ARC/NHMRC RESEARCH NETWORK FOR
PARASITOLOGY

NEWSLETTER

Issue No. 25 February 2009

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Dear Network Participant,

This month we celebrate the award of NHMRC Fellowships and Scholarships to some fine young researchers. I congratulate all of you warmly.

However, this is unfortunately overshadowed by events that have rocked Geoff McFadden's lab, and many other researchers in the Network. The McFadden lab is in mourning after losing two fine people. Tim Spurck passed away from a heart attack, and Kylie Mullin succumbed after a long battle with melanoma. Tim will be known to many in the Network for his remarkable microscopy images. His expertise in confocal microscopy, live video and electron microscopy were legendary, and he created some remarkable images of *Plasmodium*, *Toxoplasma* and *Leishmania*. Tim is survived by his wife Jun-Li. He is already sorely missed. Kylie did a PhD in Malcolm McConville's lab and co-discovered the remarkable tubular lysosome of *Leishmania*. As a postdoc in Geoff McFadden's lab she characterised the malaria parasite's apicoplast membrane transporters, collaborated with Kiaran Kirk's group on a phosphate transporter, and developed the first method to isolate apicoplasts. Kylie is survived by her husband Daryl, and two young children Katherine (aged 3) and Thomas (aged 1). Kiaran Kirk, on behalf of Kylie's friends, has set up an account to accept donations, with the money collected to be used to pay for a holiday for Kylie's family, later in the year when they feel able to get away. Donations can be made by electronic transfer, and the account will remain open for the next month. The account details are as follows:

Bank: Commonwealth Bank

Account name: Kylie Mullin Memorial Fund

BSB: 062903

Account #: 10511963

Swift Code/IBAN (for transfers from overseas): CTBAA2US

In making a donation it is not necessary to reveal your name. If you prefer not to do so, but would nevertheless like your name included on a card that will accompany the cheque to be given to Kylie's family in a month's time, please just let Kiaran know (kiaran.kirk@anu.edu.au). NB, just to be clear, the card will list the names of those who have contributed so that Kylie's family will know that she had a lot of friends who are thinking of them, but it won't list the amounts of individual contributions. Those who include their names when making the donation need not contact Kiaran directly.

As Geoff says, "The loss of two extraordinarily kind, generous and talented young people is a tragedy".

Nick

(Nick Smith, Convenor, ARC/NHMRC Research Network for Parasitology; nick.smith@uts.edu.au)

Annual Survey

Please help us fulfil our annual reporting obligations to the ARC and NHMRC by **completing the Annual Network Survey by Tuesday 10 March 2009**. The survey can be completed online. Please click on the link below or cut and paste into your browser:

http://surveys.uts.edu.au/index.cfm?surveyid=3040

Congratulations

Congratulations to **Ala Lew** (QDPI&F) who has won a Smart State Smart Women Award (Qld) for Women in the Community/Public Sector – Science).

Congratulations to **Kathy Andrews** (QIMR and Griffith University) who won an ASMR QLD Premiers Award for Medical Research (Senior Category).

Grant and Fellowship Winners

Congratulations to **Terry Speed** (WEHI) on the award of a very prestigious *Australia Fellowship* from the NHMRC.

Congratulations also to several young parasitology researchers who were recently awarded fellowships or scholarships by the NHMRC:

Marthe D'Ombrain (University of Melbourne) to investigate *Innate immune responses in the outcome of severe malaria;*

Fiona Sansom (University of Melbourne) to investigate *New ways of treating parasitic diseases;*

Rachel Lundie (University of Melbourne) to investigate *Immune responses in mice co-infected with malaria and helminth parasites;*

Magda Ellis (QIMR) to investigate *Human genetic susceptibility to bacterial invasion and the interaction with chronic helminth infections;*

Gabriela Minigo (Menzies School of Health Research) to investigate *The differences in immune responses during uncomplicated and severe falciparum and vivax malaria;*

Julie Wheway (University of Sydney) to investigate *The involvement of small membrane vesicles and their potential as therapeutic targets in malaria.*

And congratulations to **Kiaran Kirk** (ANU) on the award of an NHMRC Project grant to look into *Transport of amino acids and polyamines in the malaria parasite.*

Conference

The Sydney2009 Annual Parasitology Conference website, registration and abstract submission are now open:

The Sydney2009 conference website is **www.parasite.org.au/arcnet/conference**

and registration and abstract submission are **www.conftool.net/parasitology2009**

The Network is, once again, subsidising venue and invited speaker costs and, together with valuable support from our sponsors - The International Journal for Parasitology, Elsevier, The Queensland Institute of Medical Research, Meat and Livestock Australia, The Institute for the Biotechnology of Infectious Disease, The University of Technology, Sydney, Schering-Plough Pty Limited, Intervet and Coopers, New England Biolabs and Novartis Animal Health - this has ensured that the meeting is as affordable as possible. We have been able to keep the costs at the same low levels enjoyed for Glenelg2008 including all lunches, tea breaks, and evening meals and drinks in your registration fee.

The conference will be from **July 12-15, 2009** in the historic **Holme Building and Footbridge Theatre at The University of Sydney**, with the Conference Banquet being held in the superb **Great Hall** at The University of Sydney.

Early bird registration and abstract submission close on April 24, 2008.

Don't forget that **student ASP members are eligible for generous financial assistance to attend the conference from the ASP** provided they have been members for a minimum period before the conference – so download an ASP membership application form now from the ASP website **http://www.parasite.org.au/member.htm**

Speakers and sessions:

Opening Plenary Lecture
- Genevieve Milon (Institut Pasteur, France)

Elsevier Plenary Lectures - Host Cell Modulation
- John Boothroyd (Stanford University, USA)
- Alan Sher (National Institutes of Health, USA)

Human Helminthiases
- David Dunne (University of Cambridge, UK)
- Tom Nutman (National Institutes of Health, USA)
- David Rollinson (The Natural History Museum, UK)
- Jeff Bethony (George Washington University, USA)
- Banchob Sripa (Khon Kaen University, Thailand)
- Don McManus (QLD Institute of Medical Research, Australia)

Malaria Vaccine: Fact or Fantasy?
- Michael Good (QLD Institute of Medical Research, Australia)
- Richard Carter (University of Edinburgh, UK)
- Denise Doolan (QLD Institute of Medical Research, Australia)
- Louis Schofield (Walter and Eliza Hall Institute of Medical Research, Australia)

Immunopathology
- Georges Grau (University of Sydney, Australia)
- Christian Engwerda (QLD Institute of Medical Research, Australia)
- Nick Hunt (University of Sydney, Australia)

Environmental Health
- Nigel Beebe (University of QLD, Australia)
- Lydden Polley (University of Saskatchewan, Canada)

Ectoparasites of Livestock
- Shaun Coffey (Industrial Research Ltd, New Zealand)
- Gary Levot (Department of Primary Industries, New South Wales)

Research News

Network scientists help to set the groundwork for the development of antimalarial therapeutics that target the neutral aminopeptidases of the malaria parasite.

John Dalton, Colin Stack, Sheila Donnelly, and Jonathan Lowther from the Institute for the Biotechnology of Infectious Diseases (IBID), University of Technology, Sydney (UTS) and Tina Skinner-Adams, Franka Teusher, Don Gardiner from The Queensland Institute of Medical Research (QIMR), Sheena McGowan, James Whisstock, Ross DeGori and Ashley Buckle of Monash University, Jolanta Grembecka, University of Virginia, Pawel Kafarski and Artur Mucha, Wroclaw University, are part of a group of researchers worldwide who have recently published *"Structural basis for the inhibition of the essential Plasmodium falciparum M1 neutral aminopeptidase"* in Proceedings of the National Academy of Sciences (PNAS) published online before print February 5, 2009 http://www.pnas.org/cgi/doi/10.1073/pnas.0807398106

Plasmodium falciparum parasites are responsible for the major global disease malaria, which results in >2 million deaths each year. With the rise of drug-resistant malarial parasites, novel drug targets and lead compounds are urgently required for the development of new therapeutic strategies.

This group of scientists addressed this important problem by targeting the malarial neutral aminopeptidases that are involved in the terminal stages of hemoglobin digestion and essential for the provision of amino acids used for parasite growth and development within the erythrocyte. The team characterized the structure and substrate specificity of one such aminopeptidase, P*f*A-M1, a validated drug target. The X-ray crystal structure of P*f*A-M1 alone and in complex with the generic inhibitor, bestatin, and a phosphinate dipeptide analogue with potent in vitro and in vivo antimalarial activity, hPheP[CH2]Phe, reveals features within the protease active site that are critical to its function as an aminopeptidase and can be exploited for drug development.

John Dalton speaks to Lisa Jones about this research.

John, tell us about your collaborative work with this group of scientists.

This was a neat collaboration, one that involved biochemists, medicinal chemists, structural biologists and malariologists, all coming together with a common goal. The Polish researchers had identified a molecule that we had shown was a potent inhibitor of the P*f*A-M1 protease isolated in our laboratory and also possessed anti-malarial activity. Sheena McGowan and colleagues at Monash elucidated the structure of the P*f*A-M1 protease alone and in complex with the inhibitor.

How important is it to have research input from so many different scientists?

This was a project where collaboration was key – no one laboratory could develop all of the skills required and it was quite amazing how each part fitted like a jigsaw puzzle.

How will your research help people who are suffering from malaria?

This research has opened up a path for the development of a totally new class of anti-malarials, and directed towards the P*f*A-M1 protease. With the global spread of drug resistance to most of the currently used anti-malaria treatments there is an urgent need for the development of new drugs with new activities.

What role did Network scientists play in this process?

Here at UTS we isolated and cloned the protease gene, produced a functional recombinant enzyme and demonstrated the activity of the inhibitors against the protease. Our colleagues at Monash took the recombinant protease and used sophisticated witchcraft to crystalise it and solve its structure. The QIMR team showed that the inhibitors could kill malaria parasites using their culture systems.

What will be the next step in this research and what will your role be?

We have already begun high throughput screening of chemical libraries for better lead compounds for drug development – this is funded by the National Institutes of Health, USA. If we find new compounds they will be tested for anti-malarial activity at QIMR and then complexed into the 3-D structure at Monash to aid future medicinal chemistry to improve their potentcy.

How far away is the development of a new drug to combat malaria?

The usual 5 years!!

Network Travel Award Profiles

Professor Leann Tilley's laboratory at La Trobe University undertakes research in the areas of cell biology and drug development. Her work has been particularly concentrated on studies of the malaria parasite. Leann was a founding member of the ARC/ NHMRC Research Network for Parasitology and talks to Lisa Jones about her work.

Leann tell me about your research team at La Trobe University, the techniques you use in your research and why they are so important in parasitology research?

"My lab currently comprises 15 people, including 5 postgraduate students and 4 postdoctoral fellows. The lab members represent an impressive pool of talent with cutting edge skills in fluorescence microscopy and quantitative fluorescence imaging, electron and X-ray microscopy, including 3D reconstructions from electron tomography, and malaria parasite cell biology and genetics manipulation skills. We receive funding from the National Health and Medical Research Council and the Australian Research Council. We've also received a Wellcome grant for establishing a confocal fluorescence photobleaching facility and an Australian Research Council Large Infrastructure Equipment Fund grant for establishing a confocal fluorescence correlation facility".

Leann's lab employs a range of quantitative imaging techniques to study molecular aspects of host-parasite interactions and to probe the functions of a range of parasite proteins. Members of her lab have extensive experience in using confocal microscopy and, more recently, electron microscopy. They have developed protocols for incorporating exogenous labels into parasite-infected erythrocytes and have used molecular biology protocols to produce transfectants expressing green fluorescent protein chimeras. The application of quantitative fluorescence-based techniques to studies of the malaria parasite has enabled the dissection of the ways in which the parasite modifies its erythrocytic host. In particular, it has been shown that the host cell membrane proteins undergo a dramatic molecular reorganisation that is likely to facilitate parasite survival. Her lab has also employed electron tomography to obtain 3-D information about the cellular architecture at very high resolution and to image parasite-derived structures within the host RBC.

"We've also been able to use fluorescent molecular "beacons" to monitor changes in cell function upon treatment of parasites with antimalarial drugs and electron microscopy to confirm the changes in digestive vacuole morphology that result from drug treatments" says Leann, "And these studies have shown that both quinoline and endoperoxide antimalarial's act at the level of the parasite's digestive vacuole; they appear to act by interacting with the toxic by-products from the parasite digestion of hemoglobin."

Leann, what inspires you about your parasitology research?

"I am particularly interested in developing novel imaging technologies because of the marvellous cellular landscapes and molecular insights that are revealed when one has access to a new technique for probing parasite function. I believe that networking is very important. In modern laboratory science, no one can act alone. We all depend on a network of collaborations and interactions. I really enjoy bringing people together with different areas of expertise and interest."

Leann, you and your team have been active promoters and recipients of the ARC/NHMRC Research Network for Parasitology Travel Award Scheme. Tell us how these Travel Awards have helped your research progress.

"The ARC/NHMRC Research Network for Parasitology Travel Award Scheme funds have allowed a number of research students, Paula Hawthorne, QIMR, Silvia Haase, Bernhard Nocht Institute for Tropical Medicine, Hamburg Sheila Akinyi, Emory University, Atlanta, USA, to visit our laboratory to collaborate with us in the use of electron tomography and confocal microscopy to examine malaria parasites. They have used our expertise and high level facilities to image their samples which have included novel GFP transfectant-infected *P. falciparum* and non-falciparum species. Professor David Ferguson (Oxford Uni) visited the lab to help us set up the electron microscopy facility.

We have also used Network Travel Award funds to visit X-ray and optical microscope facilities in the laboratories of Prof John Sedat, Prof Carolyn Larabell, Prof Joe De Risi and Prof Steve Lane in the U.S.A. This gave us access to structured illumination microscopy and x-ray tomography facilities that are not available in Australia. And a Researcher Exchange visit by Professor Kiaran Kirk, ANU, provided an opportunity to exchange ideas, find areas of common interest and synergy. This has led to a joint funding application."

Network Travel Award Profiles cont...

It must be very exciting to have such a dynamic team of researchers and collaborators working with you, tell us what the future holds?

"We are very excited about the possibility that the novel imaging techniques that we are using will reveal the mechanism that this obligate intracellular parasite uses to export virulence proteins outside the boundaries of its own plasma membrane and to take up host cell haemoglobin for digestion. The molecular machinery and the mechanisms of transport involved in these unusual transport systems are not yet well understood but they appear to be different from those used in mammalian systems. My lab concentrates on increasing our molecular understanding of the parasite, which is still really very limited. In the longer term we hope that unravelling the molecular mechanisms will lead to novel antimalarial strategies. We also hope that the fluorescence technologies that we are developing might be useful for high throughput screening for antimalarial drugs or for new malaria diagnostics platforms."

Dr. Eric Hanssen is a postdoctoral scientist in the Tilley laboratory and was a recipient of a Network Travel Award for a Researcher Exchange to visit laboratories in the U.S.A.

Eric, tell me about your area of research?

"I work on malaria - more precisely on the architecture of the exporting membrane system within the host erythrocyte."

What interests you about working in this area?

"First and foremost, I believe it is a pretty important pathway that delivers the main virulence factors plus I get to play with a lot of new toys (i.e. microscopes)."

How has the Network travel award helped your research develop?

"In 2009 our Network Travel Award will bring Esther Patchlatko to Australia, she's an expert in protein pull down and other Biochemistry techniques while our lab have expertise in imaging, so that will be a nice exchange of techniques."

What advice do you have for science students who are considering parasitology as a career?

"Parasitology is a good area to work in - as long as there is a parasite there will be some form of funding for research. The little buggers are always a challenge in an area or another. Choose a lab that has a broad range of techniques available this way you can choose which one you like best and specialise a bit later on."

What do you see as the benefits of being part of the Network?

"Being part of a bigger picture; hearing about other research areas; being able to meet other scientists in the area; and the funding available for researchers who are part of the Network."

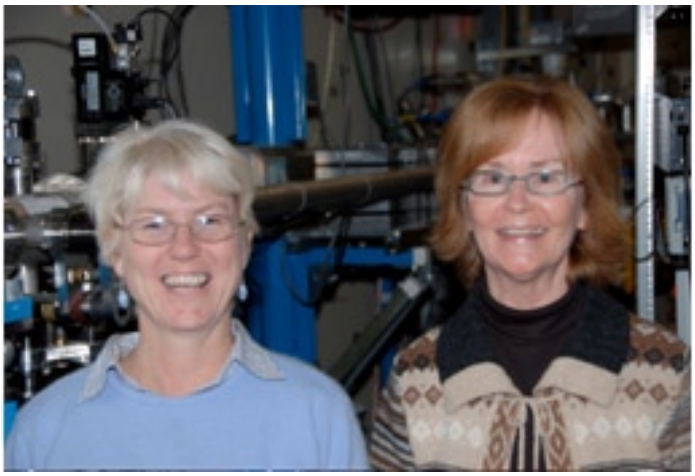
Tell me about the highlight of your science career so far?

"The number of papers accepted or published in 2008."

What would you like to do in the future?

"I would like to be a group leader with a focus on EM, or better still, the head of an EM facility with a research group."

Sheila Akinyi, Emory University, Atlanta, USA, works with Eric Hanssen to use electron tomography and confocal microscopy to examine a malaria parasite



Leann and colleagues visited X-ray and optical microscope facilities in the laboratories of Prof John Sedat, Prof Carolyn Larabell, Prof Joe De Risi and Prof Steve Lane in the U.S.A.

Network Mentorship Scheme

Early career researchers are encouraged to apply to the Network Convenor (nick.smith@uts.edu.au), in strict confidence, for funding to participate in the Network Mentorship Scheme. The scheme allows young investigators to be paired with experienced, successful researchers to discuss, plan, prioritise and set targets for their career. Typically, the early career researcher will fly to the institute of a senior parasitologist and spend a day there. Arrangements for professional development and progress to be reviewed by the pair annually can also be arranged.

Importantly, mentors need not be from an individual's home institution but can be drawn from across the Network. The scheme has proved very valuable for several young researchers and their mentors already.

To apply, simply write to Nick with a brief outline of your research interests and aspirations. You can also indicate a preferred mentor or ask Nick for advice on whom amongst the Network participants may be most suitable.

Announcements

10th International Congress On Toxoplasmosis

Hotel & Conferentieoord Rolduc, Kerkrade, The Netherlands

Friday June 19th till Tuesday June 23rd 2009

The scientific program will consist of short talks (12-15 minutes) organized thematically with poster sessions. Specific topics will be determined based upon the submitted abstracts. The program will span the whole gamut of biomedical research on *Toxoplasma gondii* with a focus on modern genomic, genetic, biochemical, and cell biological approaches to parasite biology, pathogenesis and drug development. A strength of the meeting is its tradition to bring together parasite molecular biologists and parasite immunologists, featuring several sections on host-pathogen interaction. The meeting also includes a clinically/epidemiologically oriented session providing a venue for interaction between bench scientists and physician-scientists. The absence of concurrent session fosters the breadth of interaction. There will be morning, afternoon and evening scientific sessions. Sessions will be chaired by participants selected by the organizers. The organizers encourage all attendees to present mostly unpublished work. Presentations by younger scientists (students, postdocs and new investigators) are especially encouraged.

Visit **http://www.toxomeeting.org/** for details.

The **deadline for registration & abstract submission is: March 13, 2009** (please register in a timely fashion as the capacity of the meeting site is limited).

The Tenth International Coccidiosis Conference

November 14-18, 2009, Guangzhou, China.

The International Conference of Coccidiosis (ICC) is held every 4 years for the scientists in the fields of *Eimeria* , *Toxoplasma*, *Cryptosporidium*, *Plasmodium*, *Neospora*, *Sarcocystidia* and other apicomplexan parasites to discuss science and exchange ideas. The coming 10th Conference (ICC10) will be hosted by Guangdong Academy of Agricultural Sciences and the Chinese Association of Veterinary Parasitology, and held jointly with the 10th Conference of the Chinese Association of Veterinary Parasitology in Guangzhou, China from November 14 – 18, 2009.

Visit **http://www.icc10.net/** for more details.

The Parasitology and Tropical Medicine Special Interest Group, Australian Society for Microbiology (ASM) & Standing Committee on Medical Parasitology and Zoonoses, Australian College of Tropical Medicine (ACTM) present the

Parasitology & Tropical Medicine MasterClass 2009

Hobart, Tasmania Friday 6 & Saturday 7 March 2009

visit **www.parasitologymasterclass.org** to register but be quick!