATIONAL ENGAGEMENT

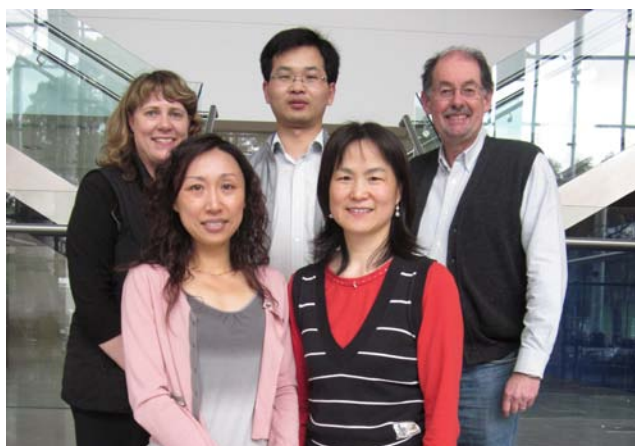
Through its extensive international network, the Centre has the privilege of hosting international scientists and students on exchange programs.

Dr Isabelle da Piedade from the University of Copenhagen spent a period of 12 months in the Centre's Adler/Boyce lab. Isabelle is a bioinformatician whose work involved developing a scheme to understand the phylogeny of bacteria of the Pasteurellaceae family, whose members are major causes of diseases of animals and humans worldwide. Isabelle's supervisor in Denmark is Prof Miki Bojesen, who spent a period of time working in the Adler lab 10 years ago.



Isabelle (bottom row, 2nd from left) with lab members from the Adler/Boyce Lab.

Since September 2010, A/Prof Xiang-Dang Du from Henan Agricultural University in Zhengzhou, China, has worked in the Centre's Rood Lab for 12 months as a Visiting Scientist. He was funded by a scholarship from the China Scholarship Council to investigate antibiotic resistance in *Clostridium perfringens*. Before he left, he presented his research (A bacitracin-resistant toxin-producing *Clostridium perfringens* strain has a mobile *bcrABDR* locus) conducted in the Rood lab at the BacPath conference.



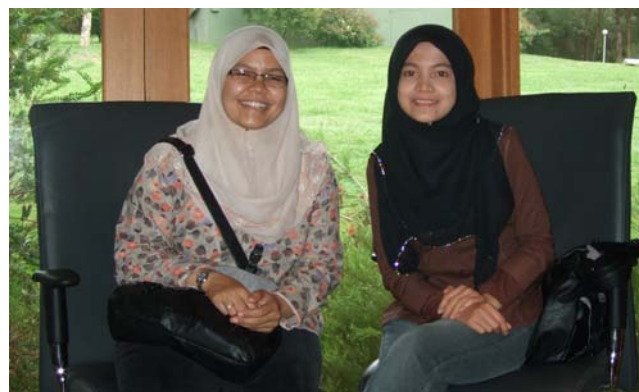
L-R Top: Trudi Bannam, Xiang-Dang Du, Julian Rood.
Bottom: Xiao-Yan Han, Xuxia Yan

Following his departure, Dr Marianne Gilhuus, a visiting PhD student from the Norway National Veterinary Institute joined the Rood lab. She will be here for 6 months and working with Dr Ruth Kennan on ovine footrot.



L-R: Marianne Gilhuus, Julian Rood and Ruth Kennan.

In the Centre's Rossjohn Lab, 2 Malaysian PhD students arrived last year to spend 5 months learning more about protein refolding and crystallisation. Noor Haza Fazlin Hashim from the National University of Malaysia and Nor Abdul Hasmaliana Manas from Universiti Teknologi Malaysia enjoyed their experience in Melbourne and hoped to bring what they have learnt back to help set up protein crystallisation facilities in their country.



Noor Haza (L) and Nor Hasmaliana (R)

Chinese Delegation Visit

A 20-member delegation from the Chongqing Animal Health Supervision Bureau in China visited the Centre on 24 November 2011. The delegation consisted of veterinarians, livestock technicians and directors of the various animal health supervision stations. They were led by the Director General of the Bureau, Ms Li Hongying, to learn more about the diseases that the Centre investigates and how we are coming up with solutions to treat and prevent them. Centre Director Prof Ben Adler and Drs Marina, Harper, Trudi Bannam, David Piedrafita gave short presentations on their work and we were fortunate to have Centre Research Fellow Dr Xiaoyan Han as our translator for all those technical details into Chinese for the delegation.



Centre Director Prof Ben Adler, Centre Research Fellows, and Chongqing Animal Health Supervision Bureau Director Ms Hongying Li with the rest of the delegates.

Leptospirosis Training Workshop

The Centre in conjunction with Queensland Health Scientific Services was invited by the Australian Department of Agriculture, Fisheries and Forestry (DAFF) and the Australian Department of Foreign Affairs and Trade (DFAT) to hold a training workshop on

Leptospirosis in Bangkok. The activity followed the formalisation of a free trade agreement between Australia and Thailand. Present were:

- Mr Simon Farbenbloom, Deputy Head of Mission, Australian Embassy,
- Dr. Vimol Jirathanawat, Director of the National Institute of Animal Health,
- Dr. Chawewan Viriyapak, Deputy Director-General of the Department of Livestock Development, Ministry of Agriculture and Cooperatives
- Dr. Suwannachai Wattanayingcharoenchai, Deputy Director-General of the Department of Disease control, Ministry of Public Health.

This "Leptospirosis Diagnostic Training Project" workshop took place at the National Institute of Animal Health from 18-20 May and was restricted to 60 selected participants from Thailand. Centre Director Prof Ben Adler who is a recognised international expert on leptospirosis led a team of presenters for the workshop, which included Dr Rudy Hartskeerl (Head of WHO/FAO/OIE Leptospirosis Reference Centre in The Netherlands) and Mr Lee Smythe (Head of WHO/FAO/OIE Leptospirosis Reference Centre in Queensland). Spread over 3 days, the workshop covered themes such as diagnostics, quality assurance programmes, training, reference laboratories, new technologies, research and public health.



Prof Ben Adler at the Leptospirosis Training Workshop in Bangkok.

ANNUAL SCIENCE MEETING

The Centre held its annual scientific meeting from 27-29 November at the Yarra Valley Conference Centre. This was the second time the Centre has used this venue. About 60 Centre students and staff, including Board members and Centre Associates attended the meeting. Among them were the new incoming Board member Prof Marshall Lightowlers who also gave the opening plenary talk on "Vaccines for control of parasitic diseases: neurosystemicercosis and hydatid disease" and the new Head of the Monash Department of Microbiology, Prof Christian

Doerig who gave a talk on "Plasmodium functional kinomics".



Science and fun at the Annual Scientific Meeting

STAFF PROFILE

Ben Adler



This newsletter we thought it was about time we profiled our director, Ben Adler. Ben is well known internationally for his work on bacterial pathogenesis and immunity spanning four decades. His passion for science has been attested by the more than 30 PhD students that he has supervised. Ben is a regular invited speaker at international conferences, especially in the areas where he is best known for his research on *Leptospira* and *Pasteurella*. In fact, he takes pride in being now recognized as the "Grand Old Man of Lepto". He was recently elected as the Chair of the Gordon Research Conference on the Biology of Spirochetes, the most prestigious conference in this field.

As well as science, Ben has had a keen interest in languages, music and motor sport. He speaks a wide range of European languages as well as Japanese and has enjoyed periods living and working in New Zealand, Japan and The Netherlands. Ben's parents hailed from Eastern Europe and he likes to point out that when he started

school in Australia, English was the fourth language he had to learn.

In his younger days, Ben dabbled in motor racing and rallying and he has driven at all of the major Victorian race circuits. Ben rues the fact that motor sport has become so expensive that the days of the amateur privateer are virtually gone. Another not so well known fact is that as an undergraduate Ben earned his pocket money as a wedding photographer and a folk singer in coffee lounges round Melbourne. He hastens to add that these days he is strictly just a keen music listener and his photos are restricted to travel snaps.

STUDENT PROFILE

Tamaryn Cashmore



Tamaryn Cashmore, or Tammy as she is known, began her postgraduate studies in clinical medicine at Stellenbosch University in South Africa, but soon realised that treatment of gunshot wounds and incomplete abortions was not for her. So she changed her career path to biomedical research. Her Honours degree involved a study

of the role of Vitamin D in the pathogenesis of HIV/AIDS. After working in many different areas for a few years, her interest was sparked by Tuberculosis (TB) – the number 1 killer of HIV-infected patients in South Africa. Subsequently, she completed her Masters at Cape Town University. This project assessed the feasibility of newer diagnostic methods of TB.

Her next big move was to Monash University. “I wanted to experience a top, world-class institution in a first world country in order to greatly further my knowledge and practical skills. I am continuing to focus on TB research as there is such a great worldwide need for new insight, interventions and qualified answers.” In her PhD project, she will be looking at specific pathways in the biosynthesis of the mycobacterial cell wall. Two novel genes are of initial, particular interest. After characterising these, she will broaden her metabolic and lipidomic study to include three others in the same protein-synthetic complex.

“Growing up in South Africa has instilled in me a great love for the outdoors. As a child, we would go on safari at least once a year; horse-riding, hiking and tennis are still favoured hobbies. Fortunately, being in Melbourne, I can cope with rainy weather too! Cuddled up with my little Maltese Poodle, a good paperback novel plus a huge bar of dark chocolate suits me just fine...”

UPCOMING EVENTS

2nd Prato Conference on Pore Forming Proteins

The Centre contributes to this conference from 17 – 20 April at the Monash Prato Centre, Italy. For more details, www.pratolysin.org

6th International Veterinary Vaccines and Diagnostics Conference

The Centre has the privilege to host the 6th IVVDC conference from 29 July – 1 August at the Cairns Convention Centre. For more details, www.ivvdc2012.org

VETPATH 2012

The Centre's flagship event is back this year in October. The 2nd Prato Conference on the Pathogenesis of Bacterial Diseases of Animals will be held from 9-12 October at the Monash Prato Centre, Italy. For more information, www.vetpath2012.org

CONTACT

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

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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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