



N E W S L E T T E R

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Immunology at the Malaghan Institute of Medical Research

Debbie Scarlett

Scientists at the Malaghan Institute of Medical Research, an independent biomedical research facility based at Victoria University's Kelburn campus, Wellington, New Zealand, believe exciting opportunities exist in targeting the immune cells to treat immune-mediated diseases. The focus of the Institute's seven research groups is the discovery of the basic immunological processes that operate during asthma, infectious diseases, cancer, arthritis and multiple sclerosis, with a view to the development of effective immunotherapies and vaccines for the treatment of these diseases. To maintain its excellent track record for translating basic research discoveries into clinical practice, the Malaghan Institute is dependent on an extensive network of international and national collaborations, as well as a close working relationship between the individual research groups from within the Institute itself.

At the core of the Malaghan Institute's research activity is the "Immunity and Immune-mediated diseases" programme, which comprises four research groups. The first of these is the **Asthma and Parasitic Diseases** group headed by **Professor Graham Le Gros**. Prof. Le Gros was appointed Research Director of the Malaghan Institute in 1994, following a three year Fogarty Fellowship at the National Institutes of Health (NIH), USA, and a five year scientist position with Ciba-Geigy in Basel, Switzerland. In 2005 Prof. Le Gros was elected as a Fellow of the Royal Society of New Zealand in recognition of his research contributions to the fields of immunology and asthma. Prof. Le Gros' overall research interest lies in understanding the basic biology of Th2 immune responses, with

a particular focus on the mechanisms and cell types involved in mediating allergic and asthmatic inflammation. Over recent years Prof. Le Gros' research group has used IL-4/GFP knock-in mice to address fundamental questions on the behaviour of IL-4-producing Th2 cells *in vivo*. The gene-targeted IL-4/GFP mice offer significant advantages over previous models in that they can be used to follow the formation, function and fate of Th2 cells without *in vitro* manipulations and the attendant artefacts. Using this model Prof. Le Gros' group has shown that there is an alternative pathway for allergic immune responses *in vivo* that doesn't involve IL-4, and has identified a new role for the poorly characterised basophil cells in Th2 immunity. A second model used by Prof. Le Gros to study allergic asthma is the nematode *Nippostrongylus brasiliensis*.



Prof. Graham Le Gros

Allergens secreted by *N. brasiliensis* can be isolated from *in vitro* parasite cultures and used to induce allergic airway disease, including airway hyper-responsiveness, airway eosinophilia, IgE and Th2 cytokine production, when administered to pre-sensitised mice. Prof. Le Gros' group is now working towards identifying the *N. brasiliensis* allergens responsible for inducing these effects. A flipside of this latter work is the identification of potential targets for developing a vaccine that can be used to treat parasitic worm diseases.

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Website

The ASI web site (www.immunology.org.au) has been fully remodelled and updated. New services include:

- Downloadable forms for ASI awards,
- Positions vacant pages,
- Jobs wanted pages,
- Upcoming conferences listings,

as well as a plethora of links to sites of immunological interest at home and abroad. If you'd like your lab home pages linked to the site, would like to advertise a job or conference, or have a favourite immunology-related site that doesn't currently appear on the ASI site, please email Judy Greer at j.greer@medicine.uq.edu.au

Email bulletin board

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EDITORIAL

December's newsletter coincides with the ASI annual conference in Auckland, and I have used this as an opportunity to highlight the exciting research being carried out in the Malaghan Institute in Wellington (p1). Hopefully we will all have the chance to hear more about this work first hand at the conference. This newsletter also provides the opportunity to reward the contributions of members to *Immunology and Cell Biology* (paper of the year, p10), and to the newsletter (annual Newsletter Prize, bottom right). Publication of *Immunology and Cell Biology* will be transferred to the Nature stable of journals from next year (as outlined by the ICB Editor Chris Parish on page 9), however I am still waiting for one of the major journals to show interest in taking over the newsletter

This issue also highlights the achievements of members with the Queensland Premier's Awards for Medical Research (p19), and a lifetime membership of ASI to Tony Basten (top right). Reports from students who have been overseas on ASI sponsored conferences (p13) provides feedback on where some of the members funds have been spent, and for a full rundown on income and expenditure, don't miss the ASI annual general meeting in Auckland! Hope to catch up with you all at the ASI conference.

Miles Davenport

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Life membership for Professor Tony Basten

At the mid-year Council meeting it was unanimously agreed to confer Honorary Life Membership on Professor Tony Basten. Prof Basten recently retired after 15 years as Director of the Centenary Institute for Cancer Medicine and Cell Biology (see Newsletter December 2005 issue). During this time he helped develop an internationally renowned immunology research environment in a new purpose-built building adjacent to the Royal Prince Alfred Hospital and the University of Sydney. Professor Basten's own research into B cells and tolerance have made a major impact worldwide and he has been a key advisor to government on clinical immunology. Professor Basten is a valued mentor, having helped supervise over 50 PhD students and fostered the careers of many researchers. He is a long time supporter of the ASI, serving as President in 1979, and presenting the 1995 Burnet Oration.



2006 Newsletter Article Winner

The 2006 ASI newsletter article of the year award was a close call between two excellent articles. Prof Tony Basten's humorous retrospective "An Immunological saga" (June, p17) detailed the trials and tribulations of his long and successful career as an immunologist and head of the Centenary Institute in Sydney. Importantly, it highlighted the role played by both serendipity and strong friendships in making an exciting and enjoyable career. However, the \$100 prize for best newsletter article of 2006 was eventually awarded to an article by Natkunam Ketheesan (James Cook University) on "Teaching in Tamil Territory" (September, p5).

Natkunam's article, which details his experiences running a medical immunobiology course for third year medical students in Jaffna University, highlights the mix of rudimentary conditions and great enthusiasm for learning that Natkunam found during his stay in Sri Lanka.



ASI has provided funds to allow Natkunam to return to teach the course again in 2006 and 2007. However, due to the unfortunate deterioration in the security situation in Sri Lanka, the 2006 visit has had to be postponed for the time being.

Immunology at the Malaghan Institute (cont)

A second group involved in the Malaghan Institute's Immunity and Immune-mediated diseases programme is the **Infectious Diseases** group, headed by **Dr Joanna Kirman**. After completing her postgraduate training in New Zealand, Dr Kirman was awarded a Fogarty Fellowship to pursue her work in vaccine development at the National Institute of Allergy and Infectious Diseases, USA. Dr Kirman returned to the Malaghan Institute in July 2002 to lead the Infectious Diseases group as a Sir Charles Hercus Research Fellow, supported by the Health Research Council of NZ. The overall aim of Dr Kirman's current research is to reduce the incidence of infectious disease in New Zealand through the development and implementation of vaccines. The primary research focus of Dr Kirman's group is to understand protective immunity to the bacterium that causes Tuberculosis (Tb). The currently available vaccine against Tb, BCG, does not provide long-term protection. To facilitate rational design of a more effective vaccine for Tb, Dr Kirman's group aims to identify the T cell populations critical for mediating memory immune responses to pulmonary Tb infections, to monitor the *in vivo* survival of the protective cell subsets, and to determine the factors that contribute to or could enhance their longevity and persistence in the airways. The Infectious Diseases group is also investigating factors that may abrogate development and maintenance of protective memory

immunity. One aspect of this work has been a study of the role of CD4+CD25+ regulatory T cells during Tb infection and during vaccination against Tb. This regulatory cell subset was found to suppress immune responses early after Tb infection, as well as after vaccination. The effect of this subset on long-term memory development is currently being investigated. In addition to the Tb research, in 2005 the Infectious Diseases group completed a study looking at how respiratory syncytial virus (RSV) subtypes have changed during consecutive epidemics in New Zealand over the last 30 years, and established a multi-centre rotavirus strain surveillance study. Results of these molecular epidemiology studies will have important implications for vaccine design and administration.

The **Cancer Immunotherapy** group headed by **Professor Franca Ronchese** is the third component of the Malaghan Institute's Immunity and Immune-mediated diseases programme. Prof. Ronchese completed her studies at the University of Padova, Italy, and spent four years as a post-doctoral researcher at the NIH, USA. She then worked as an independent Scientific Member at the Basel Institute for Immunology, Switzerland, before being awarded a Malaghan Senior Research Fellowship. With support from the Wellington Medical Research Foundation, Prof. Ronchese established the Cancer Immunotherapy group at the Malaghan Institute in 1994. Prof. Ronchese's research centres on the dendritic cell, with a particular focus on the involvement of these cells in the early phases of an immune response, and how dendritic cells can be used to best

advantage as carriers in cancer vaccines. Prof. Ronchese has shown that perforin-dependent killing of dendritic cells by cytotoxic T lymphocytes (CTL) is an important mechanism in regulating the size of an immune response. This observation has considerable significance for dendritic cell-based cancer immunotherapy trials, where repeated administrations of dendritic cells loaded with tumour antigens are used routinely in an attempt to induce effective immunity. Prof. Ronchese's group is now attempting to define the precise mechanisms by which activated CTL feed back on the immune system through killing of dendritic cells. Other projects within the group examine different aspects of anti-tumour immune responses such as CD4+CD25+ regulatory T cells, and tumour-specific CD8+ T cells, and their ability to develop into memory cells that may be able to maintain anti-tumour effector activity for an extended time. Dr Patrizia Stoitner, a Visiting Fellow within Prof. Ronchese's group, has shown recently that application of tumour antigen in a cream to the skin can induce the activation of tumour-specific T cells, and that these T cells are able to attack the tumour. This work has particular relevance to the immunotherapy of skin cancers such as melanoma, of which the Malaghan Institute is involved in a phase III clinical trial.

The phase III clinical trial of a dendritic cell-based vaccine for melanoma is being undertaken in conjunction with the Queensland Institute of Medical Research, and the Wellington Cancer Centre. Relocation of the Malaghan Institute to Victoria University's Kelburn Campus in 2004 provided a golden opportunity to develop a state-of-the-art Good Manufacturing Practice clinical production laboratory for preparation of the vaccines. It is hoped that a total of 200 melanoma patients from New Zealand and Australia will participate in the trial over a two year period. Overseeing the Malaghan Institute's current involvement in the melanoma vaccine trial is **Dr Ian Hermans**, head of the **Vaccine Research** group, and the fourth investigator involved in the Immunity and Immune-mediated diseases programme. Dr Hermans worked on dendritic cell vaccinations with Prof. Ronchese between 1995 and 2001, before taking up a position at the Tumour Immunology Unit (Weatherall Institute of Molecular Medicine), at the University of Oxford, UK. In 2005 Dr Hermans returned to the Malaghan Institute and was awarded a Sir Charles Hercus Research Fellowship from



Dr Joanna Kirman



Dr Franca Ronchese



Dr Ian Hermans

the Health Research Council of New Zealand to pursue his research into improving the potency of vaccines against cancer, asthma and infectious disease. Dr Hermans' group is also investigating a newly defined series of lipid-based compounds that can be used to activate a subset of T cells called *i*NKT cells. These cells are an excellent source of the signals required for optimal activation of dendritic cells, and can thus significantly enhance vaccine-induced immune responses. In collaboration with Professor Ronchese, Dr Hermans is exploring the possibility of including these compounds in vaccines designed to elicit T cell-mediated responses to cancer or infection.

Over the last 50 years the focus of most anticancer drug development has been on rapidly proliferating tumour cells. However, remissions are often transient, drug resistance a major problem and drug withdrawal can result in an aggressive return of the cancer. This is because the tumour-perpetuating but largely quiescent cancer stem cell is unaffected by treatments that target rapidly dividing cells. In work that complements the cancer immunotherapy and vaccine research at the Malaghan Institute, the **Cancer Cell and Molecular Biology** group headed by **Professor Mike Berridge** seeks to identify ways to eradicate the cancer stem cell. Prof. Berridge completed his postgraduate degree in Cell Biology at the University of Auckland. Following postdoctoral research at Purdue University, USA, and the National Institute for Medical Research, UK, Prof. Berridge returned to Wellington in 1976 as the second Malaghan Fellow. He currently holds a Senior Research Fellowship with the



Dr Mike Berridge

Cancer Society of New Zealand, and recently held a James Cook Fellowship in the Health Sciences. In collaboration with Dr Hermans and Prof. Ronchese, Prof. Berridge plans to investigate whether dendritic cells can be stimulated to mount an immunological response against glioblastoma cells, which are developmentally similar to melanoma. Prof. Berridge's group has also developed a novel assay for screening potential anticancer drugs that block a vital life support system used by cancer stem cells. The drug target is a high capacity plasma membrane electron transport system that is used by tumour cells to alleviate reductive stress. Using this assay, Prof. Berridge's group has identified several different groups of chemical compounds that not only interfere with the plasma membrane stress pathway, but also compromise cancer cell survival *in vitro* and inhibit tumour growth in mice. Selected compounds will now be modified to target them specifically to the outer leaflet of the cell membrane. Since the modified drugs will not be able to enter the cell, this should not only enhance their anticancer activity but also greatly reduce potential side effects.

The biodiversity of New Zealand's marine and terrestrial organisms represents huge potential for the identification of novel bioactive molecules for drug development. This unique resource is being targeted by the TerraMarine Biodiscoveries programme, a joint venture between the Malaghan Institute, the National Institute of Water and Atmospheric Research (NIWA), and Crop and Food Research. This programme uses a human microplate assay to screen New Zealand biota for novel anti-inflammatory



Dr Jacquie Harper

activity, and is the major focus of the **Arthritis and Inflammation** group headed by **Dr Jacquie Harper**. Dr Harper obtained her PhD in Chemistry and Physiology from the University of Otago. She then undertook a Fogarty Postdoctoral fellowship at the NIH, USA, before returning to New Zealand in 1999 to establish her research group at the Malaghan Institute. One of the aims of Dr Harper's research is to develop novel non-steroidal anti-inflammatory drugs for the treatment of inflammatory diseases such as arthritis. Dr Harper's group has identified several lead compounds that both inhibit the activity of the human neutrophil respiratory burst and suppress neutrophil infiltration in murine models of inflammation. These compounds are currently being tested in structure activity studies to identify the optimal structure(s) for anti-inflammatory activity. During the course of the programme some novel molecules have shown promising anti-cancer activity and are being investigated further in collaboration with Prof. Berridge. Dr Harper's group is also investigating the inflammatory responses of cells commonly linked with arthritic disease. Using a disease model of gout, they have identified discreet subpopulations of monocytes and macrophages that appear to be associated with the different stages of the inflammatory response, from initiation through to resolution. Understanding the mechanism behind this switch could lead to the development of a new treatment for the underlying cause of arthritis. Recently Dr Harper initiated a clinical

research project that will compare the inflammatory immune responses of gout patients and healthy individuals. She predicts that differences in these responses could be used as a marker of disease susceptibility, and could potentially aid in disease prognosis.

Inflammation in the form of the autoimmune disease multiple sclerosis is the focus of the final Malaghan Institute research group, headed by **Associate Professor Thomas Bäckström**. Assoc. Prof. Bäckström established the **Multiple Sclerosis Basic Research** group at the Malaghan Institute in 1997, following a one year Postdoctoral research position at the National Jewish Centre, USA, and five years as a member at the Basel Institute of Immunology, Switzerland. In 1999 Assoc. Prof. Bäckström was awarded a five year Wellcome Trust Senior Research Fellowship in Medical Science, and last year he was the recipient of a Wellington Medical Research Foundation's Malaghan Senior Haematology Research Fellowship. Over recent years Assoc. Prof. Bäckström's research focus has been on identifying mechanisms that inhibit the development and activation of autoreactive T cells. In collaboration with Professor John Fraser from the University of Auckland, Assoc. Prof. Bäckström has shown that a modified superantigen coupled to a self peptide can turn off autoreactive T cells and inhibit disease in the EAE (Experimental Autoimmune Encephalomyelitis) model of autoimmunity. The superantigen-peptide conjugate appears to do this by triggering the activation and expansion of natural regulatory T cells, a newly

defined immune cell type important for controlling autoimmune diseases. Assoc. Prof. Bäckström's group is currently investigating the mechanisms by which the superantigen-self peptide complex activates natural regulatory T cells and inhibits autoimmunity. The knowledge arising from this work will guide the pre-clinical development of the modified superantigen-peptide conjugate into a novel therapeutic agent for treating organ-specific autoimmune diseases such as multiple sclerosis. In other work Assoc. Prof. Bäckström is collaborating with Dr Hermans to develop novel inexpensive vaccine delivery systems based on 200-500 nm biopolyester particles. These biodegradable 'bio-nanoparticles' are produced by many species of bacteria, and can be engineered to deliver disease-specific antigens to the immune system. Initially Assoc. Prof. Bäckström and Dr Hermans will concentrate on using the bio-nanoparticles to produce custom-made vaccines against influenza and cancer, however the particles can also be used to generate correctly folded recombinant proteins and produce targeted drug delivery vehicles.

In summary, immune-mediated disease and the lack of immunity to infectious agents and cancer pose a significant threat to human health throughout the world. Researchers at the Malaghan Institute believe that the most effective way of dealing with this threat is going to come from solutions provided by an improved understanding of the immune system, and the pathogens that infect humans. For further information on immunology research at the Malaghan Institute visit: <http://www.malaghan.org.nz>.

Recent key publications

Ainge GD, Hudson J, Larsen DS, Painter GF, Singh Gill D, Harper JL. Phosphatidylinositol Mannosides: Synthesis and Suppression of Allergic Airway Disease. *Bioorg Med Chem Lett* (in press).
La Flamme AC, Harvie M, McNeill A, Bäckström BT. Macrophage FcγR ligation ameliorates the course of EAE by enhancing basal Th2 responses. *Immunol Cell Biol* (in press)
Matheson JW, Rich FJ, Cohet C, Grimwood K, Huang S, Penny D, Hendy MD, Kirman J. Distinct patterns of evolution between respiratory syncytial virus subgroups A and B from New Zealand isolates collected over thirty-seven years. *J Med Virol* (in press).
Min B, Le Gros G, Paul WE (2006) Basophils: A potential liaison between innate and adaptive immunity. *Allergy Int.* 55:99-104.
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Kemp R, Bäckström T, Ronchese F (2005) The phenotype of Type 1 and Type 2 CD8⁺ T cells activated *in vitro* is affected by culture conditions and correlates with effector activity. *Immunology*, 115:315-24.

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Associate Professor Thomas Bäckström

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Advance Notice

Next year's ASI conference will be held at the Manly Pacific Hotel which overlooks Manly Beach, Sydney, NSW, December 2-6, 2007

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Immunology & Cell Biology

Coming to Nature Publishing Group (NPG) in January 2007

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Immunology and Cell Biology Joins Nature Publishing

As many ASI members are probably already aware, commencing in January, 2007, *Immunology and Cell Biology* will be published by the Nature Publishing Group (NPG) and will become one of only four specialist immunology journals published by NPG, the other journals being *Nature Immunology*, *Nature Reviews Immunology* and *Genes and Immunity*. The association with NPG will greatly enhance the visibility and impact of *ICB* and should help to establish *ICB* as one of the leading immunology journals in the world.

ASI members should be aware of a number of important changes to *ICB* that will occur in 2007.

- The journal will have a new look with a totally new cover design (see below) and manuscripts being formatted in the *Nature Immunology* style.
- There will be an increase in the number of issues each year from 6 to 8.
- There will be a revamped and more international Editorial Board.
- **News and Commentary** articles will appear in each issue. These articles will have a similar format to the well known 'News and Views' articles in Nature journals. Carola Vinuesa has kindly agreed to act as the News and Commentary Associate Editor.
- Additional new article types will also be included in the journal. These include **Landmark** articles, which highlight the historical significance of a particular piece of research relevant to the journal's scope; **Editorial** articles that are brief comments written by the Editor-in-Chief or by guest editors of **Special Features**, and occasional **Meeting Reports** that briefly detail the discussions, presentations and events at a relevant recent meeting.
- The journal will continue to publish **Theoretical Articles** that report new and provocative ideas in immunology. *ICB* will also encourage the submission of **Review Articles** from outstanding graduate students.
- **Special Features** will remain an important component of *ICB* with the possibility of an increase in their frequency.
- Once accepted manuscripts will become publicly available much more rapidly via **Advanced Online Publication**.
- Finally, the journal should have a dramatically increased visibility by its new website being hosted on nature.com

ASI members will also enjoy a number of direct benefits as a result of *ICB* being published by NPG.

- A free online subscription to *ICB* will be included in the ASI subscription fee.
- If an ASI member wishes to receive a hard copy subscription of *ICB* they only need to pay a modest sum (\$29/annum in 2007).
- As part of the ASI subscription ASI members will also gain free online access to *Nature Immunology* and *Nature Reviews Immunology*.
- It is anticipated that there will be a substantial increase in the *ICB* revenue received by ASI, such funds benefiting all ASI members.

Overall the move to NPG promises to be an exciting development for *ICB* that will increase the international standing of the journal and benefit all ASI members.



Chris Parish
Editor-in-Chief
Immunology and Cell Biology

*The historic signing of the contract with NPG.
LtoR: Nick Campbell (NPG Assistant publisher
Nature Asia-Pacific), Phil Hodgkin (President,
ASI), Tony Bocquet (Associate Director, Nature
Asia-Pacific) and Chris Parish (Editor, ICB)*

ICB Paper of the Year

Erika Cretney

Based at the Peter MacCallum Cancer Centre, Dr Erika Cretney was recently awarded The Immunology and Cell Biology publication of the year award 2005 for her paper entitled "TNF-related apoptosis-inducing ligand (TRAIL)/Apo2L suppresses experimental autoimmune encephalomyelitis (EAE) in mice."

Dr Cretney's data are the first to illustrate the potential therapeutic value of recombinant TRAIL in suppressing EAE (the mouse model of autoimmune inflammation for Multiple Sclerosis (MS)). Exogenous administration of recombinant TRAIL from the point of disease induction suppressed relapsing-remitting EAE in NOD/Lt mice. Suppression of disease was characterized by a significant reduction in the proliferation of myelin oligodendrocyte glycoprotein (MOG)-specific T cells. Although phase I clinical trials of recombinant TRAIL produced by Genentech Incorporated and Amgen have recently commenced in cancer patients, Dr Cretney's findings raise the possibility that recombinant TRAIL or therapeutics that manipulate the TRAIL pathway might also be effective in suppressing T-cell-mediated autoimmune diseases.

The research described in the winning paper was completed by Dr Cretney, under the supervision of Associate Professor Mark Smyth, as part of her PhD studies. The project was undertaken in collaboration with Drs Claude Bernard and Jonathan McQualter from the Department of Biochemistry at Latrobe University who provided essential expertise with the EAE model. A fruitful collaboration was also formed with Drs Avi Ashkenazi and Iqbal Grewal from the Departments of Immunology and Molecular Oncology at Genentech Incorporated to obtain recombinant TRAIL for therapy experiments.

Dr Cretney completed her Bachelor of Science and postgraduate studies at The University of Melbourne, and is currently a Senior Research Fellow in



the Cancer Immunology Program at the Peter MacCallum Cancer Centre in Melbourne. Her PhD and post-doctoral studies, both under the supervision of Associate Professor Mark Smyth, have helped elucidate the roles of endogenous host TRAIL in disease. This is her 13th paper on the subject of TRAIL, and her first focusing on the role of TRAIL in EAE. Her TRAIL research has spanned a number of diverse areas including studies that examined the role of TRAIL in tumor immunosurveillance, immunoregulation, T cell development and homeostasis, and control of EAE/MS. In 2004, she won The Peter MacCallum Cancer Centre Postgraduate Research Medal for Outstanding Achievement and Scientific Excellence, and obtained a Cancer Council Victoria Postdoctoral Research Fellowship. In 2005 she won a High Commendation in the Premier's Award for Medical Research and obtained a prestigious Victoria Fellowship.

In 2007 Dr Cretney is moving to the Walter and Eliza Hall Institute of Medical Research to undertake post-doctoral studies with Dr Stephen Nutt in the Immunology Division. During these studies, she aims to investigate the functions of B lymphocyte induced maturation protein-1 (Blimp-1) in T cell homeostasis and self-tolerance. She plans to use this award to attend an international conference on her new area of research and to purchase books relevant to this subject from Blackwell Publishing Asia.

Brisbane Immunology Group meeting on the Gold Coast, 17/18 August 2006 – see report in ASI Councillors' News (p.12)



Dr Michelle Wykes (QIMR) and Prof Jonathan Sprent (Garvan Institute of Medical Research)

Below: Dr Adriana Baz, Ms Regina Gary, and Dr Norbert Kienzle (all QIMR)



Right: Dr Rachel De Kluyver (Centre for Immunology and Cancer Research, Brisbane) and Prof. Bob Tindle (Sir Albert Sakzewski Virus Research Centre, Brisbane)

ASI Councillors' News

N.S.W. News

It has been a busy couple of months for the NSW branch of ASI. On September 22 we had a Branch Research Meeting, which was a great success. Seventeen speakers from six institutions across NSW came to talk about their work. My thanks to all participants, both speakers and audience members alike, who joined in to make it such an informative and interesting day. We covered a diverse range of topics over the day, highlighting the breadth and depth of immunology in NSW. The best Student Presentation of the day was awarded airfare and registration to this year's ASI conference in Auckland, and congratulations go to Bennett Shum, from the Garvan Institute, for his presentation on "The Requirement for the adipocyte fatty acid binding protein aP2 in allergic airway inflammation" Well done Bennett.

Along with our research meeting we have also have the pleasure of hosting two visiting ASI speakers recently: Philip Greenberg from the University of Washington, USA and Graeme Pawelec from the University of Tübingen, Germany. Both gave excellent seminars that stimulated some lively discussions.

On top of all that, we are making great progress in organizing the ASI annual meeting to be held in Sydney in 2007. The meeting will be held at the Manly Pacific Hotel, overlooking beautiful Manly Beach from 2-6 December. We already have a host of great international scientists lined up, so make sure to keep those dates free in 2007.

Cheers

*Bernadette Saunders
Councillor*

Sustaining Membership

ASI Inc acknowledges the support of the following sustaining members:

- Jomar Diagnostics
- Dynal Biotech Pty Ltd

S.A./N.T. News

Hi all

We have had a very exciting past few months with the ASI Sponsored Speaker, Dr Graham Pawelec, coming into Adelaide and spending a few days at various institutes throughout the State, sharing his knowledge on tumour immunology and senescence. Graham was a delight to meet and his breadth of knowledge in his area was a great source to tap into. Thank you to Su Heinzl for arranging his visit throughout Australia.

A small group of local ASI members have also come together recently to try and identify where ASI may be more active in SA/NT and attempt to run more ASI events in the future. We are intending to line up student-only lunches with any ASI invited speakers to allow the students an opportunity to meet and interact with the speakers outside of their normal schedule. We'll let you know how this goes. Speaking of students, I'd like to congratulate Emma Beukema for being awarded an ASI Travel Bursary to attend the Annual Meeting in Auckland. We look forward to our next visiting speaker, Prof Ari Theofiloupoulos, in a few weeks and I'd like to now move on to a report of our annual retreat.

The Second Adelaide Immunology Retreat (AIR) 2006 was held at the Warrawong Wildlife Sanctuary in the Adelaide Hills, 27th-28th October 2006.

AIR was organized by the local ASI state branch and was designed for students, as well as young and established scientists to get to know not only each other but also the science going on in Adelaide. Like last year, we again had a mixture of great science and social activities.

We continued our tradition of inviting a well accomplished scientist from South Australia as well as one from interstate to join us at the retreat. We were very please that Simon Barry from the WCH in Adelaide agreed to be our 'local' speaker. Likewise, we were absolutely delighted that Australian of the Year 2006, Prof Ian Frazer and his wonderful wife Caroline could join us. They could not be a more lovely, humble and easy-going couple and Ian's generosity with his time, especially this year, exemplifies what a wonderful role model he is for us all.

Day 1, the Friday morning started early in the idyllic setting of the sanctuary with the vibrant Assoc/Prof Simon Barry openly describing his scientific journey as one of highs and lows but filled with enough of the good, the bad and the ugly to keep him coming back for more!!!! His depth of immunological knowledge, his love/hate relationship with regulatory T cells as well as his overall energy and enthusiasm was just one of the many great things about the weekend. For more information on Simon, check him out at the Women's and Children's Hospital site (<http://www.chri.com.au/MolecularImmunology.htm>). The rest of the morning saw five great delegate talks from different corners of Adelaide before we went out exploring. We dove straight into the wildlife where we met the Barking Owl, the Barn Owl, the Kestrel, the Wedged tail Eagle and learnt about the day to day life of Australia's endangered 'birds of prey'. We then treated ourselves to some delicacies from the McLaren Vale area with Mark Potter from 'Blessed Cheese' trying to teach us the finer art of combining cheese and wine. We had some absolutely divine combos and enjoyed the wines so much we drank them well beyond the tasting session. We then took a stroll along the boardwalks around the sanctuary wetlands to get a closer look at the freshwater turtles and elusive platypus followed the meandering paths through the beautiful Australian bush setting to see kangaroos relaxing on the hillside, wallabies and potoroos scurrying through the shrubs and trees. Su even spotted a koala swaying and grunting in the gum trees! Feasting on the roo after the walk wasn't for everyone, but there was a great menu selection... The cool cabins had quite a few people huddle together 'networking' into the wee hours of the morning...

Day 2, started off with an eagerly awaited talk by Ian Frazer. He shared with us his career journey and the current developments on the first vaccine to fight cervical cancer (<http://www.cicr.uq.edu.au/>). Following Ian we had another 6 great talks from the delegates. This year we had a great mix of Honours students, PhD students, RAs, post-docs and lab heads at the retreat and the quality of presentations was outstanding. Both invited speakers were fantastic in their

mixing and mingling with the students throughout the event and were more than happy to share their advice and knowledge. We were a very sociable group, energized by each others work, sharing our experiences and advice and really just getting to know each other and enjoying each others company. We ended the retreat as we started, with fun and laughter but left with a few more friends. We believe that this is a great way to promote science made in SA to some of our very best. Ian Frazer also commented that not only was he impressed by the high standard of the presentations but that he might spread the word that it's not all cold down in SA but that there's some pretty hot science going on.

It is an absolute honour to run these events but it would not be at all possible without the financial support (for AIR 2006 we would like to sincerely thank Hanson Institute, IMVS, Ozgene, BD, Jomar Diagnostics, Adelab Scientific and John Morris Scientific) and we are already looking forward to AIR 2007!!!!

*Claudine Bonder and Susanne Heinzl
Convenors of AIR 2006*

A.C.T. News

The ACT Branch has had an active schedule for the last few months with a line-up of outstanding immunologists who visited and delivered seminars. In August we had Professor John Harley (Oklahoma University Health Sciences Center) who gave two talks: "The Genetics of Human Lupus: In the New Data Rich World" and "The Case for EBV as the cause of Lupus". In the same month, Dr Chris Engerweda from the Queensland Institute for Medical Research presented a seminar entitled "Balancing immunity and pathology in experimental cerebral malaria".

Dr Philip Hodgkin (The Walter and Eliza Hall Institute of Medical Research) visited us in September and presented a seminar entitled "Insights into the regulation of lymphocyte growth and survival from quantitative modelling". His seminar certainly generated a lot of discussion. Professor Jonathan Sprent (Garvan Institute of Medical Research) visited us next in October and delivered a brilliant talk on "Homeostasis of CD8 T cells".

Our next visitor will be Professor Thomas Blankenstein (Max-Delbrueck-Center for Molecular Medicine and Institute of Immunology of the Charite) who will be attending the ASI Inc Annual Scientific Meeting in Auckland in December. The grand finale for this year will be marked by a visit by Professor Marc Feldman (Imperial College) in December. He will travel to Auckland to give the Burnett Oration at the Annual Scientific meeting this year after which he will visit Canberra. His travel to Canberra is organized by the Australian Academy of Science.

We had a record number of applications (9) from the ACT Branch for the ASI Inc student travel bursaries this year. We congratulate Ivan Poon from the ACT for being awarded one of these bursaries by the ASI Executive. We would also like to congratulate Donna Easton, Julia Ellyard, Di Yu and Isaac Sakala for being awarded bursaries (\$600 each) by the ACT Branch to attend the meeting in Auckland this year. Di Yu has been selected for an oral presentation in the Young Investigator Award session.

*Guna Karupiah
Councillor*

Victorian News



The Immunology Group of Victoria
A branch of the Australasian Society for Immunology

We are all looking forward to the upcoming ASI conference at the University of Auckland, New Zealand from December 3–7. John Fraser and the rest of the committee have done a wonderful job assembling an excellent list of national and international speakers for this event. The Tumour Immunology Workshop preceding the main conference is always a worthwhile day to attend. The workshop will cover both basic and translational research in tumour immunology and will include presentations from several prominent international and local scientists. ASI is also a participating society at the Australian Health Medical Research Congress (AHMRC) meeting in Melbourne from 26 November–1 December and has organised two symposia.

On the local front, the IgV meeting at Beechworth was held again after a year's absence because of the ASI conference in Melbourne. From all reports there were many outstanding presentations from both senior scientists and students. The meeting

format allowed most students who attended to present their work and encouraged their active participation during question time. The trivia night hosted by Dale Godfrey and Anne Fletcher was also a highlight and we hope they can be convinced to run this again in future meetings. I would like to thank the entire IgV committee for the successful organisation of the meeting.

As a reminder, the next scheduled visiting ASI speaker is Professor Thomas Blankenstein from the Delbrueck-Center for Molecular Medicine who is head of the Institute of Immunology of the Charite Hospital, Berlin, Germany. He will be presenting at the ASI symposium at AHMRC in Melbourne and also at the Tumour Immunology Workshop and ASI conference in Auckland.

Finally I would like to congratulate the following students who were awarded travel bursaries to attend the ASI conference in Auckland: Kate Gartlan, Susan Johnson, Anja Scholzen, Sandro Prato, Desiree Anthony and Anne Fletcher.

*Phillip Darcy
Councillor*

Queensland News

The lead-up to our December meeting in Auckland has created much excitement among ASI members, planning the pre- or post-meeting bungee jumps and white water rafting, or even just contemplating the stellar line-up of keynote speakers. The best way to Auckland for students, of course, was to win an ASI bursary. Three Queensland ASI candidates were externally ranked as deserving of this plum prize—congratulations to Michelle Neller (Queensland Institute of Medical Research), Annelie Vulink and Jennifer Freeman (both from the Mater Medical Research Institute). Since our Treasurer, Dr Norbert Kienzle (QIMR), was feeling particularly generous, this year (as in 2005) the award covered both airfare and registration.

Other ASI members with reason to celebrate include Drs Scott Burrows and Maher Gandhi (both from QIMR) who were awarded NHMRC fellowships in this year's round – Scott at the level of SRFB, and Maher a Clinical Career Development Award.

ASI's vibrant visitor program assisted Prof Graham Pawelec (Center for Medical Research, University of Tübingen) to visit

cont. p20

Travel Award Conference Reports

Rachel Lundie

The Walter and Eliza Hall Institute of Medical Research
1st Joint Meeting of European National Societies of Immunology,
16th European Congress of Immunology
September 6–9, Paris, France

The 1st Joint Meeting of European National Societies of Immunology, 16th European Congress of Immunology, was held at the impressive Palais des Congres, Paris. Over three days, more than 4000 delegates attended 41 symposia and 61 workshops designed to cover the physiology and pathology of the immune system. The conference format was diverse, with general symposia sessions in the morning, more in-depth workshop sessions in the afternoon, and poster sessions during the lunch break and at the end of each day. All sessions ran concurrently to allow for the breadth of topics to be covered adequately, and oral presentations covered both innate and adaptive immunity as well as immunopathology and immune intervention. This format allowed a large number of delegates to present their work, however at times it was difficult to choose between concurrent sessions and seat numbers were limited in some of the smaller seminar rooms. Rolf Zinkernagel delivered the keynote lecture during the opening ceremony, discussing vaccination against Tuberculosis and HIV. This was followed by the welcome cocktail reception, which was a relaxed way to mingle with the other delegates while sampling authentic French cuisine and wine.

Of the symposia sessions, Adrian Hayday (UK) covered the hot topic of “unconventional” $\gamma\delta$ T cells and their functional and developmental integration with conventional $\alpha\beta$ T cells.



LtoR: Marian Turner, Kirsten Fairfax, Petra Schnorrer, Anna Proietto, Louise Young, Rachel Lundie (on our way to dinner)

Discussions focussed on the thymus, which gives rise to both of these T cell lineages. The current dogma is that $\alpha\beta$ and $\gamma\delta$ T cells develop in the thymus independently of one another, and that $CD4^+CD8^+$ (double positive) thymocytes are simply the progenitors of $CD4^+$ and $CD8^+$ $\alpha\beta$ T cells. However, recent gene profiling studies and experiments in mice lacking double positive thymocytes ($TCR\beta^{-/-}$) indicated that double positive cells regulate the differentiation of functional $\gamma\delta$ T cells, by a mechanism dependent on the transcription factor $ROR\gamma t$, and the lymphotoxin β receptor, suggesting that there is “cross-talk” between these two T cell lineages during development.

The workshop session on vaccination and immunotherapy against parasitic diseases was also particularly interesting, covering both malaria and leishmaniasis. Scott Draper from Adrian Hill's group (UK) presented results from a promising study in which complete protective immunity against blood-stage malaria was induced in mice following a heterologous prime-boost vaccination strategy. This involved a ‘priming’ immunisation with an adenoviral vector, followed by a ‘boost’ with a poxvirus vector, both of which expressed a recombinant form of merozoite surface protein (MSP)-1, a major blood-stage vaccine candidate. Importantly, immunised mice generated protective T cell and antibody responses following challenge with lethal *Plasmodium yoelii* YM blood-stage parasites or sporozoites (natural mode of infection), strongly supporting this strategy for further pre-clinical studies and clinical trials.

Educational courses were also held each day and were designed to cater to the large cohort of PhD students and young post-docs attending the conference. Expert speakers presented an overview of fundamental and applied aspects of immunology, and topics were extremely diverse, covering allergy, rheumatology, innate immunity, antibody deficiencies and novel immunological approaches to control infectious diseases. Antonio Lanzavecchia (Switzerland) explained the use of human B cells to

produce monoclonal antibodies for infectious disease therapy. In one example, memory B cells isolated from individuals recovered from SARS coronavirus infection were immortalised and cloned *in vitro*, to allow the selection of those producing virus-specific neutralising monoclonal antibodies. Advantages of using human B cells to produce monoclonal antibodies include the minimal risk of cross-reactivity with self antigens, since the antibodies have been selected in the human body, and that the human immune response is directed against the virulent pathogen, and can therefore target all the components necessary for infection and virulence, including those which may be invisible to the immune system of a different host (e.g. the mouse). This “analytic vaccinology” approach will be useful not only to isolate therapeutic antibodies for passive vaccination, but also to analyse the antibody repertoire in immune or vaccinated individuals to identify neutralising, enhancing or even irrelevant epitopes, particularly for highly variable viruses (e.g. HIV) or highly complex pathogens (e.g. *Plasmodium*).

9th International Conference Dendritic Cells **September 16–20, Edinburgh, Scotland**

The 9th International Conference on Dendritic Cells (DCs) was held at the Edinburgh International Conference Centre, right in the heart of historic Edinburgh. The Welcome Reception was a night to remember, where we were treated to a traditional performance of the Highland fling and a beautiful selection of Gaelic folksongs before embarking upon the well-known tourist attraction, Edinburgh Castle. Here, we were treated to a striking Edinburgh sunset and a customary bagpipe performance by a group of Scotsmen in kilts (no experience of Scotland is complete without this!). Those attending the conference dinner reported that the Haggis ceremony was a highlight, and afterwards we all enjoyed participating in the Gala Ceilidh, a traditional Scottish social dance. The Ceilidh dancing was fast and lively, and all the dances were made up of a sequence

of formations, so even if you had never danced before (or had two left feet!) it was easy, entertaining and enjoyable to take part. Overall, the conference organisers did a fantastic job showcasing the unique Scottish culture.

The scientific programme spanned four full days of symposia sessions, the format of which consisted of an opening plenary symposia, followed by a series of shorter presentations, on topics related to the therapeutic use of dendritic cells for the treatment of infectious diseases and autoimmune and allergic conditions. Given the limited opportunity for oral presentations, the majority of delegates presented posters during one of two designated sessions, arranged into themes such as functional immunobiology, immunophysiology, molecular cell biology and immunopathology.

Functional differences between DC subsets were covered by a variety of speakers, including Jacques Banchereau (USA), who explained that Langerhans cells (located in the epidermis) were potent inducers of cellular immunity whereas interstitial DCs (found in the dermis) preferentially activate humoral immunity. William Heath (Australia) presented data on the essential role of trafficking DCs during herpes simplex virus or influenza infection, and Ken Shortman (Australia) explored the development of DCs using a Flt3 ligand stimulated bone marrow culture system which generates equivalents of all steady-state splenic DC subsets.

Toll-like receptors (TLRs) and control of adaptive immunity was another interesting session, where Colin Watts (UK) presented data showing that activation of dendritic cells through TLR signalling induces changes in the actin cytoskeleton that result in an early, transient phase of enhanced endocytosis. This boosts antigen capture and presentation to T cells, prior to the eventual down-regulation of endocytosis that accompanies dendritic cell maturation. In the same session, Matthew Albert (France) covered the broad and contrasting effects of type I interferons in innate and adaptive immunity, explaining that mature DCs (but not immature DCs) exposed to IFN- α/β showed an enhanced ability to cross-present viral antigens to influenza-

specific CD8⁺ T cells *in vitro*.

A number of prominent immunologists in the field of parasitology presented exciting *in vivo* data on DC function during acute and chronic parasitic infections. Alan Sher (USA) reported on the role of *Toxoplasma gondii* profilin as an immunodominant antigen governing CD4⁺ T cell responses to the pathogen, via MyD88-dependent signalling through TLR11 on CD8 α ⁺ dendritic cells. Jean Langhorne (UK) suggested that populations of splenic DCs have different but overlapping roles during chronic malaria infection. Experiments using a TCR transgenic mouse specific for MSP-1 demonstrated that initial uptake and presentation of antigen to CD4⁺ T cells was performed by CD8⁺ DCs, while the CD8⁻ DCs appeared to play a later role in antigen presentation, suggesting that they may support the Th2 and CD4⁺ T cell-mediated B cell response that is required for control of the infection. Paul Kaye (UK) presented interesting data on the role of tissue stromal cells in regulating DC development and function under steady-state conditions and during experimental visceral leishmaniasis, while Rick Maizels (UK) highlighted the controversy surrounding DC activation in the field of Helminth immunology.

In summary, I had a fantastic time at both conferences, scientifically and socially, and I would like to thank ASI for supporting my attendance at these international events. I would also like to thank the Edith Moffat Fund (WEHI) for the opportunity to visit laboratories for my future post-doctoral placement during this time. This experience has been extremely motivational and has facilitated and strengthened my international network across both parasitology and immunology fields.



LtoR (top to bottom) Chris Smith, Rachel Lundie, Meredith O'Keefe, Anna Proietto, Nick Wilson, Louise Young, Shalin Naik, David Vremec (this was after the Gala Ceilidh)

Lukasz Kedzierski
Walter and Eliza Hall Institute of
Medical Research
XIth International Congress of
Parasitology, Glasgow
August 6-11, 2006

This year ICOPA was held in Glasgow, which I thought was an unusual choice of a location for the conference. It all made a perfect sense to me when I read a bit on the Scots' encounters with tropical diseases and parasitology. My favourite parasitic disease, leishmaniasis, was named after the Glaswegian William Leishman; David Livingstone, a man who found that quinine can keep malaria at bay was born just a few miles south of Glasgow, and Patrick Mason, the "Father of Tropical Medicine," was also born in Scotland. Others include Sir David Bruce who was born in Melbourne, but to Scottish parents and one of the most famous, Sir Roland Ross whose family descended from Scotland. No wonder that the conference was organised in Glasgow.

This is a huge conference organised once every four years. This year there were over 300 invited speakers and more than 1500 abstracts from 70 countries. The congress was held in the Scottish Exhibition and Conference Centre also known as "Armadillo", although names such as a lobster or a Sydney opera house copy were also used. Due to the number of delegates there were 13 concurrent sessions, and I was only able to stick to Leishmania and Trypanosoma themes with occasional visits to malaria and some other talks. All aspects of parasitology were covered from population biology of nematodes and parasites of aquatic animals to apoptosis, immunology and drug resistance.



"Armadillo", the ICOPA venue

Each day started with a plenary session, and to me the most interesting included Kevin Marsh's (Kenya) talk on immunity to malaria or Robin Gasser's (Australia) presentation on parasite genomics and genetics. These sessions were followed by a day full of talks on specific topics and I found presentations delivered by Chris Peacock (UK), Rob

McMaster (Canada), Jim McKerrow (USA) or Shyam Sundar (India) of particular interest to my research. Afternoon sessions were devoted to posters. Red and white wine was generously served and facilitated contacts between researchers from different fields and different countries. It was good to catch up and talk to parasitologists from my home country, Poland, and to see what kind of research is going on over there. Unfortunately, they do not research tropical diseases such as leishmaniasis or malaria, so it was hard to establish any collaborations.

There was enough spare time to explore Glasgow, a city that features quite a few interesting museums (free of charge) and a good selection of pubs. As true scientists do, we "researched" single malt whiskeys and cask conditioned real ales, while haggis with tatties and neeps or a clapsnot provided energy for the long nights. The conference dinner also gave us an opportunity to taste local culture and to master a few steps of traditional Scottish dances. Without a proper protocol to follow, we constantly bumped into each other, while the Scots present on the dance floor watched in horror.

We all meet again in Melbourne in 2010.

My thanks go to ASI for providing me with the financial assistance through the Postdoctoral International Travel Prize.



LtoR: Dr Svetozar Kovacevic (Monash Uni), Lev Kats (Monash Uni), Lukasz Kedzierski (WEHI)

LtoR: Zuopeng Wu, PhD student, Immunogenomics Lab, JCSMR, ANU, Canberra; Di Yu, PhD student, Immunogenomics Lab, JCSMR, ANU; Lisa Miosge, Post-doc fellow, MRC, National Institute of Medical Research, London (ex-PhD student in Immunogenomics Lab, JCSMR, ANU); Katherine Gosling, PhD student, School of Biochemistry and Molecular Biology, ANU, Canberra

Di Yu
JCSMR, ANU

1st Joint Meeting of European National Societies of Immunology / 16th European Congress of Immunology

I was sponsored by ASI to attend the 1st Joint Meeting of European National Societies of Immunology / 16th European Congress of Immunology (16th ECI) held in Paris, France from September 6–9, 2006. With more than 4000 participants, 16th ECI made itself huge, thus different from ASI annual meeting in size, which I think more efficient for communication. However, such a big conference provided a chance for every delegate to find lots of talks and posters quite related to his/her field of research, or even projects undergone. Moreover, I was able to broaden my vision in the whole immunology by approaching excellent research in fields other than my own through a variety of presentations.

It has turned out not so easy to locate famous master pieces such as "*Portrait of Mona Lisa*", "*Winged Victory of Samothrace*" and many more in 35,000 works of art collected in Musée du Louvre. At the beginning, I had the problem to find abstracts of my interests. Thank the conference organizer for providing searching function on the conference website and in the abstract CD-ROM. After typing in key words (autoimmunity, ICOS, etc.), I could finally track down my targets from more than 1000 abstract and draw a route map for the next day, directing me to shuttle among presentation rooms.

The scientific program in 16th ECI was composed of four tracks: Innate Immunity, Adaptive Immunity, Diseases of the Immune System and Immune Interventions with a total of 38 symposia, 60 workshops and lots of educational and sponsored sections in addition to hundreds of posters. My PhD studies include two projects, one on germinal center B cells and the other on the regulation of co-stimulation in autoimmunity. Therefore, I took the chance to attend

various sessions about autoimmunity, co-stimulation, germinal center reaction, B cell signalling, etc.

My oral presentation, "The ubiquitin ligase roquin regulates T and B cell tolerance through posttranscriptional regulation of ICOS expression", was arranged in the session "Costimulation, accessory molecules and activation signals". A seven-minute presentation and a two-minute discussion were just enough for me to outline our research and highlight the main discovery. There was no doubt that people interested in my talk would follow up for more details. A researcher from Finland talked with me about her findings on the effects of human single nucleotide polymorphisms (SNPs) in ICOS on its expression which had attracted lots of my attention when I went through posters. And ... (OK, that's the most exciting moment during the conference) a researcher from Singapore talked with me about his lab's studies on ICOS. I was then pleased with their data supporting my discovery by a different means. So, two labs have built up the collaboration soon after.

Many Australian colleagues were present in the conference. After flying for 20 hours, Carola Vinuesa (JCSMR, ANU, Canberra), Fabienne Mackay (Garvan Institute, Sydney), Kirsten Fairfax (WEHI, Melbourne) and Jose Villadangos (WEHI, Melbourne) were still able to show the high quality research of immunology in Australia.

Thank you ASI to provide me the opportunity to attend the conference. What a rewarding trip.



ASI Visiting Speakers Program

Professor Ronald N. Germain,
Lymphocyte Biology Section, Laboratory
of Immunology, National Institutes of
Health, Bethesda, MD, USA.

One of the icon living immunologists, Prof. Germain started his prolific career in Brown University, Rhode Island where he completed his *Summa cum laude* degree in biology (Sc.B. and Sc.M) in 1970. He then completed his PhD (*Magna cum laude*) and MD degrees at Harvard (1976) where he remained until 1982 as Associate Professor. Since that date, Prof. Germain has been at the NIH where he heads the Lymphocyte Biology Section (LBS). Besides being deputy chair of the Laboratory of Immunology at the NIH, he serves in numerous editorial boards and committees both in the USA.

The LBS studies basic aspects of how white blood cells called T lymphocytes recognize foreign substances known as antigens. The work of the laboratory is organized around three themes within this larger topic: 1) the formation of peptide complexes with major histocompatibility complex (MHC) molecules, which are the ligands for the antigen-specific receptors (TCR) of $\alpha\beta$ T cells; 2) the role of recognition of self-peptide:MHC molecule ligands in the development of T cells in the thymus gland; and 3) the biochemical mechanisms involved in allowing TCR to discriminate between self and foreign peptide-associated MHC molecules, including the control of T-cell differentiation by the TCR signals generated by these recognition events.

Recent work in this area includes the identification of a novel transport signal within class II molecules themselves and the first direct evidence that antigen presentation by MHC class II molecules involves binding to large protein fragments and not peptides, followed by cleavage of the bound protein to peptide length. This latter finding provides new insight into why the MHC class II molecule evolved a binding site with open ends — namely, to accommodate the large proteins that are its preferred substrates. LBS has also pioneered the development of reagents (monoclonal antibodies) that can detect specific



peptide-MHC molecule complexes, and the use of these tools for the *in vivo* visualization of antigen presentation to T cells. This work has led to a new understanding of which cells actually process and present antigen, the kinetics of presentation, and the role of inflammatory signals in effective dendritic cell antigen processing and colocalization with T cells for the initiation of adaptive immune responses.

A second major focus of the LBS is on the consequences of T-cell receptor recognition of peptide-MHC molecule complexes, especially how binding events are translated into intracellular signals that regulate T-cell differentiation. Among the major previous accomplishments of LBS in this area are the identification of the site(s) of CD4:MHC class II interaction, description of TCR antagonists and partial agonists, and discovery that such ligands induce a distinct set of early intracellular tyrosine phosphorylation events.

Ongoing work centres on understanding the differences in intracellular signals generated by agonist versus partial agonists/antagonists, examining the molecular interactions that account for normal and altered signaling, and exploring the biological consequences of altered signalling in immunity. Very exciting data are now emerging from these studies, which have revealed previously unsuspected feedback regulatory pathways that help the T cell achieve fine discrimination between ligands of closely related structure. Such selectivity is at the heart of physiologic self/nonself-discrimination by the immune system. These experiments also have clarified the role of

negative regulatory molecules, such as SHP-1, in the phenomenon of TCR antagonism and in regulating the strength and duration of TCR signalling by activating ligands.

Finally, we have continued to study the development of T cells in the thymus. Our work in this area has led to a new and increasingly accepted model of the stages of thymocyte differentiation. We have now developed a new model system for examining the role of antigen-specific and -unspecific signals in T-cell lineage (CD4 versus CD8) choice, as well as the nature of TCR signalling leading to effective positive and negative selection. This work is closely dovetailed with the biochemical studies on TCR signalling and recently has led to the novel finding that the TCR changes its perception of ligand during maturation in a highly selective manner that supports self/nonself discrimination in the periphery. These biochemical and developmental studies are being integrated with modern methods for global gene expression analysis to reveal the changes that accompany and control each step of maturation.

Selected Publications

Germain RN, Miller MJ, Dustin ML, Nussenzweig MC. Dynamic imaging of the immune system: progress, pitfalls and promise. *Nat Rev Immunol*. 2006 Jul;6(7):497-507.

Qi H, Egen JG, Huang AY, Germain RN. Extrafollicular activation of lymph node B cells by antigen-bearing dendritic cells. *Science*. 2006 Jun 16;312(5780):1672-6.

Castellino F, Huang AY, Altan-Bonnet G, Stoll S, Scheinecker C, Germain RN. Chemokines enhance immunity by guiding naive CD8+ T cells to sites of CD4+ T cell-dendritic cell interaction. *Nature*. 2006 Apr 13;440(7086):890-5.

Bajenoff M, Breart B, Huang AY, Qi H, Cazareth J, Braud VM, Germain RN, Glaichenhaus N. Natural killer cell behavior in lymph nodes revealed by static and real-time imaging. *J Exp Med*. 2006 Mar 20;203(3):619-31.

Melbourne, April 10-11

Host: Sarah Russell, Peter Mac Cancer Research Institute, (03) 96563727; sarah.russell@petermac.org

Canberra, April 12

Host: Guna Karupiah, John Curtin School of Medical Research, ANU, (02) 61254562; guna.karupiah@anu.edu.au

Sydney, April 3, 14

Host: Bernadette Saunders, Centenary Institute, (02)-9565-6114; b.saunders@centenary.usyd.edu.au

Brisbane, April 16, 17

Host: J. Alejandro López, Queensland Institute of Medical Research, (07) 3845 3794; alejL@qimr.edu.au

Auckland, April 18

Host: Peter Hunter, Bioengineering Institute, University of Auckland, (09) 373 7599 ext 88395
p.hunter@auckland.ac.nz

Wellington, April 19-20

Host: Franca Ronchese, Malaghan Institute, (04) 4996914 ext 828; fronchese@malaghan.org.nz

Please, contact the local ASI councillor or the respective visit hosts for further details of the Seminars planned.

Also confirmed for 2007 (October 8–28), Jacques Banchereau, Baylor Institute for Immunology Research, Dallas, TX, USA

UPCOMING LECTURES & CONFERENCES

Australasian Society for Infectious Diseases
 ASM

March 22–24, 2007

Hobart, Tasmania

Email: Conference.Mailbox@ashm.org.au

Website: www.racp.edu.au/asid/asm.htm

4th IAS Conference on HIV Pathogenesis,
 Treatment & Prevention

July 22–25, 2007

Sydney, NSW

Email: cammi.webb@ashm.org.au

Website: www.ias2007.org

The Walter and Eliza Hall Institute of Medical Research

WEHI Seminars on the Web:
www.wehi.edu/seminars/

ICB Online Manuscript Submission

Online manuscript submission for
 Immunology and Cell Biology now
 available via:

<http://mc.manuscriptcentral.com/icb>

All manuscript submissions to ICB
 should in future be made online via this
 web site to speed up the reviewing and
 acceptance of manuscripts.

Chris Parish, Editor-in-Chief
 Immunology and Cell Biology

Adelaide Immunology Retreat (AIR) – A Student's Experience

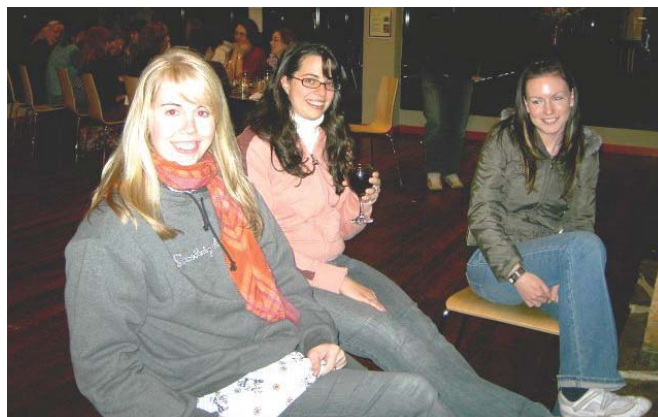
The AIR was held at Warrawong Wildlife Sanctuary in the Adelaide Hills on October 27–28. Around 30 delegates attended including Honours and PhD students, postdocs and senior researchers, all of whom enjoyed 1½ days of learning, networking, marsupial spotting, and drinking! We were lucky enough to be joined by Ian Frazer from the University of Queensland and Simon Barry from the Women's and Children's Hospital in Adelaide, who both gave us insightful talks not only about the work in their laboratories but also about the challenges and successes they have encountered in their careers thus far. This was an excellent opportunity for junior researchers to get some practical advice on how to have a successful career, invaluable advice for every young researcher!

This meeting also allowed students and postdocs to present their work and receive some feedback in a relaxed setting. The talks were diverse and of a very high standard. Networking and scientific discussions also

took part over an afternoon of cheese and wine tasting held by Blessed Cheese from McLaren Vale, an evening guided walk around the sanctuary where we viewed many furry native creatures, and a lengthy (and in some cases) slightly inebriated dinner, so it wasn't all hard work!

This retreat is highly recommended to all students. Not only is it a great opportunity to get to know people that work in your field in your city, it is also a relaxed forum in which to get practice presenting your work in a public setting and a chance to get ideas from people removed from your specific field. We strongly encourage you to attend and support these events in your State and to try and convince other people in your lab to come along as well as not only was this a great learning experience but fun was had by all.

Sarah Haylock-Jacobs



ASI STUDENT PAGE

So it seems my time as student rep is almost up. I thought since this was my last student page, I would include my favourite grad student comic. I was sent this early on in my PhD but didn't quite appreciate it like I do now. The comic comes from **Piled Higher and Deeper** by Jorge Cham. It's about Life (or the lack thereof) in Academia. If you want to view more (and I recommend that you do for your own sanity) then go to <http://www.phdcomics.com/comics.php>. Some other favourites of mine include "Things to do while waiting for your experiments" and "Graph – Work output", which is a grad student's week. If you are ever having one of those weeks, and we all know they happen a lot over the course of a PhD, then take a few minutes to read some and I guarantee you will feel better.

The student BBQ at this year's ASI conference is looking like it will be a goodie. Over 50 students have signed up and the menu is very mouth watering. Pork, chicken and lamb spit roast with lots

of tasty salads and don't forget there will be drinks to help break the ice. Hopefully this will end up being a regular occurrence at ASI conferences. A good chance for you to mingle with some of the keynote speakers and meet others going through what you are.

One last thing before I sign off. Don't forget that the 13th International Congress of Immunology is in Rio in August next year. If you have ever wanted an excuse to get to Brazil, then here is your chance. This will be a large international conference that has over 360 invited speakers. Check out the web site for more information <http://www.immunorio2007.org.br/> and start thinking of ways to get yourself there.

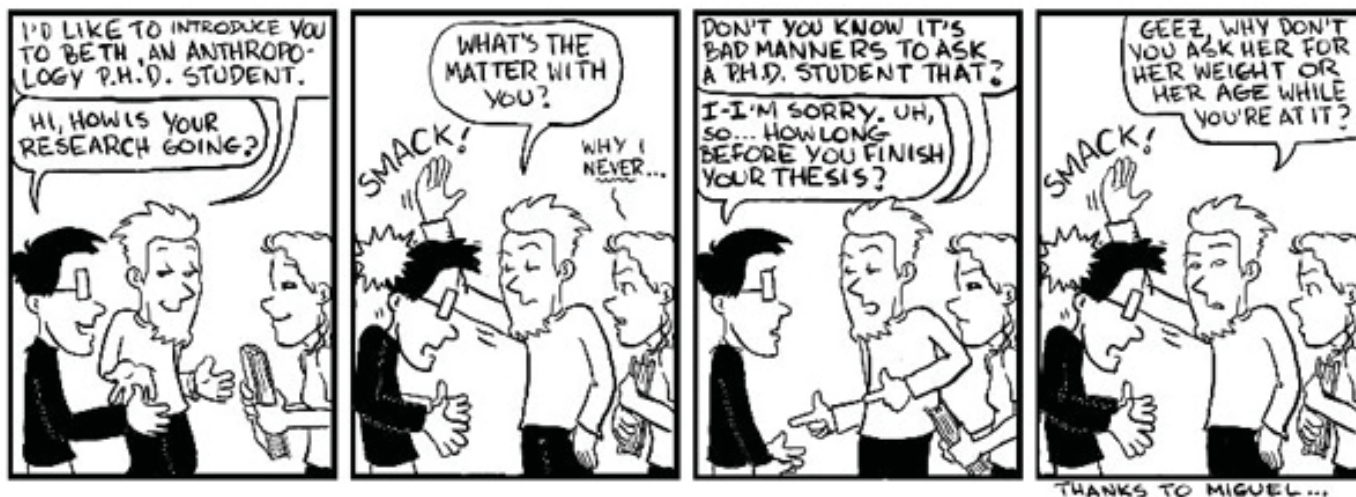
So that's all from me. I'll be handing the title onto someone from Sydney as the 2007 ASI Conference will be held there. Unfortunately, as I discovered it, doesn't come with a crown. I'm sure I'll be meeting a lot of you at the grad student BBQ. Ciao until then.

Amanda Taylor

An invitation and a request to all ASI members

to contribute copy that they think might be interesting, useful, historical, humorous or thought provoking.

- We invite our student membership to voice their views on issues that interest or directly concern them.
- It's our newsletter, so let's support it and strive to make it even better.
- The ASI newsletter comes out 4 times a year and we welcome your contributions.
- **AND NOW YOU COULD WIN \$100 FOR THE BEST ARTICLE PUBLISHED IN THE NEWSLETTER!**



JORGE CHAM ©THE STANFORD DAILY

Submission of photos with articles

When submitting articles, reports, etc. to the newsletter, please do not embed the photos in the Word article, but always send as separate jpeg files - preferably no larger than around 200kb. Embedded photos/graphics cannot be imported into the desktop publishing program nor edited if required and delays occur in requesting photographs to be re-sent. High resolution jpeg files are not necessary and only take extra time to download.

Thank you for your co-operation.

Queensland Taken by Storm

This year two ASI members show cased the success of immunology in Queensland by winning prestigious ASMR Premier's Awards for Medical Research. They shared in a booty of over \$25,000, with Premier Peter Beattie on hand to give the prizes. The award in the post-graduate student category went to Alberto Pinzon-Charry and in the senior Post-doctoral level to Chris Schmidt. Interestingly, the research interests of both winners from the Queensland Institute of Medical Research (QIMR) revolve around the use of dendritic cells for cancer immunotherapy.

Since the discovery of dendritic cells (DC) a couple of decades ago, their potential as initiators of immune responses has been extensively described. Their ability to elicit responses against novel and self antigens has made them obvious candidates to be tested for cancer immunotherapy.

"Because of their central role in controlling anti-tumor immunity there has been a lot of interest in exploiting DC for cancer immunotherapy. Many trials have been conducted yielding some exciting results particularly in the case of melanoma. However, clinical outcomes have not met the high expectations raised by early results" says Dr Pinzon-Charry from the QIMR.

"It's been puzzling to see that most clinical trials have evolved from vaccines formulated to mimic 'successful' murine models with limited understanding of what's happening in patients during cancer development. We simply wanted to see what was going on with DC during cancer progression. So we looked at DC in patients with different types of solid tumours and tested a few ways to improve them".

Dr Pinzon-Charry discovered that tumours may cause the premature death of DC while in blood by apoptosis and that they halt the natural differentiation of DC and other lineages leading to the accumulation of a large number of immature cells in the circulation. The addition of CD40L protects DC from dying too early and the function of DC and immature cells abundant in cancer patients could be rescued.

"I believe our findings provide a better understanding of the complexities behind cancer development and aid in enhancing the effectiveness of DC immunotherapy

particularly for breast and prostate cancer".

Dr Pinzon-Charry's research was conducted within the group of A/Prof. JAlejandro López through the University of Queensland and the QIMR. He published nine papers during his PhD, including a publication in Breast Cancer Research, ranked amongst the top 10 most visited of the journal's website.

Dr Pinzon-Charry, 30, completed medical training overseas prior to his PhD. Previous to the Premier's Award, he also received various distinctions including Travel Awards from the Queensland Cancer Fund and ASI as well as the Paul Mackay Bolton Foundation Scholarship for Excellence in Cancer Research. Other prizes include Best Scientific Presentation during the Australian Society of Medical Research Postgraduate Conferences. He was finalist to the Young Investigator Award at a previous ASI Meeting in 2005. Most recently, he was awarded the Early Career Research Award from the ARC/NHMRC network for Parasitology for work on malaria that followed his PhD, in the group of Prof. Michael Good at the QIMR – a return to his early research interests.

Chris Schmidt, head of the Cancer immunotherapy Laboratory at the QIMR has for many years focused on understanding the "foe within" and presented a vivid immunological insight into the death of cancers at the ASMR Queensland Premier's Awards this year.

"Many patients believe that the key to curing advanced cancer lies within. Spontaneous cures are rare, but many studies show that the same complex system that has protected higher animals from viruses for hundreds of millions of years has the potential to eliminate tumours. And, unlike many toxic chemicals now in use, it can do so without leaving a trace of evidence, either of itself or of its foe. In these rare cases, the extraordinary fact is that usually, the cancer does not return. We remain ignorant of how immunity works, just as we misunderstand how it fails," said Dr Schmidt.

"Cancers are organs that survive at the expense of other cells. If we can see them, they have clearly avoided the armies of T cells that apparently lie idle. But this hides the more subtle truth: we now speak of immunity "sculpting" the

cancer, a true Darwinian struggle. The evidence for this is that cancer cells sometimes relinquish those surface features that make them recognizable to our sophisticated T cells. Even then, more primitive mechanisms of immunity must be overcome. Natural killer cells are capable of detecting changes in these recognition structures, but cancers can express decoys that mimic normality. The evidence of these changes in tumours suggests that the immune system may kill cancer cells at some stage, but the unequal battle has them lose sight of the enemy.

"This raises the most important question: what allows the immune system to prevail? To answer this, we must find ways of coaxing the immune system into action. To avoid T cells, cancers can subvert the means by which they are activated. One way, of course, is simply to lie there, pretending to be normal – which, as far as the immune system is concerned, they pretty much are. Perhaps because of the local nuisance that the growing tumour causes, this can't last forever, but maybe long enough for the cancer to release its own toxins to inhibit those fragile, tentacled immune activists, the dendritic cells. This inhibition might be avoided if the dendritic cells were taken out of the patient's body (and so away from the cancer) long enough to nourish them with cytokines, arm them with cancer antigens, and poise them at the point of activating a waiting but ignorant army of T cells.

"We used this approach, loading patients' dendritic cells with their own cancer cells as the source of antigen. We reasoned that to distinguish friend from foe, those accumulated mutations peculiar to cancer might be the only effective flags for the T cells. And, we reasoned that repeated attacks would be necessary, as long as the cancer remained.

"In four separate clinical studies we have performed in collaboration with clinical investigators at the Mater and Royal Brisbane and Women's Hospital, a few patients have responded with complete regression of all detectable disease.

"Luckily, we had immortalized some of the cancer cells to grow in our laboratory, so we could measure the immune response against them. You would think this was easy, but perversely most cancer cells do not grow where they are wanted. Melanomas, though, are different. We were surprised how strongly the patients' T cells reacted to their cancer, and how numerous they were. Even in the face of this immune onslaught, one patient took a year and a half finally to eliminate his cancer. In each case, this was achieved without major side effects. Only the patients who had complete tumour regressions had these strong T cell responses – patients who eliminated some of their tumours, only to have others grow elsewhere, had responses as low as those who showed no signs of regression.

"The key to understanding why just these patients had such dramatic responses may lie in their cancers. Firstly, these patients had less disease; none survived that started with bulky cancers. And, it appears, their cancers did not play the evasive tricks mentioned above. Their cancer cells show no sign of losing the surface structures that allow them to be recognized by



Chris Schmidt and Alberto Pinzon-Charry at the Queensland ASMR Premier's Award for Medical Research prize ceremony

the immune system. So, of course, there is now another question: why would one patient's melanoma cells all remain intact, while another's become a faceless enemy? In science, there are no final answers. But, perhaps one day, finally a cure."

Chris, who is also the ASI Councillor for Queensland, has completed his career in Brisbane, starting with a BSc in mathematics from the University of Queensland, was seduced by the uncertainties of biology and Immunology and completed his PhD thesis in 1996. He has since worked at the QIMR and co-ordinated several clinical trials.

Queensland news cont.

Brisbane, and his talk on "Immunotherapy, immunosenescence, suppression and tumour progression" (October 25, QIMR) generated a lengthy discussion among those attendant.

Professor Anne Kelso (QIMR) has been recruited as the new director of the Commonwealth-funded World Health Organisation Collaborating Centre for Reference and Research on Influenza in Melbourne (<http://www.health.gov.au/internet/ministers/publishing.nsf/Content/health-mediarel-yr2006-ta-abb140.htm>). Of course, Anne hails from Victoria, but we have been lucky to call her a Queenslander since 1992, when she joined the QIMR. She has a distinguished career as an immunologist here and abroad, and has made many contributions to the international scientific community, as a former President of the ASI (1995–1996), Secretary-General of the International Union of Immunological

Societies (2001–2004) and Director of the Cooperative Research Centre for Vaccine Technology (2000–2006). Anne is certainly not leaving academia, and will hold an honorary appointment in the Department of Microbiology and Immunology at the University of Melbourne. The appointment begins in February, and Anne takes with her our very best wishes.

The strong focus on vaccine research in Australia will find a new voice in the Australian Centre for Vaccine Development. Under the directorship of Assoc. Prof. Rajiv Khanna (Rajiv.Khanna@qimr.edu.au), ACVD will facilitate collaboration between scientists at the QIMR and other national and international centres. Education and training are central objectives, but assistance with commercial links is also part of the strategy.

We hope the ACVD will play a role in future Brisbane Immunology Group meetings. This

year's meeting (August 17/18, Gold Coast) was a great success, and featured a very impressive list of national and international visiting speakers. Prof Phil Greenberg was a guest courtesy of the ASI's visiting speaker program. Jane Lattin (Institute for Molecular Bioscience, University of Queensland) won the prize for best oral presentation, and Tammy Maxwell (QIMR) and Margaret Jordan (James Cook University) won the poster prizes. Oddly, I was not invited to any of the after-dinner parties that make BIG such a desirable destination. You will need to attend the next meeting yourself to learn more ...

*Chris Schmidt
Councillor*

See BIG photos on page 10.