N E W S L E T T E R

Australasian Society for Immunology Incorporated

PP 341403100035 ISSN 1442-8725 June 2012

The NKT Cell Laboratory

Dale Godfrey
Department of Microbiology and Immunology, University of Melbourne

When immunologists refer to T cells, they are usually talking about lymphocytes that express T cell antigen receptors (TCRs) that are specific for peptide antigens presented by Major Histocompatibility Complex (MHC) encoded antigen presenting molecules. It is widely accepted that there are two populations of T cells: CD4 T cells that recognize peptide antigens presented by MHC class II, and CD8 T cells that recognize peptide antigens presented by MHC class I. However, there is a third population, termed "NKT cells" that do not respond to peptide antigens and are not MHC restricted. Instead, they represent a distinct arm of the immune system that specifically recognizes lipid-based antigens presented by an MHC-like antigen-presenting molecule known as CD1d.

LtoR: Adam Uldrich, Garth Cameron, Marcin 'Marty' Ciula, Catarina Almeida, Nick Gherardin, Fiona Ross, Rhiannon Clanchy, Daniel Pellicci, Dale Godfrey. (Not present: Kirsty MacPherson, John Waddington, Huey-Fern Koay, Ben O'Sullivan)

NKT cells are present in most mammalian species and their TCR specificity is remarkably conserved, such that mouse NKT cells can recognize lipid antigens presented by human CD1d and vice versa. This conservation over ~100 million years of evolution suggests that these cells must play a fairly important role in the immune system. We now know that NKT cells can recognize lipid antigens derived from various types of bacteria, parasites, fungi, pollens and house dust extract, as well as a range of self-lipid antigens. When activated, NKT cells can abundantly produce a broad range of cytokines such as Interferon-γ, Interleukin-4 (IL-4) and IL-17. Moreover, they produce these cytokines within minutes to hours of antigenic challenge, which puts their peptide-MHC reactive T cell cousins to shame. Accordingly, NKT cells are implicated as key players in a broad range of immunological settings, including infection, allergy, asthma, cancer, atherosclerosis and allograft rejection. Just as we are starting to develop a good understanding of these cells, the field is getting more complicated as we realise that there are several, functionally distinct subsets of these cells, as well as related T cells that are restricted to other MHC-like antigen presenting molecules including CD1a, CD1b, CD1c, and MR1. Collectively, these 'non-conventional' T

cont.p4

Contents

The NKT Cell Laboratory	1
Editorial	3
Student News	3
Graham Jackson Memorial Prize for MI	9
Jomar Biosciences MI Poster Prize	12
Major Poster Prize Winner	13
Australian Bioresearch Poster Prize	14
Councillors' News	17
Hon. Secretary's News	18
Visiting Speaker Program	19
FIMSA Training Course Report	20
Travel Award Conference Reports	21
Publications List	25
Upcoming Conferences	27

ASI Inc. COUNCIL

President
Dr David Tarlinton
Walter & Eliza Hall Institute of Medical Research
1G Royal Parade, Parkville Vic 3050
Ph: 61 3 9345 2615
Email: tarlinton@wehi.edu.au

Vice President
Professor Dale Godfrey
Dept Microbiology & Immunology
University of Melbourne
Royal Parade, Parkville Vic 3010
Ph: 61 3 8344 6831
Email: godfrey@unimelb.edu.au

Honorary Secretary
Professor Rosemary Ffrench
Burnet Institute
GPO Box 2284
Melbourne Vic 3001
Ph: 61 3 9282 2285
Email: ffrench@burnet.edu.au

Honorary Treasurer
Dr Pablo Silveira
Garvan Institute
384 Victoria Street
Darlinghurst NSW 2010
Ph: 61 2 9295 8429
Email: P.silveira@garvan.org.au

State Councillors

New South Wales
Dr Marcel Batten
Ph: 61 2 9295 8412
Email: m.batten@garvan.org.au

Victoria & Tasmania
Dr Stuart Berzins
Ph: 61 3 5320 2039
Email: s.berzins@ballarat.edu.au

Queensland
Dr Ashraful Haque
Ph: 61 7 3362 0414
Email: ashraful.haque@qimr.edu.au

South Australia & Northern Territory
Dr Michele Grimbaldeston
Ph: 61 8 8222 3083
Email: michele.grimbaldeston@health.sa.gov.au

Western Australia
Dr Alec Redwood
Ph: 61 8 9346 2512
Email: aredwood@cyllene.uwa.edu.au

Australian Capital Territory
Dr Stephen Daley
Ph: 61 2 6125 7605
Email: stephen.daley@anu.edu.au

New Zealand
Dr Anne LaFlamme
Ph: 64 4 463 6093
Email: anne.laflamme@vuw.ac.nz

FIMSA Councillor
Dr Guna Karupiah
Ph: 61 2 6125 4562
Email: guna.karupiah@anu.edu.au

Non-Voting Councillors:

Newsletter Editor
Dr Simon Apte
Ph: 61 7 3362 0380
Email: Simon.Apte@qimr.edu.au

Journal Editor
Dr Gabrielle Belz
Ph: 61 3 9345 2544 Fax: 61 3 9347 0852
Email: belz@wehi.edu.au

Visiting Speakers Co-ordinator
A/Prof J. Alejandro Lopez
Queensland Institute of Medical Research
CBCRC/I, Post Office
Royal Brisbane Hospital Qld 4029
Ph: 61 7 3845 3794 Fax: 61 7 3845 3510
Email: Email: alejL@qimr.edu.au

Council Member of IUIS
Dr Franca Ronchese
Ph: 64 4 499 6914 ext 828
Email: fronchese@malaghan.org.nz

Honorary Archivist & Webmaster:
Dr Judith Greer
Ph: 61 7 3346 6018
Email: j.greer@uq.edu.au

Administrative Correspondence
Ms Judi Anderson
ASI Inc. Secretariat
PO Box 7108
Upper Ferntree Gully Vic 3156
Ph: 61 3 9756 0128 Fax: 61 3 9753 6372
Email: asi@21century.com.au

ASI Student Representatives
Ms Julia Marchingo
Ph: 61 3 9345 2609
Email: marchingo@wehi.edu.au
Ms Maria Demaria
Ph: 61 3 9903 0700
Email: maria.demaria@monash.edu

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

We have another packed edition of the Newsletter with fabulous contributions by Dale Godfrey and his team and very impressive articles by prize-winning researchers from ASI2011.

Dale's story is a great example of how a fascination with basic immunology can be translated into significant outcomes, both in our understanding of basic immunology, and in clinical translation. Perhaps the most surprising part of Dale's story is that he could have possibly been tempted away from research and into Chartered Accounting! Surely he was joking about that.

I hope you have time to glance through the publication list and to read the articles by the prize-winners, they attest to the incredible variety and quality of the research being conducted by ASI members – I personally find it very inspiring.

Finally, welcome to our two new Student Representatives. I know the future of our Society, and immunology in general, looks promising when our students prefer to communicate in limericks.

Simon Apte

ASI Student News

Hi Everyone,

Welcome to the first edition of the student news for 2012. Firstly, we'd like to say a big thank you to the previous student representatives Kiwi Sun and Kate Parham and their committee for their fabulous work over the last year to bring us the awesome student function at the ASI Adelaide Conference. We all had a blast!

We're already very excited about the upcoming 42nd ASI Annual Meeting in Melbourne and are particularly looking forward to showcasing Melbourne at the student function. We want to make sure this event is as fun as possible so if you have any ideas about how to make this an unforgettable night please let us know. Any suggestions can be sent to marchingo@wehi.edu.au or maria.demaria@monash.edu.au.

Stay tuned for news about this and other student events by joining the student Facebook group, "Student Members of the Australasian Society for Immunology".

Finally, as your student representatives for 2012, we'd like to give you a little introduction about who we are and what we do. Given how pumped we are already for the ASI 2012 Conference, we decided what better way to do this than through limerick? So here goes ….

There once was a student named Julia
Who found cell expansion peculiar
T cell division
She gauged with precision
Cessation vs death did not fool her

A PhD student named Maria
Had a wonderful idea
Cell surface organisation
Drove her to procrastination
Tetraspanin function? Mamma mia!

Julia Marchingo & Maria Demaria

The NKT Cell Laboratory, cont.

cells, some of which are CD4+, some CD8+ and some CD4-CD8-, can represent up to 20% of human PBMC. Without realizing it, immunologists and clinicians have probably been studying these cells for many years as part of standard T lymphocyte assays.

How did my lab end up in this area of research?

I am occasionally asked this question, and the answer is that it all started long ago. As a PhD student in the late '80s, I started out in the field of intrathymic T cell development under the supervision of Richard Boyd at Monash University. My PhD project was about thymic stromal cell diversity and stromal cell molecules that regulated T cell development. Perhaps surprisingly, I made it through the PhD in just over three years, with much credit to Richard who kept me on track when the lure of a career in chartered accounting or management consulting occasionally distracted me. A very important lesson that I learnt way back then is that if two cells appear to be different, they probably are, and you won't have much chance of understanding them if you keep lumping them together. This shaped much of my future research. I embarked on a brief, one-year postdoctoral stint at Hoffman La-Roche in New Jersey followed by a 3-year run at DNAX Research Institute in California under the supervision of Albert Zlotnik. Over this time, my focus shifted from thymic stromal cells to early CD4-CD8- (double negative, DN) thymocyte development, and my claim to fame (sort of) was mapping a 4 step pathway (imaginatively termed DN1-DN4) that these cells followed as they rearranged and expressed their TCR genes. Whilst working with DN thymocytes, the Zlotnik lab was also very interested in a population of mature DN T cells that expressed CD3 and either γδ or αβTCRs. The latter cells, which were called αβDN cells, were receiving very little attention in the literature in those days but we were intrigued by the fact that they produced an abundance of cytokines including IL-4, IFN-γ, TNF and they also expressed some Natural Killer cell markers such as NK1.1. They looked very different from other T cells.

Upon my return to Australia, I took up a postdoctoral position at the Centenary Institute in Sydney under the supervision of Roland Scollay. I wanted to carve out my own niche in the field of T cell development, but this was difficult because Roland's existing projects spanned most aspects of this field. However, he had left out one cell type in his research agenda … αβDN T cells. Thus, these cells formed a key part of my NHMRC grant applications, my research projects, and ultimately, my research career (at least up till now). Alan Baxter started at the Centenary Institute the same week that I did. We hit it off straight away, which was fortunate as we both found ourselves as essentially the sole inhabitants of the new Centenary Institute building, which had only just opened when we arrived. Both recognizing the importance of collaboration, we joined forces, which was quite fortuitous as we soon discovered that NOD mice (Alan's field) had a selective deficiency in αβDN T cells (my field) and that this was linked with diabetes susceptibility. We were both hooked and this provided some of the earliest insight into the fact that αβDN T cells were functionally distinct from other T cells in an important disease model, which highlighted their therapeutic potential. We were unhappy with the name 'αβDN T cells' and alternative names that were creeping into the literature, such as NK1.1+ T cells, were no better. After much debate, and unable to agree on "Godfrey-Baxter cells" or "Baxter-Godfrey cells", we ultimately settled on "NKT cells". Despite the assertions of one or two of my witty colleagues, this does NOT stand for "Not Kwite T cells".

I returned to Melbourne to set up my "NKT laboratory" at Monash University, Department of Immunology in 1997, where I worked for six years, and gradually built up a team of talented PhDs, postdocs and RAs. While my 'NKT cell niche' was now becoming well established, I continued to study conventional T cell development, and forged several valuable new collaborations including Tim Cole, Richard Boyd, and Andreas Strasser, investigating the factors that regulate intrathymic positive and negative selection. A new collaboration with Mark Smyth at this time was a major factor in shaping my research directions over the years ahead. Mark, a leader in the field of tumour immunology and I found a common interest in understanding how NKT cells respond to cancer. These studies helped demonstrate the great immunotherapeutic potential of NKT cells in this disease and this became an important focus for both of us. This resulted in my teaming up on an NHMRC program grant with Mark, Joe Trapani and Ricky Johnstone at the Peter MacCallum Cancer Center, a grant that is now in its third iteration and going strong. These studies have evolved into some exciting pre-clinical and translational studies with NKT cells in mouse and human cancer, including more recent members of our NHMRC program at the Peter Mac (Miles Prince, David Ritchie, Paul Neeson).

In 2003, I took the NKT laboratory 'across the Yarra' and moved my lab from Monash to University of Melbourne, Department of Microbiology and Immunology, where I am currently based and looking forward to being a founding member of the new Peter Doherty Institute in 2014. Here, I have added several terrific new collaborations that have influenced my research projects over the last few years. In particular, I have been fortunate to enter into collaborative studies with Jamie Rossjohn (Monash) and Jim McCluskey (UoM). Using protein chemistry, molecular immunology and crystallography, these guys have been making great progress in understanding TCR-peptide-MHC recognition and we soon realized that there was a great opportunity to apply this approach to understanding glycolipid antigen recognition by NKT cells. This has been instrumental in helping us understand the fundamental feature that defines NKT cells and distinguishes them from other T cell types – that is, CD1d-restricted lipid antigen specificity. This has shown us how the same basic αβTCR complex that is normally associated with peptide-MHC recognition, can confer reactivity to such distinct antigenic targets as lipid antigens presented by CD1d. Furthermore, this work is informing us about the molecular constraints that govern self and foreign lipid antigenicity, and TCR diversity within the NKT cell family, and extending to the broader family of non-MHC restricted, innate-like T cells including: γδ T cells, CD1a, CD1b, CD1c-restricted T cells, and MR1-restricted MAIT cells. One thing that I am becoming increasingly certain of: the more we look, the more we realize how much we don't yet understand in the field of immunology!

While I have mentioned some of my key collaborators that have influenced my research directions, it goes without say that these studies could never have progressed without the fantastic and tireless efforts of the many Honours and PhD students, postdocs, and research assistants that I have worked with in my team, and my collaborators teams, over the years since my return to Australia. There are too many to mention here, but I am extremely grateful to all of

them. I would like to mention one person, Dr Jared Purton, whose burgeoning research career was tragically cut short when he was killed in a car accident two years ago while working as a senior postdoc in San Diego. Jared undertook a very successful honours, PhD and first postdoc appointment under the supervision of Tim Cole and myself. He was well on his way to running his own independent team while working at Scripps Research Institute. He was a great scientist, a lovely fellow, and he is sadly missed.

For a little more detail on some of the current projects underway in 'The NKT cell lab', I will hand it over to the individuals that make up the current team, who can be seen day and night slaving away at the bench in the NKT laboratory.

Catarina Almeida, PhD student

I am conducting a PhD under the co-supervision of Dale and Dr Adam Uldrich. I completed Biochemistry (2007) at the University of Lisbon, Portugal where I developed a big interest in immunology, consequently, pursued the objective to do a MSc thesis in one of the two best Portuguese research institutes in this field –Instituto de Medicina Molecular (IMM), at the Faculty of Medicine in Lisbon – the Cellular Immunology Unit directed by Dr. Luis Graca, being also an external group from Instituto de Gulbenkian para a Ciência (IGC). There I focused on the plasticity and modulation of Type I NKT cells in immune mediated diseases, recurring to animal models of asthma and multiple sclerosis. After two years of lab work I decided to chase a PhD down to Australia with one of the most well known groups in the field of NKTs. So, now I am trying to understand how Type II NKT cells recognize, interact and respond to CD1d bound to different glycolipids. Although I'm still chasing just a few dots on a dot plot, my approach has a strong biochemical component as I try to express and refold several Type II TCRs. One of my non-lab favorite activities is kayaking. In Portugal I was the national vice-champion of sea kayaking. Here in Australia I paddle for Ivanhoe Northcote Canoe Club doing some marathons and adventure races. I am also the Vice-president of SPASIM, the postgraduate student association for the Dept of Microbiology and Immunology.

Garth Cameron, PhD student

I completed a Bachelor of Science (Biotechnology) at RMIT before moving over to the University of Melbourne in 2009 to do Honours in the Godfrey lab. I am currently in the third year of my PhD investigating the range of different glycolipid antigens recognized by the NKT cell TCR, with a focus on tumour-associated glycolipid antigens. I am interested in the way the NKT cell functional response can be modulated by modifications in glycolipid structure, which particular glycolipid antigens are important in tumour recognition, and identifying how sequence diversity within the β-chain of the semi-invariant NKT cell TCR participates in glycolipid antigen specificity.

Marcin Ciula, Research Assistant & Lab Co-ordinator

I am Monash graduate having completed my Honours project in Dr Ashley Mansell's group on TLR STAT3 signaling in 2008. I joined the Godfrey lab in 2009 working as a research assistant under the supervision of Dr Sumone Chakravarti. As of this year, I work directly for Dale as a research assistant and lab co-ordinator. My research work has encompassed various facets of NKT cells using in vitro and in vivo experiments to study their development and function, including their role in regulating EAE. More recently, alongside Daniel Pellicci, my work has also involved antigen recognition by NKT TCRs. In addition to my research, my work involves managing the regulatory, safety, training and everyday running needs of the laboratory as well as working with a great group of scientists.

Rhiannon Clanchy, Honours student

The field of immunology first captured my interest in late high school while I was undertaking VCE Biology. It developed into a passion during my undergraduate degree at the University of Melbourne, an institute where I was fortunate enough to be exposed to many aspects of immunology and a variety of research projects. As a result, my fascination with immunology grew and, therefore, it is not surprising that I find myself completing an Honours degree in a joint venture between the Godfrey and Doherty/Turner labs to employ a retrogenic mouse model to explore the development and functional characteristics of three distinct types of NKT cells. Thus far, this has been a fascinating and thrilling introduction to research science and one I hope to continue into a PhD and hopefully a career as an immunologist.

Nick Gherardin, PhD student

After completing a Bachelor of Biomedicine at the University of Melbourne, I developed a keen interest in human disease, and particularly the role of the immune system.

I pursued this interest during an Honours year last year, and have recently started my PhD. I am currently a member of two laboratories – both the Godfrey Lab at the University of Melbourne, as well as the Haematology Immunology Translational Research Lab (HITRL) at the Peter MacCallum Cancer Centre. My project focuses on studying the role of unconventional T lymphocyte subsets in the setting of cancer. My work in the Godfrey Lab involves characterisation of MAIT and CD1-restricted human lymphocyte subsets across phenotypic, functional and molecular levels, while HITRL allows me to translate this knowledge into the disease setting, with a focus on multiple myeloma. Working at the interface between fundamental immunology research and translation to the clinic is a particularly exciting aspect of my work.

Dale Godfrey, Head of NKT cell laboratory at University of Melbourne

NHMRC Senior Principal Research Fellow and Vice President 2012/incoming President for the Australasian Society for Immunology

Hui-Fern Koay (Fern), PhD student

My research experience started in the Peter MacCallum Cancer Centre, working in conjunction with the Godfrey lab, where we explored the potential responses of T and NKT cells induced by activated B-chronic lymphocytic leukemic cells. With that I received my Honours degree from the University of Melbourne in 2011, and I am now excited to commence my PhD studies in the Godfrey Laboratory, co-supervised by Dale and Dr Jamie Rossjohn at Monash University. I am interested in the molecular constraints that govern foreign versus self-lipid antigenicity, and the functional outcomes of NKT cell activation by distinct types of lipid antigens. Hence my PhD project will employ a combination of cellular and molecular approaches to investigate how distinct NKT cell types respond to a broad range of self and foreign lipid antigens.

Kirsty MacPherson, Research Assistant

I have been a member of the NKT lab since 2009, when I signed on as a research assistant under the supervision of Dr Sumone Chakravarti, working on functionally distinct subsets, their role in EAE, and (in collaboration with Steve Turner), the epigenetic basis for their distinct cytokine profiles. I am now working under the cosupervision of Dale and Dr Adam Uldrich where my primary project is exploring the diversity of CD1d restricted T cells in humans, including γδ and αβ NKT cells.

Ben O'Sullivan, Research Assistant

A simple country lad, my science career began when I moved to the city to study a Bachelor of Biotechnology at Monash University. I completed my Honours year focusing on aetiology of Type 1 Diabetes in 2010 with Robyn Slattery in Monash's Dept of Immunology. My focus was directed towards NKT cells as a Research Assistant

in Dale's lab at the University of Melbourne in mid-2011. Recently, I have once again succumbed to the lure of tertiary education by commencing a Bachelor of Medicine at Deakin University in 2012. Fortunately I am maintaining part-time RA work, and a link with the cutting edge world of science, in Dale's lab which also provides a means to support my Medicine venture. I hope to eventually meld my research and medical experience to actualise improved community health outcomes.

Daniel Pellicci, PhD student

I am in the process of completing my PhD (co-supervised by Dale and Jim McCluskey), after having worked for many years in the Godfrey 'NKT' lab where I started out as a Research Assistant in 1999 when the lab was still based at Monash University. I have worked on many different facets of NKT cell biology, including mouse NKT cell development and function, using in vivo and in vitro models. A few years ago I delved headlong into glycolipid biochemistry in search of CD1d restricted tumour antigens in a collaboration between Dale, Mark Smyth, and Malcolm McConville, and more recently I have transformed into a molecular immunologist, where my focus has been the study of foreign and self glycolipid antigen recognition by NKT TCRs at the molecular level, working in a collaborative project between Dale, Jim McCluskey and Jamie Rossjohn.

Fiona Ross, PhD student

I completed a BSc at the University of Melbourne with a Microbiology/ Immunology major. Following this I completed my Honours year in the Godfrey Laboratory under the supervision of Dale and Stuart Berzins, focusing on the role of NKT cells in the NOD mouse model of Type 1 Diabetes. After enjoying the year immensely, I continued on to a PhD, also supervised by Dale and Stuart, however my interest shifted to the interaction between NKT cells and different types of antigen-presenting cells. More recently, following the flow of the lab, I have also been delving into the role of phospholipid antigens in NKT cell activation.

Adam Uldrich, Postdoc

After completing my undergraduate degree at Monash University, I undertook a PhD under the co-supervision of Dale and Richard Boyd on the maturation of T cells and NKT cells in the thymus. Pursuing my interest in innate immunity I then moved to the Peter MacCallum Cancer Centre working with Mark Smyth where, with the assistance of a Doherty training fellowship, I studied the role of NKT cells in tumour surveillance. I am now working at Melbourne University as a senior postdoc in Dale's lab and in close collaboration with Jamie Rossjohn, continuing my studies of NKT cells and glycolipid immunity. I have been working in the exciting area of cell discovery, identifying previously unrecognized subsets of lipid-antigen reactive NKT cells.

John Waddington, Research Assistant

I have just started as a Research Assistant in the NKT Laboratory at Melbourne University. My previous employment has been mainly in the Victorian Agriculture Department where I worked in cell culture and virology and gained extensive experience in culturing primary cell cultures and continuous cell lines, animal virus production, protein purification and immunology. I am delighted to have joined such a very enthusiastic and hard working group and I am keen to assist and learn from other members of the team about the important role played by NKT TCRs in the recognition of self and non-self recognition glycolipid antigens.

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.

Below, LtoR: Dale Godfrey, Daniel Pellicci, Rhiannon Clanchy, Adam Uldrich, Catarina Almeida, John Waddington, Marcin 'Marty' Ciula and Fiona Ross

Key Dates

May 2012 - Abstracts Open

June 2012 - Registration Open

1 September 2012 - Early Bird Registration Close & Abstracts Close

2 - 6 December 2012 - Meeting Dates

Organising Committee

Co-chairs: Prof. Stephen Turner & A/Prof. Rose Ffrench
A/Prof. Frank Alderuccio
Dr. Susanne Heinzel
Dr. Nicole La Gruta
Dr. Meredith O'Keefe
Dr. Stuart Mannering
Dr. Ed Hawkins
Dr. Stuart Berzin
Prof. Phil Hodgkin
Dr. Daniel Layton

Scientific Advisory Committee

Chair: Prof. Stephen Turner
A/Prof. Rose Ffrench
A/Prof. David Tarlinton
Prof. Fabienne Mackay
Prof. Paul Hertzog
Prof. Mark Smyth
Prof. Dale Godfrey
Prof. Sharon Lewin
Prof. Anne Kelso
Prof. Bill Heath
Dr. Li Wu
Prof. Charles Mackay
Dr. James Beeson

Conference Managers

arinex Pty Ltd
91-97 Islington Street
Collingwood, VIC 3066
P: + 61 3 9417 0888
F: + 61 3 9417 0899
E: asi2012@arinex.com.au

MELBOURNE 2-6 DECEMBER
2012

42ND ANNUAL SCIENTIFIC MEETING OF THE
AUSTRALASIAN SOCIETY FOR IMMUNOLOGY

Invited Speakers

- **Prof. Xuetao Cao**
  Zhejiang University, School of Medicine, China
- **Prof. Eicke Latz**
  University of Massachusetts, USA
- **Prof. Eric Vivier**
  Centre d'Immunologie de Marseille-Luminy, France
- **Dr. Sidonia Fagarasan**
  Riken Research Centre for Allergy and Immunology, Japan
- **Prof. Pippa Marrack**
  Jewish Medical Centre, USA
- **Prof. Bali Pulendren**
  Emory University, USA
- **Prof. Olivier Lantz**
  Harvard University, USA
- **Dr. Rafael Casellas**
  National Cancer Institute, USA
- **Prof. John Cambier**
  University of Colorado, USA
- **Prof. Sarah Rowland-Jones**
  John Radcliffe Hospital, UK
- **Dr. Jedd Wolchock**
  NYU Medical Centre/Bellevue Hospital , USA

www.asi2012.org

Graham Jackson Memorial Prize for Mucosal Immunology

Inflammation in the Gut 'Stresses Out' Secretory Cells

Sumaira Z. Hasnain

Immunity, Infection and Inflammation Program, Mater Medical Research Institute and the University of Queensland

I would like to thank the editor for inviting me to contribute to ASI newsletter and allowing me to share our recent work at the Mater Medical Research institute. I would also like to take this opportunity to thank the ASI for awarding me the Graham Jackson Mucosal Immunology Prize for this work which I presented at the ASI annual conference in December 2011.

I have always had a keen interest in gastrointestinal inflammation and during my Medical Biochemistry degree I became fascinated with the host-parasite relationship. What distinguishes parasites from other modes of life is its adaptive interaction with the host, where both are concerned with their own survival. How this balance between the parasite and the host is achieved was the initial curiosity that led me to pursue a PhD at the University of Manchester (UK), which focussed on exploring the role of the intestinal mucosal barrier in nematode (worm) infections. We discovered a pivotal role of mucosal barrier components as effectors that facilitate worm expulsion, and demonstrated how the worm manipulates the immune response to exert its effects on the mucosal barrier in order to promote its own survival within the host [1,2]. So after graduating with my doctorate in December 2010 I moved to the Mater Medical Research Institute to Prof. Michael McGuckin's internationally reputed laboratory to explore the role of inflammation in the maintenance of mucosal barrier function.

The intestinal mucosal barrier is a highly dynamic first layer of defence that has evolved to be highly responsive to physiological and immunological stimuli. In fact, the intestine is the largest reservoir of commensal microbiota and the impermeable extrinsic mucus layer covering the epithelium ensures that our immune system does not overreact to the microbiota. This mucus layer is not just "slime" but an organised extracellular matrix containing a complex mixture of inorganic salts, water and large glycoproteins called mucins which determine the rheological gel-like properties of the mucus barrier [3]. The secretory 'goblet' cells within the crypts of the intestinal epithelium invest a large amount of energy in the production and storage of mucins within granules, which are then released constitutively or in response to specific stimuli [4].

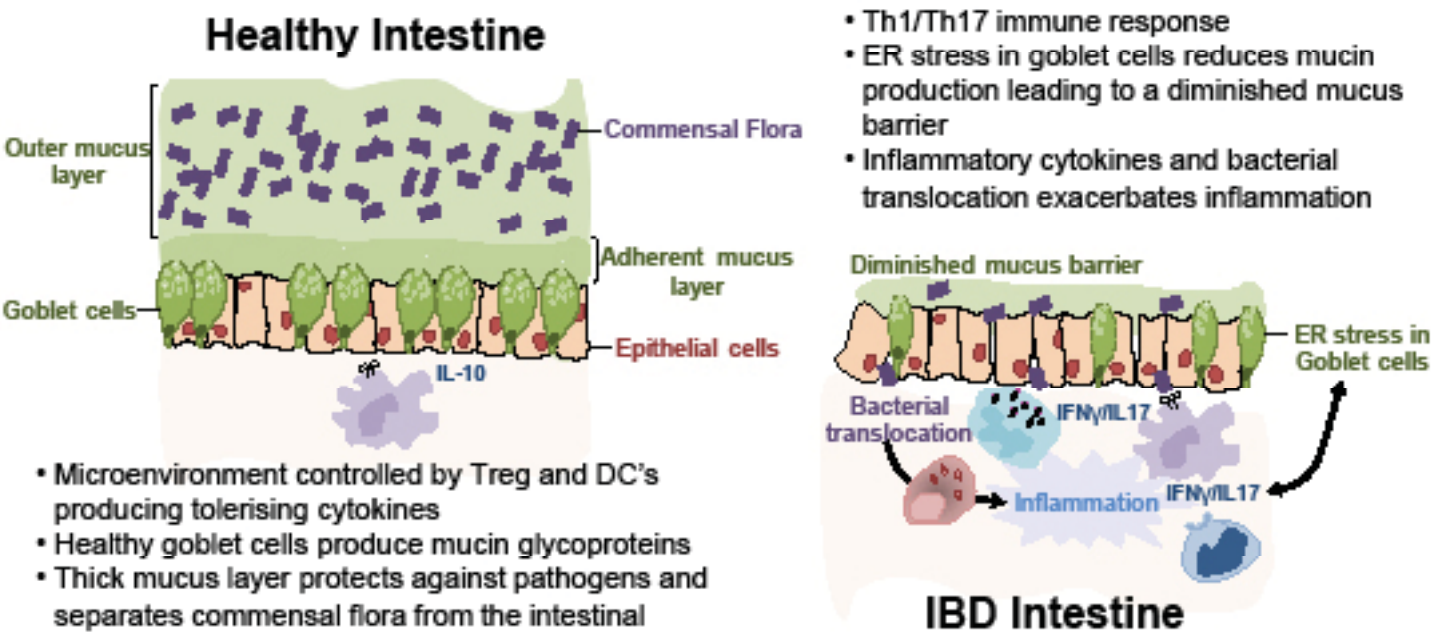
The intestinal mucin MUC2 is a large >5000 amino acid protein synthesised in the endoplasmic reticulum (ER) where it dimerises before it is densely decorated with O-glycan sugars in the Golgi. Once secreted, there is over a 100-fold expansion of the glycosylated domains of the secreted mucins due to hydration resulting in an extensive organised network within the mucus layer. MUC2 requires the biosynthesis of 31 N-glycans and contains 215 cysteines, therefore it is not surprising that it presents a substantial challenge for correct folding in the ER. Interestingly, a proportion of all proteins misfold during biosynthesis and with an increase in the complexity of the protein there is an increase in protein misfolding. However, secretory cells such as goblet cells with a high throughput of complex protein synthesis have evolved mechanisms to cope with protein misfolding by initiating the unfolded protein response (UPR). Consequently, resolving ER stress by decreasing protein synthesis, facilitating

folding and degrading misfolded proteins through the ER associated degradation (ERAD) pathway [5]. During inflammation there is an increase in the demand for the production of mucins which can lead to an increase in protein misfolding and ER stress, and chronic ER stress can trigger inflammation [6].

ER stress has been linked to the pathophysiology of several diseases including autoimmune diseases such as diabetes and spondyloarthropathy as we reviewed recently [6]. We have proposed

L-R: Penny Jeffery, Ran Wang, Alice Chen, Sumaira Hasnain, Indrajit Das, Mike McGuckin, Thu Tran, Kirsten Gerloff, Yong Sheng

Figure 1



that protein misfolding and ER stress in intestinal secretory cells is a significant contributor to inflammatory bowel disease (IBD). Data from several murine models unequivocally demonstrate that intestinal secretory cells are susceptible to ER stress due to high rates of protein biosynthesis, and that environmental ER stressors, mutations in secreted proteins, alterations to their post-translational modifications and disturbances to the UPR can perturb homeostasis leading to colitis. Therefore, understanding and modulating cellular ER stress during inflammation has therapeutic potential for IBD. In collaboration with Chris Goodnow and the Australian Phenomics Facility Mike McGuckin's laboratory was the first to report and fully characterise the *Winnie* mouse model [7,8], where misfolding of the Muc2 mucin in goblet cells due to a single missense mutation is the initiating event leading to spontaneous colitis. The accumulation of misfolded Muc2 in the ER, results in the initiation of the UPR and ER stress leading to a reduction in fully formed glycosylated mucin production and therefore a depleted mucus layer. The diminished mucus barrier could result in exacerbating inflammation, not only due to increased foreign toxin and antigen exposure but also because of the commensal flora coming into contact with epithelium (*Figure 1*). The *Winnie* mice develop complex Th1/Th17 immune response akin to that observed in ulcerative colitis, and it is clear that inflammation plays an important role in exacerbating the pathophysiology. *RaW* mice (*Winnie* mice crossed with immunodeficient *Rag1* knockouts) develop innate inflammation but have reduced colitis, and treatment of *Winnie* mice anti-inflammatory drugs which is common practice in IBD reduces ER stress, restores mucin production and ameliorates colitis.

Deciphering the fundamental issue of whether the initiation of ER stress is a primary or secondary event which leads to inflammation is challenging. However, another way of dissecting this "chicken or egg" question is to ask where and how ER stress intersects with inflammation. Using the *Winnie* model and an *in vitro* intestinal secretory cell model we have we have uncovered a novel role for the colitis-associated pro-inflammatory cytokines, IFNγ and IL-17, in inducing ER stress and a role for the regulatory cytokine IL-10 in suppressing ER stress. IFNγ and IL-17 induced *XBP1* splicing, which is a direct measure of the activity of the UPR endonuclease IRE1 activated by ER stress and this was abolished when cells were concomitantly treated with IL-10. Importantly, IL-10 also alleviated ER stress caused by the N-glycosylation inhibitor tunicamycin which causes protein misfolding. We have discovered that IL-10 suppresses ER stress by altering the ER microenvironment, enhancing the degradation of misfolded proteins and promoting the correct folding of MUC2, and its successful exit from the ER, O-glycosylation and secretion into the mucus layer.

Corroborating these *in vitro* observations, blocking IL-10 signalling *in vivo* in *Winnie* mice, in which mucin misfolding initiates ER stress and colitis, rapidly exacerbated inflammation and ER stress including increased accumulation of misfolded Muc2. This suggested that IL-10 might not only control inflammation, but also directly suppress ER stress. Strikingly, *Winnie* mice haplosufficient for IL-10 and IL-10$^{-/-}$ mice carrying a single *Muc2*^{Win} allele developed very severe inflammation through all regions of the intestine.

Overall, this study highlights new insights into how ER stress arises and how it is integrated with inflammation. Anti-inflammatory therapy is one of the most common treatments for IBD illustrating that ongoing immunosuppression in the face of chronic inflammation is important. However, broad immunosuppressive

therapy leads to secondary complications by compromising immunity to infections. Therefore, understanding the nature of ER stress and the inflammatory cues that contribute to ER stress such as those defined in this study will lead to the development of specific and appropriate drugs and biologicals.

Acknowledgements

First and foremost I would like to thank my mentor at the MMRI, Mike McGuckin, for his invaluable advice and encouragement. Thank you to Prof. Tim Florin for his continuous help and support. I would also like to thank all the members of the Immunity, infection and Inflammation group, in particular the authors (Sharyn Tauro, Indrajit Das, Alice Chen, Penny Jeffery, and Victoria McDonald) for their contribution to this study.

References

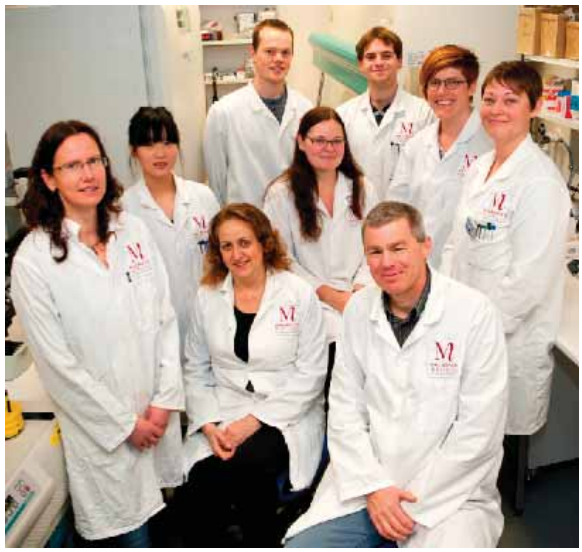
1. Hasnain SZ, Evans CM, Roy M, Gallagher AL, Kindrachuk KN, et al. (2011) Muc5ac: a critical component mediating the rejection of enteric nematodes. J Exp Med.
2. Hasnain SZ, Wang H, Ghia JE, Haq N, Deng Y, et al. (2010) Mucin Gene Deficiency in Mice Impairs Host Resistance to an Enteric Parasitic Infection. Gastroenterology 138: 1763-1771.
3. McGuckin MA, Linden SK, Sutton P, Florin TH (2011) Mucin dynamics and enteric pathogens. Nat Rev Microbiol 9: 265-278.
4. Hasnain SZ, Thornton DJ, Grencis RK (2011) Changes in the mucosal barrier during acute and chronic Trichuris muris infection. Parasite Immunol 33: 45-55.
5. Walter P, Ron D (2011) The unfolded protein response: from stress pathway to homeostatic regulation. Science 334: 1081-1086.
6. Hasnain SZ, Lourie R, Das I, Chen AC, McGuckin MA (2012) The interplay between endoplasmic reticulum stress and inflammation. Immunol Cell Biol.
7. Eri RD, Adams RJ, Tran TV, Tong H, Das I, et al. (2011) An intestinal epithelial defect conferring ER stress results in inflammation involving both innate and adaptive immunity. Mucosal Immunol 4: 354-364.
8. Heazlewood CK, Cook MC, Eri R, Price GR, Tauro SB, et al. (2008) Aberrant mucin assembly in mice causes endoplasmic reticulum stress and spontaneous inflammation resembling ulcerative colitis. PLoS Med 5: e54.

Mucosal Immunology Poster Prize

Supported by Jomar Bioscience

Winner: Marcus Robinson

Malaghan Institute of Medical Research, New Zealand



Graham Le Gros' lab group (LtoR): Mel Prout, Shiau-Choot Tang, Mali Camberis, Marcus Robinson, Cat Plunkett, Ryan Kyle, Prof. Graham Le Gros, Helen Mearns, Dr Liz Forbes-Blöm.

ASI 2011, held in Adelaide last December, was my first international conference. I was pleased to find that students, post-docs and established scientists are willing to discuss their work before it is available in the literature. Thank you, organisers, for a full and informative meeting. I also thank Ian and Rodney at Jomar Biosciences for the Mucosal Immunology poster prize.

I am a PhD candidate under the supervision of Prof. Graham Le Gros at the Malaghan Institute of Medical Research. In collaboration with Dr Ali Hodgkinson at AgResearch, we have set out to elucidate: i) Why goat milk may be a weaker allergen than cow milk; and ii) How CD4+ T cells contribute to the post-sensitization phase of food allergy. The poster I presented at ASI 2011 focussed on the latter, examining the role of CD4+ T cells and IL-3 in the generation of intestinal priming that results in oral allergen-induced diarrhoea.

We used a murine model of intestinal anaphylaxis (1), in which mice are first sensitized to ovalbumin (OVA) by intraperitoneal injection of OVA plus Alum adjuvant, then orally challenged with OVA. This induces an allergic response in the intestine, resulting in transient, mast cell- and IgE-dependent diarrhoea (1).

One of the intriguing aspects of this system is that at least two oral allergen challenges are required before mice present with diarrhoea. That is, there is an oral priming process that precedes disease elicitation. Previous investigations have suggested a role for CD4+ T helper type 2 (Th2) cells in oral allergen hypersensitivity (2-5). Therefore, I tested the hypothesis that CD4+ T cells are required to generate gastric priming. To address this, CD4+ T cells were depleted with GK1.5, and this prevented both mastocytosis and allergic diarrhoea. When CD4+ T cells were replenished, allergic diarrhoea began to develop. The converse, however, did not appear to be true – if CD4+ T cells were depleted following established allergic diarrhoea, most mice remained susceptible to allergen-induced diarrhoea. These findings suggest that at least two components are involved in the intestinal allergic response; CD4-dependent priming and susceptibility to the development of allergic diarrhoea, and CD4-independent disease maintenance. These results may explain, at least in part, why desensitization strategies can require multiple doses over a significant period of time – if IgE-loaded mast cells can be repeatedly activated in the absence of allergen specific Th2 CD4+ T cells, there is a potential disconnect between adaptive tolerance (loss of allergy-promoting CD4+ T cell and B cell function) and the loss of clinical reactivity.

Finally, we addressed the mechanism by which CD4+ T cells induce mastocytosis in the small intestine. IL-4 and IL-9 knock-out mice are protected from the development of allergic diarrhoea(2, 6), and along with IL-3(7) these cytokines contribute to helminth-induced intestinal mastocytosis(8, 9). We asked whether IL-3 also contributes to mastocytosis driven by oral priming to OVA. Following oral challenge, mice deficient in IL-3 had fewer mast cells in the small intestine than wildtype mice, and were protected from allergic diarrhoea. However, IL-3$^{-/-}$ mice, like IL-9$^{-/-}$ mice (2), still showed signs of oral priming (including increases in serum IgE over mock-challenged mice). We are currently investigating the possibility that IL-3, in addition to augmenting mastocytosis, promotes the development of functionally specialised pro-allergic intestinal mast cells. We hope to have the answer soon. If you are at the New Zealand ASI branch meeting, perhaps I'll be able to tell you then. Otherwise, I hope to get to the conference in Melbourne and see what will be happening in Australasian immunology in 2013.

References

1. Brandt, E.B., Strait, R.T., Hershko, D., Wang, Q., Muntel, E.E., Scribner, T.A., Zimmermann, N., Finkelman, F.D., and Rothenberg, M.E. 2003. Mast cells are required for experimental oral allergen-induced diarrhea. *Journal of Clinical Investigation* 112:1666-1677.
2. Forbes, E.E., Groschwitz, K., Abonia, J.P., Brandt, E.B., Cohen, E., Blanchard, C., Ahrens, R., Seidu, L., McKenzie, A., Strait, R., et al. 2008. IL-9- and mast cell-mediated intestinal permeability predisposes to oral antigen hypersensitivity. *Journal of Experimental Medicine* 205:897-913.
3. Knight, A.K., Blazquez, A.B., Zhang, S., Mayer, L., Sampson, H.A., and Berin, M.C. 2007. CD4 T cells activated in the mesenteric lymph node mediate gastrointestinal food allergy in mice. *American Journal of Physiology – Gastrointestinal and Liver Physiology* 293: G1234-G1243.
4. Blazquez, A.B., Knight, A.K., Getachew, H., Bromberg, J.S., Lira, S.A., Mayer, L., and Berin, M.C. 2008. A Functional Role for CCR6 on Proallergic T Cells in the Gastrointestinal Tract. *Gastroenterology* 138:275-284.e274.
5. Kweon, M.N., Yamamoto, M., Kajiki, M., Takahashi, I., and Kiyono, H. 2000. Systemically derived large intestinal CD4 + Th2 cells play a central role in STAT6-mediated allergic diarrhea. *Journal of Clinical Investigation* 106:199-206.
6. Brandt, E.B., Munitz, A., Orekov, T., Mingler, M.K., McBride, M., Finkelman, F.D., and Rothenberg, M.E. 2009. Targeting IL-4/IL-13 signaling to alleviate oral allergen-induced diarrhea. *Journal of Allergy and Clinical Immunology* 123:53-58.
7. Lantz, C.S., Boeslger, J., Song, C.H., Mach, N., Kobayashi, T., Mulligan, R.C., Nawa, Y., Dranoff, G., and Galli, S.J. 1998. Role for interleukin-3 in mast cell and basophil development and in immunity to parasites. *Nature* 392:90-93.
8. Faulkner, H., Renauld, J.C., Van Snick, J., and Grencis, R.K. 1998. Interleukin-9 enhances resistance to the intestinal nematode Trichuds muris. *Infection and Immunity* 66:3832-3840.
9. Finkelman, F.D., Shea-Donohue, T., Morris, S.C., Gildea, L., Strait, R., Madden, K.B., Schopf, L., and Urban Jr, J.F. 2004. Interleukin-4- and interleukin-13-mediated host protection against intestinal nematode parasites. *Immunological Reviews* 201:139-155.

Major Poster Prize Winner

Wai-Yan (Kiwi) Sun
IMVS, University of Adelaide

People in research always say "join one or two professional societies and go to their annual meetings, it is always good for networking because you never know when you need help and collaboration." I cannot agree more. I joined ASI as my first ever professional society in my Honours year in 2006 and since then, I have been involved in organizing our state student events, attended the annual meetings and I even co-organized the ASI student function in 2011 where I made a lot of friends and gained advice and mentorship for my research project.

Last year, it was easy enough for me to attend the annual meeting as it was held in my home town, Adelaide. In the 5-day ASI annual meeting, I presented my PhD work in the Allergy poster session on the second day and my poster was awarded one of the top student presentation prizes.

The focus of my PhD is the regulation of allergic inflammation. In my studies, I aim to investigate new therapeutic approaches to tackle mild to severe allergic inflammation which currently affect 20-25% of the population world-wide and result in AU$7 billion medical costs annually. Literature well describes that allergic inflammation is initiated by the presence of allergens, which is then presented by antigen presenting cells and T-helper cells for the subsequent B cells production of specific IgE antibodies to trigger mast cell activation. As important, endothelial cells (EC) lining the inside of blood vessels control the recruitment of leukocytes from the circulation as well as vaso-permeability which leads to leukocyte emigration to the sites of inflammation. This mechanism of leukocyte recruitment by ECs is adhesion molecule-dependent. For example, P-selectin is expressed by ECs within minutes of exposure to histamine and

promotes the immediate increase in leukocyte tethering and rolling along the vasculature which then allows the circulating leukocytes to reduce their velocity prior to firm adhesion and transmigration. Precisely, how P-selectin is expressed on ECs within the immediate/ early stages of allergic inflammation and whether regulation of P-selectin surface expression can attenuate this disease is yet to be determined.

Under the supervision of Dr Claudine Bonder in the Vascular Biology and Cell Trafficking Laboratory at the Centre for Cancer Biology, Adelaide, South Australia, we are investigating whether sphingosine kinase (SK) is a key regulator of allergic inflammation via its control of P-selectin expression. SK is a lipid kinase which catalyses the phosphorylation of sphingosine to form sphingosine-1-phosphate (S1P). Both SK catalytic activity and the product S1P are important to determine cell fate, such as proliferation, survival and activation.

In April, we published 'Rapid histamine-induced neutrophil recruitment is sphingosine kinase-1 dependent' in Am J Pathology. Briefly, we have shown that human umbilical cord endothelial cells (HUVEC) rapidly express surface P-selectin within five minutes of histamine exposure which mimics the early phase of allergic inflammation where the ECs are activated for initial leukocyte interactions (Figure 1). Inhibition studies using specific inhibitors antagonize either SK or its pathway exhibited a decrease in histamine-induced P-selectin surface expression. To examine the biological function of histamine-induced P-selectin by HUVECs, we utilized a parallel plate flow chamber (in vitro system mimicking the interactions of blood cells and ECs under shear stress). Our results show that 5 minutes of histamine perfusion causes a significant increase in leukocyte rolling events on HUVECs per field of view under flow, and such histamine-induced rolling events were attenuated when HUVECs were pre-treated with either P-selectin blocking antibody or SK pathway inhibitors (SKi or DMS). This observation is important as P-selectin is well described to be responsible for rapid leukocyte recruitment during allergic inflammation. Thus, abrogation of P-selectin expression by HUVECs may be one of the keys to controlling an inflammatory response.

To investigate our hypothesis in a more complex biological system, we used our scientific and social networking advantage to collaborate with A/Prof Michael Hickey and his team for in vivo mouse model at the Medical Centre of Monash University, Melbourne (that's why becoming a member of a professional society is important!). We examined the effect of SKi treatment for histamine-induced leukocyte recruitment using the 2-photon intravital microscopy.

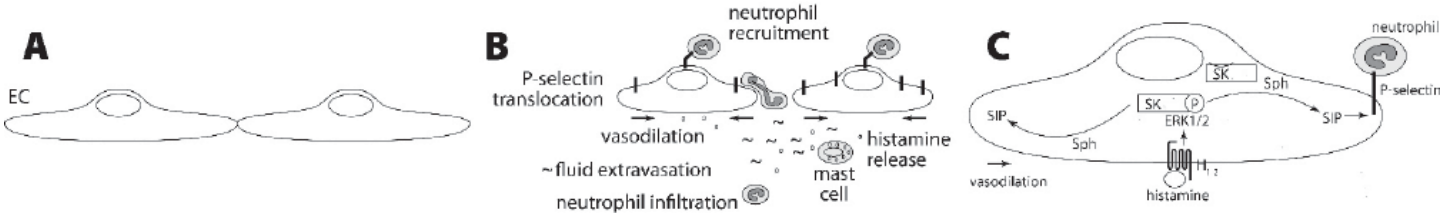


Figure 1

A role for SK in allergic inflammation. In (A), endothelial cells (EC) form a tight junction. In (B), allergen exposure causes mast cells to release histamine, ECs become activated, vasodilate & express P-selectin which recruits neutrophils. In (C), histamine-induced neutrophil recruitment occurs via histamine activation of the SK which translocates to the plasma membrane to convert sphingoinse to S1P and subsequent P-selectin expression.

In a post-capillary venule of a cremaster muscle of anethesized mice, leukocyte rolling numbers in response to histamine superfusion was increased significantly at the peak of 5 minutes post perfusion. Then, the rolling events subsided gradually to basal levels over time. By contrast, mice pretreated with SKi by subcutaneously injection prior to histamine perfusion exhibited a reduction in leukocyte rolling when compared to controls.

Future direction of this project is to focus on new therapeutic approach to treat and prevent allergic inflammation. Fingolimod is an oral pro-drug interfering the SK pathway and has been approved in clinical use for patients with multiple sclerosis. In addition to Dr Claudine Bonder's supervision, I am currently getting advice from Dr Michele Grimbaldeston (Centre for Cancer Biology, Adelaide; present SA/NT State Councillor of ASI) for the animal models of passive cutaneous anaphylaxis and histamine-induced local inflammation with the treatment of Fingolimod. Our ultimate goal is to combat allergic inflammation by using small molecule treatment. The significance of this study will help reduce anaphylaxis caused mortality, reduce the massive medical cost and increase quality of life.

Finally, as a second year PhD student, I truly understand and agree that having a good scientific and social network does help me a lot with my research project. Although I still have a mile to go till the end of my PhD journey, I appreciate all mentors and collaborators who have contributed and will continue to contribute to my research road. Of course, I thank the little black furry fellows (in the photo with me) who are "involved" in my experiment too!

Australian Biosearch Poster Prize

Bone marrow gene therapy following non myeloablative pre conditioning to induce immune tolerance

Zeyad Nasa

The Autoimmunity and Gene Therapy Laboratory, Department of Immunology, The Alfred Hospital Medical Research Precinct (AMREP), Monash University

To begin with, I would like to thank the ASI and the newsletter editor for giving me the opportunity to briefly describe my winning poster. I was one of the lucky ones to have been awarded the Poster Encouragement Award at the 41st meeting of the Australian Society for Immunology in Adelaide (Nasa, Chung J. et al. 2011). The work presented in the poster is part of my PhD study carried out in the Autoimmunity and Gene Therapy Laboratory (AGTL) at the Department of Immunology, Monash University. The AGTL is headed by Associate Professor Frank Alderuccio who has had a long-standing interest in understanding mechanisms of tolerance and developing novel strategies for the treatment of autoimmune disease.

Autoimmune diseases such as multiple sclerosis, type 1 diabetes, systemic sclerosis, and rheumatoid arthritis are characterized by a chronic adaptive immune response that targets self-antigens and leads to clinical pathology. Current treatments of autoimmune diseases are often non-specific and do not address the cause, but aim to reduce symptoms and they may be associated with unwanted side effects. Multiple sclerosis (MS) and its animal model experimental autoimmune encephalomyelitis (EAE) are autoimmune diseases of the central nervous system and used as experimental models in our laboratory to develop a gene therapy approach to the treatments of autoimmune diseases with known autoantigens. The gene therapy approach involves the use of a retroviral vector to introduce defined self-antigens into bone marrow stem cells of donor animals and transferred into recipient mice (Figure 1).

The concepts revolve around the notion that gene therapy can be used to promote immunological tolerance and that this may be used in a clinical setting to treat autoimmunity. The underlying protocol would be similar to that currently used to cure children with X-linked SCID in which retrovirus encoding the cytokine common gamma chain is used ex vivo to transduce autologous bone marrow prior to re-transfusion (Chinen, Davis et al. 2007; Aiuti, Cattaneo et al. 2009).

We have previously shown that transplantation of bone marrow (BM) cells transduced with retrovirus encoding the myelin autoantigen

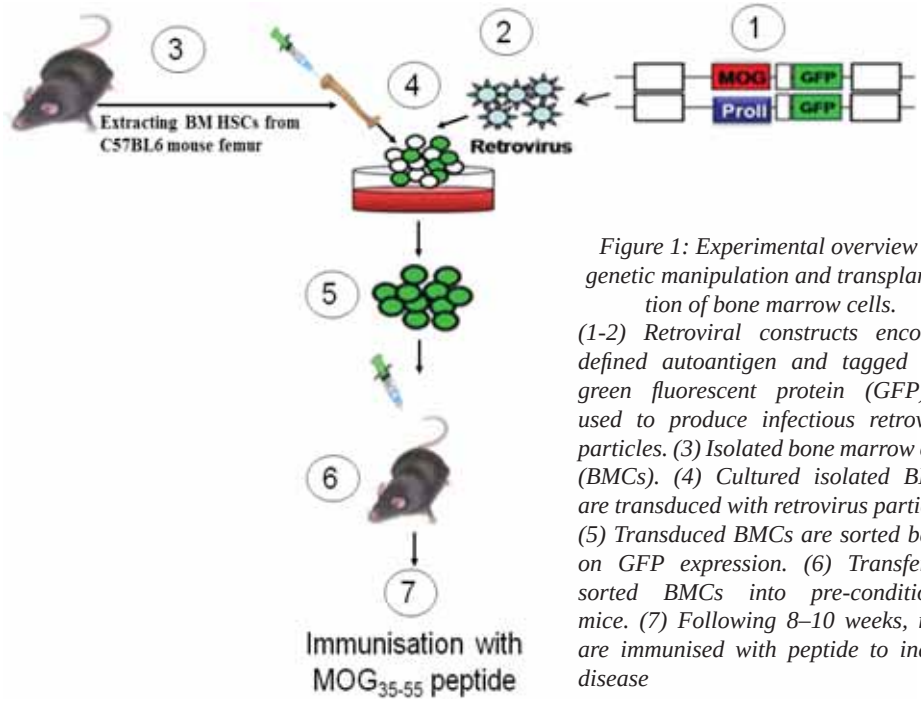
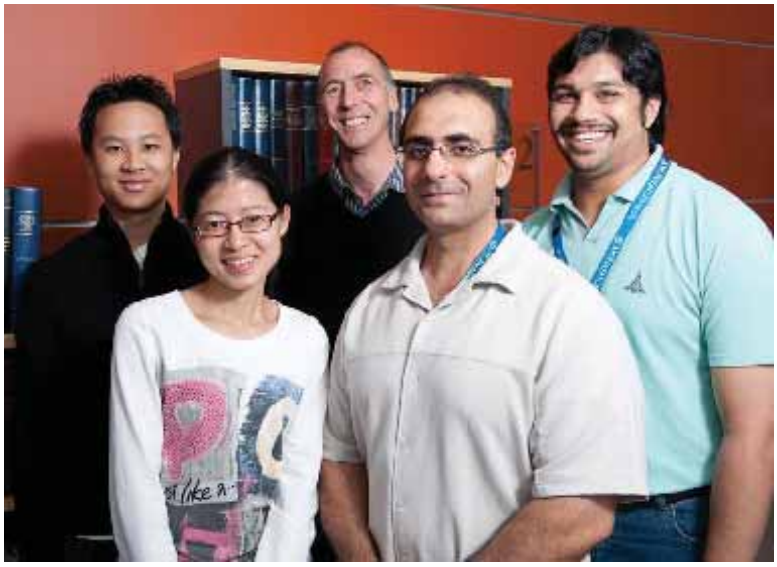


Figure 1: Experimental overview of genetic manipulation and transplantation of bone marrow cells. (1-2) Retroviral constructs encoding defined autoantigen and tagged with green fluorescent protein (GFP) is used to produce infectious retrovirus particles. (3) Isolated bone marrow cells (BMCs). (4) Cultured isolated BMCs are transduced with retrovirus particles. (5) Transduced BMCs are sorted based on GFP expression. (6) Transfer of sorted BMCs into pre-conditioned mice. (7) Following 8–10 weeks, mice are immunised with peptide to induce disease

Myelin Oligodendrocyte Glycoprotein (MOG) into total body irradiated mice can prevent the initiation of EAE (Chan, Ban et al. 2008). This work has shown the potential of utilising BM gene therapy to cure autoimmune diseases. However, the undesirable side effects or use of lethal total body irradiation remain an obstacle for translation to the clinic, therefore the search for a less toxic regimen is becoming increasingly important. In my study, we have investigated the use of Treosulfan as a less toxic preconditioning regime and assessed the induction of tolerance and disease susceptibility to provide potential clinical feasibility assessment. Treosulfan is mainly used in the treatment of ovarian cancer and recently used as preconditioning regimen for allogeneic haematopoietic stem cells transplantation in children with haematological malignancies (Glowka, Karazniewicz-Lada et al. 2008; Slatter, Rao et al. 2011).

Transfer of BM expressing MOG into myeloablated and non-myeloablated mice using Treosulfan had resulted in molecular chimerism and robust protection from the induction of EAE. Of particular interest, we find that only low levels of chimerism; in the order of a few percent, is sufficient to promote tolerance. We are currently working towards unravelling the potential mechanisms of tolerance but have previously shown that thymic deletion is active. Whether other mechanisms in central lymphoid organs or periphery are active remains to be determined. Moreover, in clinically relevant scenario of established EAE, we could also promote immune tolerance and long-lasting remission with non-myeloablative conditioning following transfer of transduced BM, even upon subsequent rechallenge with MOG-peptide. This work has recently been accepted for publication in *The American Journal of Transplantation* (Nasa, Chung et al. 2012).

These results add to the growing body of knowledge that shows immune tolerance to defined autoantigens can be promoted by transfer of genetically manipulated BM. In addition, the finding that it is also successful with lower toxic preconditioning regimes highlights potential clinically application and feasibility.



Members of the Autoimmunity and Gene Therapy Lab
LtoR: Jie-Yu Chunk (PhD student), Cai Zhank (PhD student), Frank Alderuccio (Lab head), Zeyad Nasa (PhD student) and Amit Joglekar (PhD student)

References:

Aiuti, A., F. Cattaneo, S. Galimberti, U. Benninghoff, B. Cassani, L. Callegaro, S. Scaramuzza, G. Andolfi, M. Mirolo, I. Brigida, A. Tabucchi, F. Carlucci, M. Eibl, M. Aker, S. Slavin, H. Al-Mousa, A. Al Ghonaium, A. Ferster, A. Duppenthaler, L. Notarangelo, U. Wintergerst, R. H. Buckley, M. Bregni, S. Marktel, M. G. Valsecchi, P. Rossi, F. Ciceri, R. Miniero, C. Bordignon and M. G. Roncarolo (2009). "Gene therapy for immunodeficiency due to adenosine deaminase deficiency." *N Engl J Med* **360**(5): 447-458.

Chan, J., E. J. Ban, K. H. Chun, S. Wang, B. T. Backstrom, C. C. Bernard, B. H. Toh and F. Alderuccio (2008). "Transplantation of bone marrow transduced to express self-antigen establishes deletional tolerance and permanently remits autoimmune disease." *J Immunol* **181**(11): 7571-7580.

Chinen, J., J. Davis, S. S. De Ravin, B. N. Hay, A. P. Hsu, G. F. Linton, N. Naumann, E. Y. Nomicos, C. Silvin, J. Ulrick, N. L. Whiting-Theobald, H. L. Malech and J. M. Puck (2007). "Gene therapy improves immune function in preadolescents with X-linked severe combined immunodeficiency." *Blood* **110**(1): 67-73.

Glowka, F. K., M. Karazniewicz-Lada, G. Grund, T. Wrobel and J. Wachowiak (2008). "Pharmacokinetics of high-dose i.v. treosulfan in children undergoing treosulfan-based preparative regimen for allogeneic haematopoietic SCT." *Bone Marrow Transplant* **42 Suppl 2**: S67-70.

Nasa, Z., J. Chung, J. Chan, B. T. Toh and F. Alderuccio (2012). "Non-myeloablative conditioning generates autoantigen-encoding bone marrow that prevents and cures an experimental autoimmune disease." *American Journal of Transplantation* **Accepted for publication**.

Nasa, Z., Chung J., Joglekar A., Chan J., Toh B.H. and F. Alderuccio (2011). "Bone marrow gene therapy following non myeloablative pre conditioning to induce immune tolerance." *Poster session presented at the 41st meeting of the Australasian Society for Immunology* (December 11–15, 2011; Adelaide, South Australia).

Slatter, M. A., K. Rao, P. Amrolia, T. Flood, M. Abinun, S. Hambleton, Z. Nademi, N. Goulden, G. Davies, W. Qasim, H. B. Gaspar, A. Cant, A. R. Gennery and P. Veys (2011). "Treosulfan-based conditioning regimens for hematopoietic stem cell transplantation in children with primary immunodeficiency: United Kingdom experience." *Blood* **117**(16): 4367-4375.

Contributions sought for the ASI Newsletter

You could win $200 !!

Deadline for the next issue: 1st August 2012

Please email your contributions to the Secretariat by the above date.
asi@21century.com.au

Coming soon...

Clinical & Translational Immunology

Nature Publishing Group and the Australasian Society of Immunology are proud to announce the upcoming launch of their newest title ***Clinical & Translational Immunology***, which will extend their publishing partnership as they already co-publish the prestigious and well-established journal *Immunology & Cell Biology*.

Topics of particular interest will be:

- cutting edge approaches including in vivo models of human disease that shed light on the mechanisms of immunity
- clinical studies with relevance to autoimmunity transplantation and tumor immunotherapy
- cutting edge immunoassays for monitoring clinical trials/patient responses
- infection and immunity – correlates of protection
- immunotherapies in relation to autoimmunity, primary and secondary immunodeficiencies, complement disorders and allergies
- pathogenesis and correlates of protection for autoimmune and endocrine disorders, infectious disease, malignancy and transplantation

CTI will publish Original Articles, Reviews and Case Reports and will begin accepting submissions in July 2012.

The CTI editorial team is to be led by Editor-in-Chief Dr. Gabrielle Belz together with Deputy Editors Dr. Adrian Liston and Dr. Stuart Tangye. An editorial board of distinguished physicians and immunology researchers from across the globe will provide their experience and expertise to support the journal and the editorial team.

Clinical & Translational Immunology will be an open access, online-only journal covering basic, translational, and clinical studies in all aspects of human immunology, including experimental models specific to human diseases.

Why not consider sending your next excellent paper to CTI !

nature publishing group npg

ASI Councillors' News

W.A. News

The Western Australian Branch of ASI has had two well supported visits this year. In March, Professor JoAnne Flynn from the University of Pittsburgh gave a very interesting talk entitled "Latent Tuberculosis: A moving target". In May we had a visit from Professor Ed Mocarski from Emory University. Professor Mocarski's visit was co-sponsored by Mariapia Degli-Esposti from the Lions Eye Institute. Prof. Mocarski gave two talks, these were "Suppressive impact of inflammatory monocytes on antiviral CTL responses" and "Role of extrinsic apoptosis and necrosis in antiviral host defense; what cytomegalovirus inhibitors have rendered".

Last year the local organizing committee of ASI organized the Perth Immunology Group (PIG) meeting. This was a very successful event and typically we hold these meetings every two years. This year your committee is trialling something new. We have teamed up with the Combined Biological Sciences Meeting (CBSM) to hold two immunology sessions during this one-day meeting. The CBSM meetings are an institution in Perth and this will be the 22nd annual meeting. The format is still being teased out but at this stage there will be a national keynote speaker, invited by ASI to speak at one of two sessions dedicated to immunology. One of these sessions will be given over to local invited speakers. The other session will be for student presentations. The immunology sessions are at the end of the day so that we can spill out into the post-meeting sundowner for drinks and nibbles. The CBSM meeting is scheduled for 24th August. I will provide more details as they come to hand. If the local ASI members support this initiative, the plan will be to hold combined meetings with CBSM every two years, with the PIG meetings held in alternate years.

Alec Redwood
Councillor

N.S.W. News

The 2012 combined NSW/ACT Branch Retreat will be held on the Thursday/Friday 23/24 August and will again be at Craigieburn Resort and Conference Centre in Bowral. This year we are fortunate to have plenary seminars from Prof. Tony Cunningham (Westmead Millennium Institute for Medical Research) and Dr Michele Grimbaldeston (Division of Human Immunology, Centre for Cancer Biology, SA Pathology) as well as a special seminar by Prof. Tony Basten (Garvan Institute) and a flow cytometry update from Dr Adrian Smith (Centenary Institute). As always, there will also be plenty of opportunities for students and early career researchers to present and prizes will be awarded for the best presentations.

This meeting is always a lot of fun and a great chance to form collaborative relationships with our neighbors. We'd love to see people there from as many institutions across NSW and ACT as possible. The registration site is now on line at http://www.garvan.org.au/symposiums/asinsw

All the best until next time,

Marcel Batten
Councillor

S.A./N.T. News

After a very busy 2011, there are some great events ahead in Adelaide later this year. In November (25-28) the 6th Australian Health and Medical Research Congress will be held at the Adelaide Convention Centre. Some of the participating societies include ASMR, Molecular and Experimental Pathology Society of Australasia, Australian Society for Stem Cell Research, Australian Vascular Biology Society and the Australian Society for HIV Medicine. The line up of international speakers is impressive with Plenary presentations from Elaine Dzierzak (Netherlands), Craig Logsdon (USA), Colin Sibley (UK). For more information, please see the advertisement in this newsletter issue and for all those social networkers out there, please visit the page and keep up to date on what's happening. The Facebook link is: https://www.facebook.com/events/294241793979659/

On another note: we will soon be forming the committee for the 8th Adelaide Immunology Retreat (AIR) for PhD students, Honours students and research assistants to be held in late August/early September of this year. An advertisement of the exact date and call for abstracts will be sent out by email to all SA/NT ASI members in June. Please support this event if you are a supervisor by encouraging your students and staff to attend as it is a great opportunity for them to give an oral presentation to their peers in a relaxed environment. Another incentive is that there will be 3 prizes conferred for the Best Presentations given by a PhD Student, Honours Student and Research Assistant (at least one in each category). We are looking forward to another great AIR event this year. For queries or more information, I can be contacted by email at michele.grimbaldeston@health.sa.gov.au. We look forward to seeing you there!

Finally, at the end of this year my term as the ASI SA/NT Branch Councillor will come to an end. In June/July there will be a call for nominations for the new SA/NT State Councillor. Please look out for this and start to consider who you would like to have as a representative on Council for the next three years. I have greatly enjoyed my time serving the Society and look forward to aiding the induction of the next Councillor.

Michele Grimbaldeston
Councillor

N.Z. News

The 2012 NZ ASI has just wrapped up in Dunedin, and we are looking forward to our next meeting – ASI 2013 at the Michael Fowler Centre in Wellington, New Zealand. Work is well underway planning the scientific programme, and we are proud to have many confirmed international speakers including Alan Sher, Richard Locksley, Bill Paul, Kristin Hogquist, Helen Heslop, and Takashi Saito. The conference will start on Monday, 2 December 2013 and will be preceded by the traditional workshops on Sunday. Presently, our website with all of the details will be made available. Jo Kirman and I have organized only sunny days for the week so mark your calendars and bring your sunscreen.

Anne La Flamme
Councillor

Victorian News

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

Much of the focus of the local Immunology community has been organizing the upcoming ASI Annual Scientific meeting to be held this year in Melbourne. This meeting is the highlight of the Immunology calendar in Australia and the Melbourne event is always extremely well attended, with organisers expecting over 800 registrants this year. The line up of invited International speakers is outstanding (as will be the local line up no doubt) and registrations and abstracts will soon be called for. Please keep an eye out for more information on the conference website (www.asi2012.org). As always, ASI will be offering scholarships as a benefit to its members so please watch for details about how to apply. Given the timing of the ASI conference, the annual Immunology Group of Victoria meeting will not be held this year, but IgV will contribute directly to the ASI conference in a number of ways, including through additional student scholarships.

There are several Immunologists coming to Melbourne in 2012 as part of the ASI Visiting Speakers Program. Provisionally, these include Hidde Ploegh (from MIT), Mark K. Jenkins (Minnesota) and John Wherry (Pennsylvania). The IgV Winter seminar is also coming soon (August 1), with Mariapia Degli-Eposti the invited speaker. Further details about all these seminars will be sent out to all members by email.

The highlight of the last few months has been the highly successful Day of Immunology activities held on April 26. This event continues to grow and it is particularly pleasing to see the interest in Immunology being generated amongst school students through the Immunology in Schools competition, the public lectures and the over-subscribed full day Immunology program held at GTAC. Our thanks go to the fantastic organising committee of the DoI and to all those who volunteered to help and/or attended the day's activities. The day is becoming an important element of publicizing our discipline to the community and it seems like it will continue to grow.

Lastly, please look out for emails from me that publicize upcoming events and notices of interest to local members (information about this year's Immunology Masterclass are coming soon). Unfortunately, we are still in the process of updating the ASI and IgV websites so these are not always as up-to-date as they could be, although we expect this to be fixed soon with new website designs. If you have any questions about ASI or IgV events, please don't hesitate to contact me (sberzins@ballarat.edu.au).

Stuart Berzins
Councillor

ASI Secretariat
PO Box 7108,
Upper Ferntree Gully,Vic. 3156
Australia
Tel: +61 3 9756 0128
Fax: +61 3 9753 6372
Email: asi@21century.com.au

HONORARY SECRETARY'S NEWS

FIMSA conference

I had the opportunity to attend the FIMSA Conference in New Delhi in March this year, and was very impressed by the quality and breadth of the immunology research presented there. Over 600 delegates attended and we were fortunate that the IUIS committee members chose to also have their meeting at the conference, as this bolstered the program with some outstanding presenters. There was a strong contingent from Australia at the meeting, including outgoing FIMSA President Prof Nick King, Prof Jim McCluskey, Prof Jonathan Sprent, Prof Miles Davenport, Dr Cindy Ma, Dr Helen Thomas, Dr David Martino and A/Prof Guna Karupiah. The meeting was also enhanced by the presence of FIMSA patron Prof Sir Gustav Nossal who was honoured during the opening ceremony and made his usual excellent contribution to questions and discussion of the presentations. The quality of the presentations and posters from the local students was very impressive, and demonstrated a focus on TB and parasitic diseases from the region. I also had the opportunity to participate in a panel discussion on gender equity in immunology, which highlighted the challenges some countries face in terms of striving for gender equity, and comparatively how well Australasia is doing in this area. The conference was followed by the Advanced Immunology Training Course, which also had some excellent faculty including Prof Abul Abbas and Prof Vijay Kuchroo, and allowed for a lot of interaction and discussion between the young researchers and senior presenters. I would congratulate Prof Narinder Mehra and his team on an excellent conference and training course, and encourage fellow immunologists to attend this important regional meeting in future.

First Round ASI International Travel Awards

There were a large number of excellent applications for the first round of the ASI international travel awards in late April. Judging of these awards was not complete at the time of writing, so successful awardees will have been notified by email in early June, and published in the next edition of the Newsletter.

ASI 2012 conference in Melbourne, 2–6 December

The preparations for the ASI annual scientific meeting in Melbourne are almost complete. An excellent range of international plenary speakers have accepted to come, and national speakers will be invited in the coming weeks. The meeting will be held in the outstanding new Melbourne Convention and Exhibition Centre on the Yarra River, right in the centre of the city. Abstracts and registration are now open (www.asi2012.org) and will close on 1st September. Calls for applications for travel bursaries for students and early post-docs will appear on the website and be sent out by email notice in the coming months. The larger venue will provide more opportunities for junior researchers to present their work orally. We expect it will be a fantastic meeting, and we welcome all ASI members and fellow immunology researchers from Australia and New Zealand, as well as colleagues from further afield to come and experience the very high quality science presented and also enjoy the great food, wine and nightlife that this exciting city has to offer!

Rose Ffrench

THE ASI VISITING SPEAKER PROGRAM 2012

We would like to remind you of the opportunities to propose and host high calibre speakers relevant to your field of research. The program facilitates the visit of distinguished immunologists to your own location opening opportunities for strengthening or initiating collaborations for your research. We do look forward to hearing your proposals.For details on the process, visit the ASI website.

Scheduled visits for 2012

August 2012

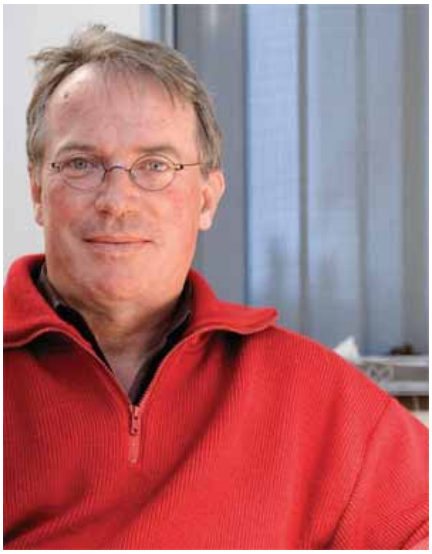
Dr Pam Schwartzberg
National Human Genome Research Institute
NIH, Bethesda, MD, USA
Hosted by Stuart Tangye, Sydney (Garvan Institute)
Details of the tour will be provided timely by local Councillors.

October 2012

Professor Hidde Plegh
Whitehead Institute for Biomedical Research; Massachusetts Institute of Technology (MIT), Boston, USA

Hosted by Jose Villadangos, University of Melbourne
Details of the tour will be provided timely by local councillors.

Hidde Ploegh was born in 1953 in the Netherlands. He attended the University of Groningen, where he obtained his undergraduate (majors in biology and chemistry) and master's degrees. He performed the work for his PhD in the laboratory of Jack Strominger (Harvard University) and obtained his doctorate from the University of Leiden. He joined the University of Cologne's Institute for Genetics as a junior group leader and in 1984 became a staff member at the Netherlands Cancer Institute, Amsterdam, The Netherlands. In 1992 he accepted a position as Professor of Biology at MIT, Cambridge, Mass. In 1997 Hidde became the director of the graduate program in immunology at Harvard Medical School, where he was the incumbent of the Mallinckrodt chair in Immunopathology from 1997-2005.



Hidde returned to MIT in 2005, where he is currently a member of the Whitehead Institute for Biomedical Research and a Professor in MIT's Department of Biology. He is a member of EMBO, a corresponding member of the Royal Dutch Academy of Sciences and a member of the American Academy of Arts and Sciences.

Current interests in the Ploegh Laboratory include studies of the various tactics that viruses employ to evade immune responses, and the ways in which the immune system – both innate and adaptive – distinguishes friend from foe. The findings have illuminated not only hostpathogen interactions, but also aspects of protein quality control, an area to which the lab applies chemistry-based strategies. Other technologies include new methods for protein labelling and for the production of mouse models by somatic cell nuclear transfer.

Hidde Ploegh has received multiple prizes, including the Avery-Landsteiner Prize, the Havinga Medal and the Meritorious Career Award of the American Association of Immunologists. He is the author of over 400 papers.

Selected Publications

Lee CC, Avalos AM, Ploegh HL. Accessory molecules for Toll-like receptors and their function. *Nat Rev Immunol*. 2012 Feb 3;12(3):168-79.
Park B, Buti L, Lee S, Matsuwaki T, Spooner E, Brinkmann MM, Nishihara M, Ploegh HL. Granulin is a soluble cofactor for toll-like receptor 9 signaling. *Immunity*. 2011 Apr 22;34(4):505-13.
Kim YM, Brinkmann MM, Paquet ME, Ploegh HL. Kirak O, Frickel EM, Grotenbreg GM, Suh H, Jaenisch R, Ploegh HL. Transnuclear mice with predefined T cell receptor specificities against Toxoplasma gondii obtained via SCNT. *Science*. 2010 Apr 9;328(5975):243-8.
Park B, Spooner E, Houser BL, Strominger JL, Ploegh HL. The HCMV membrane glycoprotein US10 selectively targets HLA-G for degradation. *J Exp Med*. 2010 Aug 30;207(9):2033-41.
Hu CC, Dougan SK, Winter SV, Paton AW, Paton JC, Ploegh HL. Subtilase cytotoxin cleaves newly synthesized BiP and blocks antibody secretion in B lymphocytes. *J Exp Med*. 2009 Oct 6;206(11):2429-40.
Park B, Brinkmann MM, Spooner E, Lee CC, Kim YM, Ploegh HL. Proteolytic cleavage in an endolysosomal compartment is required for activation of Toll-like receptor 9. *Nat Immunol*. 2008 Dec;9(12):1407-14.
Kim YM, Brinkmann MM, Paquet ME, Ploegh HL. UNC93B1 delivers nucleotide-sensing toll-like receptors to endolysosomes. *Nature*. 2008 Mar 13;452(7184):234-8.
Vyas JM, Van der Veen AG, Ploegh HL. The known unknowns of antigen processing and presentation. *Nat Rev Immunol*. 2008 Aug;8(8):607-18.
Loureiro J, Lilley BN, Spooner E, Noriega V, Tortorella D, Ploegh HL. Signal peptide peptidase is required for dislocation from the endoplasmic reticulum. *Nature*. 2006 Jun 15;441(7095):894-7.
Love JC, Ronan JL, Grotenbreg GM, van der Veen AG, Ploegh HL. A microengraving method for rapid selection of single cells producing antigen-specific antibodies. *Nat Biotechnol*. 2006 Jun;24(6):703-7.
Tirosh B, Iwakoshi NN, Glimcher LH, Ploegh HL. XBP-1 specifically promotes IgM synthesis and secretion, but is dispensable for degradation of glycoproteins in primary B cells. *J Exp Med*. 2005 Aug 15;202(4):505-16.
Lilley BN, Ploegh HL. A membrane protein required for dislocation of misfolded proteins from the ER. *Nature*. 2004 Jun 24;429(6994):834-40.
Boes M, Cerny J, Massol R, Op den Brouw M, Kirchhausen T, Chen J, Ploegh HL. T-cell engagement of dendritic cells rapidly rearranges MHC class II transport. *Nature*. 2002 Aug 29;418(6901):983-8.
Wiertz EJ, Tortorella D, Bogyo M, Yu J, Mothes W, Jones TR, Rapoport TA, Ploegh HL. Sec61-mediated transfer of a membrane protein from the endoplasmic reticulum to the proteasome for destruction. *Nature*. 1996 Dec 5;384(6608):432-8.
Wiertz EJ, Jones TR, Sun L, Bogyo M, Geuze HJ, Ploegh HL. The human cytomegalovirus US11 gene product dislocates MHC class I heavy chains from the endoplasmic reticulum to the cytosol. *Cell*. 1996 Mar 8;84(5):769-79.
Hill A, Jugovic P, York I, Russ G, Bennink J, Yewdell J, Ploegh H, Johnson D. Herpes simplex virus turns off the TAP to evade host immunity. *Nature*. 1995 Jun 1;375(6530):411-5.

Report on FIMSA Advanced Immunology Training Course

Cindy Ma

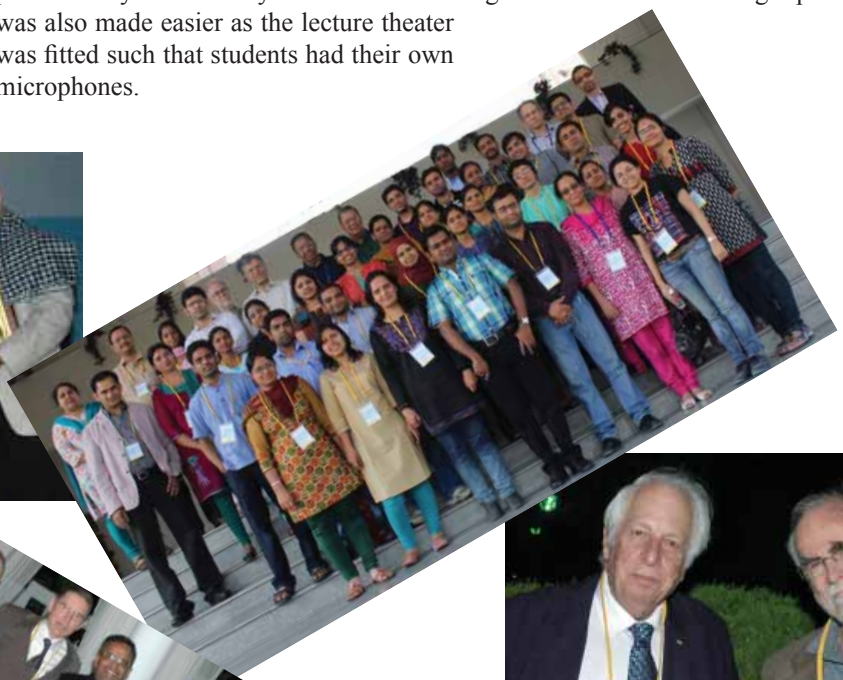
(Garvan Institute of Medical Research, NSW)

An advanced course on basic and translational immunology was held immediately following the 5th Congress of the Federation of Immunological Societies of Asia Oceania (FIMSA) in New Delhi from 18-20 March. Again, due to the generous support of ASI, the teaching faculty had a strong Australian contingent, consisting of Jonathan Sprent, Miles Davenport, Rose Ffrench, Cindy Ma, Guna Karupiah, and Nicholas King. The other members of the teaching faculty were Abul Abbas, Vijay Kuchroo and Ram Raj Singh from the USA.

The advanced training course was attended by ~75 students most of whom were selected through an application process. The course was run in a "residential course" format whereby the faculty members and students stayed at the same location at the Institute for Defence Studies and Analyses. The format of the course consisted of six lots of 1-hour basic immunology lectures from Abul and Vijay, followed by 1-hour lectures given by the rest of the faculty members, spread over the three days. The students made posters on their work and on the last day 20 students were selected to give oral presentations, with quite generous monetary awards presented to the two best student posters, oral presentations and best participant during the course.

The majority of the students were from India with a few from other countries in the Asia Oceania region. The format of the course was informal which meant students were able to ask questions throughout the lectures provided by the faculty members. This was also made easier as the lecture theater was fitted such that students had their own microphones.

Overall the quality of the presentations and work performed by the students was impressive, as were the scientific discussions that were held throughout the duration of the course. The one short coming, if there had to be one, would be the lack of "breakout" sessions to further encourage group discussions and interactions between students and faculty members. That said, the schedule was quite intense, with a large amount of topics covered, and a chance to take a break or explore the surrounds in New Delhi was welcomed by most of the participants. We all found our involvement in the teaching course to be an extremely worthwhile experience and once again we are grateful to ASI for making it possible.



TRAVEL AWARD CONFERENCE REPORTS

15th International Congress of Mucosal Immunology

Maria Kaparakis-Liaskos
Monash Institute of Medical Research, Melbourne

Last July, I was fortunate to escape the Melbourne winter and attend the 15th International Congress of Mucosal Immunology (ICMI) in Paris. ICMI is widely recognised as the pre-eminent conference on mucosal immunology, and this biennial meeting is organised by the International Society for Mucosal Immunology. The meeting was held in the picturesque and historic Latin Quarter of Paris, at the Université Paris Descartes. The location could not have been more ideal. My daily stroll to the conference took me along part of the Louvre, the river Seine, across the Pont des Arts and past the breathtaking Parisian antique stores nestled along the narrow streets. It was a refreshing change from my usual one hour morning drive across Melbourne in peak-hour traffic, to say the least.

The conference had a total of 960 attendees and 144 oral presentations that focused on various aspects of mucosal immunology, ranging from innate and adaptive immunity, mucosal pathogenesis, epithelial cell barrier responses of almost all mucosal surfaces, mucosal immunity to viruses, vaccine development, inflammatory bowel disease (IBD), Crohns disease and anything else "mucosally" related. There was a greater focus on bacterial pathogenesis and innate immune receptors compared to previous ICMI meetings that I have attended, so the meeting was highly relevant for me, as my research focuses predominately on these two areas.

The conference began with a keynote presentation by Professor Philippe Sansonetti, Director of the Unit of Molecular Microbial Pathogenesis at the Institut Pasteur, a member of the French Academy of Sciences and an international leader in the field of bacterial pathogenesis. Professor Sansonetti presented unpublished findings generated using a powerful and novel microscopy imaging technique performed in his laboratory. This technique enabled his team to visualise with intricate detail the bacterium *Shigella* interacting with innate and adaptive immune cells within the lymph node of a live animal.

I was scheduled to talk the following day about my recent work examining the role of the human pathogen recognition molecule NOD1 in the induction of autophagy in response to bacterial outer membrane vesicles. In addition to being provided with a travel grant from ASI to attend the meeting and present my work, I was also awarded one of the 16 Young Investigator travel awards from the Society for Mucosal Immunology.

During the five day conference, there was a plethora of presentations from postdoctoral fellows and distinguished laboratory heads. Of these, there were a few notable presentations that are worth mentioning. Professor Warren Strober presented an overview of the IL-12–IL-23 axis in gut inflammation, and summarised over a decade of his research in the fields of experimental colitis and human IBD. Professor Richard Blumberg discussed the key role of autophagy in immune responses at mucosal surfaces. Daniel Littman presented some of his recent findings regarding the plasticity of T cell subsets and James Di Santo informed us of novel intestinal natural killer cell subsets. In addition, I was particularly interested in two studies. The first was presented by Catharina Svanborg, who identified a novel innate immune receptor called Hamlet, which has a key role in cellular apoptosis and inflammation. Secondly, Andrew McKenzie introduced us to a new hematopoietic derived, IL-13-producing cell, which he and others have named the nuocyte. This cell requires IL-25 and IL-33 signalling to expand, and Andrew McKenzie's research team and a second group of researchers simultaneously identified that the nuocyte has a key role in the generation of Th2-induced immune responses *in vivo*.

Overall, I found the quality of the science presented at this meeting outstanding and very informative. In addition, there were plenty of opportunities to interact with other delegates in the poster sessions and during the social events. I look forward to attending the next ICMI, to be held in Vancouver in July 2013.

The week following the meeting, I visited senior scientists at the Institut Pasteur: Dr Hilde De Reuse, head of the Helicobacter Pathogenesis laboratory, and Professor Sansonetti. I had excellent discussions with these scientists and members of their laboratories. We discussed our common interests, and both Dr De Reuse and Professor Sansonetti gave me scientific and mentoring advice for my future research endeavours. Ultimately, my visit to the Institut Pasteur resulted in strengthening collaborations between our research groups, and provided me with the opportunity to organise a return visit to the Institut Pasteur to perform collaborative work within Philippe Sansonetti's laboratory.

My week at the Pasteur concluded with a personalised tour through the apartment of Louis Pasteur. I was amazed at the preservation of his hand-labelled reagents, laboratory equipment and personal belongings within the apartment, giving the impression that he had only just been in there yesterday. I was unaware that the Institut Pasteur was purpose built to give Louis Pasteur sufficient laboratory space to allow visiting researchers

to conduct collaborative laboratory work and receive training from the great scientist himself. If only we could all have a place built for ourselves to perform research with our friends! The tour ended in the gold mosaic encased crypt underneath the Institute, where Louis Pasteur is buried. Indeed, it is a fitting burial place for the true founder of the Institute. Finally, my week in Paris ended with the chance to fulfil one of my childhood dreams and a real treat, seeing the 14th of July Bastille Day fireworks at the Eiffel Tower.

I would like to thank ASI for providing me with an International Postdoctoral Travel grant that enabled me to attend the ICMI and visit scientists at the Institut Pasteur. I believe that the knowledge and opportunities presented to me during this two week trip will contribute to my future development and research endeavours.

Keystone Symposium, Innate Immunity: Sensing the Microbes and Danger Signals

Elizabeth Forbes-Blom
Malaghan Institute of Medical Research, New Zealand

The microbiome heralds a new era in medical research; and we are now more aware than ever before of its impact upon immunity. The Keystone symposium, "Innate Immunity: Sensing the Microbes and Danger Signals", was held at Keystone Resort from 4–9 March 2012. This conference took me out of my scientific 'comfort zone' as I consider myself neither an innate immunologist nor a microbiome whizz kid. Yet, these all have profound impact on our gastrointestinal allergy and inflammation research as understanding how to exploit host receptor crosstalk mechanisms is essential for developing interventions for allergic diseases or IBD.

The goal of this Keystone symposium was to "gather scientists working on innate immunity to discuss cutting edge research on the mechanisms that regulate the activation of the immune system by microbes as well as by endogenous damage signals, and to integrate such knowledge in the context of inflammation, homeostasis, host defence and disease". They achieved this goal and the presentations throughout this conference highlighted that whilst we understand the initial sensing of microbes, the interplay between recognition of commensal versus pathogenic microbes on the host immune system is only beginning to be uncovered. In particular, the concurrent microbiome meeting enhanced the opportunity for interdisciplinary interaction, and gave insight into how one can design and execute studies of the microbiota in your favourite niche (= in my opinion, to stick with point one and collaborate with the experts, as that 16S sequencing and bioinformatics stuff is in a 'league of their own'). Personal highlights for the meeting included David Artis' presentation on their elegant studies demonstrating that pattern recognition of commensal bacteria by B cells reduces allergic inflammation in mice and a chance to discuss our findings with one of the great minds of immunology, Alan Sher.

As the conference was late winter, and the snow had not been as plentiful as it can during the season, we were unsure what the ski conditions would be – we lucked out as the Americans would say, with clear skies and good conditions that resulted in a few stories of black routes that should not have been taken and some off piste action for fellow scientists during the week. Following the symposia I headed down the mountain and off to Chicago for lab visits and presentations at Northwestern and the University of Chicago. This award enabled me to network with world leaders in this field as well as conduct discussions on future collaborations, both critical to the success of my future career. Thank you ASI, for making this possible.

Right: Liz at Keystone Resort

Above: Liz at Cloud Gate, Chicago. "The Bean"is a public sculpture by British artist Anish Kapoorand weighs in at over 110 tons, is 66 ft long and 33 ft high. It was created using a huge number of individual stainless steel plates and the seamless surface is the result of thousands of hours of polishing

Sustaining Membership

ASI Inc acknowledges the support of the following sustaining member:

• Jomar Bioscience

FIMSA 2012 – India Rising

David Martino
Murdoch Children's Research Institute, Melbourne

March this year saw India host the 5th congress of the Federation of Immunological Societies of Asia-Oceania (FIMSA). Hosted at the stunning Le Meridian Hotel New Delhi, this conference represented a key achievement for immunology in developing India. About 600 delegates from 30 plus countries around the world attended the four-day event themed: Translational Immunology in Health and Disease.

GP Talwar gives a Master Lecture on fertility

The quality of the scientific program was commendable, featuring 10 of the most eminent names in Immunology providing the 'Master Lecture' series, followed by symposia covering immune regulatory networks, host-pathogen interactions, infection and immunity, autoimmunity and tolerance, stem cell biology and cell therapy, vaccines and HIV.

Personal highlights included Prof Abdul Abbas' unique mouse model of skin inflammation challenging traditional paradigms of immune homeostasis initiated by Tregs. James McClusky provided fascinating insights into specificity of immunity through HLA-peptide complexes showing compelling data on Abacavir hypersensitivity in the B5701 haplotype. Vijay Kuchroo's lecture on Th17 gene networks in autoimmunity nearly evoked a standing applause, second only in decibel level to the announcement that Sachin Tendulkar had achieved his 100th century for India against Bangladesh in the Asia Cup – a feat that sent locals and cricket fans alike into a frenzy of applause.

I was particularly impressed by the quality of work by the young Indian PhD students and their enthusiastic approach to networking and question time.

A novel format this year included the e-Poster sessions where posters were digitally displayed on 48 inch flat screens, perhaps the future of poster sessions on the conference circuit, but not without its share of IT issues.

This was truly an experience for a young scientist like myself as each morning my taxi passed scores of the homeless and poverty to arrive (after gun-point security checks) at the immaculate Le Meridian Hotel. One truly got the sense that, despite its challenges, India is ready to pursue its place on the world stage of immunology.

My sincere thanks to ASI for funding my attendance at FIMSA this year.

On the streets of Delhi

Dinner with Sir Gustav Nossal (left) & Prof Natvig (right); author is second from right

World Immune Regulation Meeting-VI, Davos, Switzerland

Erika Cretney
Walter & Eliza Hall Institute, Melbourne

Who could think of a better way to recuperate from grant writing than a trip to Europe? Just two days after NHMRC grants were due I flew to Switzerland to attend the World Immune Regulation Meeting-VI in Davos, 18–21 March 2012. Davos is located in the Swiss Alps and is the highest city in Europe. After flying to Zurich I caught the Rhatische Bahn train which over a period of 2½ hours crossed a breathtaking countryside of mountains and lakes and climbed to ~1500m above sea level, reaching the ski fields of Davos, the site of the meeting.

Upon my arrival I decided to forgo dinner and slept for 13 hours (the combined effects of travelling and grant writing had completely sucked the energy out of me). The next morning the conference commenced at 8.30am. I made it on time, bright- eyed and cheery despite experiencing my first fall on slippery ice (by the end of the meeting I managed to fall five times, only one fall was preceded by conference drinks). More than 500 people attended the conference, amongst them only a small handful of Aussies. Conference days were long (8.30am-~10pm) but allowed for long lunch breaks to digest symposia (or sleep or ski …).

The conference itself was packed with a broad range of topics including inflammation, innate immune responses, effector and regulatory cells, development of tissues and secondary lymphoid organs, innate lymphoid cells in the tissues and self tolerance. The conference attracted me because there were topics focusing on regulatory T cell development (I was fortunate enough to get a talk) and transcriptional regulation.

A conference highlight for me was a talk by Kenya Honda whose recent research, published in *Science,* demonstrated that mouse colonic regulatory T cells are induced by commensal Clostridia. Honda presented unpublished follow-up research aimed at translating these important findings into humans. His group are currently optimising a cocktail of human intestinal bacteria, composed mainly of Clostridia, and have demonstrated that this cocktail can induce regulatory T cells in the colon of germ free mice. Future studies are now required to ascertain whether oral administration of regulatory T cell-inducing commensal Clostridia in humans can be used as a treatment for autoimmune/inflammatory diseases.

Another highlight was a talk by Frederica Sallusto who presented her human Th17 cell research (unpublished at the time of the conference but since published in the April issue of *Nature*). Using *in vitro*-primed and *ex vivo* memory cells her team demonstrated that *Candida albicans* and *Staphylococcus aureus* elicit different types of T_H17 cells that produce IL17 together with either IFNγ or IL-10 respectively. They also revealed an important role for IL-1β in the regulation of human Th17 cells at priming and at the effector stage.

Following the meeting, I travelled to Paris to visit Dr Nabila Seddiki (Universite Creteil, Faculte de médecine Henri Mondor) to meet researchers working on human regulatory T cell development, and give a seminar on my research. Dr Seddiki's group has identified a human counterpart of the Blimp-expressing effector regulatory T cells that we have identified in mice. Dr Seddiki's research is yet to be published, so we were keen to meet up to compare and contrast our findings, and set up important networks enabling future collaboration between our research groups. Dr Seddiki made sure that I did not leave Paris without eating escargot (snails drenched in garlic butter). They were delicious though even an old boot soaked in sauce that good would have tasted superb. I also sampled foie gras but stopped short of trying viande de cheval (every man I spoke to in Switzerland and France said they loved it but every woman said they hated it – who to trust?!).

Thank you to ASI (and its paid up members) for funding a good portion of my trip. I have come back inspired and more motivated than ever to continue my immunology research and feel fortunate to have the support of a great society behind me. If only the NHMRC would feel the same about my grant …

Erika Cretney (left) with fellow ASI member Stephane Chevrier on the ski slopes of Davos

Erika in Paris

Publications List

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

Affandi, J.S., Aghafar, Z.K., Rodriguez, B., Lederman, M.M., Burrows, S., Senitzer, D., Price, P., 2012. Can immune-related genotypes illuminate the immunopathogenesis of cytomegalovirus disease in human immunodeficiency virus-infected patients? Hum Immunol 73, 168-174.

Aghafar, M.Z., Witt, C., Kamarulzaman, A., Ismail, R., Lederman, M.M., Rodriguez, B., Senitzer, D., Lee, S., Price, P., 2012. Genetic variations in loci relevant to natural killer cell function are affected by ethnicity but are generally not correlated with susceptibility to HIV-1. Tissue Antigens 79, 367-371.

Arendts, G., Stone, S.F., Fatovich, D.M., van Eeden, P., MacDonald, E., Brown, S.G., 2012. Critical illness in the emergency department: lessons learnt from the first 12 months of enrolments in the Critical Illness and Shock Study. Emerg Med Australas 24, 31-36.

Barclay, T., Ginic-Markovic, M., Johnston, M.R., Cooper, P., Petrovsky, N., 2012a. Observation of the keto tautomer of D-fructose in D(2)O using (1)H NMR spectroscopy. Carbohydr Res 347, 136-141.

Barclay, T., Ginic-Markovic, M., Johnston, M.R., Cooper, P.D., Petrovsky, N., 2012b. Analysis of the hydrolysis of inulin using real time 1H NMR spectroscopy. Carbohydr Res 352, 117-125.

Brennan, R.M., Petersen, J., Neller, M.A., Miles, J.J., Burrows, J.M., Smith, C., McCluskey, J., Khanna, R., Rossjohn, J., Burrows, S.R., 2012. The impact of a large and frequent deletion in the human TCR beta locus on antiviral immunity. J Immunol 188, 2742-2748.

Brown, S.G., Stone, S.F., 2011. Laboratory diagnosis of acute anaphylaxis. Clin Exp Allergy 41, 1660-1662.

Brown, S.G., Wiese, M.D., van Eeden, P., Stone, S.F., Chuter, C.L., Gunner, J., Wanandy, T., Phillips, M., Heddle, R.J., 2012. Ultrarush versus semirush initiation of insect venom immunotherapy: A randomized controlled trial. J Allergy Clin Immunol.

Bruder, J.T., Semenova, E., Chen, P., Limbach, K., Patterson, N.B., Stefaniak, M.E., Konovalova, S., Thomas, C., Hamilton, M., King, C.R., Richie, T.L., Doolan, D.L., 2012. Modification of Ad5 hexon hypervariable regions circumvents pre-existing Ad5 neutralizing antibodies and induces protective immune responses. PLoS One 7, e33920.

Bulek, A.M., Cole, D.K., Skowera, A., Dolton, G., Gras, S., Madura, F., Fuller, A., Miles, J.J., Gostick, E., Price, D.A., Drijfhout, J.W., Knight, R.R., Huang, G.C., Lissin, N., Molloy, P.E., Wooldridge, L., Jakobsen, B.K., Rossjohn, J., Peakman, M., Rizkallah, P.J., Sewell, A.K., 2012. Structural basis for the killing of human beta cells by CD8(+) T cells in type 1 diabetes. Nat Immunol 13, 283-289.

Bull, C.F., Mayrhofer, G., Zeegers, D., Mun, G.L., Hande, M.P., Fenech, M.F., 2012. Folate deficiency is associated with the formation of complex nuclear anomalies in the cytokinesis-block micronucleus cytome assay. Environ Mol Mutagen 53, 311-323.

Campbell, H.G., Slatter, T.L., Jeffs, A., Mehta, R., Rubio, C., Baird, M., Braithwaite, A.W., 2012. Does Delta133p53 isoform trigger inflammation and autoimmunity? Cell Cycle 11, 446-450.

Chang, P.P., Barral, P., Fitch, J., Pratama, A., Ma, C.S., Kallies, A., Hogan, J.J., Cerundolo, V., Tangye, S.G., Bittman, R., Nutt, S.L., Brink, R., Godfrey, D.I., Batista, F.D., Vinuesa, C.G., 2012. Identification of Bcl-6-dependent follicular helper NKT cells that provide cognate help for B cell responses. Nat Immunol 13, 35-43.

Chen, A.T., Cornberg, M., Gras, S., Guillonneau, C., Rossjohn, J., Trees, A., Emonet, S., de la Torre, J.C., Welsh, R.M., Selin, L.K., 2012. Loss of anti-viral immunity by infection with a virus encoding a cross-reactive pathogenic epitope. PLoS Pathog 8, e1002633.

Chuan, Y.P., Zeng, B.Y., O'Sullivan, B., Thomas, R., Middelberg, A.P., 2012. Co-delivery of antigen and a lipophilic anti-inflammatory drug to cells via a tailorable nanocarrier emulsion. J Colloid Interface Sci 368, 616-624.

Clanchy, F.I., Hamilton, J.A., 2012. HUVEC co-culture and haematopoietic growth factors modulate human proliferative monocyte activity. Cytokine.

Clybouw, C., Merino, D., Nebl, T., Masson, F., Robati, M., O'Reilly, L., Hubner, A., Davis, R.J., Strasser, A., Bouillet, P., 2012. Alternative splicing of Bim and Erk-mediated Bim(EL) phosphorylation are dispensable for hematopoietic homeostasis in vivo. Cell Death Differ 19, 1060-1068.

Davies, J.M., Li, H., Green, M., Towers, M., Upham, J.W., 2012. Subtropical grass pollen allergens are important for allergic respiratory diseases in subtropical regions. Clin Transl Allergy 2, 4.

Deane, J.A., Abeynaike, L.D., Norman, M.U., Wee, J.L., Kitching, A.R., Kubes, P., Hickey, M.J., 2012. Endogenous regulatory T cells adhere in inflamed dermal vessels via ICAM-1: association with regulation of effector leukocyte adhesion. J Immunol 188, 2179-2188.

Ebert, L.M., MacRaild, S.E., Davis, I.D., Cebon, J., Chen, W., 2012. A novel method for detecting antigen-specific human regulatory T cells. J Immunol Methods 377, 56-61.

Fernandez, S., French, M.A., Price, P., 2011. Immunosenescent CD57+CD4+ T-cells accumulate and contribute to interferon-gamma responses in HIV patients responding stably to ART. Dis Markers 31, 337-342.

Fernando, G.J., Chen, X., Primiero, C.A., Yukiko, S.R., Fairmaid, E.J., Corbett, H.J., Frazer, I.H., Brown, L.E., Kendall, M.A., 2012. Nanopatch targeted delivery of both antigen and adjuvant to skin synergistically drives enhanced antibody responses. J Control Release 159, 215-221.

Ferrer, P.E., Frederick, P., Gulbis, J.M., Dewson, G., Kluck, R.M., 2012. Translocation of a Bak C-terminus mutant from cytosol to mitochondria to mediate cytochrome C release: implications for Bak and Bax apoptotic function. PLoS One 7, e31510.

Fogarty, R.D., Abhary, S., Javadiyan, S., Kasmeridis, N., Petrovsky, N., Whiting, M.J., Craig, J.E., Burdon, K.P., 2012. Relationship between DDAH gene variants and serum ADMA level in individuals with type 1 diabetes. J Diabetes Complications.

Gagliardi, L., Ling, K.H., Kok, C.H., Carolan, J., Brautigan, P., Kenyon, R., D'Andrea, R.J., Van der Hoek, M., Hahn, C.N., Torpy, D., Scott, H.S., 2012. Genome-wide gene expression profiling identifies overlap with malignant adrenocortical tumours and novel mechanisms of inefficient steroidogenesis in familial ACTH-independent macronodular adrenal hyperplasia. Endocr Relat Cancer.

Glaser, S.P., Lee, E.F., Trounson, E., Bouillet, P., Wei, A., Fairlie, W.D., Izon, D.J., Zuber, J., Rappaport, A.R., Herold, M.J., Alexander, W.S., Lowe, S.W., Robb, L., Strasser, A., 2012. Anti-apoptotic Mcl-1 is essential for the development and sustained growth of acute myeloid leukemia. Genes Dev 26, 120-125.

Gorman, S., Tan, D.H., Lambert, M.J., Scott, N.M., Judge, M.A., Hart, P.H., 2012. Vitamin D(3) deficiency enhances allergen-induced lymphocyte responses in a mouse model of allergic airway disease. Pediatr Allergy Immunol 23, 83-87.

Gras, S., Wilmann, P.G., Chen, Z., Halim, H., Liu, Y.C., Kjer-Nielsen, L., Purcell, A.W., Burrows, S.R., McCluskey, J., Rossjohn, J., 2012. A structural basis for varied alphabeta TCR usage against an immunodominant EBV antigen restricted to a HLA-B8 molecule. J Immunol 188, 311-321.

Gugasyan, R., Horat, E., Kinkel, S.A., Ross, F., Grigoriadis, G., Gray, D., O'Keeffe, M., Berzins, S.P., Belz, G.T., Grumont, R.J., Banerjee, A., Strasser, A., Godfrey, D.I., Tsichlis, P.N., Gerondakis, S., 2012. The NF-kappaB1 transcription factor prevents the intrathymic development of CD8 T cells with memory properties. EMBO J 31, 692-706.

Guinovart, C., Dobano, C., Bassat, Q., Nhabomba, A., Quinto, L., Manaca, M.N., Aguilar, R., Rodriguez, M.H., Barbosa, A., Aponte, J.J., Mayor, A.G., Renom, M., Moraleda, C., Roberts, D.J., Schwarzer, E., Le Souef, P.N., Schofield, L., Chitnis, C.E., Doolan, D.L., Alonso, P.L., 2012. The role of age and exposure to Plasmodium falciparum in the rate of acquisition of naturally acquired immunity: a randomized controlled trial. PLoS One 7, e32362.

Hamilton-Williams, E.E., Cheung, J., Rainbow, D.B., Hunter, K.M., Wicker, L.S., Sherman, L.A., 2012. Cellular mechanisms of restored beta-cell tolerance mediated by protective alleles of Idd3 and Idd5. Diabetes 61, 166-174.

Hamilton, J.A., Davis, J., Pobjoy, J., Cook, A.D., 2012. GM-CSF is not essential for optimal fertility or for weight control. Cytokine 57, 30-31.

Happo, L., Strasser, A., Cory, S., 2012. BH3-only proteins in apoptosis at a glance. J Cell Sci 125, 1081-1087.

Hearps, A.C., Maisa, A., Cheng, W.J., Angelovich, T.A., Lichtfuss, G.F., Palmer, C.S., Landay, A.L., Jaworowski, A., Crowe, S.M., 2012. HIV infection induces age-related changes to monocytes and innate immune activation in young men that persist despite combination antiretroviral therapy. AIDS 26, 843-853.

Irvine, K.M., Gallego, P., An, X., Best, S.E., Thomas, G., Wells, C., Harris, M., Cotterill, A., Thomas, R., 2012. Peripheral blood monocyte gene expression profile clinically stratifies patients with recent-onset type 1 diabetes. Diabetes 61, 1281-1290.

John, L.B., Howland, L.J., Flynn, J.K., West, A.C., Devaud, C., Duong, C.P., Stewart, T.J., Westwood, J.A., Guo, Z.S., Bartlett, D.L., Smyth, M.J., Kershaw, M.H., Darcy, P.K., 2012. Oncolytic virus and anti-4-1BB combination therapy elicits strong antitumor immunity against established cancer. Cancer Res 72, 1651-1660.

Kaufmann, T., Strasser, A., Jost, P.J., 2012. Fas death receptor signalling: roles of Bid and XIAP. Cell Death Differ 19, 42-50.

Kazenwadel, J., Secker, G.A., Liu, Y.J., Rosenfeld, J.A., Wildin, R.S., Cuellar-Rodriguez, J., Hsu, A.P., Dyack, S., Fernandez, C.V., Chong, C.E., Babic, M., Bardy, P.G., Shimamura, A., Zhang, M.Y., Walsh, T., Holland, S.M., Hickstein, D.D., Horwitz, M.S., Hahn, C.N., Scott, H.S., Harvey, N.L., 2012. Loss-of-function germline GATA2 mutations in patients with MDS/AML or MonoMAC syndrome and primary lymphedema reveal a key role for GATA2 in the lymphatic vasculature. Blood 119, 1283-1291.

Keely, S., Feighery, L., Campion, D.P., O'Brien, L., Brayden, D.J., Baird, A.W., 2011. Chloride-led disruption of the intestinal mucous layer impedes Salmonella invasion: evidence for an 'enteric tear' mechanism. Cell Physiol Biochem 28, 743-752.

Keely, S., Talley, N.J., Hansbro, P.M., 2012. Pulmonary-intestinal cross-talk in mucosal inflammatory disease. Mucosal Immunol 5, 7-18.

Kenna, T.J., Davidson, S.I., Duan, R., Bradbury, L.A., McFarlane, J., Smith, M., Weedon, H., Street, S., Thomas, R., Thomas, G.P., Brown, M.A., 2012. Enrichment of circulating interleukin-17-secreting interleukin-23 receptor-positive gamma/delta T cells in patients with active ankylosing spondylitis. Arthritis Rheum 64, 1420-1429.

Lacey, D.C., Achuthan, A., Fleetwood, A.J., Dinh, H., Roiniotis, J., Scholz, G.M., Chang, M.W., Beckman, S.K., Cook, A.D., Hamilton, J.A., 2012. Defining GM-CSF- and Macrophage-CSF-Dependent Macrophage Responses by In Vitro Models. J Immunol 188, 5752-5765.

Lenzo, J.C., Turner, A.L., Cook, A.D., Vlahos, R., Anderson, G.P., Reynolds, E.C., Hamilton, J.A., 2012. Control of macrophage lineage populations by CSF-1 receptor and GM-CSF in homeostasis and inflammation. Immunol Cell Biol 90, 429-440.

Li, M., Knight, D.A., Smyth, M.J., Stewart, T.J., 2012a. Sensitivity of a novel model of mammary cancer stem cell-like cells to TNF-related death pathways. Cancer Immunol Immunother.

Li, R., Dooley, H., Wang, T., Secombes, C.J., Bird, S., 2012b. Characterisation and expression analysis of B-cell activating factor (BAFF) in spiny dogfish (Squalus acanthias): cartilaginous fish BAFF has a unique extra exon that may impact receptor binding. Dev Comp Immunol 36, 707-717.

Liu, Y.C., Chen, Z., Burrows, S.R., Purcell, A.W., McCluskey, J., Rossjohn, J., Gras, S., 2012. The energetic basis underpinning T-cell receptor recognition of a super-bulged peptide bound to a major histocompatibility complex class I molecule. J Biol Chem 287, 12267-12276.

Ludlow, L.E., Zhou, J., Tippett, E., Cheng, W.J., Hasang, W., Rogerson, S.J., Jaworowski, A., 2012. HIV-1 inhibits phagocytosis and inflammatory cytokine responses of human monocyte-derived macrophages to P. falciparum infected erythrocytes. PLoS One 7, e32102.

Ma, C.S., Avery, D.T., Chan, A., Batten, M., Bustamante, J., Boisson-Dupuis, S., Arkwright, P.D., Kreins, A.Y., Averbuch, D., Engelhard, D., Magdorf, K., Kilic, S.S., Minegishi, Y., Nonoyama, S., French, M.A., Choo, S., Smart, J.M., Peake, J., Wong, M., Gray, P., Cook, M.C., Fulcher, D.A., Casanova, J.L., Deenick, E.K., Tangye, S.G., 2012. Functional STAT3 deficiency compromises the generation of human T follicular helper cells. Blood 119, 3997-4008.

Maine, C.J., Hamilton-Williams, E.E., Cheung, J., Stanford, S.M., Bottini, N., Wicker, L.S., Sherman, L.A., 2012. PTPN22 Alters the Development of Regulatory T Cells in the Thymus. J Immunol 188, 5267-5275.

Manetsch, M., Seidel, P., Heintz, U., Che, W., Hughes, J.M., Ge, Q., Sukkar, M.B., Ammit, A.J., 2012. TLR2 ligand engagement upregulates airway smooth muscle TNFalpha-induced cytokine production. Am J Physiol Lung Cell Mol Physiol 302, L838-845.

McKee, S.J., Young, V.L., Clow, F., Hayman, C.M., Baird, M.A., Hermans, I.F., Young, S.L., Ward, V.K., 2012. Virus-like particles and alpha-galactosylceramide form a self-adjuvanting composite particle that elicits anti-tumor responses. J Control Release 159, 338-345.

Melville, J.M., Bischof, R.J., Meeusen, E.N., Westover, A.J., Moss, T.J., 2012. Changes in Fetal Thymic Immune Cell Populations in a Sheep Model of Intrauterine Inflammation. Reprod Sci.

Merino, D., Strasser, A., Bouillet, P., 2011. Bim must be able to engage all pro-survival Bcl-2 family members for efficient tumor suppression. Oncogene.

Murchison, E.P., Schulz-Trieglaff, O.B., Ning, Z., Alexandrov, L.B., Bauer, M.J., Fu, B., Hims, M., Ding, Z., Ivakhno, S., Stewart, C., Ng, B.L., Wong, W., Aken, B., White, S., Alsop, A., Becq, J., Bignell, G.R., Cheetham, R.K., Cheng, W., Connor, T.R., Cox, A.J., Feng, Z.P., Gu, Y., Grocock, R.J., Harris, S.R., Khrebtukova, I., Kingsbury, Z., Kowarsky, M., Kreiss, A., Luo, S., Marshall, J., McBride, D.J., Murray, L., Pearse, A.M., Raine, K., Rasolonjatovo, I., Shaw, R., Tedder, P., Tregidgo, C., Vilella, A.J., Wedge, D.C., Woods, G.M., Gormley, N., Humphray, S., Schroth, G., Smith, G., Hall, K., Searle, S.M., Carter, N.P., Papenfuss, A.T., Futreal, P.A., Campbell, P.J., Yang, F., Bentley, D.R., Evers, D.J., Stratton, M.R., 2012. Genome sequencing and analysis of the Tasmanian devil and its transmissible cancer. Cell 148, 780-791.

Oakes, S.R., Vaillant, F., Lim, E., Lee, L., Breslin, K., Feleppa, F., Deb, S., Ritchie, M.E., Takano, E., Ward, T., Fox, S.B., Generali, D., Smyth, G.K., Strasser, A., Huang, D.C., Visvader, J.E., Lindeman, G.J., 2012. Sensitization of BCL-2-expressing breast tumors to chemotherapy by the BH3 mimetic ABT-737. Proc Natl Acad Sci U S A 109, 2766-2771.

Palendira, U., Low, C., Bell, A.I., Ma, C.S., Abbott, R.J., Phan, T.G., Riminton, D.S., Choo, S., Smart, J.M., Lougaris, V., Giliani, S., Buckley, R.H., Grimbacher, B., Alvaro, F., Klion, A.D., Nichols, K.E., Adelstein, S., Rickinson, A.B., Tangye, S.G., 2012. Expansion of somatically reverted memory CD8+ T cells in patients with X-linked lymphoproliferative disease caused by selective pressure from Epstein-Barr virus. J Exp Med 209, 913-924.

Parker, W.T., Ho, M., Scott, H.S., Hughes, T.P., Branford, S., 2012. Poor response to second-line kinase inhibitors in chronic myeloid leukemia patients with multiple low-level mutations, irrespective of their resistance profile. Blood 119, 2234-2238.

Parlane, N.A., Grage, K., Mifune, J., Basaraba, R.J., Wedlock, D.N., Rehm, B.H., Buddle, B.M., 2012. Vaccines displaying mycobacterial proteins on biopolyester beads stimulate cellular immunity and induce protection against tuberculosis. Clin Vaccine Immunol 19, 37-44.

Peperzak, V., Vikstrom, I.B., Tarlinton, D.M., 2012. Through a glass less darkly: apoptosis and the germinal center response to antigen. Immunol Rev 247, 93-106.

Price, P., Haddow, L.J., Affandi, J., Agarwal, U., Easterbrook, P.J., Elliott, J., French, M., Kumar, M., Moosa, M.Y., Oliver, B., Singh, S., Sola, M., Saphonn, V., Vun, M.C., 2012. Plasma Levels of Vitamin D in HIV Patients Initiating Antiretroviral Therapy Do Not Predict Immune Restoration Disease Associated with Mycobacterium tuberculosis. AIDS Res Hum Retroviruses.

Quelhas, D., Puyol, L., Quinto, L., Nhampossa, T., Serra-Casas, E., Macete, E., Aide, P., Sanz, S., Aponte, J.J., Doolan, D.L., Alonso, P.L., Menendez, C., Dobano, C., 2012. Intermittent preventive treatment with sulfadoxine-pyrimethamine does not modify plasma cytokines and chemokines or intracellular cytokine responses to Plasmodium falciparum in Mozambican children. BMC Immunol 13, 5.

Reantragoon, R., Kjer-Nielsen, L., Patel, O., Chen, Z., Illing, P.T., Bhati, M., Kostenko, L., Bharadwaj, M., Meehan, B., Hansen, T.H., Godfrey, D.I., Rossjohn, J., McCluskey, J., 2012. Structural insight into MR1-mediated recognition of the mucosal associated invariant T cell receptor. J Exp Med 209, 761-774.

Ruutu, M., Thomas, G., Steck, R., Degli-Esposti, M.A., Zinkernagel, M.S., Alexander, K., Velasco, J., Strutton, G., Tran, A., Benham, H., Rehaume, L., Wilson, R.J., Kikly, K., Davies, J., Pettit, A.R., Brown, M.A., McGuckin, M.A., Thomas, R., 2012. Beta-glucan triggers spondyloarthropathy and Crohn's-like ileitis in SKG mice. Arthritis Rheum.

Saade, F., Petrovsky, N., 2012. Technologies for enhanced efficacy of DNA vaccines. Expert Rev Vaccines 11, 189-209.

Sakaguchi, S., Benham, H., Cope, A.P., Thomas, R., 2012. T-cell receptor signaling and the pathogenesis of autoimmune arthritis: insights from mouse and man. Immunol Cell Biol 90, 277-287.

Secombes, C.J., Wang, T., Bird, S., 2011. The interleukins of fish. Dev Comp Immunol 35, 1336-1345.

Stent, A., Every, A.L., Sutton, P., 2012. Helicobacter pylori defense against oxidative attack. Am J Physiol Gastrointest Liver Physiol 302, G579-587.

Stone, S.F., Brown, S.G., 2012. Mediators released during human anaphylaxis. Curr Allergy Asthma Rep 12, 33-41.

Subharat, S., Shu, D., de Lisle, G.W., Buddle, B.M., Wedlock, D.N., 2012. Altered patterns of toll-like receptor gene expression in cull cows infected with Mycobacterium avium subsp. paratuberculosis. Vet Immunol Immunopathol 145, 471-478.

Tan, S.Y., Cavanagh, L.L., d'Advigor, W., Shackel, N., de St Groth, B.F., Weninger, W., 2012. Phenotype and functions of conventional dendritic cells are not compromised in aged mice. Immunol Cell Biol.

Tangye, S.G., Brink, R., 2012. A helping hand from neutrophils in T cell-independent antibody responses? Nat Immunol 13, 111-113.

Tangye, S.G., Deenick, E.K., Palendira, U., Ma, C.S., 2012. T cell-B cell interactions in primary immunodeficiencies. Ann N Y Acad Sci 1250, 1-13.

Thomas, R., 2012. Autoimmunity: innovation in pathogenesis and therapy. Immunol Cell Biol 90, 255.

Ting, R.D., Keech, A.C., Drury, P.L., Donoghoe, M.W., Hedley, J., Jenkins, A.J., Davis, T.M., Lehto, S., Celermajer, D., Simes, R.J., Rajamani, K., Stanton, K., 2012. Benefits and safety of long-term fenofibrate therapy in people with type 2 diabetes and renal impairment: the FIELD Study. Diabetes Care 35, 218-225.

Vujanic, A., Snibson, K.J., Wee, J.L., Edwards, S.J., Pearse, M.J., Scheerlinck, J.P., Sutton, P., 2012. Long-term antibody and immune memory response induced by pulmonary delivery of the influenza Iscomatrix vaccine. Clin Vaccine Immunol 19, 79-83.

Wadley, A.L., Lombard, Z., Cherry, C.L., Price, P., Kamerman, P.R., 2012. Analysis of a Previously Identified "Pain-Protective" Haplotype and Individual Polymorphisms in the GCH1 Gene in Africans With HIV-

Associated Sensory Neuropathy: A Genetic Association Study. J Acquir Immune Defic Syndr 60, 20-23.

Wang, X., Laan, M., Bichele, R., Kisand, K., Scott, H.S., Peterson, P., 2012. Post-Aire maturation of thymic medullary epithelial cells involves selective expression of keratinocyte-specific autoantigens. Front Immunol 3, 1-16.

Whitehouse, A.J., Holt, B.J., Serralha, M., Holt, P.G., Kusel, M.M., Hart, P.H., 2012. Maternal serum vitamin D levels during pregnancy and offspring neurocognitive development. Pediatrics 129, 485-493.

Wilkinson, R., Woods, K., D'Rozario, R., Prue, R., Vari, F., Hardy, M.Y., Dong, Y., Clements, J.A., Hart, D.N., Radford, K.J., 2012. Human kallikrein 4 signal peptide induces cytotoxic T cell responses in healthy donors and prostate cancer patients. Cancer Immunol Immunother 61, 169-179.

Win, S.J., McMillan, D.G., Errington-Mais, F., Ward, V.K., Young, S.L., Baird, M.A., Melcher, A.A., 2012. Enhancing the immunogenicity of tumour lysate-loaded dendritic cell vaccines by conjugation to virus-like particles. Br J Cancer 106, 92-98.

Woodward, E.A., Kolesnik, T.B., Nicholson, S.E., Prele, C.M., Hart, P.H., 2012. The anti-inflammatory actions of IL-4 in human monocytes are not mediated by IL-10, RP105 or the kinase activity of RIPK2. Cytokine 58, 415-423.

Yan, J., Read, S.J., Henderson, R.D., Hull, R., O'Sullivan, J.D., McCombe, P.A., Greer, J.M., 2012. Frequency and function of regulatory T cells after ischaemic stroke in humans. J Neuroimmunol 243, 89-94.

Young, A.R., Barcham, G.J., McWilliam, H.E., Piedrafita, D.M., Meeusen, E.N., 2012. Galectin secretion and binding to adult Fasciola hepatica during chronic liver fluke infection of sheep. Vet Immunol Immunopathol 145, 362-367.

Zeng, L., Sullivan, L.C., Vivian, J.P., Walpole, N.G., Harpur, C.M., Rossjohn, J., Clements, C.S., Brooks, A.G., 2012. A structural basis for antigen presentation by the MHC class Ib molecule, Qa-1b. J Immunol 188, 302-310.

Ziolkowski, A.F., Popp, S.K., Freeman, C., Parish, C.R., Simeonovic, C.J., 2012. Heparan sulfate and heparanase play key roles in mouse beta cell survival and autoimmune diabetes. J Clin Invest 122, 132-141.

Upcoming Conferences

15th Biennial Meeting of the European Society for Immunodeficiencies
October 3–6, 2012
Florence, Italy
www.kenes.com/esid2012

ASI2012, 42nd ASM
December 2–6, 2012
Melbourne, Australia
www.asi2012.org

52nd Midwinter Conference of Immunologists
January 26-29, 2013
Pacific Grove (Monterey) California
www.midwconfimmunol.org

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

15th International Congress of Immunology
August 22–27, 2013
Rome, Italy
ici2013@triumphgroup.it
www.ici2013.org

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 YOU COULD WIN $200 FOR THE BEST ARTICLE PUBLISHED IN THE NEWSLETTER!**

The Walter and Eliza Hall Institute of Medical Research

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

2nd Network of Immunology Frontiers Winter School on Advanced Immunology

Singapore, 20–25 January 2013

The NIF Winter School, co-organized by the Singapore Immunology Network & Immunology Frontier Research Center, provides a unique training and networking opportunity to young immunologists. Sixteen International Faculty members and 50 young scientists, selected out of 200, participated in the inaugural event at Awaji Island in January 2012. It is intended to organize the School on an annual basis and to alternate the event between Osaka and Singapore.

The second School offers five days of intensive immunology lectures to young researchers in January 2013. 50 participants will be selected on a competitive basis. Participants are required to give poster and short oral presentations.

Travel fellowships will be awarded on a competitive basis. Accommodation will be fully covered. Registration fee (400 SGD) required of accepted participants.

Eligibility: PhD students and post-doc fellows within 3 years after PhD degree.

Further information:
http://ifrec-sign-winterschool.org/index.html