



N E W S L E T T E R

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Infection Immunity and Immunogenetics Unit, Pathology and Laboratory Medicine, University of Western Australia

Can a HIV patient who once progressed to AIDS ever regain a normal immune system on antiretroviral therapy (ART)? Why do some HIV patients beginning ART have an uneventful immune recovery, whilst others develop immune restoration disease? Are the effects of CMV similar in HIV patients, transplant recipients and healthy aging? Why is HCV disease more severe in HIV patients and what determines how HCV patients respond to therapy?

Patricia Price and Martyn French manage the Infection Immunity and Immunogenetics Unit of the School of Pathology and Laboratory Medicine of the University of Western Australia based at Royal Perth Hospital, with post-doctoral scientists, Silvia Lee and Sonia Fernandez. Projects addressing the outcome of infection with HIV, CMV, HCV and mycobacteria include investigations of the effects of pathogen-specific immune responses, host genotype and drug treatments. They are designed to answer some important questions.

How does immune activation influence immune reconstitution in HIV patients given ART?

Up to 30% of HIV patients receiving ART fail to achieve a normal CD4⁺ T cell count. Such individuals are at an increased risk of death and experience higher rates of cancer, cardiovascular disease and kidney disease. Our comparisons between patients with poor or good CD4⁺ T cell recovery on ART have



Back Row LtoR: Martyn French (Clinical co-ordinator), James Taylor (research assistant)
Middle Row LtoR: Sonia Fernandez (Scientist), Sara Tanascovic (PhD student), Samantha Bunt & Alfred Laiman (Honours students)
Front Row LtoR: Silvia Lee (Scientist) Lilian Cha, Nandini Makwana, Laila Abudulai, Henny Saraswati, Jacquita Affandi (PhD students), Patricia Price (Research co-ordinator).
Henny is completing her PhD within our project in Jakarta.

identified two important factors. Firstly, CD4⁺ T cell deficiency parallels lower naïve CD4⁺ T cell counts and is associated with evidence of a small or inactive thymus. Secondly, CD4⁺ T cell deficiency is closely associated with persistently increased immune activation which may induce CD4⁺ T cell senescence and increase rates of apoptosis. Sonia Fernandez demonstrated that the effects of immune activation are most evident on the naïve CD4⁺ T cell population, particularly in individuals with a small thymus. We are now characterising deficiencies in the immune system of patients with low CD4⁺ T cell recovery and investigating the causes of immune activation. Projects include:

The causes of persistent immune activation. Lines of investigation include the roles of type I interferons and underlying viral infections such as CMV.

cont.p4

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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@uq.edu.au

Email bulletin board

To subscribe to the ASI bulletin board, send an email to majordomo@explode.unsw.edu.au with the message: subscribe anz-imm.

EDITORIAL

One aspect of the role of Newsletter Editor is hard to anticipate and difficult to describe. The Newsletter plays an important role in reporting the death of Immunologists who are members of ASI or their colleagues. In this edition we report the death of two significant immunologists – Gordon Ada and Bill Boyle. I knew neither of them personally, but the respect and affection of their colleagues is palpable in their obituaries. As Editor, I read the obituaries and usually find myself researching further on the Web and this is always a humbling and inspirational experience: humbling because of the volume and significance of the work (and the inverse then apparent in my own career) and inspirational because it seems they achieved their greatness by being good. By that I mean that they were good scientifically and professionally and those are two things we can all strive for.

In this issue we have reprinted two articles Gordon Ada wrote as unsolicited submissions to the Newsletter in 2004 (there were three published in 2004). I urge you to have a look online at the transcript of an interview with Gordon Ada by Frank Fenner on the Australian Academy of Science website. This gives a tremendous insight into the personality of Gordon and his fascinating career. So, although the passing of friends and colleagues is a sad event, it is a time for recognising their achievement and the role of the Newsletter (with mixed emotions) is to bring their stories and inspiration to the wider ASI community.

I wish everyone a safe and relaxing holiday season and hope you come back invigorated and ready to submit your next grant.

Simon Apte

THE MOST FUN YOU'LL EVER
HAVE AT A NETWORKING EVENT!

IMMUNOLOGY

Speed Dating

iQ, the Queensland Branch of the Australasian Society for Immunology (ASI), invites ALL Honours, Masters and PhD students studying any aspect of Immunology to meet for an evening of "Immunology Speed Dating".

To register for this **FREE** event, please e-mail iQ committee secretary, Danielle Stanisic at d.stanisic@griffith.edu.au, with your name, institute, and whether you are studying Honours, Masters or PhD (1st, 2nd or 3rd year) by **25 January 2013**.

(ASI-members and non-members are welcome).

Cash Prizes for the best "dates"!

Friday 8th Feb 2013
4-7pm
Venue TBA (Central Brisbane)



Infection Immunity and Immunogenetics Unit, Pathology and Laboratory Medicine, University of Western Australia (cont.)

Homeostatic maintenance of the peripheral naïve CD4⁺ T cell pool in HIV patients on long-term ART. This study looks at the proliferative potential of CD4⁺ T cells (particularly naïve cells) in response to both general stimuli and IL-7.

The effects of interferon- α on homeostasis of CD4⁺ T cells and memory B cells. Our data associate low CD4⁺ T cell counts after long-term ART with increased interferon activity. IFN- α appears to alter CD4⁺ T cell homeostasis by interfering with the IL-7 mediated pathway of proliferation. The work also addresses memory B cells, as this population is also deficient in some HIV patients responding to ART.

Why do some HIV patients experience Immune Restoration Disease?

Immune restoration disease is a clinical phenomenon seen in some immunocompromised HIV patients whose immune function is restored after starting ART. It is characterised by exaggerated or atypical inflammatory reactions or worsening of pre-existing infectious disease. Worldwide the most important IRD associated with tuberculosis.

Our studies in Cambodia, India, South Africa and Malaysia provided evidence that T-cell and innate immune responses contribute to the immunopathology of IRD associated with *M. tuberculosis* or cryptococcal infection. Increased T-cell and/or dendritic cell responses to *M. tuberculosis* or cryptococcal antigens could be demonstrated in many patients with 'paradoxical' exacerbations of partially treated tuberculosis but were not diagnostic. Patients also displayed perturbations of chemokine levels. Interestingly low levels of CCL2 pre-ART show promise as a marker of risk, whereas immunogenetic markers show no consistent pattern across ethnicities. Low CCL2 levels may generate a high bacterial load pre-ART – this is likely a key component of risk. A study of cryptococcosis-associated IRD undertaken in Durban, South Africa has demonstrated the importance of CD4⁺ T-cell deficiency and high pathogen load.

Our research in Indonesian HIV patients starting ART is centred on HCV IRD. Dr Evy Yuniastuti (PhD completed 2010) showed that low levels of anti-HCV antibodies

predicted IRD. This is consistent with the notion that IRD develop when there are high levels of antigen when the patients begin ART. Studies of T-cell responses to HCV that may associate with IRD are nearing completion.

What is the lasting footprint of CMV infection?

Cytomegalovirus (CMV) infection is usually asymptomatic, but can cause a mononucleosis-like illness in some individuals. CMV disease can manifest as a syndrome or as an acute infection of an organ or tissue. CMV retinitis is prevalent in 46% of patients with untreated HIV infection, and remains a common cause of blindness in resource limited settings. This will be addressed in our new project in Indonesia.

In considering the role of CMV in human health, many studies have overlooked the fact that 50-90% of all populations are seropositive. As the virus has the capacity for latency and is known to be reactivated by "stress" (immunosuppression), most people harbour latent virus. Sensitive PCR-based viral load assays are available, but these are only routinely applied in patients likely to have acute disease. There is little probability of detecting latent CMV. We are working on a tool to evaluate the lifelong effects of CMV on human health – the "footprint" of CMV. The footprint may include:

1. CMV DNA detected by a sensitive PCR assay of blood, saliva or urine.
2. CMV-peptide/HLA tetramer positive CD8 T-cells.
3. IFN γ responses of CD4 and CD8 T-cells to CMV antigens.
4. Anti-CMV antibody detected by ELISA.
5. Enhanced expression of NK receptors on NK cells and T-cells.

In older CMV-seropositive adults, up to 23% of the T-cell population can be CMV-specific. Their accumulation correlates with immunologic aging or "immunosenescence" evident in the entire T-cell population assayed *ex vivo*. Repeated sub-clinical CMV infections may expand CMV-specific T-cells clones until they suppress homeostatic expansion of other T-cells. CMV infects endothelial cells in acute stages of infection. The resulting inflammation may lead to atherosclerosis.

CMV may have long-term effects in HIV patients. Treatment of systemic CMV disease is expensive and protracted, so prophylaxis is suspended once patients are stable on ART. CMV reactivation is triggered by inflammatory mediators, including TNF. Immune activation in HIV disease increases levels of this cytokine, so frequent subclinical reactivation of CMV is expected. We investigated HIV patients who began antiretroviral therapy (ART) with extreme immunodeficiency and maintained a virological response until they were >50 years old. One can assume that they had a high burden of CMV pre-ART as many had experienced CMV retinitis. These HIV patients retained high titres of antibody reactive with CMV after 14 (13-16) years on ART and displayed elevated IFN γ responses to an immediate early peptide of CMV (*unpublished data*). This constitutes a "heavy footprint" of CMV likely arising from frequent reactivations. CMV and thymic insufficiency may be synergistic in their effects on T-cell profiles. It may be important that HIV disease also depresses NK cell function – these mechanisms are under investigation.

CMV remains an important pathogen after renal transplantation. In Australia, prophylaxis (valganciclovir) is routinely administered for 12-26 weeks after transplantation, according to a formula that considers donor and recipient CMV seropositivity and clinical risk. CMV remains a significant cause of graft loss despite prophylaxis and in the longer term, CMV reactivations are implicated in deterioration in renal function, exhaustion or senescence of T-cells and cardiovascular disease. We are now addressing this in a cross-sectional study focussing on the role of NK cells in resistance to CMV. The resulting holistic view of the immune response in man will identify phenotypes associated with protection and those individuals who will benefit most from CMV prophylaxis.

Can a response to HCV therapy be predicted?

Dr Silvia Lee has a programme of research investigating the correlation between treatment outcome, disease status and immunological status during hepatitis C virus (HCV) infection. These studies have resulted from ongoing collaborations with clinicians at Royal Perth Hospital (Dr James Flexman and Dr Wendy Cheng) and researchers at

Murdoch University and Fremantle Hospital (Dr Mark Watson and Dr Jane Allan). Recent projects include:

The effects of HCV and IFN-based therapy on DC responses. Therapy impaired IL-12 and IFN α production by DCs and reduced production of IFN α by PBMC after stimulation with ligands for TLR3, TLR7/8, TLR9 and RIG-I. This was independent of a patients' response to therapy and was not accompanied by reduced expression of pertinent TLR on dendritic cells. These data implicate TLR signaling pathways in immune dysfunction associated with HCV disease and its treatment.

The effects of HCV and IFN-based therapy on natural killer (NK) cells and T-cells. Frequencies of CD56^{dim} NK cells expressing perforin and CD16 were lower on therapy, irrespective of outcome, whilst proportions of effector CD4 and CD8 T-cells only declined in patients who achieved a virological response. Similarly production of IFN γ to HCV antigens declined in responders but not in non-responders. Therapy may promote the expansion of NK cells able to produce cytokines, whilst decreased HCV-specific CD4 T-cell responses during therapy may be associated with reduction in effector memory CD4 T-cells in the circulation of patients with a sustained virological response.

The potential of genotype cross-reactive HCV neutralising antibody. We are interested in the ability of antibody to neutralise HCV infectivity using the HCV genotype 2a virus (JFH1) cell culture model. Plasma samples were collected from 108 chronic HCV-infected patients prior to therapy. All patients had antibodies that reacted to the JFH-1 antigen by ELISA and 96% of patients had detectable neutralising antibodies. We now plan to examine neutralising antibody titres in samples collected during and after therapy and assess antigen recognition by western blot. This includes patients co-infected with HIV receiving ART.

With Kathy Davern (Monoclonal Antibody Facility, WAIMR), Silvia is producing human monoclonal antibodies that can neutralize HCV infection. This is important for the management of transplant recipients and for prophylaxis. Using cryopreserved cells from chronic HCV-infected patients fused to a human myeloma cell line, hybridomas have been prepared. Supernatants were tested by ELISA for recognition of HCV antigen and

by immunohistochemistry for inhibition of HCV infectivity in a hepatoma cell line.

Why do some HIV patients experience sensory neuropathy?

HIV-associated sensory neuropathy (HIV-SN) is a length-dependent peripheral neuropathy that is frequently painful and is a common complication of HIV infection. HIV-SN is defined as present if the patient had both symptoms and signs of peripheral neuropathy detected using the AIDS Clinical Trials Group (ACTG) Brief Peripheral Neuropathy Screen. SN can be caused by HIV itself, but symptoms can also be triggered by ART. This is most common in patients receiving older nucleoside analogue reverse transcriptase medications (usually stavudine), but neuropathy is also seen in Australians with HIV. My collaborator, Dr Kate Cherry, confirmed that 44% of patients treated at the Alfred Hospital (Melbourne) are affected.

I established collaborations in SE Asia and South Africa to address why some patients suffer SN whilst others do not when treated with the antiretroviral drug stavudine. This will help clinicians decide which patients may be treated safely with stavudine and who should be prioritized for expensive alternatives. The South African Department of Health now recommends use of tenofovir as first line treatment, but many people remain on stavudine and or live with the side effects. Stavudine is still prescribed in other resource-poor countries.

Genetic studies in Australian, Asian and African cohorts. Disordered inflammation may be central to the pathogenesis of SN. Our first study found that alleles of *TNFA* and *IL12B* (encoding TNF α and IL-12p40) distinguished Australian patients who developed SN within six months of ART from those who did not. We then tested HIV patients in Jakarta and Kuala Lumpur, confirming that neuropathy is common among Asian patients. We showed that increasing patient height and increasing age are risk factors for SN.

Initial genotyping of Indonesian patients confirmed an association with TNFA-1031*2, an allele associated with SN in Australians. This provided a link with alleles in the TNF haplotype block, but linkage disequilibrium of this region hampers disease association studies. Constance Chew (PhD student) first

analysed the role of TNF block haplotypes as a predictor of risk for sensory neuropathy in HIV patients. Constance reconstructed 38-SNP haplotypes in healthy control cohorts of different ethnic backgrounds. Haplotypes associated with SN in Caucasian, Malay and Chinese patients were determined.

To extend this work, 404 Black HIV-positive Africans from the Virology Clinic of the Charlotte Maxeke Academic Hospital Johannesburg in collaboration with Ms Antonia Wadley (PhD submitted 2012) and Prof Peter Kamerman (University of Witwatersrand). Of those exposed to stavudine, 57% had HIV-SN and 74% of these people described the syndrome as painful. SNPs and haplotypes from *TNF* and adjacent genes from the MHC were assessed. There was no association with TNF-1031, but the haplotypes incorporating TNF-1031 and associated with SN in Asians and Caucasians were not found in Africans. Hence critical haplotypes are slightly better defined and TNF-1031 itself is exonerated. Novel associations were identified between HIV-SN protection and five other SNPs found in a single haplotype block were associated with SN for the first time. We also found novel associations with minor alleles of polymorphisms in *IL4*. These data support an inflammatory etiology to HIV-SN.

The search for immunological correlates of SN: Learning from the genes. Confocal microscopy was used to visualise CD14⁺ macrophages and TNF production in skin biopsies from HIV patients with active (painful) and "burned-out" (numb) neuropathy. 50 μ m sections were triple-stained to mark PGP9.5⁺ dermal and epidermal nerves (red), CD14⁺ macrophages (green) and cell nuclei (blue). Parallel sections were stained to mark TNF (green). Images derived from 15-40 focal planes were compiled, so nerve fibres could be followed through the tissue. In active neuropathy, biopsies from the ankle and thigh displayed dense infiltrates of CD14⁺ macrophages, with a distribution consistent with migration from dermal blood vessels to concentrate around damaged nerves. In late-stage neuropathy, ankle biopsies demonstrated extensive focal nerve damage (often with no nerves visible) and few macrophages. The results suggest that activated macrophages producing TNF may instigate epidermal nerve fibre damage.



Patricia Price



Sylvia Lee



Sonia Fernandez

Studies of HIV in the majority world: the JakCCANDO project

ART is becoming more widely available in Asia, so many HIV patients with advanced disease (AIDS) and untreated opportunistic infections are starting therapy. JakCCANDO stands for Jakarta CMV, Cardiovascular, Antiretroviral, Neuropathy, Dental, Ophthalmology. It is our third and largest project based in the Cipto Mangunkusumo Hospital affiliated with the University of Indonesia. We will investigate the recovery of immune function and the role of CMV in HIV patients beginning ART. Preliminary data shows antibody responses to HIV are extremely high in Indonesian patients with a significant (but undocumented) burden of disease. This project will support four Clinical/Biomedical PhD projects (at UI), plus graduate students enrolled through UI and UWA. Studies of candida immunology are a new initiative.

Evidence of repeated CMV reactivation (the “footprint” of CMV) will include CMV DNA (by PCR), antibodies and CD8 T-cell responses. This will be correlated with ...

- a) immune activation, immunosenescence and T-cell homeostasis
- b) clinical outcomes previously associated with CMV in other contexts, specifically ocular, cardiovascular and neurological sequelae assessed by expert physicians

Natural killer cells will be considered as a mechanism affecting the “footprint” of CMV, including an evaluation of the importance of genetically-determined variations in NK activity.

Key members of the team at UWA

Patricia Price (PhD,1985) runs several projects investigating HIV disease with a focus on the consequences of beginning ART with very low CD4 T-cell counts, as this is reality for many patients worldwide. To this end, she has initiated and run collaborations with institutions in Africa and Asia. Patricia is now returning to a long-standing interest in CMV in relation to human disease; specifically the varied manifestations of CMV infection and how consequences arise from the infection of so few cells. The characterization of CMV genes encoding proteins homologous to components of human inflammatory pathways presents many avenues for study. These can now be applied to real clinical situations—evaluating the roles of immune activation, CMV burden and T-cell competency in HIV patients, renal transplant recipients and healthy aging donors.

Martyn French is a Winthrop Professor in Clinical Immunology in the School of Pathology and Laboratory Medicine of UWA and also a Consultant Clinical Immunologist/Immunopathologist at Royal Perth Hospital. He has had a research and clinical interest in primary and secondary immunodeficiency disorders for over 30 years. His current research is focused on immune restoration disease in patients commencing ART, immune activation and dysfunction in patients on long-term ART and phagocytosis-inducing antibodies in the control of HIV infection. He also contributes to multi-centre research studies on the molecular pathology and genetics of primary antibody deficiency disorders.

Sylvia Lee completed her PhD in 2004 and has continued a focus on research into the immune responses of patients who

are infected with HIV and/or HCV and the effects of antiviral therapy. She has published several articles which utilised real-time PCR to evaluate mRNA expression of viral genes and critical cytokines in viral infections. More recently she has focussed on characterisation of humoral responses to HCV and has developed and exploited a novel assay for neutralising antibody.

Sonia Fernandez completed her PhD in 2007. Since then she has continued to work in the field of HIV immunology. Her main research interest is the immune recovery of HIV infected patients receiving antiretroviral therapy with a focus on the immunological mechanisms that underlie immune activation. Current projects include the role of IFN α in immune activation and characterisation of T-cell and B-cell homeostasis in HIV patients.

Ben Oliver completed his PhD in 2012. His thesis investigated whether plasmabiomarkers may inform about the immunopathogenesis of immune restoration disease associated with *Mycobacterium tuberculosis* (TB-IRD) or have a role in prediction and diagnosis. He found that inflammatory mediators of the innate immune system may influence the immunopathogenesis of TB-IRD, while T cell responses may aid in diagnosis.

Constance Chew completed her PhD in 2012. She analysed the role of TNF block haplotypes as a predictor of risk for sensory neuropathy in Caucasian, Malay, Chinese and South African HIV patients. Genotypes were then reconstructed into TNF block haplotypes and their effects on HIV-SN disease were determined. Constance identified chemokines as molecules likely to mediate neuropathy and used confocal microscopy to visualise infiltrating macrophages around the damaged nerves.



Sara Tanaskovic & Zayd Aghafar



Naamah Laila Abudulai

Sara Tanaskovic is in the final year of a PhD investigating naive T-cell homeostasis in HIV patients responding to ART. She demonstrated the importance of the thymus in the generation of naive T-cells, naive T-cell homeostasis and apoptosis as a cause of naive T-cell loss. Data based on Stat5 implicate perturbations to IL-7 signalling. The associated reduced expression of CD27 and CD28 may impede CD4⁺ T-cell homeostasis or compound the functional deficit.

Laila Abudulai is a third year PhD student addressing the impairment of memory B-cell IgG isotype switching as a cause of decreased phagocytosis-enhancing antibody responses in chronic HIV infection. The impairment of IgG subclass diversification by blocking isotype switching may be a mechanism used by the HIV virus to evade the immune system and impede phagocytosis-enhancing antibody responses. Therefore, stimulating IgG2 antibody production might be a means of developing a novel HIV vaccine.

Lilian Cha has recently started her PhD investigating IFN α and immune activation in HIV patients receiving ART. She is building on evidence that IFN- α may be involved in HIV pathogenesis, with a positive correlation between chronic immune activation and levels of IFN α and interferon-stimulated genes. Lilian will investigate the effect of IFN α on CD4 T-cell and memory B cell homeostasis, and examine the expression of the type I interferon pathway transcriptome in HIV patients with good and poor recovery of CD4 T-cells.

Nandini Makwana is a first year PhD student investigating if (and how) persistent CMV infections induce changes in Natural Killer (NK) cell function and phenotype and drive NK and T cell immunosenescence in renal transplant recipients. She will correlate the CMV footprint with NK genotype and phenotype, including investigations of NK senescence. Whilst this has been described in elderly individuals and CMV is known to promote senescence in T-cells, it is unclear whether CMV drives NK immunosenescence.

Zayd Aghafar is an MSc student addressing KIR diversity and the role of NK cells in CMV infection. NK genotypes may influence CMV disease in HIV patients but do not affect susceptibility to HIV. To assess NK cell function, purified NK cells activated with IL-2 are co-cultured with CMV-infected or uninfected human fibroblasts. CMV down-regulates NK activation assessed with CD107a. Factors influencing this down regulation are under investigation.



Lilian Cha

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Obituary – Emeritus Professor Gordon L. Ada

Professor Sir Gustav Nossal

This piece appeared originally as an obituary for the Members of the Australian Academy of Science.

Gordon L. Ada died peacefully on 25 September after a brief illness, aged 89. His wife Jean pre-deceased him by several years; our sympathy goes out to his children and grandchildren.

Ada, a Sydney University graduate in science, began his career at the Commonwealth Serum Laboratories in Melbourne. In 1948, Sir Macfarlane Burnet recruited him to The Walter and Eliza Hall Institute of Medical Research to work on biochemical aspects of the influenza virus under Alfred Gottschalk (later FAA). His most important discovery was that influenza virus was an RNA, not DNA virus, very novel at that time.

Initially just plain Mr Ada, Gordon eschewed the normal PhD pathway but submitted his published work for a DSc which he received and shortly after which he was elected to the Fellowship.

Burnet changed the Institute's direction from virology to immunology in 1957, but Ada was slow to follow. In the early 1960s he teamed up with the author of this note and began a felicitous five year collaboration, the purpose of which was to determine how antigen exerted its stimulatory action through tracing radioactively-labelled antigen through the body (in the rat) using autoradiography, including electron-microscopic detection. This resulted in about 20 publications, the most important of which discovered the follicular dendritic cell. This extraordinary cell type had the capacity to capture antigen and hold it on the surface of long dendritic processes for prolonged periods (up to at least nine months). B lymphocytes were attracted to the vicinity and a germinal centre was set up, which was critical to the process of immunological memory. Another important finding was that single antibody-producing cells did not contain antigen (even where four molecules could have been detected). This disproved the direct template hypothesis of antibody formation.

In 1968, Professor Frank Fenner invited Ada to Canberra to head the Department of Microbiology of the John Curtin School of Medical Research of the Australian National University. Here, Ada surrounded himself with an outstanding group of colleagues. He managed to combine the disciplines of virology and immunology in a creative fashion. Helped by Robert Blanden, this created the atmosphere within which Peter Doherty and Rolf Zinkernagel were able to make their Nobel Prize-winning discovery of how T lymphocytes “saw” antigenic peptides in association with “self” molecules of the major histocompatibility complex. The author was privileged to be at a Brook Lodge Symposium in 1974 where Ada gave this amazing discovery its first international airing. Curiously, it caused little stir – it was just too novel – but the world pretty soon caught on. Ada continued to give exemplary leadership to the group until his retirement. He was also very influential in education in immunology, through reviews and popular books.

Ada's retirement was clouded by a serious and prolonged illness of his beloved wife Jean. He looked after her with loving care to the very end.



Ada was also actively involved in the Australian Society of Immunology and the Australian Academy of Science amidst his many editorial and administrative duties. He was universally admired for his gentle and gentlemanly leadership and his impeccably high standards of scientific rigour and integrity. He will be sorely missed.

*GJV Nossal
The University of Melbourne*



Emeritus Professor Frank Fenner (left) relaxing with Gordon Ada

Thanks to Geeta Chaudhri for providing all Gordon Ada photographs used in this tribute

What does it take to be a great scientist?

Gordon Ada

Originally published in ASI Newsletter, June 2004

Preamble

What does it take to be a great scientist? It takes brilliance of course and persistence, and this can involve being prepared to fight very hard for your ideas and beliefs. The extent to which this can be pursued was brought home to me by a brief interaction with virologist Albert Sabin very late in his career.

After I retired in 1987, I spent three years at Johns Hopkins School of Hygiene and Public Health in Baltimore and became Director of a Center for AIDS Research. This brought me into close contact with the AIDS Program scientists at the NIH in Washington and I was invited to give talks at various meetings there. Shortly after I returned to Canberra, I was asked to join a new NIH committee – an HIV Vaccine Working Group which was to meet three or four times a year in Washington. I was the only non-USA citizen on the committee and was appointed because I was thought to know something about cell-mediated immune responses generated following vaccination. I was also invited to give talks at various scientific meetings usually held at NIH. At one meeting – a Bob Gallo meeting – I gave a talk on what is called the common mucosal immune system. There was increasing evidence that stimulating at one mucosal site could result in a specific immune response at another site. For example, adenovirus infects via the respiratory tract, but the adenoviral vaccine is administered orally and gives good protection from a subsequent respiratory challenge.

It had become clear that increasing numbers of women became infected after unprotected sexual intercourse with HIV-infected partners. It was known that the female vagina is not well endowed with lymphoid tissue. In fact, the vaginal flora can include seven different non-pathogenic bacteria, five pathogenic bacteria and seven pathogenic viruses, and yet they induce poor immune responses. Normally, the non-pathogenic bacteria induce an environment which inhibits other infections. So in my talk, I stressed the need to find out whether an HIV vaccine might be effective if given via another mucosal site (we now know the respiratory tract can be quite effective as an immunisation route for this purpose).

The next talk after mine at the meeting was given by Albert Sabin, the virologist who developed the oral poliovirus vaccine (OPV). For this he was almost revered in the USA. But he was recognised to be a somewhat difficult person: a young scientist, having worked with him once, rarely repeated the experience. Shortly after he started his talk, he stopped, glared at me sitting in the third row at this large meeting, and said in a very loud voice – “DRADA, YOU MUST IMMUNISE AT THE SITE OF INFECTION.” I felt like creeping under the chair in front of me. I learnt later that he had spent much time seeing if he could vaccinate young children with measles vaccine by the respiratory route rather than by injection. This was possible but not feasible on a large scale. But how could I respond?

Early in 1992, a paper appeared in the *Proceedings of the National Academy of Sciences* (1) by Dr Sabin in which he stressed the improbability of being able to vaccinate against HIV infecting by the vaginal route. The reason was because infected semen contained latently infected cells (containing only viral DNA but no viral particles) which could persist in the recipient indefinitely and later initiate an infection. At the next meeting of the HIV Vaccine group, I pointed out the flaws in this argument – mainly that such cells would, in nearly all recipients, be recognised as foreign and very rapidly destroyed by the recipient’s immune system (host-versus-graft reaction).

Because of his high standing, none of my US colleagues wished to criticise Sabin; would I do something about it? Back in Canberra, Bob Blanden and Arno Mullbacher joined me in writing a short article gently pointing out the flaws in Sabin’s paper. We were also concerned that it might inhibit research aimed at developing HIV vaccines. Our article was published in *Nature* under the heading – *HIV: to vaccinate or not to vaccinate* (2). There was no immediate response. In March, 1993, Sabin died and was buried in the Arlington National Cemetery. Almost to the day, *Nature* advised me that they had just received a statement for publication sent by Dr Sabin before his death in which he stated he did not accept our arguments mainly because we had not actually shown such cells being destroyed in the recipients. Did I want to reply? I said there was now no point in replying; let Dr Sabin rest in peace. But I thought that I had yet to meet an immunologist who would disagree with our argument.

Postscript: The WHO polio eradication campaign was initiated in 1988, but the time limit was finally extended to 2005. The year 1994 may go down in medical history as the time when the last case of natural infection worldwide was detected. Though many countries have now switched to the use of the inactivated virus vaccine (IPV), the use of the OPV was absolutely crucial in achieving the great success to date.

(1) Sabin, A. B. Proc. Nat. Acad. Sci., USA. 89: 8852 (1992)

(2) Ada, G., Blanden, B., Mullbacher, A. Nature 359: 572 (1992)



Gordon Ada, winner of the first award for best newsletter article for three contributions published in 2004 newsletters, two of which are reprinted here

The Importance of Mother's Milk

Gordon Ada

Originally published in ASI Newsletter, June 2004

On becoming Director of the Walter and Eliza Hall Institute in 1942, Macfarlane Burnet and colleagues began a major investigation of the influenza virus with the hope that they might be able to learn how to control an influenza pandemic like the one which killed at least 20 million people after the First World War. The virus was grown in embryonated chicken eggs. When harvesting the allantoic fluid from the infected eggs, Burnet noticed that the red blood cells (RBCs) were often in clumps (agglutinated). But it was George Hirst in New York who found that after incubating such agglutinated cells at 37°C for a few hours, the clumps of cells broke up, and adding more of the same virus no longer caused those cells to agglutinate. Hirst thus showed that the influenza virus contained an enzyme which would destroy a receptor for the virus on the RBC. Burnet soon confirmed this, but remembered a paper published years earlier which showed that *V. cholerae* grown in culture secreted a factor which affected the properties of RBCs. Burnet then showed that RBCs incubated in such a culture could no longer be agglutinated by the influenza virus. Thus, the culture was shown to contain an influenza virus-like receptor-destroying enzyme (RDE) and this became a very important tool in the influenza virus work. Alfred Gottschalk in the Institute then started work to elucidate the nature of the bond split by RDE which eventually he achieved. I thought his work would be facilitated if the enzyme could be purified.

So in the mid 1950s I started such a programme, using a crude broth as the culture fluid for the Cholera organisms and Eric French agreed to carry out the assays for RDE activity. Despite using adsorption to RBCs at 4°C followed later by the elution of the enzyme at 37°C as an important step in the purification, the enzyme preparation was still not pure enough. An important visitor to the Institute in 1956-7 was Joshua Lederberg, who in 1958 was to share the Nobel Prize in Physiology or Medicine for his work on the genetic properties of bacteria. On telling him of my frustration, he said, "Gordon, you must grow the bacteria in a purely synthetic medium." This I achieved, but - you've guessed it, absolutely no RDE was secreted. RDE was thus an inducible enzyme! (It would be fascinating to know how the decision is made to secrete or not secrete the enzyme.) At this stage, the specificity of RDE was unknown. So, where would I find a rich source of an appropriate substrate which desirably would have a low molecular weight, and thus make purification of the enzyme easier?

My wife had recently had her fourth (and last) baby and as I was watching her breastfeeding him one day, it suddenly struck me - her milk must be an extraordinarily rich source of a great variety of different substances in order for the baby to survive and grow so quickly. My wife agreed to my having a small sample of her milk which I added to the synthetic culture medium. The bacteria were added and the culture incubated overnight,

the bacteria then removed by centrifugation and the supernatant given to Eric French for assaying. Some hours later, Eric burst into my room, exclaiming, "Gordon, lots of RDE activity!" My wife then kindly agreed to my having another small sample of her milk. This I dialysed against some of the synthetic medium, then added the bacteria to the dialysate and incubated it. Fortunately, most of the active factor(s) was dialysable and (later), one component was found to be sialyl lactose.

We found bovine colostrum to be a rich source of the dialysable active factors and this led to my being able to produce enough and subsequently to obtain crystals of the enzyme. Burnet was told about it before he left on an overseas trip. As I wanted to be absolutely sure my technique was reproducible, I prepared crystals of the enzyme (now called neuraminidase) from three successive batches before we submitted a paper to *Nature* with pictures of the crystals. It was accepted but one week before the paper came out in 1959, *Nature* published a paper with German authors claiming crystallization of the enzyme, but showing no pictures. I became a world supplier of the pure enzyme for about three years before Sigma became a supplier. Graeme Laver in the Department of Microbiology in the John Curtin School isolated and crystallized the neuraminidase (sialidase) from the virus about 20 years later. This led in due course to the synthesis of a compound which neutralised the neuraminidase activity of the influenza virus.

Contributions sought for the ASI Newsletter

You could win \$200 !!

Deadline for the next issue: 1st February 2013

Please email your contributions to the Secretariat by the above date.
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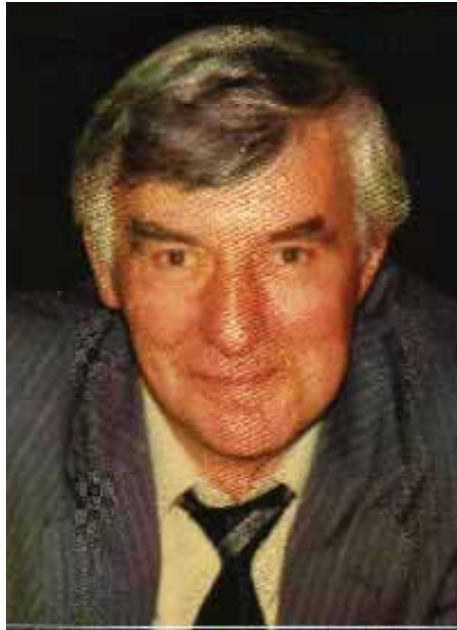
Obituary – Dr William (Bill) Boyle

Ian Mackenzie & Sandra Uren

On Friday 9 November, one of our former colleagues and ASI member William “Bill” Boyle passed away. Bill was Associate Professor and Reader in Immunology in the Department of Microbiology and Immunology at the University of Melbourne from 1970 until his retirement in 1998.

Bill was born in Glasgow in 1933, and undertook a Science degree with first class honours, and subsequently his PhD from Glasgow University. He worked with Allan Davies on mouse tissue cell antigens at the Microbiological Research Establishment in England where he was Senior Research Officer. In 1963 he joined the Division of Immunology at Duke University Medical Centre where he worked with Bernard Amos. During this time he pioneered the use of several now routine techniques including the isolation of leucocyte populations by Ficoll barrier centrifugation, and the use of the ^{51}Cr release assay for cytotoxicity.

By 1970 he and his wife Mary had three young children, and they decided that the best opportunities for their young family were to be found in Australia. He joined the Department of Microbiology (as it was then known) at the University of Melbourne, where his research interests included the areas of T cell activation, histocompatibility antigens and transplantation, and macrophage biology. His work was published in many journals including *Nature* and *J Exp Med*. He supervised a large number of Honours and Masters students and was a very expert co-ordinator of the department’s Honours



program for many years. He was also PhD supervisor for many students, including Keryn Williams, Anne Kelso, Bill Heath, Robyn Sutherland and Andrew Nash. Bill served on NHMRC Assignor’s panels and Regional Grants Committees and was an active member of many professional societies, including the Australian Tissue Typing Association (ATTA), the Transplantation Society of Australia and New Zealand (TSANZ) and ASI, where he was Chair of the Education Committee in 1993-4.

Bill also took a major role in teaching to undergraduate students where, together with Christina Cheers and Ian Mackenzie (in the Department of Pathology until 1995),

he developed the Immunology major for Science students at Melbourne University. He also provided medical students with an introduction to immunology that provided a framework for the new paradigms that they would encounter in the future.

After Bill retired from Melbourne University, he took up a part-time consulting role at the Austin Research Institute (ARI) at the Austin Hospital until the Institute merged with the Burnet Institute at the Alfred Hospital. At the ARI, Bill was most closely associated with Prof Mauro Sandrin’s Transplantation Lab where he was warmly welcomed by all. At the ARI, Bill was also a consultant for Prima Biomed Ltd—a public company commercializing the ARI’s inventions—where Bill was an active member of the Scientific Advisory Board (SAB) and he was also a member of the SAB for Roche’s CARG grants. Mark Hogarth, Director of the ARI at the time, recalled that of all the lecturers he had at Melbourne Uni, Bill’s were the only ones he remembered!

Indeed, it is as a teacher and mentor that Bill will be most remembered and sadly missed. His enthusiasm for all aspects of immunology and cell biology was palpable and infectious, and his approach to science was thoughtful and rigorous. Bill’s contributions to both research and teaching to a generation of science and medical students leave a lasting legacy that many of us have much to be grateful for. He leaves behind his wife Mary, four children and five (nearly six) grandchildren.

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HONORARY SECRETARY'S NEWS

ASI International travel award recipients

We received a large number of excellent applications for the October round of the ASI international Travel Awards, and the following awards of \$3000 each were made:

Owen Siggs (University of Oxford); IgN Winter School, Singapore

Mehmet Yabas (ANU); Keystone Symposia "B cell Development and Function", Colorado, USA

Erika Duan (Monash University); American Association of Immunology Centennial meeting, Honolulu, USA

Connie Duong (Peter Mac); Keystone Symposium: Cancer Immunology and Immunotherapy, Vancouver, Canada

Stephen Mattarollo (University of Queensland); Keystone Symposium: Cancer Immunology and Immunotherapy, Vancouver, Canada

Jason Waithman (Telethon Institute for Child Health/UWA); Keystone Symposium: Understanding Dendritic Cell Biology to Advance Disease Therapies, Colorado

ASI 2012 conference

At time of writing, preparations are nearly complete for the ASI 2012 annual scientific meeting, which will be held in Melbourne from 2-6 December at the new Melbourne Convention and Exhibition Centre. We have had a great response with more than 550 abstracts and over 700 registrants to date. Many thanks to my co-chair Prof Steve Turner from the University of Melbourne, who has presided over the scientific program for the meeting, and all of the members of the local organising committee who have worked so hard behind the scenes to secure sponsorship, review abstracts, assist in programming and budgeting, and helping to prepare the social program, including

the conference dinner at the MCG which we hope will be a highlight. Members of the Local Organising Committee include Frank Alderuccio (meeting treasurer), Meredith O'Keeffe, Nicole La Gruta, Stuart Mannering, Su Heinzl, Daniel Layton, Phil Hodgkin, and Edwin Hawkins. The student reps for 2012 are Julia Marchingo and Maria Demaria, and they have done a great job with organising the student dinner. Others involved in the SIGs and workshops include John Stambas, Nicole Haynes and Emma Grant (Postgraduate Symposium), Seth Masters (Infection and Immunity SIG), Odilia Wijburg (Mucosal Immunity SIG) and Phil Darcy (Tumour Immunology SIG).

Election of new council members

There was a call for nominations for the positions of state/regional councillors for WA, SA/NT and ACT in October, as well as for the executive position of ASI Treasurer. After nominations were received and a ballot conducted the following new council members were elected;

WA: Dr Andrew Currie

SA/NT: Dr Cara Fraser

ACT: Dr Anselm Enders

ASI Treasurer: Dr John Stambas

We would like to take the opportunity to express our sincere gratitude to the outgoing state/regional councillors – Dr Alec Redwood, Dr Michele Grimbaldston and Dr Stephen Daley (ACT) – who have worked so hard over the past three years to represent the ASI members in their region, and organise branch activities and annual meetings. Special thanks should also go to the outgoing ASI Treasurer Dr Pablo Silveira, who has done a fantastic job in the quite onerous position of Treasurer for the past three years.

ASI Travel Bursaries

There were a large number of applications from students and early post-docs for travel bursaries to attend the ASI 2012 annual scientific meeting in Melbourne. The following were selected for funding:

Dino Tan (UWA)

Malcolm Starkey (Newcastle University)

Sumaira Hasnain (Mater Institute)

Alison Carey (Griffith University)

Michelle Vo (Centenary Institute)

Alvin Pratama (ANU)

Md Ashik Ullah (University of Sydney)

Sally Mujaj (QIMR)

Zahra Sabouri (ANU)

Taryn Osmond (Malaghan Institute, NZ)

Brooke Dobson (University of Otago, NZ)

James Q. Wang (ANU)

Roy Ramiscal (ANU)

Connor O'Meara (QUT)

Fatima El-Assaad (University of Sydney)

Meru Sheel (QIMR)

Marie Kharkrang (Victoria University, NZ)

Cameron S Field (Malaghan Institute, NZ)

Tessa Gargett (University of Adelaide)

Megan Ives (Garvan Institute)

Aline Nocon (University of Sydney)

Michael Wong (ANU)

Pallave Dasari (University of Adelaide)

Sarrabeth Stone (Victoria University, NZ)

Jason Lynch (University of Queensland)

Laura Cook (UNSW)

Roland Ruscher (University of Queensland)

*Rose Ffrench
Honorary Secretary*

ASI STUDENT NEWS

Hi All,

That time of year has come. The ASI conference is all over and the student function held at The Common Man was a great success and enjoyed by all. We just wanted to give a big thank you to the student committee who helped us organize this great event: Emma Grant, Eleanor Livingston Jones, Aislin Meehan, Rangsim Reantragoon and Alison West. And of course, thank you to all of you who attended for making it a night to remember!

For photos of the night don't forget to visit our ASI student facebook page "Student members of the Australasian Society for Immunology".

As we head towards the end of year break we thought we'd give you a comic or two to help you brains unwind for the year.

For another great procrastination tool or just something to help you get through a tough day in the lab visit <http://whatshouldwecallgradschool.tumblr.com/> for a guaranteed laugh.

Thanks for having us as your students reps for 2012. We've had a great time putting together the quarterly newsletter articles, running the student facebook page and organizing the student function. We hope to see you at future ASI events!

Julia Marchingo and Maria Demaria

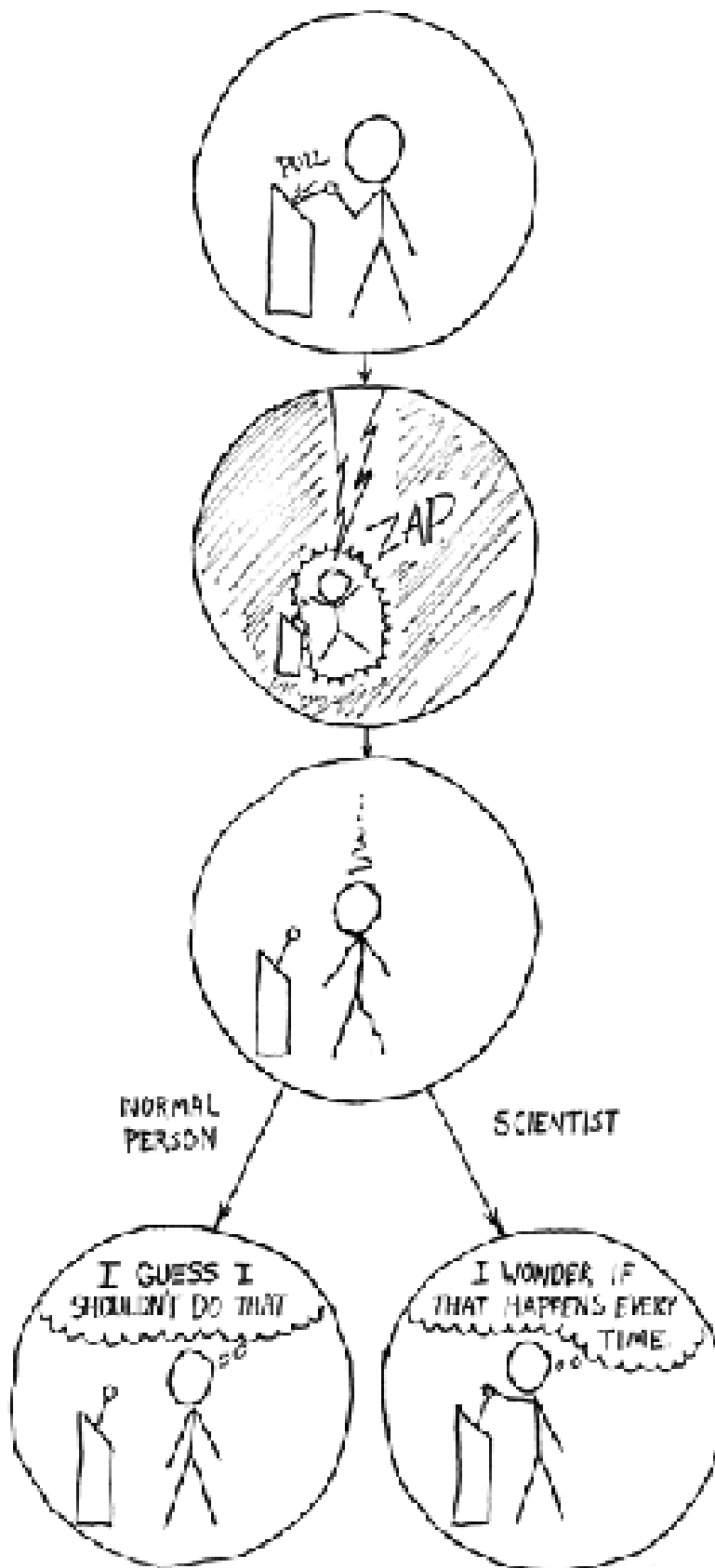


Image from <http://xkcd.com/>

ASI Councillors' News

Queensland News

In an effort to enhance communications and collaborations for our Queensland-based ASI members, and immunologists in general, September saw the formation of iQ (Immunology Queensland). This ASI sub-committee consists of 10-15 student and post-doc ASI members from various immunology hubs across Brisbane, the Gold Coast and Townsville (UQ, QUT, Griffith University, QIMR, MMRI, JCU) and will organise events of interest to local immunologists.

The following positions were appointed:
 Chairperson: Dr Ashraf Haque,
 Secretary: Dr Danielle Staniscic, and
 Treasurer: Marcela Gatica-Andrades.

iQ can be contacted through the secretary d.staniscic@griffith.edu.au.

iQ has already been very busy with two Brisbane-based events planned for the first half of next year. The first event is a night of "Immunology Speed Dating" on Friday 8th February for immunology students. It will be a fun and informal way to meet students from other institutions, to hear about what they are doing and to think about how best to communicate one's research in a few short minutes. Cash prizes will be awarded to the students who can best impress their "immunology dates" with a summary of their research.

iQ's second event will be open to the general public, and will coincide with the Day of Immunology in late April. Watch this space for more details in the next newsletter.

*Ashraf Haque
 Councillor*

W.A. News

The WA branch of ASI has had a busy 2012. In association with the Combined Biological Sciences Meeting (CBSM), we introduced immunology sessions into the annual CBSM meeting. CBSM is an institution in WA and has been running annual scientific meetings in Perth for the past 22 years. We were very fortunate to be able to convince David Tarlinton to come over to Perth and give our keynote address. This excellent talk was then backed up by two full immunology sessions for mid career researchers and students.

The mid career scientists invited to speak were: Dr Shelley Gorman (Sunlight, inflammation and obesity-related metabolic diseases: a hypothesis), Dr Andrew Lucas (Abacavir hypersensitivity, poster child for the altered peptide generation), Dr John Waitman (Immuno-surveillance of melanoma by dendritic cells) and Dr Anna Johansson (Tumour targeted TFN α improves vessel function and enhances active immune therapy).

Student presentation were selected from abstracts; the four selected speakers were Scott Cornwall (The Effect of Mesothelioma on Dendritic Cell Subsets), Laila Abudulai (Diversification of IgG Antibody Responses to Pneumococcal Polysaccharides in HIV Patients), Shruti Krishnan (Tumour eradication and induction of memory against murine mesothelioma by combined immunotherapy) and, finally, Joanne Gardner who took out the Western Australian Institute of Medical Research Student Oral Presentation Award for her presentation entitled "Mesothelioma tumours modulate dendritic cell lipid content, phenotype and function". ASI also supported a student poster prize and this was awarded to Dino Tan for an excellent poster describing the study "Treg function and induction of CTLA-4 are impaired in patients with chronic obstructive pulmonary disease".

At this stage we plan to run concurrent sessions with CBSM every two years, interspersed with our P.I.G meetings. If anyone has another view please let me know, but we on your local committee thought the initiative with CBSM worked very well this year.

This is my last official duty as State Councillor for WA. To be honest, I was a little reticent about taking on the role when first approached, it seemed a lot of extra work. And while there have been moments where things got a bit hectic, the experience has been well worth it. I have had an opportunity to meet and work with other Councillors and the Executive and it really has been a great pleasure and, to be honest, a privilege. It has been an experience to see how our society works and to meet the people who ensure it continues. So thanks to ASI and welcome to the new State Councillor.

*Alec Redwood
 Councillor*

Victorian News

The highlight of 2012 for Immunology in Victoria/Tasmania is undoubtedly the 42nd Annual Meeting of the Australasian Society of Immunology, which runs from December 2-6 at the Melbourne Convention and Exhibition Centre. The organising committee, headed by Stephen Turner and Rose Ffrench, have been working hard all this year and they all deserve a great deal of credit for the work they have done to make the conference a huge success.

Given the location of the Annual Meeting in Melbourne, the Immunology Group of Victoria did not hold their normal annual retreat. However, IgV was still heavily involved in other activities, including providing significant financial support to local members attending the ASI conference. Many IgV members are also heavily involved in organising the national meeting. This year saw IgV run a competition to design a new logo, with the winner to be announced at the ASI conference.

This year Victoria hosted a visit by Prof Pam Schwartzberg who was sponsored by the ASI Visiting Speakers Program. Pam was a very popular speaker and next year ASI visiting speakers will include John Wherry (visiting in February, hosted by Scott Mueller), Branch Moody (visiting in March – Dale Godfrey hosting), Ed Palmer (hosted by Su Heinzel) and Mark Jenkins. Please contact the hosts if you would like to meet the speakers and let me know if you have nominations for international speakers to visit Victoria or Tasmania under this program, or if your institute wants to host a seminar by one of the aforementioned speakers.

Next year will see the return of the IgV conference as well as the other initiatives that support immunology, including sponsored seminars, the Masterclass, Day of Immunology and student and postdoctoral travel awards to visit conferences and deliver seminars interstate and overseas. I will advise members about all these events as they draw near. Please contact me if you have any suggestions or queries. Renewal forms accompany this newsletter so please renew ASAP so that you receive all the updates and notifications about ASI and IgV. Please let your new students and colleagues know about signing up too!

*Stuart Berzins
 Councillor*

S.A./N.T. News

8th Adelaide Immunology Retreat (AIR-7) 2012 Report

Once again, the Adelaide Immunology Retreat (AIR) for PhD students, Honours students and research assistants was a great success. It was held at the Comfort Inn in the lovely surrounds of the Clare Valley on 7-8 September. The retreat was opened with a terrific seminar by Prof Lynn Corcoran (WEHI, Vic), our invited national speaker. This was followed by presentations from PhD students, Honours students and research assistants. Overall the standard of the presentations was exceptional. Congratulations go to the following students and research assistant who received awards:

Nicole Christie (AIR-8 Best PhD Presentation)

Tessa Gargett and Heidi Neubauer (both received the award of 2nd PhD Presentation Prize)

Nikhil Thyagaraja (Best Honours Presentation)

Bianca Van Dierman and Lih Tan (both received the award of 2nd Honours Presentation Prize) and

Daniella Penko (Best Research Assistant/Masters Presentation).

To strengthen links between SA and NT, our invited 'local' speaker was Dr Gabi Minigo (Menzies, NT). Next year we are hoping to sponsor at least two Northern Territory students to attend AIR-9 in order to provide

opportunities for them to network with the ASI student body in Adelaide.

In addition to the very high standard of science presented, we also participated in wine tasting at the historic Seven Hills Winery. This was a very popular function – not only due to the quality juice of the vine sampled but also because of the interesting history of the winery – it was set up in the 1800s by Catholic monks to provide sacramental wine for parishes throughout South Australia.

Finally, I would like to thank the AIR-8 organizing committee members – Cara

Fraser, Erin Lousberg, Susan Christo, Nicole Christie, Dave Yip, Natasha Kolesnikoff, Houg Taing, Kevin Fenix, Yuka Harata-Lee, Natalie Stevens and Iain Comerford – for all their hard work and enthusiasm for the meeting. Also a BIG thank you to all our sponsors: Miltenyi, Sapphire Bioscience, Jomar, Uni SA, Adelaide Uni, Roche Diagnostics Australia, BioRad, AdeLab Scientific, Karl Zeiss, Geneworks, BD Biosciences, Genesearch, Life Technologies, Epitope Technologies, Qiagen, Australian Bioscience, Beckman Coulter and STEMCELL Technologies. Without their generous financial support the event each year could not be held.



Above: AIR-8 award winners

Below: AIR-8 participants



Out with the Old and in with the New SA/NT State Branch Councillor

My term as the ASI SA/NT State Branch Councillor will come to an end at the Melbourne ASI Annual Meeting. I have greatly enjoyed my time as councillor – it has been a privilege to serve the Society and the SA/NT membership in this capacity. Highlights have been convening the Adelaide Immunology Retreats for the past three years and also taking on the task of the Program Chair at the 41st ASI Annual Meeting that was held last year in Adelaide. It has been extremely rewarding interacting with the ASI SA student body during the AIR meetings and watching their burgeoning careers develop over each subsequent year I convened the meeting. It is with this in mind that I hand over the councillor position to Dr Cara Fraser, who is the new incumbent for the next three years. Cara has always impressed me with her enthusiasm and dedication to the Society. Below, I have included her short bio that she

attached to her nomination form. Cara will make a terrific councillor and I look forward to supporting her in this role. Congratulations on your appointment, Cara!

Cara Fraser Bio

Dr Cara Fraser has been an active member of the ASI since 2004, during which time she has made an increasingly substantial contribution to national and local Society activities. In 2010/2011 Dr Fraser was a member of the organising committee for the 41st Annual Scientific Meeting of the ASI and was the sole convenor of the Tumour Immunology Workshop. This involved inviting international and national speakers, compiling the program, liaising with delegates and chairing sessions. Dr Fraser has also participated in organizing five Adelaide Immunology Retreats, progressively taking on more responsibility and gaining experience in all aspects of event organisation including obtaining sponsorship, organising

accommodation, catering and transport and receiving registrations. In 2009 Dr Fraser participated in school visits promoting understanding of immunology for the World Day of Immunology.

Dr Fraser’s research interests include tumour immunology and immunotherapy, kinase inhibition, adjuvants, vaccines and infectious diseases. Currently Dr Fraser manages the Experimental Therapeutics Laboratory, which requires liaison between the RAH, SA Pathology, UniSA, and UA for everything from OGTR, ethics, financial reconciliation and student co-supervision. Collectively, Dr Fraser’s past involvement with ASI, managerial experience and diverse research interests afford her the necessary skills to make a positive contribution to ASI as the SA/NT ASI Councillor.

*Michele Grimaldeston
Councillor*

NSW/ACT Retreat

The 4th Annual NSW/ACT retreat was held in idyllic surrounds at Bowral on 23–24 August. Seventy-six delegates attended this year’s meeting and enjoyed fantastic presentations all round. As always, it was a great meeting and hopefully fruitful in terms of forming new links and collaborations.

For their keynote presentations, we would like to warmly thank Professor Tony Cunningham, Dr Michele Grimaldeston, Professor Tony Basten, and Dr Adrian Smith.

Thanks also to Scott Byrne for helping to organize the program, Marian Fernandez for organizing the judging and Julie Wheway for

co-hosting a very couth trivia contest (apart from the risqué bits).

The recipients of awards were:

Honours Student prize (shared): Felix Marsh-Wakefield (USyd) and David McDonald (Centenary Institute)

PhD student prizes:

- 1st Hannes Bergmann (JCSMR)
- 2nd Manu Singh (JCSMR)
- 3rd Zahra Sabouri (JCSMR)

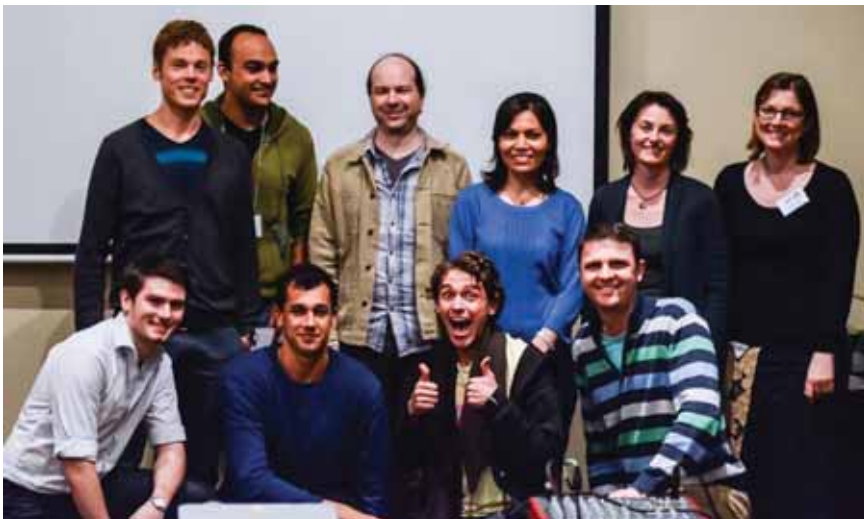
Post Doc Prize (\$500 voucher from Invitrogen): Ian Parish (JCSMR)

Question asking prize: Yogesh Jeelall

Thank you so much to our wonderful meeting sponsors: BD Biosciences, Miltenyi, Jomar Bioscience, Stemcell Technologies, Australian Biosearch, Life Technologies and In Vitro. Their support allows us to bring you the meeting at a very reasonable price and invite some great plenary speakers.

We look forward to seeing you all at the 2013 meeting!

*Marcel Batten (NSW Councillor)
Stephen Daley (ACT Councillor)*



Back row LtoR: Hannes Bergmann (PhD talk prize), Ian Parish (Early Career Researcher Prize), Dr Adrian Smith (Plenary), Zahra Sabouri (PhD talk prize), Michele Grimaldeston (Plenary), Marcel Batten (NSW Councillor).

Front row LtoR: David McDonald (Honours prize), Manu Singh (PhD talk prize), Felix Marsh-Wakefield (Honours prize) and Stephen Daley (ACT Councillor)

THE ASI VISITING SPEAKER PROGRAM 2012

The opportunity to establish or to strengthen collaborations with leading immunologists abroad is greatly encouraged by the ASI Visiting Speaker Program. It allows bringing key overseas players in the various fields of research in Immunology for them to interact with local groups. During 2012, the ASI VSP facilitated the visits by JoAnne Flynn from the University of Pittsburgh (hosted by Michael Good) and Pam Schwartzberg from the NIH (hosted by Stuart Tangye). Both visits were very well received in the various branches.

We already have a good line-up of speakers for 2013 and will let you know details as they become available. However, we are always eager to receive your proposals for new speakers and are willing to accommodate your suggestions. We do look forward to hearing from you with your proposals. For details on the process, visit the ASI website.

FEBRUARY 2013

A/Professor E. John Wherry, University of Pennsylvania, Department of Microbiology, Philadelphia, PA, USA
Hosted by Scott Mueller, University of Melbourne

Sydney, 1st
Brisbane, 4th & 5th
Melbourne, 6th – 8th
Auckland, 11th

MARCH 2013

Dr Branch Moody, MD, Brigham and Women's Hospital, Harvard University, Boston, USA
Hosted by Dale Godfrey, University of Melbourne



Melbourne, 18th – 20th
Sydney, 21st & 22nd
Wellington, 25th

Dr Moody has been investigating the cellular mechanisms by which CD1 proteins, MHC class II proteins and Toll-like receptors control T cell activation. CD1 proteins are a family of evolutionarily conserved antigen presenting molecules that bind lipid antigens for presentation to T cells. Using mass spectrometry to study the lipid content of the cell wall of *M. tuberculosis*, his team has discovered lipid ligands for CD1a, CD1b, CD1c and CD1d proteins. They are studying the cellular mechanisms of lipid loading onto CD1 proteins in endosomal compartments of dendritic cells and the roles of Toll-like receptors in promoting cellular antigen presentation. They are using these lipids to study the function of CD1-restricted T cells in human patients with tuberculosis, autoimmune thyroiditis and drug hypersensitivity reactions.

Selected Recent Publications

Layre E, Moody DB. Lipidomic profiling of model organisms and the world's major pathogens. *Biochimie*. 2012 Aug 23. doi: pii: S0300-9084(12)00336-7. 10.1016/j.biochi.2012.08.012.

Hong S, Cheng TY, Layre E, Sweet L, Young DC, Posey JE, Butler WR, Moody DB.

Ultralong C100 mycolic acids support the assignment of *Segniliparus* as a new bacterial genus. *PLoS One*. 2012;7(6):e39017.

Zeissig S, Murata K, Sweet L, Publicover J, Hu Z, Kaser A, Bosse E, Iqbal J, Hussain MM, Balschun K, Röcken C, Arlt A, Günther R, Hampe J, Schreiber S, Baron JL, Moody DB, Liang TJ, Blumberg RS. Hepatitis B virus-induced lipid alterations contribute to natural killer T cell-dependent protective immunity. *Nat Med*. 2012 Jul;18(7):1060-8.

Madigan CA, Cheng TY, Layre E, Young DC, McConnell MJ, Debono CA, Murry JP, Wei JR, Barry CE 3rd, Rodriguez GM, Matsunaga I, Rubin EJ, Moody DB.

Lipidomic discovery of deoxysiderophores reveals a revised mycobactin biosynthesis pathway in *Mycobacterium tuberculosis*. *Proc Natl Acad Sci U S A*. 2012 Jan 24;109(4):1257-62.

Layre E, Sweet L, Hong S, Madigan CA, Desjardins D, Young DC, Cheng TY, Annand JW, Kim K, Shamputa IC, McConnell MJ, Debono CA, Behar SM, Minnaard AJ, Murray M, Barry CE 3rd, Matsunaga I, Moody DB. A comparative lipidomics platform for chemotaxonomic analysis of *Mycobacterium tuberculosis*. *Chem Biol*. 2011 Dec 23;18(12):1537-49.

Huang S, Cheng TY, Young DC, Layre E, Madigan CA, Shires J, Cerundolo V, Altman JD, Moody DB. Discovery of deoxyceramides and diacylglycerols as CD1b scaffold lipids among diverse groove-blocking lipids of the human CD1 system. *Proc Natl Acad Sci U S A*. 2011 Nov 29;108(48):19335-40.

Kasmar AG, van Rhijn I, Cheng TY, Turner M, Seshadri C, Schiefner A, Kalathur RC, Annand JW, de Jong A, Shires J, Leon L, Brenner M, Wilson IA, Altman JD, Moody DB. CD1b tetramers bind $\alpha\beta$ T cell receptors to identify a mycobacterial glycolipid-reactive T cell repertoire in humans. *J Exp Med*. 2011 Aug 29;208(9):1741-7.

Yakimchuk K, Roura-Mir C, Magalhaes KG, de Jong A, Kasmar AG, Granter SR, Budd R, Steere A, Pena-Cruz V, Kirschning C, Cheng TY, Moody DB. *Borrelia burgdorferi* infection regulates CD1 expression in human cells and tissues via IL-1 β . *Eur J Immunol*. 2011 Mar;41(3):694-705.

de Jong A, Peña-Cruz V, Cheng TY, Clark RA, Van Rhijn I, Moody DB. CD1a-autoreactive T cells are a normal component of the human $\alpha\beta$ T cell repertoire. *Nat Immunol*. 2010 Dec;11(12):1102-9.

MAY 2013

Professor Marc Jenkins, Distinguished McKnight University Professor, Department of Microbiology, University of Minnesota, Minneapolis, MN, USA
Hosted by David Tarlinton, WEHI



Prof. Jenkins will visit **Melbourne, Sydney** and **Canberra** between May 18 and 26; detailed dates to be defined.

Mark has made many outstanding contributions to both T and B cell activation and differentiation. Recently he has perfected the detection of rare, antigen specific B and

T cells in the naive repertoire and followed their entry into the immune response. This has led to some striking insights into the requirements for immunity and the capacity of these cells to sustain themselves as memory cells. Mark has also applied this technology to follow CD4 T cell responses to intracellular pathogens. Jenkins and his colleagues investigate CD4+ helper T and B cell activation in vivo at a level that can only be achieved by directly tracking antigen-specific cells. Using gene-targeted recipients or antibody blocking approaches, they identify molecules that are critical for in vivo T and B cell signal transduction, proliferation, lymphokine production, survival, and differentiation. The goal is to achieve a basic understanding of these processes so that they can be manipulated to improve vaccines and prevent autoimmunity.

Selected Recent Publications

Jenkins MK, Moon JJ. The role of naive T cell precursor frequency and recruitment in dictating immune response magnitude. *J Immunol.* 2012 188(9):4135-40.
Taylor JJ, Pape KA, Jenkins MK. A germinal center-independent pathway generates unswitched memory B cells early in the primary response. *J Exp Med.* 2012;209(3):597-606.
Pepper M, Pagán AJ, Igyártó BZ, Taylor JJ, Jenkins MK. Opposing signals from the Bcl6 transcription factor and the interleukin-2 receptor generate T helper 1 central and effector memory cells. *Immunity.* 2011;35(4):583-95.
Moon JJ, Dash P, Oguin TH 3rd, McClaren JL, Chu HH, Thomas PG, Jenkins MK

Quantitative impact of thymic selection on Foxp3+ and Foxp3- subsets of self-peptide/MHC class II-specific CD4+ T cells. . PNAS U S A. 2011;108(35):14602-7.
Pepper M, Jenkins MK. Origins of CD4(+) effector and central memory T cells. *Nat Immunol.* 2011 Jun;12(6):467-71.
Pape KA, Taylor JJ, Maul RW, Gearhart PJ, Jenkins MK. Different B cell populations mediate early and late memory during an endogenous immune response. *Science.* 2011;331(6021):1203-7.
Chu HH, Moon JJ, Kruse AC, Pepper M, Jenkins MK. Negative selection and peptide chemistry determine the size of naive foreign peptide-MHC class II-specific CD4+ T cell populations. *J Immunol.* 2010;185(8):4705-13.
Jenkins MK, Chu HH, McLachlan JB, Moon JJ. On the composition of the preimmune repertoire of T cells specific for Peptide-major histocompatibility complex ligands. *Annu Rev Immunol.* 2010;28:275-94. Review.
Catron DM, Pape KA, Fife BT, van Rooijen N, Jenkins MK. A protease-dependent mechanism for initiating T-dependent B cell responses to large particulate antigens. *J Immunol.* 2010;184(7):3609-17.
Pepper M, Linehan JL, Pagán AJ, Zell T, Dileepan T, Cleary PP, Jenkins MK. Different routes of bacterial infection induce long-lived TH1 memory cells and short-lived TH17 cells. *Nat Immunol.* 2010; 11(1):83-9.
Chu HH, Moon JJ, Takada K, Pepper M, Molitor JA, Schacker TW, Hogquist KA, Jameson SC, Jenkins MK. Positive selection optimizes the number and function of MHCII-restricted CD4+ T cell clones in the naive polyclonal repertoire. *Proc Natl Acad Sci U S A.* 2009;106(27):11241-5.

UPCOMING CONFERENCES

Lorne Infection & Immunity Conference
 20-22 February 2013
 Mantra Lorne, Victoria
www.lorneinfectionimmunity.org

Immuno 2013,
 March 11–12, 2013
 Barcelona, Spain
<http://www2.kenes.com>

WIRM-VII
 World Immune Regulation Meeting
 “Innate and Adaptive Immune Response and Role of Tissues in Immune Regulation”
 March 13–16, 2013
 Davos, Switzerland
 Email: wirminfo@wirm.ch
<http://www.wirm.ch>

Immunology 2013
 May 3-7, 2013
 Honolulu, Hawaii, USA
www.immunology2013.org

30 Years of HIV Science – Imagine the Future
 May 21-23, 2013
 Paris, France
<http://www.pasteur.fr> 15th International Congress of Immunology
 August 22–27, 2013
 Rome, Italy
ici2013@triumphgroup.it
www.ici2013.org

ACA 2013
 6th Asian Congress of Autoimmunity
 November 21-23, 2013
 Hong Kong
<http://www2.kenes.com/autoimmunity2013>
 Email: aca@kenes.com

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 \$200 FOR THE BEST ARTICLE PUBLISHED IN THE NEWSLETTER!**

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TRAVEL AWARD CONFERENCE REPORTS

7th International EMBO Workshop on Antigen Presentation and Processing

Eleanor Jones

Monash University, Melbourne

The 7th International EMBO Workshop on Antigen Presentation and Processing was held in the beautiful city of Amsterdam this year (24–27 April) and I was lucky enough to be able to attend thanks to help from a special travel award. The opening address by Paul Roche set the tone of the conference with him threatening to hit anyone who spoke too long with a convenient gavel, and introduced everyone with comical pictures (no doubt from previous conferences). The workshop's tradition dictates that all presentations must be on data that has not yet been published, leading to some happy embarrassment on Thursday, when Nilabh Shastri had to change his topic at the last minute when his paper was accepted to *Nature Immunology* on the weekend. The tradition, and a decision on the part of the selection committee, also meant an unusually strong showing of early career researchers, including Eva Huber, Alex Theodossis and Mariolina Salio.

More informal than most conferences, the workshop also included daily forums with open discussion. The first day's topic was commercial and clinical demands on scientists, and inspired lots of impassioned comments that arguments over funding came at the cost of patients' lives. After thanking the organizers with books (one on how to write clearly met with much laughter), the second day's forum included the two extremely controversial topics of the contribution of DRiPs to antigen presentation, and the main source of *in vivo* cross presentation. Truly, if in a less civilized setting, there might have been a brawl, with both topics encouraging loud and vigorous discussions (at one point one very prominent member of the field was heard to exclaim: "You're wrong!" to be met with cries of "Maybe he needs a book on manners!"). The third day's forum, hosted by a number of students in the field, was perhaps a more polite ending.

For me, one of the most valuable experiences was being able to talk to leaders from around the world during breaks, as well as getting constructive feedback during the poster session. Spread throughout the first two days, the posters were also eligible for invited talks on the last day. Although I missed out, fellow Australian Hannah Siddle was selected, giving a fascinating presentation on Tasmanian devil facial tumour disease.

Overall, not only was the conference highly educational and entertaining, the experience allowed me to gain insight into many facets of antigen presentation and meet some of the most well respected (for good reasons!) members of the field, all made possible by the support of ASI.

Eleanor enjoying a fresh stroopwafel, a national dish of the Netherlands



One of the tables at the conference dinner involved in lively discussion

Tuberculosis Vaccines for the World 2012 International Conference

Lindsay Ancelet

Malaghan Institute of Medical Research, Wellington, New Zealand

I recently attended the Tuberculosis Vaccines for the World 2012 International Conference (TBV 2012) in Orlando, Florida, US.

Although TBV2012 was a small meeting, it was packed full of influential talks by some of the worlds leading TB scientists and clinicians. The meeting was opened with a very informative talk by David Murray addressing the so-called “myths” surrounding the TB vaccine BCG. Highlights included the presentation of preliminary clinical trial results by Dr Helen McShane and Dr Willem Hanekom, and a fantastic talk by Dr Andrea Cooper delineating the role of IL-17 and IL-27 in immunity to TB.

I was very fortunate to have the opportunity to present my research to such an impressive audience. My talk focused on the ability of a novel lipid-formulated oral BCG vaccine to induce long-term CD4⁺ memory T cell responses in the lung. My presentation was well received, and gave me an excellent opportunity to network with TB immunologists, and gain valuable feedback on my research.

While in the US I also travelled to Washington DC where I visited Dr Robert Seder at the Vaccine Research Center at the National Institute of Health. I was given a tour of the NIH and his laboratory and gave a seminar presentation of my research.

Along with my collaborators from Immune Solutions Ltd, the inventors of the oral vaccine, we presented our oral BCG vaccine research platform to the TB vaccine partnership Aeras. I presented my research findings to the Aeras senior leadership team and staff, which included the Chief Scientific Officer, Dr Tom Evans, and the Vice President of Scientific Affairs, Dr Ann Ginsberg. It was



Meeting at Aeras with Lew Barker, Director of Clinical Development, Aeras (left), Lindsay Ancelet, Frank Aldwell, Head of Research and Director, Immune Solutions Ltd (right).

an amazing experience being able to present and defend my research to such high caliber scientists. The meeting was very successful, and Aeras agreed to trial our vaccine in a novel natural infection study alongside their top candidate TB vaccines.

Finally, I presented a seminar of my work at the Vaccine and Infectious Disease Organization/International Vaccine Center (VIDO/InterVac) in Saskatoon Canada. I was fortunate to be given a very escorted tour of the brand new, world-leading \$140 million Containment Level 3 facility, which was due to open the following week.

My attendance at TBV 2012 conference, lab visits in the US and Canada, as well as my meeting with Aeras, made this trip very busy and exciting. I was able to network and form future collaborations with leading vaccine researchers, which is critical to my success as a young scientist. I felt very proud to present New Zealand research to such an international audience and am extremely grateful to ASI for providing me with such a brilliant opportunity.

Contributions sought for the ASI online immunology quiz

As part of World Day of Immunology events, we have developed an online immunology quiz (see <http://www.immunology.org.au/immquiz1.html>)

on the ASI website. This quiz is targeted at the general public, but it would be good to add a few more questions (especially some with an Australian flavour), and maybe even add an “Advanced Level”, with questions that undergrad students might find useful for revising for exams. All that’s needed now are the questions and answers.

If you would like to contribute any multiple choice questions for either the general quiz or an advanced version, please send them to Judith Greer at j.greer@uq.edu.au.

4th Annual Antigen Processing and Presentation Workshop, Amsterdam, 2012

Damien Zankar

Ludwing Institute for Cancer Research, Victoria

The 4th annual Antigen Processing and Presentation Workshop was held alongside the beautiful canals of Amsterdam, The Netherlands. The meeting was attended by a broad range of scientists from our immunological niche ranging from stalwarts in the field to young and upcoming scientists, with the calibre of research presented of a continuous high standard.

A large proportion of the research presented focused on a major trend in the field of trying to understand more detail about the peptide loading complex (PLC) and how peptides are loaded into the MHC cleft. This included analysis of the crystal structures of various parts of the complex, the importance of specific residues for binding to the Class II DO and DM proteins, the exact protein composition of the PLC, as well as timelines for the peptide binding and loading processes. Data involving alternate presenting molecules such as CD1s were

also reported, highlighting the importance of saposin facilitation of lipid binding in endosomal compartments. The important mechanism of cross presentation of antigens was unanimously agreed upon that it does exist, however the underlying mechanisms behind the phenomenon are still yet to be fully described and more investigation is required. The exact contribution of cross presentation versus directly presented antigens is also an elusive topic that remains to be fully understood. The demonstration of visualising this phenomenon *in vivo* using imaging techniques was highlighted as a goal for the future.

Indeed most controversial of all, the debate of the DRiP hypothesis remains a hot topic. This hypothesis suggests that a major proportion of peptides are generated from Defective Ribosomal Products (DRiPs) rather than from degradation of correctly folded stable proteins. Conflicting data was

presented from several lab groups using a similar degradation/peptide rescue approach, investigating the contribution of DRiPs to the overall peptide pool. While it was agreed that DRiPs do exist, further research is required as to their exact contribution to the overall peptide pool, in a range of antigenic scenarios. However, it is clear that new and exciting instalments into this debate will arise shortly in the future.

From this data and other exciting observations presented at this workshop, it is evident that the Antigen Processing and Presentation field is strong and will be fruitful in the future.

This meeting provided me personally with new insights into the field and the directions into which current research is headed. I'd like to thank the ASI for the Travel Grant I received for both the intellectual stimulation I received as well as the chance to talk to fellow researchers and pioneers in the field about my scientific work.



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3rd European Congress of Immunology, Glasgow

Sabine Kuhn

Malaghan Institute of Medical Research, Wellington, New Zealand

On 5-8 September 2012, for the third time immunologists from all over Europe gathered at one big conference to present and discuss their latest research. The range of topics was extremely diverse with sessions covering innate and adaptive immune responses, therapy, regulation, signalling, infectious diseases as well as autoimmunity and cancer. Up to 12 concurrent sessions spoil the delegates for choice.

With over 4000 participants, this was the largest conference I have attended so far. In addition, it was also my first paperless meeting. Going green, the conference organisers provided free wifi and a smartphone app to search for abstracts, instead of a printed monster of a conference programme. While technical hiccups led to some spontaneous gatherings around one of the few printed programmes, the paperless idea is definitely worthwhile, especially for such a large meeting.

The symposium sessions and workshops featured many impressive presentations by postdoctoral fellows and distinguished laboratory heads. Among my personal highlights was Caetano Reis e Sousa's talk. Earlier this year, both his team and Ken Shortman and Mireille Lahoud's groups from Australia identified F-actin as the ligand for the receptor DNGR-1 (Clec9A). Investigating the down-stream effects of this interaction in more detail, he showed data indicating that DNGR-1 binding of F-actin initiates syk-signalling, which in turn alters endosome trafficking, increasing antigenicity rather than adjuvanticity of

dying cells. Eric Vivier presented his recent findings on the tuning of NK cell functions via NKp46, where blocking of this activating receptor leads to hyperresponsiveness of NK cells.

Matthew Albert's contribution "Biomarkers lie!" initiated a lively discussion about the validation, benefits and clinical implementation of biomarkers. In addition, his identification of a dominant-negative cleavage variant of CXCL10 shed light on the paradoxical correlation of high CXCL10 levels with impaired hepatitis C clearance and highlighted the caveat of common detection kits that cannot distinguish the two CXCL10 forms. A study presented by Panayotis Verginis identified decreased recruitment and functional alteration of inflammatory DCs as a mechanism of Treg mediated immune-suppression. This finding particularly intrigued me as I observed a correlation between the accumulation of inflammatory DCs and increased anti-tumour immune responses after adjuvant treatment in my work.

Overall, I found the presentations at the ECI meeting very informative. In addition, it also provided a great overview of the exciting immunology research in Europe and the opportunity to interact with other delegates during the poster sessions and coffee breaks.

Fitting in several laboratory visits before and after the conference, I had the pleasure



Sabine in front of the "Armadillo", part of the Scottish Exhibition and Conference Centre in Glasgow, where the meeting was held

to meet Doug Fearon, Ken Smith, Paul Klenerman, Vincenzo Cerundolo and their groups. I was impressed with the diversity of their projects and learned much about their brilliant research in the regulation of immune responses in infection, autoimmunity and cancer. I also had the opportunity to present my own work on the use of adjuvants for tumour-immunotherapy, leading to interesting discussions and providing me with valuable feedback.

On my way back to New Zealand I stopped over in Singapore to meet Christiane Ruedl and discuss a collaborative project. Jean-Pierre Abastado shared insights into his spontaneous melanoma model and kindly gave me the opportunity to give a talk at the Singapore Immunology Network (SIgN).

A big thank you to ASI, as well as the NZ Cancer Society and the Kathleen Stewart Scholarship for making this invaluable experience possible for me.



Glaswegian pipers getting everyone into the spirit at the ECI opening

23rd Annual Scientific Meeting of the Australasian Society of Clinical Immunology and Allergy (ASCIA)

Wai Yan (Kiwi) Sun

Centre for Cancer Biology, SA Pathology, Adelaide

I was very delighted to be awarded the ASI Postgraduate International Travel Grant to travel to New Zealand for (1) visiting laboratories and presenting at the Malaghan Institute, (2) attending the 23rd Annual Scientific Meeting of the Australasian Society of Clinical Immunology and Allergy (ASCIA) on 5-8 September 2012 in Wellington, and (3) visiting the “Kiwi birds”.

The ASCIA conference is a top tier conference for me to attend as my PhD focuses on using a small molecule as a new therapy to treat allergic inflammation. Thus, meeting with the top scientists in this field is highly beneficial for my study and future direction. To start off my journey, I visited a few laboratories at the Malaghan Institute in Wellington, where I met with a number of senior postdoc researchers and PhD students from the Allergic Diseases Research Lab led by Prof Graham Le Gros, the Immune Cell Biology Lab led by Prof Franca Ronchese and the Arthritis & Inflammation Lab led by Dr Jacquie Harper. I was fortunate enough to present and share my PhD work with them and as a result I received a lot of valuable comments, which will help with my current research and future career.

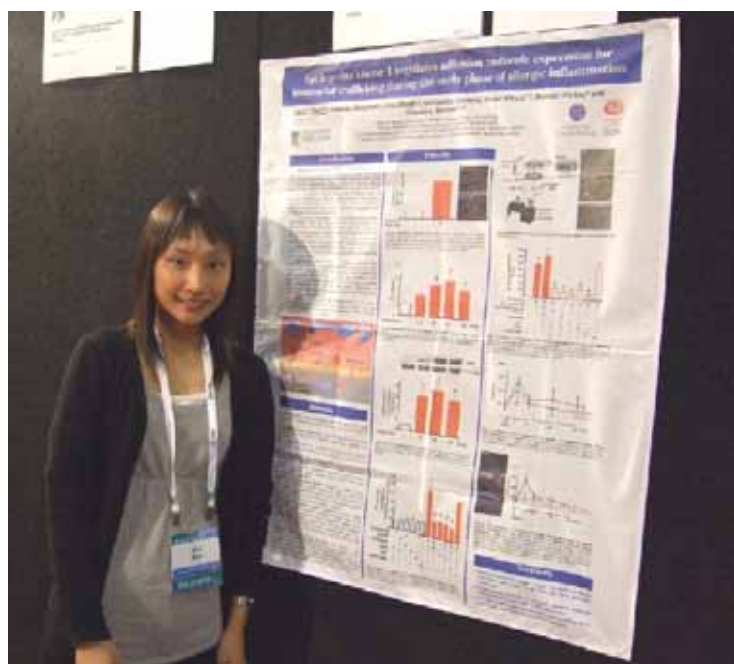
The next part of my trip was to attend the conference and workshop. It was well organized and divided into sessions which covered (1) primary immune deficiency, (2) allergy prevention, (3) inflammatory eye disease, (4) immunotherapy, (5) autoimmunity, (6) food allergy, (7) anaphylaxis and (8) vitamin D and the immune system. There were ~300 delegates from both clinical and research backgrounds who contributed to the programme and discussions. All sessions were interesting and informative. I was particularly attracted to the work of A/Prof Mimi Tang (Paediatric Clinical Immunologist, Melbourne) who presented on Oral Immunotherapy and Tolerance. She discussed the roles of Treg cells in terms of tolerance and desensitization in response to a single high dose antigen challenge versus multiple low dose antigen challenge. Her work showed that only the multiple low dose administration can upregulate the inducible Treg cells, which suggests a better immunotherapeutic approach to induce oral tolerance.

Another highlight of this conference included the impressive presentation by Dr Jorg Kleine-Tebbe (Allergy and Asthma Centre, Berlin, Germany). He discussed the current issue of IgE testing for food and

skin allergies wherein the ratio of specific IgE and total IgE was often not considered and thereby causing misleading test results. He also showed that the levels of IgE in serum do not correlate with the severity of allergic symptoms and advised that a sensitivity test alone should not be used as the only read out system to define allergy in clinic.

There were about 50 posters, mainly by students and trainees. I presented a poster based on my current PhD work and was honoured to be selected for further discussion on the third day of the conference. At the discussion session, I had the opportunity to talk to some clinicians and researchers where I received very positive feedback as well as excellent ideas for future directions.

At the end of my trip, I went to visit the cute little Kiwi birds. I have always wanted to meet this unique bird as we share the same name, Kiwi. I was so excited when I saw one Kiwi and had to stop myself from touching it. But I know it is virtually impossible ... why? Because Kiwi birds can run very fast, up to 45 mph (which is almost as fast as a car on a road)! They are small but very powerful!!



Overall, the conference was well attended with outstanding presentations, venue and catering. I learnt a lot of new information about allergy, not only scientific but also clinical. This was an excellent experience for me and will greatly aid the completion of my PhD. Finally, I would like to sincerely thank ASI for providing me with this opportunity to present and attend the ASCIA conference in New Zealand.

Publications List

Congratulations to ASI members who have published their following work in the last three months (articles with an ePub date between July and September 2012)

- Londrigan SL, Tate MD, Brooks AG, Reading PC. **Cell-surface receptors on macrophages and dendritic cells for attachment and entry of influenza virus.** *J Leukoc Biol* 2012; **92**(1): 97.
- Hamilton JA, Davis J, Pobjoy J, Cook AD. **GM-CSF is not essential for optimal fertility or for weight control.** *Cytokine* 2012; **57**(1): 30.
- Tan SY, Cavanagh LL, d'Advigor W, Shackel N, Fazekas de St Groth B, Weninger W. **Phenotype and functions of conventional dendritic cells are not compromised in aged mice.** *Immunol Cell Biol* 2012; **90**(7): 722.
- Sheng YH, Hasnain SZ, Png CW, McGuckin MA, Linden SK. **Techniques for assessment of interactions of mucins with microbes and parasites in vitro and in vivo.** *Methods Mol Biol* 2012; **842**: 297.
- Song KD, Hwang S, Yun CH. **T cell receptor signaling that regulates the development of intrathymic natural regulatory T cells.** *Immune Netw* 2011; **11**(6): 336.
- Song KD, Kim DJ, Lee JE, Yun CH, Lee WK. **KLF10, transforming growth factor-beta-inducible early gene 1, acts as a tumor suppressor.** *Biochem Biophys Res Commun* 2012; **419**(2): 388.
- Melville JM, Bischof RJ, Meeusen EN, Westover AJ, Moss TJ. **Changes in fetal thymic immune cell populations in a sheep model of intrauterine inflammation.** *Reprod Sci* 2012; **19**(7): 740.
- O'Keeffe M, Fancke B, Suter M, Ramm G, Clark J, Wu L, Hochrein H. **Nonplasmacytoid, high IFN-alpha-producing, bone marrow dendritic cells.** *J Immunol* 2012; **188**(8): 3774.
- Kang SS, Jeon JH, Woo SJ, Yang JS, Kim KW, Yun CH, Han SH. **IFN-gamma renders human intestinal epithelial cells responsive to lipopolysaccharide of *Vibrio cholerae* by down-regulation of DMBT1.** *Comp Immunol Microbiol Infect Dis* 2012; **35**(4): 345.
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- Good-Jacobson KL, Tarlinton DM. **Multiple routes to B-cell memory.** *Int Immunol* 2012; **24**(7): 403.
- Lacey DC, Achuthan A, Fleetwood AJ, Dinh H, Roiniotis J, Scholz GM, Chang MW *et al.* **Defining GM-CSF- and macrophage-CSF-dependent macrophage responses by in vitro models.** *J Immunol* 2012; **188**(11): 5752.
- Huynh J, Kwa MQ, Cook AD, Hamilton JA, Scholz GM. **CSF-1 receptor signalling from endosomes mediates the sustained activation of Erk1/2 and Akt in macrophages.** *Cell Signal* 2012; **24**(9): 1753.
- Woodberry T, Minigo G, Piera KA, Amante FH, Pinzon-Charry A, Good MF, Lopez JA *et al.* **Low-level *Plasmodium falciparum* blood-stage infection causes dendritic cell apoptosis and dysfunction in healthy volunteers.** *J Infect Dis* 2012; **206**(3): 333.
- Cliffe ST, Bloch DB, Suryani S, Kamsteeg EJ, Avery DT, Palendira U, Church JA *et al.* **Clinical, molecular, and cellular immunologic findings in patients with SP110-associated veno-occlusive disease with immunodeficiency syndrome.** *J Allergy Clin Immunol* 2012; **130**(3): 735.
- Kang SS, Kim HJ, Jang MS, Moon S, In Lee S, Jeon JH, Baik JE *et al.* **Gene expression profile of human peripheral blood mononuclear cells induced by *Staphylococcus aureus* lipoteichoic acid.** *Int Immunopharmacol* 2012; **13**(4): 454.
- Jalilian I, Peranec M, Curtis BL, Seavers A, Spildrejorde M, Sluyter V, Sluyter R. **Activation of the damage-associated molecular pattern receptor P2X7 induces interleukin-1beta release from canine monocytes.** *Vet Immunol Immunopathol* 2012; **149**(1-2): 86.
- Scott NM, Ng RL, Strickland DH, Bisley JL, Bazely SA, Gorman S, Norval M *et al.* **Toward homeostasis: regulatory dendritic cells from the bone marrow of mice with inflammation of the airways and peritoneal cavity.** *Am J Pathol* 2012; **181**(2): 535.
- Fernandez CS, Cameron G, Godfrey DI, Kent SJ. **Ex-vivo alpha-galactosylceramide activation of NKT cells in humans and macaques.** *J Immunol Methods* 2012; **382**(1-2): 150.
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- Ancelet L, Rich FJ, Delahunty B, Kirman JR. **Dissecting memory T cell responses to TB: concerns using adoptive transfer into immunodeficient mice.** *Tuberculosis (Edinb)* 2012; **92**(5): 422.
- Dudgeon K, Rouet R, Kokmeijer I, Schofield P, Stolp J, Langley D, Stock D *et al.* **General strategy for the generation of human antibody variable domains with increased aggregation resistance.** *Proc Natl Acad Sci U S A* 2012; **109**(27): 10879.
- Ma CS, Deenick EK, Batten M, Tangye SG. **The origins, function, and regulation of T follicular helper cells.** *J Exp Med* 2012; **209**(7): 1241.
- Sutton VR, Sedelies K, Dewson G, Christensen ME, Bird PI, Johnstone RW, Kluck RM *et al.* **Granzyme B triggers a prolonged pressure to die in Bcl-2 overexpressing cells, defining a window of opportunity for effective treatment with ABT-737.** *Cell Death Dis* 2012; **3**: e344.
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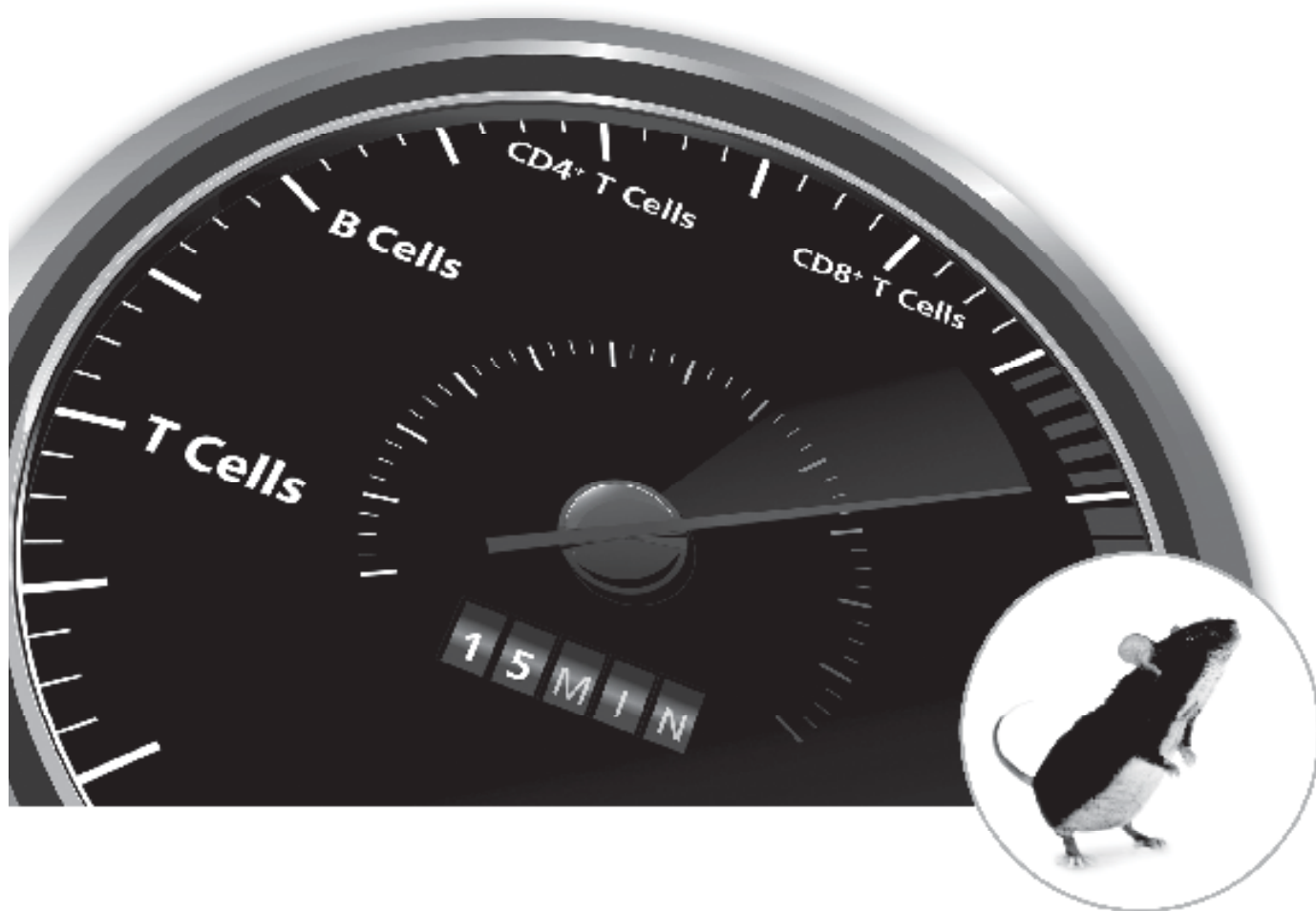
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