



N E W S L E T T E R

Australasian Society for Immunology Incorporated

PP 341403100035

ISSN 1442-8725

June 2006

Overview of the JCSMR Immunogenomics Laboratory 2006

Gerard Hoyne

Overview

The Immunogenomics Laboratory at the John Curtin School of Medical Research in Canberra comprises four research groups working in concert to develop an integrated understanding of how our immune system is controlled at the cellular and molecular level by circuits that are specified in our genome sequence. Each of the groups focuses on a different element of a fundamental set of immune system decisions made at the level of individual immune system cells: either to fight or to disarm. The process of deciding which immune cells should fight and which should disarm is key to our ability to resist infection and parasitism. Mistakes in this process result in incurable infections, autoimmune diseases, allergy, lymphoma, and leukaemia. Moreover, drugs and other ways to alter fight or disarm decisions are sorely needed to improve the success of organ transplantation and treatment of autoimmune diseases and metastatic cancer.

For a long time it was not possible to see how memory and effector cells are made, nor how self-reactive lymphocytes disarm themselves. **The Immunogenomics Laboratory** headed by **Chris Goodnow** has pioneered ways to visualize these processes in genetically modified transgenic mice. By studying cells from the transgenic mice, we have discovered that each immune cell must run through a complex series of fight or disarm checkpoints before it can be fully launched into an immune response. In some ways, the process resembles the sequence of fight/disarm decisions in a military missile launch, which serve a similar purpose of preventing friendly fire and optimising targeting against invaders. Together with Adrian Liston a former PhD student in the lab

they were able to reveal that the autoimmune regulator gene AIRE, which is expressed by a subset of thymic epithelial cells, plays a critical role in establishing T cell tolerance to self antigens in the thymus. In addition, Adrian also identified that defective signals to cell death genes account for the inherited resistance of T lymphocytes to clonal deletion in the thymus of NOD mice. Upon infection with a virus or bacteria, B lymphocytes with the right antigen receptors to neutralize infection are stimulated to switch the isotype of their receptor from IgM to IgG, and at the same time secretion of antibodies by these switched cells is dramatically increased. A previous PhD student, Dr Steve Martin, discovered that the switched receptor – and indeed a small tail segment uniquely found in switched receptors – explains the dramatic elevation of antibody secretion that serves as the cardinal measure of immunological memory. It was thought that the IgG tail would enhance antibody production by enhancing a signal within B lymphocytes,

but Dr Horikawa, a postdoctoral fellow in the lab, has made the remarkable finding that the exact opposite is the case. The memory B cell receptor is less active at inducing a subset of genes, and in this case less signal means more antibody formation.

Carola Vinuesa heads the **Humoral memory and Autoimmunity Group**.

Her group is investigating the cellular and molecular events that regulate production and selection versus elimination of memory B cells which is of critical importance to understand how best to harness immune responses against infection, and to mitigate against autoimmunity. One approach utilised by Vinuesa's group is to survey the mammalian genome by ENU mouse mutagenesis to identify single point mutations that predispose to systemic

cont. p4

Chris Goodnow



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ASI Inc. COUNCIL

President

Dr Philip Hodgkin
Walter & Eliza Hall Institute
1G Royal Parade
Parkville Vic 3050

Ph: 03 9345 2609 Fax: 03 9347 0852

Email: hodgkin@wehi.edu.au

Honorary Secretary

Dr Jose Villadangos
Walter & Eliza Hall Institute
1G Royal Parade
Parkville Vic 3050
Ph: 03 9345 2532 Fax: 03 9347 0852
Email: villadangos@wehi.edu.au

Vice President

Professor Alan Baxter
CGC, James Cook University
Townsville Qld 4811
Ph: 07 4781 6265 Fax: 07 4781 6078

Email: Alan.Baxter@jcu.edu.au

Honorary Treasurer

Dr Norbert Kienzle
Queensland Institute of Medical Research
300 Herston Road
Brisbane Qld 4006
Ph: 07 3362 0379 Fax: 07 3362 0105
Email: norbertK@qimr.edu.au

Non-Voting Councillors:

Newsletter Editor

Dr Miles Davenport
Ph: 02 9385 2762 Fax: 02 9385 1389
Email: m.davenport@unsw.edu.au

Journal Editor

Professor Chris Parish
Ph: 02 6125 2604 Fax: 02 6125 2595
Email: christopher.parish@anu.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: 07 3845 3794 Fax: 07 3845 3510
Email: alejL@qimr.edu.au

Council Member of IUIS

Professor Chris Parish
Ph: 02 6125 2604 Fax: 02 6125 2595
Email: christopher.parish@anu.edu.au

Honorary Archivist & Webmaster:

Dr Judith Greer
Ph: 07 3365 5133 Fax: 07 3365 5462
Email: j.greer@medicine.herston.uq.edu.au

Administrative Correspondence

Ms Judi Anderson
ASI Inc. Secretariat
PO Box 7108
Upper Ferntree Gully Vic 3156
Ph: 03 9756 0128 Fax: 03 9753 6372
Email: asi@21century.com.au

State Councillors

New South Wales

Dr Bernadette Saunders
Ph: 02 9565 6114 Fax: 02 9565 6101
Email: b.saunders@centenary.usyd.edu.au

Victoria & Tasmania

Dr Phillip Darcy
Ph: 03 9656 3769 Fax: 03 9656 1411
Email: phil.darcy@petermac.org

Queensland

Dr Christopher Schmidt
Ph: 07 3362 0313 Fax: 07 3362 3510
Email: chriss@qimr.edu.au

South Australia & Northern Territory

Dr Claudine Bonder
Ph: 08 8222 3852 Fax: 08 8232 4092
Email: claudine.bonder@imvs.sa.gov.au

Western Australia

Dr Chris Andoniou
Ph: 08 9381 0799 Fax: 08 9381 0700
Email: cadoniou@cyllene.uwa.edu.au

Australian Capital Territory

Dr Guna Karupiah
Ph: 02 6125 4562 Fax: 02 6125 2595
Email: guna.karupiah@anu.edu.au

New Zealand

Prof John Fraser
Ph: +64 9 373 7599 ext 86036 Fax: +64 9 373 8774
Email: jd.fraser@auckland.ac.nz

FIMSA Councillor

Professor Nicholas King
Ph: 02 9351 4553 Fax: 02 9351 3429
Email: nickk@med.su.oz.au

Contact for Tasmania

Dr Greg Woods
Tel: 03 6226 4830 Fax: 03 6226 4833
Email: g.m.woods@utas.edu.au

Website

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

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

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

Email bulletin board

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

EDITORIAL

This quarter's newsletter brings exciting details of the upcoming annual conference in Auckland in December. A list of speakers is included on pages 13-15, and conference details can be found at the website below.

A new addition to the newsletter is the annual audit of ASI's finances (p8-11). The Council thought it important to share this with members so we can all know our membership funds are being managed well. If reading this is not enough of a challenge, we also have our first "immunology crossword" by our student representative Amanda Taylor (p12) to test your mental agility.

Finally, some reflections by Tony Basten on pages 17-20. Tony retired as director of the Centenary Institute earlier this year and his article is a very humorous and interesting recount of his adventures during a life in immunology.

Miles Davenport

The Day of Immunology – April 29, 2006

For the second consecutive year the European Federation of Immunological Societies (EFIS) has organised the Day of Immunology (DoI) on April 29. This year, the emphasis was on delivering information about the discipline of Immunology to school kids. Most of the activities took place in Germany (Berlin, Hannover, Munich, Erlangen) and Denmark and included conferences and meetings of general interest dealing with subjects such as antibody-therapy, avian influenza and multiple sclerosis.

The main project was the launching of the prize for "Partners in Immunology and Education" (PIE) which will reward proposals fostering the interactions between research institutes and schools that facilitate the understanding of Immunology by school children. The prize of €1 500 will be awarded during the coming European Immunology Congress in Paris (Sept. 2006).

This year, the president of the International Union of Immunological Societies (IUIS), Rolf Zinkernagel made an appeal to all societies to join a coordinated International effort to promote public awareness for Immunology in a Global Day of Immunology on April 29 2007.

A report from the founder of the initiative Stefan Kaufman was recently published in *Immunity* 24,349, 2006. Further details on the initiative can be found in <http://www.dayofimmunology.org>

Treasurer's report on the Financial Audit for ASI for 2004/2005

ASI passed its inaugural financial audit with flying colours. As stated previously to the membership, record growth (note, not net) income and Victorian Government laws made it necessary that ASI underwent an independent audit for the financial year from 1 November 2004 to 31 October 2005. Margaret Crossley from WHK Day Neilson in Melbourne undertook the audit and her findings are to be found on pages 8–11 of this newsletter.

As stated in the summary of income and expenditure, ASI has a total of \$333,743 in accumulated funds including a surplus of \$50,520. These figures are slightly higher as the ones stated in the Treasurer's Report in the minutes of the AGM 2005 (printed in the last issue of the Newsletter); however the AGM calculations reflected operational accumulated funds and surplus including a pre-existing commitment of ~\$24,000 for the annual ASI branch funding.

Overall ASI Council is very grateful to Margaret for her professional assessment and has decided on an annual financial audit for the future.

*Norbert Kienzle
Honorary Treasurer*

**Contributions
sought for the
ASI Newsletter**

**You could win
\$100 !!**

**Deadline for the
next issue :
1st August 2006**

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

**2006 ASI annual conference
Auckland, New Zealand
December 3–7, 2006.
www.asi2006.auckland.ac.nz**

**Sustaining
Membership**

ASI Inc acknowledges the support of the following sustaining members:

- Jomar Diagnostics
- Dynal Biotech Pty Ltd

Overview of the JCSMR Immunogenomics Laboratory 2006 (cont)



Carola
Vinuesa

autoimmune disease. This screen has led to the discovery of Roquin, a key piece in what appears to be a crucial pathway for repressing formation of lupus autoantibodies through regulating the function of T follicular helper (T_{FH}) cells. Work by Dr Diego Silva, a postdoctoral fellow, has revealed Roquin also plays a critical role in peripheral T cell tolerance to pancreatic antigens and is a potent suppressor of autoimmune diabetes. Carola's group is now also investigating whether genetic defects in the Roquin pathway may account for a fraction of patients with SLE or type 1 diabetes. This work is being carried out by Michelle Linterman, a PhD student, in collaboration with John Harley (OMRF, US). In partnership with Dr Matthew Cook, they have launched in the last year the "APOSLE" study, with the aims of establishing an Australian DNA collection from patients with SLE that can be screened for mutations in candidate lupus genes.

Finally, in order to elucidate the molecular signals that regulate memory B cell formation, Vinuesa's group has also taken advantage of a model system in which germinal centres can be produced without T cells. After cell sorting and microarray profiling in collaboration with Professor Ian MacLennan's group (Birmingham, UK), Di Yu has confirmed the differential pattern of expression of a group of genes found in normal centrocytes undergoing T cell-driven selection, but not expressed in centrocytes from sterile germinal centres.

Gerard Hoyne leads the **T Cell**



Gerard
Hoyne

Development and Regulation Group. The main emphasis of Gerard's group has been involved in a genome wide ENU mutagenesis screen to identify new autoimmune variant genes that predispose to organ-specific autoimmune disease using a transgenic model of type 1 diabetes. Through a joint NH&MRC/JDRF funded program grant more than 40 new strains that develop type 1 diabetes have been identified and several of these have entered mapping. In addition two strains have been identified that develop obesity and type 2 diabetes. Other interests in the group is associated with the role of Notch signaling during T cell development exploring the link between Notch and Ikaros in the development of T cell leukaemia, and in collaboration with Dr Sally Dunwoodie at the Victor Chang Cardiac Institute in Sydney, we have been investigating the function of the Notch ligand Delta3 in the immune system.

Ed Bertram is the leader of the **Anti-Viral T cell Costimulation and Memory group** which was established in 2005. Ed is also currently the Head of Scientific Programs at the Australian Phenomics Facility (www.apf.edu.au). Ed's main research interest is in the regulation of CD8+ T cell immune responses using influenza virus as a model pathogen and the role that costimulatory molecules such as LIGHT:HVEM and 4-1BBL:4-1BB, as well signals transduced from costimulatory molecules via Carma-1 influence the differentiation of CD8 + T cells. This work has involved collaboration with Dr Steve Turner and lab members at the University of Melbourne.



Ed
Bertram

A unique collection of C57BL/6 mouse libraries at the Australian Phenomics Facility, bearing chemically induced single DNA changes across the genome have been undergoing a systematic screen to identify pedigrees with genes controlling lymphocyte development and migration, autoimmunity, humoral immune responses, and NK cells. The large-scale project involves Chris Goodnow and Carola Vinuesa's groups as well as Drs Lewis Lanier, Art Weiss, Jason Cyster from University of California San Francisco. Ed will make use of some of these libraries to embark on a new ENU screen to identify genes that regulate the development of CD8 T cell memory and recall to influenza virus.

PhD positions and other research opportunities exist for scientists wishing to join these groups. More information on individual groups can be found at:

Chris's lab web page:
<http://immunogenomics.jcs.anu.edu.au>

Carola's lab web page:
<http://immunogenomics.jcs.anu.edu.au/staff/vinuesa.htm>

Gerard's lab web page:
<http://immunogenomics.jcs.anu.edu.au/staff/hoyne.htm>

Ed's lab web page:
<http://immunogenomics.jcs.anu.edu.au/staff/bertram.htm>

Recent Key Publications:

Miosge LA, Blasioli J, Blery M, Goodnow CC. Analysis of an Ethylnitrosourea-generated Mouse Mutation Defines a Cell Intrinsic Role of Nuclear Factor kappaB2 in Regulating Circulating B Cell Numbers. *J Exp Med* 2002;196:1113-9

SIG Mucosal Immunology Update

Liston A, Lesage, S., Wilson J, Townsend M, Goodnow C. Organ-specific T cells escape thymic censoring as a result of autoimmune polyendocrinopathy syndrome 1 mutation. *Nat Immunol.* 2003;4:350-354.

Jun J, Wilson, LE, Vinuesa, CG, Lesage, S., Blery, M., Miosge, LA, Cook, MC, Kucharska, EM, Dolmanshenz, H, Hong, NA, Glynn, RJ, Hara, H, Penninger, JM, Nelms, KA, Goodnow, CC. Selectively crippled immunogenic responses and atopy in mice with an ENU induced point mutation in the PDZ protein Carma-1. *Immunity* 2003;18:751-76.

Suh WK, Gajewska BU, Okada H, Gronski MA, Bertram EM, Dawicki W, et al. The B7 family member B7-H3 preferentially downregulates Thelper 1-mediated immune responses. *Nature Immunol.* 2003 4:899-906.

Papathanasiou P, Perkins AC, Cobb BS, Ferrini R, Sridharan R, Hoyne GF, et al. Widespread failure of hematolymphoid differentiation caused by a recessive niche-filling allele of the Ikaros transcription factor. *Immunity* 2003;19:131-44.

Liston A, Gray D, Lesage S, Fletcher A, Wilson J, Webster K, et al. Gene Dosage-limiting Role of Aire in Thymic Expression, Clonal Deletion, and Organ-specific Autoimmunity. *J Exp Med* 2004;200:1015-1026.

Liston A, Lesage S, Gray D, O'Reilly L, Strasser A, Fahrer A, et al. Generalized Resistance to Thymic Deletion in the NOD Mouse: A Polygenic Trait Characterized by Defective Induction of Bim. *Immunity* 2004;21:817-830.

Bertram EM, Dawicki W, Sedgmen B, Bramson JL, Lynch DH, Watts TH. A switch in costimulation from CD28 to 4-1-BB during primary versus secondary CD8 T cell response to influenza in vivo. *J Immunol.* 2004 172: 981-988.

Dawicki W, Bertram EM, Sharpe AH, Watts TH. 4-1BB and OX40 act independently to facilitate robust CD8 and CD4 recall responses. *J Immunol.* 2004 173: 5944-5951.

Vinuesa C, Goodnow CC. Illuminating autoimmune regulators through controlled variation of the mouse genome sequence. *Immunity* 2004;20:669-679

Vinuesa C, Cook M, Angelucci C, Athanasopoulos V, Rui L, Hill K, et al. A RING-type ubiquitin ligase family member required to repress follicular helper T cells and autoimmunity. *Nature* 2005;435:452-458.

Goodnow CC, Sprent J, Fazekas de St. Groth B, Vinuesa C. Cellular and genetic mechanisms of self tolerance and autoimmunity. *Nature* 2005;435:590-597.

Vinuesa C, Tangye, SG, Moser B, Mackay CR. *Nature Rev Immunol.* 2005 5:853-865.

A very successful Mucosal Immunology Symposium took place at the ASI meeting held in Melbourne in December. The Symposium was attended by approximately 130 of the conference delegates. Dr Hiroshi Kiyono, President of the International Society for Mucosal Immunology, travelled from Japan to give the Key Symposium talk on "A Potential New Mechanism for the Induction of Orally Infused Tolerance." The standard set by Dr Kiyono was followed by engaging talks from Dorothee Bourges, Sanda Stankovic, Susan Johnson and Phil Sutton.

The Symposium was followed by a meeting of the Special Interest Group to decide on the future directions of the Special Interest Group and on how Mucosal Immunology can be promoted more broadly in the ASI membership. The Special Interest Group in Mucosal Immunology was formed in 1993 and successfully lobbied for the 9th International Congress of Mucosal Immunology, which was held in Sydney in August 1997.

Dr Kiyono briefed the meeting on his vision for greater engagement with the International Society and communicated that issues relating to the focus of Mucosal Immunology was not only a problem peculiar to our own Special Interest Group. At the Melbourne meeting there were only three posters in Mucosal Immunology poster session and it was obvious that Mucosal Immunology related abstracts, particularly those relevant to mucosal vaccines, had been placed in other sessions. As a result, the SIG decided to extend this year's Graham Jackson Memorial poster prize to include orally presented papers from the Symposium. It is important that the SIG promote its activities and particularly the fact that the SIG provides a \$200 prize for the best Mucosal Immunology Poster at the annual ASI meeting.

Dr Kiyono indicated that the 2007 International Mucosal Immunology meeting will be held in Tokyo and seeks input from the SIG on the style of that meeting. Please email any suggestions to Ken Beagley (ken.beagley@newcastle.edu.au).

Ken Beagley briefed the meeting on his activities as the region's councillor on the Council of the Society for Mucosal Immunology and indicated that it was

highly likely that a limited number of travel bursaries would be available for young Australian researchers to attend the international meeting in Tokyo in 2007.

There was general discussion concerning ways in which to advance the SIG and it was decided that a one-day mucosal immunology workshop would be proposed to coincide with the 2007 ASI meeting. It is planned that this workshop will cover gut, respiratory and reproductive aspects of mucosal immunity. In addition, the SIG will continue to support the Graham Jackson Memorial Poster Prize at the annual ASI scientific meetings.

Allan Cripps was confirmed as the ongoing convenor of the Special Interest Group and an Executive Committee was appointed to assist him with the organisation of the SIG and planning of the 2007 workshop. The SIG Executive consists of:

Allan Cripps, convenor

(allan.Cripps@griffith.edu.au)

Ken Beagley

(ken.beagley@newcastle.edu.au)

Margaret Dunkley

(mdunkley@mail.newcastle.edu.au)

Phil Sutton (psutton@unimelb.edu.au)

The SIG Executive Committee would be delighted to receive suggestions and advice with respect to the SMI 2007 meeting in Tokyo as well as the workshop planned for the ASI meeting in 2007.

Congratulations to Sanda Stankovic who was awarded the Graham Jackson Memorial Poster Prize. Dorothee Bourges was provided an award as the runner-up.

*Allan W Cripps
Convenor, SIG Mucosal Immunology*

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
Office hours:
8.30am - 4.30pm

ASI Councillors' News

Queensland News

Each year the ASI sponsors a prize of student membership for the top immunology student at the James Cook University, which is topped up by JCU with a bookshop voucher. This year the prize went to Sharne Beatson. Congratulations also to Queensland ASI member Margaret Jordan (Comparative Genomics Centre, James Cook University), who received the prize for the Best Oral Presentation by a New Investigator at Thymoz 2006 on Heron Island, April 4-10, 2006. She was awarded a year's subscription to *Science* by *Science* editor Stephen Simpson.

This would not be a Queensland News column without mention of Ian Frazer (director, CICR). He has been awarded the Smart State Premier's Fellowship, following his recent Australian of the Year award for his work in developing a vaccine for cervical cancer. The fellowship is valued at \$1.25 million.

This serves as a reminder that the extraordinary impact of Australian immunology research on health worldwide well justifies the increases in medical research funding recently announced in the Federal budget.

Finally, announcement of two immunology meetings now open for registration:

- The Mater Medical Research Institute's 8th Annual Dendritic Cell Symposium will focus on the topic of Antigen processing, and this year the keynote speaker is Prof Ken Shortman, Walter and Eliza Hall Institute. The symposium will be held on the 13-14 July (<http://www.mmri.mater.org.au/> for up-to-date information). Registration is free, but early enquiries are encouraged.
- From August 17-18, the Hotel Watermark (Gold Coast) will host this year's Brisbane Immunology Group Retreat (www.qimr.edu.au/big - registration/abstract deadline July 14). The BIG Retreat is somewhat of a misnomer given that it is never held in Brisbane, not to mention the

attendance by immunologists residing several thousand kilometers from Queensland's excentric capital. But it has become the highlight of our immunology calendar, and achieves an extraordinarily high level of interest, attracted by both the caliber of the scientific program, as well as the extracurricular activities. Last year: polar bears - this year, who knows? ASI Queensland sponsors awards (ASI memberships, medals, and cold hard cash) for the best postgraduate presentation and the best poster. In addition, ASI members receive a \$25 discount (~10%) on the cost of the meeting. Prof David Hume (Institute for Molecular Bioscience, University of Queensland) will feature as this year's Icon (you have to attend the meeting to understand the implications of this), and invited interstate speakers include ASI President Phil Hodgkin (WEHI), Prof Pat Holt (University of Western Australia), Dr Carola Vinuesa (John Curtin School of Medical Research), and Dr Stephen Turner (Department of Microbiology and Immunology, University of Melbourne). Phil Greenberg's talk will be another highlight of the meeting, as part of his ASI-sponsored tour of Australia as an Invited Speaker. Prior to the meeting Phil will be visiting the JCU in Townsville.

*Chris Schmidt
Councillor*

ICB Online Manuscript Submission

Online manuscript submission for Immunology and Cell Biology now available via:
<http://mc.manuscriptcentral.com/icb>

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

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

Victorian News



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

Following last year's successful ASI conference in Melbourne, this year's conference at the University of Auckland, New Zealand also promises to be an equally worthwhile event with a number of national and international invited speakers already confirmed. Details for registration and abstract submissions can be found at the ASI web site. <http://www.wehi.edu.au/collegiate/ASI/>

The next event scheduled for local members is the annual IgV techniques workshop. Details of registration, program and location will soon be available on the IgV website. Another meeting of immunological interest is the Australasian Vaccines and Immunotherapeutics Development Meeting. This inaugural meeting will take place in the Bio21 Institute, Melbourne from May 31 to June 1.

As part of the ASI visiting speaker program, Victoria will be hosting Professor Phil Greenberg on August 7 & 8. Phil is currently co-director of the Immunology Program of the University of Washington Center for AIDS Research and the Head of the Immunology Program at the Fred Hutchinson Cancer Research Center. His research interests include the immunobiology of host T cell responses to infectious viruses and transformed cells and he has pioneered adoptive transfer of T cells for treatment of cancer and viral diseases. It is anticipated that Prof Greenberg will visit a couple of centres in Melbourne and will be available for interaction with ASI members. Information regarding talks and potential interaction will be emailed to members as they become available. We encourage all members to support this worthwhile program.

Just another reminder for benefits of being an ASI member. This includes eligibility for a variety of bursaries and awards. There are great opportunities for postdocs and postgraduate students to receive international travel awards. There are also travel bursaries available for students to attend the annual ASI meeting. Details concerning awards can be found on the ASI website.

*Phillip Darcy
Councillor*

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The Spirit of Adventure



3 March, 2006

The Committee of Management
Australian Society of Immunology Inc.
Secretarial PO Box 710b
UPPER FERNHILL GULLY 3156 Victoria

Dear Committee Members

We are pleased to advise that we have completed the audit of the Australian Society of Immunology Inc. for the year ended 31 October 2005 and subject to the Committee signing the accounts will issue an unqualified audit report.

This letter includes all matters and issues arising from our audit, which we consider appropriate for consideration by the Board and is intended solely for the use of the Committee.

Overview of the Audit Process

We performed our audit for the year ended 31 October 2005 of Australian Society of Immunology Inc. in accordance with Australian Auditing Standards in order to provide reasonable assurance that the financial statements are free of material misstatement. The nature of audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control, and the availability of persuasive rather than conclusive evidence. Therefore an audit cannot guarantee that all material statements have been detected.

1. Confirmation Process

We conducted an independent audit in order to express an opinion to the members of the Society. Our audit was conducted in accordance with Australian Auditing Standards, in order to provide reasonable assurance as to whether the financial report is free of material misstatement. The nature of the audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control and the availability of persuasive, rather than conclusive, evidence. Therefore, an audit cannot guarantee that all material misstatements will be detected.

We performed procedures to assess whether in all material respects the financial report present fairly, in accordance with the Association Incorporation Act, including the compliance with Accounting Standards and other mandatory financial reporting requirements in Australia, a view which is consistent with our understanding of the society's financial position and their performance, as represented by the results of the operations and cash flows.

Accountants & Advisers

An Investor Group firm Suite 2 & 30 Little Collins Street Melbourne Victoria 3000



Offices also in Geelong, Orton Grove and Drysdale



Telephone 03 8686 5688 Facsimile 03 8686 5689
e: info@dayneilson.com.au www.dayneilson.com.au
WHK Day Neilson Audit Partnership ACN 61 917 986 081

We formed an opinion on the basis of these procedures, which included:

- Examining, on a test basis, information to provide evidence supporting the amounts and disclosures in the financial report; and
- Assessing the appropriateness of the accounting policies and disclosures used and the reasonableness of significant accounting estimates made by the directors.

While we considered the effectiveness of management's internal controls over financial reporting when determining the nature and extent of our procedures, our audit was not designed to provide assurance controls.

As a result of the audit we confirm the following:-

1. There have been no disputes with management over the preparation of the current year financial report.
2. All material balance sheet accounts reported as at 31 October 2005 are supported by general ledger accounts reconciliation.
3. We confirm that there are no material errors requiring audit adjustment or that remain unadjusted.
4. We have not detected any fraud or defalcation during our normal review procedures. Such procedures are designed primarily to form an opinion on the financial statements and we have not conducted tests of systems or procedures beyond those required in forming our review opinion.

We have not been made aware of any fraud or defalcation by management.

2. Significant Accounting Policies

There has been no change in accounting policies during the year. It is not anticipated that there will be any significant impact on the financial statements following the adoption of the Australian Equivalents of International Financial Reporting Standards for the year ending 31 October 2006.

3. Management Letter

In carrying out the audit, certain matters arose that were rectified during the course of the audit. However, there are no matters we believe require further action.

As indicated in the engagement letter forwarded to you, we assume no responsibility to design audit procedures to identify matters to report to you, but would communicate any matters encountered during the course of our audit that we believe should be brought to your attention.

The audit review was not a comprehensive review of all systems and procedures and was not designed to uncover all weaknesses, breaches and irregularities in those systems and procedures. Inherent limitations in any management process and system of internal control may mean that errors or irregularities might occur and not be detected. The audit review did not constitute a complete examination of all relevant data and was not designed to uncover all processing errors and therefore, may not have detected all breaches and irregularities that have occurred.

We would like to take this opportunity to thank Dr. Norbert Kienzle and Ms. Judith Anderson for their assistance during the audit.

If you would like to discuss any of the matters raised in this report further, please do not hesitate contact us.

Yours faithfully

WIK Day Neilson



Margaret Crossley
Principal Melbourne office

Hold that date!

The 2006 ASI annual conference will be held in Auckland, New Zealand from December 3–7, 2006.

Invited speakers include Richard Flavell, Marco Colonna, Ian Orme, Bob Coffman and Pam Bjorkman.

More information on the 2006 conference can be found at:

www.asi2006.auckland.ac.nz

AUSTRALIAN SOCIETY OF IMMUNOLOGY INC.**STATEMENT OF INCOME AND EXPENDITURE
FOR THE YEAR ENDED 31 OCTOBER 2005**

	Note	2005	2004
		\$	\$
INCOME			
Conference Income		25,856	-
FIMSA Income		124,404	-
ICB Royalty Income		43,782	47,230
Interest		20,490	10,418
Newsletter advertising		808	696
Porth Income		-	44,063
State Branch		2,941	3,927
Subscriptions		72,812	64,311
Sundry Income		<u>2,604</u>	<u>7,602</u>
		<u>293,695</u>	<u>178,247</u>
EXPENDITURE			
Administration		27,587	21,228
Awards		16,200	17,000
Bank fees		3,309	2,629
Bursary		6,050	21,475
Conferences		3,918	3,507
Council meetings		3,208	-
FIMSA ASI Training Course		124,788	-
Membership fees		3,889	2,649
Productivity Bonus		22,007	-
Publishing		17,535	17,500
Sponsorship		2,000	-
State Branch		6,984	25,419
Speakers		<u>5,740</u>	<u>19,457</u>
		<u>243,175</u>	<u>130,864</u>
SURPLUS FOR YEAR		<u>50,520</u>	<u>47,383</u>
Accumulated Funds at 1 November 2004		<u>283,223</u>	<u>235,840</u>
ACCUMULATED FUNDS AT 31 OCTOBER 2005		<u>333,743</u>	<u>283,223</u>

ASI STUDENT PAGE

It occurred to me when I was looking at the column from the last issue that the heading was "ASI student page" and that maybe I should start thinking about other things to fill up a whole page. I then realised that no way could I waffle on for a whole page so I had to start thinking about other ways to keep you all entertained that might take up a whole page.

The result of this is the first ASI student crossword and, as I'm sure you can all tell, it is the first crossword I have ever made. It's something to keep you busy on those cold winter nights or to burn if you need a way to keep warm. It's all based around that subject most dear to your heart, and no, it's not about sports, food or the opposite sex. Anything that might seem a bit random will be found somewhere in the newsletter.

If anyone else feels like they have something to share to give us all a laugh, feel free to send it to me and if it's not indecent then I will try and include it in the next newsletter. (Assuming I don't get banned after this issue's crossword attempt). Maybe you have a gift for drawing cartoons or even if someone

has emailed you something that you think is good value, just forward them on to me at amanda.taylor@auckland.ac.nz.

Last but by no means least, don't forget about the ASI conference at the end of the year in Auckland. It's a great chance to find out what is happening in the world of Immunology down under (and of course score a free trip to NZ) and for those of you getting close to finishing, think about all those potential employers. They are so much easier to approach after a few wines at the conference dinner.

Now to leave you, here are a few words that don't exist that should that I got emailed a while back. I can't take any credit for these.

Datajinx: The tendency for preliminary data to become unrepeatable once you've told your colleagues about it.

Western spot: Getting high background in your Western blot.

Eppileft: The single, unused eppendorf tube that remains after setting up an experiment. Eppilefts are never actually used in experiments; they are typically thrown away as contaminated waste.

Floater: The tubes you forgot in the ice

bucket overnight.

Amanda Taylor

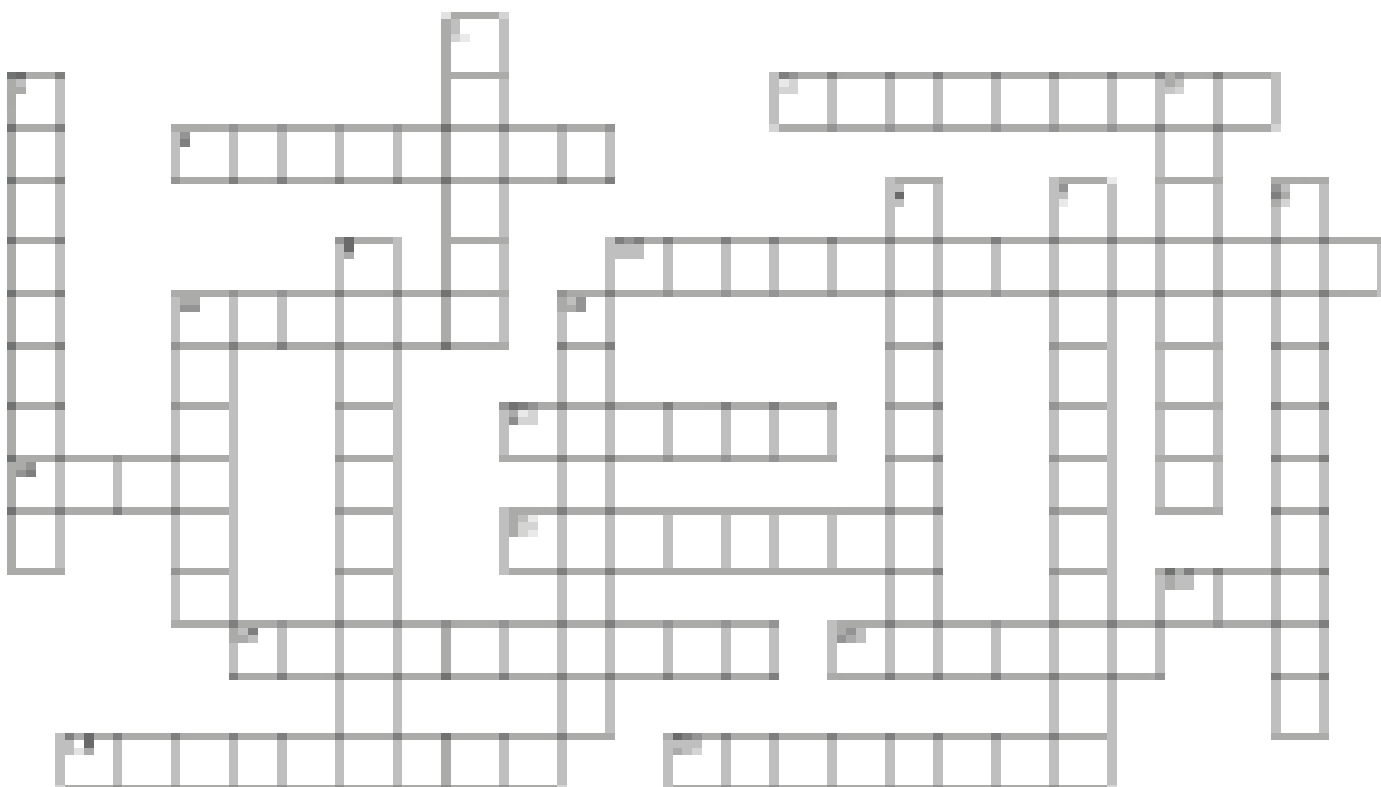
Crossword clues

Across

- 3 DCs in the skin
- 5 Location of ASI conference
- 10 Antibody molecules
- 11 An abnormal growth
- 13 A state of non-responsiveness
- 14 CD54
- 15 Forms membrane pores
- 16 A member of the TNF family
- 17 Small cytokines
- 18 Infection of the blood stream
- 19 A family of cell surface adhesion molecules
- 20 A substance that induces mitosis

Down

- 1 Surname of the NZ council rep
- 2 Programmed cell death
- 4 Enhances an immune response
- 6 Failure to response to an antigen
- 7 White blood cells important in parasitic infections
- 8 Movement of leukocytes through blood vessels
- 9 Found in the blood and act together
- 11 Site of T cell development
- 12 Genetically identical except at one loci



ASI Annual Meeting: “Immunology – From Bench to Bedside” Auckland, December 3–7, 2006

The ASI annual conference will be held in Auckland, New Zealand and we're delighted to invite you all to what will be a meeting that again celebrates all that is exciting about Immunology and its applications. The meeting will be held in the newly constructed Engineering complex on Symonds Street, in the heart of Auckland University and very close to downtown Auckland, hotels and university accommodation. If you have not been to Auckland, this is a golden opportunity to experience Auckland hospitality and combine some excellent science with a great social programme.

The theme of the 2006 meeting is “From Bench to Bedside” stressing the importance of applying basic immunology to resolving clinical problems. Our Burnett orator has been chosen carefully with this theme in mind. Professor Marc Feldman, an Australian now domiciled in London, is best known for his work in developing anti-TNF reagents that are now widely used in the treatment of rheumatoid arthritis and other inflammatory diseases. Professor Feldman was the 2003 recipient of the Albert Lasker Prize in Medicine for his contribution to the treatment of rheumatoid arthritis.

We have a superb line-up of international speakers covering the spectrum of current immunology (see below). In addition, 24 separate symposia that cover the usual themes of Immunology are planned throughout the four days. A special symposium/workshop is planned this year on Immunology teaching.

Specialist workshops

The Tumour Immunology and postgraduate training workshop will be held on Sunday 3rd before the opening of the meeting. As usual, separate registration for TIW and the postgraduate workshop is required.

Registration

All registrations will be conducted on-line. The web-site, www.asi2006.auckland.ac.nz, will be accepting registrations from around the middle of May.

Young Investigator Award

This will be offered again in 2006 and finalists will be selected by a panel from submitted

abstracts. When registering, please signify that you wish to be eligible for the Young Investigators Award.

Accommodation

We offer a five star hotel, Langhams, located at the top of Symonds Street. Rooms at Langhams are \$180/night. A mid-priced hotel, Quest on Mount, offers a slightly cheaper alternative, and budget accommodation has been organised at O'Rorke Halls of Residence at \$55/night. Each is within easy walking distance to the meeting. Contact details for hotels are available on the website.

Invited speakers

Professor Richard Flavell (Yale University)

Prof. Flavell is Sterling Professor of Immunobiology at Yale University School of Medicine, and an Investigator of the Howard Hughes Medical Institute. He received his BSc (Honors) in 1967 and PhD in 1979 in biochemistry from the University of Hull, England, and performed postdoctoral work in Amsterdam (1970–72) and Zurich (1972–73). Before accepting his current position in 1988, Prof. Flavell was first Assistant Professor at the University of Amsterdam (1974–79); then Head of the Laboratory of Gene Structure and Expression at the National Institute for Medical Research, Mill Hill, London (1979–82); and subsequently President and Chief Scientific Officer of Biogen Research Corporation, Cambridge, Massachusetts (1982–88). Prof. Flavell is a Fellow of the Royal Society and a member of the National Academy of Sciences. Richard Flavell uses transgenic and gene-targeted mice to study T cell tolerance and activation in immunity and autoimmunity, apoptosis, and regulation of T cell differentiation.



Dr Caetano Reis e Sousa (London Research Institute)

Caetano Reis e Sousa obtained a BSc(Hons) in Biology in 1989 from Imperial College, London, and a DPhil in



Immunology in 1992 from the University of Oxford. He subsequently spent 5½ years as a postdoctoral fellow at the National Institutes of Health, USA. In 1998, he joined the Imperial Cancer Research Fund, now Cancer Research UK London Research Institute, as head of the Immunobiology Laboratory. He is currently a Principal Scientist and holds honorary appointments at University College London and Queen Mary, London. His research centres on the regulation of adaptive immunity by antigen-presenting cells and innate recognition mechanisms leading to immune activation.

Dr Marco Colonna (Washington University)

Marco Colonna obtained his MD degree from the School of Medicine, University of Parma and completed post-doctoral training at the National Cancer Institute of Genova, Roswell Park Memorial Institute, and Harvard University. He established an independent laboratory at the Basel Institute for Immunology in 1994 and was appointed Professor of Pathology, Immunology and Medicine at the Washington University School of Medicine in St Louis, MO, in 2001. He focuses on receptors mediating innate immune responses, a field in which his accomplishments include identification and characterization of the Killer cell Ig-like receptors and HLA-C polymorphisms as their inhibitory ligands, as well as discovering the LILR and TREM inhibitory and activating receptor families.



Dr Ian Orme (Colorado State University)

Ian Orme is Professor of Microbiology, Immunology and Pathology at Colorado State University in Fort



Collins, Colorado. He worked as a technician in the Immunology Department at the Institute of Child Health in London before attending the University of London where he graduated in 1977 with a First Class Honors degree in Physiology. He then worked in the Immunobiology Department at Burroughs Wellcome while studying for an external PhD degree in Immunology, which was awarded in 1981. From 1981–1986 he did his post-doctoral training at the Trudeau Institute, Saranac Lake, New York State under the supervision of Dr Frank Collins. He joined the faculty at CSU in 1986 and was promoted to Professor in 1995. He has published over 230 publications on the immunology of tuberculosis in the mouse and guinea pig models. He has been the recipient of multiple awards, including the Roussell prize, the Charles H. Shepard award, and the CSU Scholar Impact Award. In 2002 he was elected Fellow of the American Academy of Microbiology.

Professor Steve Henry (Auckland University of Technology)

Professor Steve Henry is the Chief Executive of the Auckland University of Technology Biotechnology Research Institute and is the founder and CEO of the biotechnology company Kiwi Ingenuity Limited. Steve leads a team of 16 biotechnology researchers focusing on commercially viable cell surface modification/manipulation (KODE technology) of cell surfaces. Steve originally trained as a medical laboratory scientist specializing in transfusion medicine and later completed PhDs in biochemistry and transplantation medicine. He has published over 100 scientific papers, abstracts and international patent applications.



Dr Alan Aderem (Institute of Systems Biology, Seattle)

Alan Aderem has studied the interface between the innate and adaptive immune system for more than



twenty years. He obtained his PhD at the University of Cape Town, South Africa. He completed a postdoctoral fellowship at The Rockefeller University in the laboratory of Dr Zanvil Cohn. Dr Aderem rose through the ranks at The Rockefeller University, becoming head of the laboratory of Signal Transduction in 1991. In 1996, he accepted a professor of Immunology and Medicine position at the University of Washington in Seattle. In 2000, Dr Aderem co-founded the Institute for Systems Biology (ISB) with Drs Leroy Hood and Ruedi Aebersold. The ISB is an interdisciplinary institute that focuses on global analysis of complex systems including the immune system. Dr Aderem has been the editor of several journals including the *Journal of Experimental Medicine*. He has also organized a number of scientific meetings including the Gordon and Keystone Conference on immunology and systems biology. He was a Pew Scholar in the Biomedical Sciences and has a MERIT Award from NIAID. Dr Aderem has a longstanding interest in developing world medicine. He serves as a science advisor to the South African government and chaired a Parliamentary Review Commission of the South African Medical Research Council in 1996 and 2001.

Dr Bob Coffman (Dynavax, Berkeley)

Dr Robert L Coffman is the Vice President and Chief Scientific Officer of Dynavax Technologies in Berkeley, CA. Prior to joining Dynavax in 2000, Dr Coffman was a founding member of the Scientific Staff of the DNAX Research Institute in Palo Alto, CA. He has devoted the past 20 years to unravelling the pathways of immune regulation by T cells and cytokines. In 1985, Dr Coffman discovered that Interleukin-4 and Interferon-gamma were the principal cytokines regulating IgE production in allergic responses. In 1986, with colleague Dr Tim Mosmann, he defined the two principal subtypes of helper T cells, termed Th1 and Th2 cells, and demonstrated subsequently that the three major features of allergic responses, IgE, eosinophilia and mast cell hyperplasia, were co-ordinately regulated by the Th2 subset of T cells. Dr Coffman demonstrated that Interleukin-4 mediated class switching to IgE by controlling rearrangement of immunoglobulin genes and discovered the



parallel mechanism for the regulation of IgA responses by Transforming Growth Factor-beta. Over the past decade, Dr Coffman's laboratory has studied the functions of T cell regulation a number of immunological diseases. These include studies of asthma and allergic disease mechanisms, the genetic basis for differences in Th1 or Th2 responsiveness, and the importance of Th1 cells in causing and regulatory CD4+ T cells in preventing inflammatory bowel disease. In addition, his laboratory has made important contributions to understanding the role of T cell and cytokine responses in determining the form and severity of several tropical parasitic diseases. Dr Coffman has authored over 200 scientific publications. In 1997, he received the William S. Coley Award for research in Basic and Clinical Immunology.

Professor Pamela Bjorkman (California Institute of Technology)

Professor Pamela J. Bjorkman is the Max Delbrück Professor of Biology and an HHMI investigator at the California Institute of Technology and Adjunct Professor of Bio-chemistry at the University of Southern California School of Medicine, Los Angeles. She received a BA degree in chemistry from the University of Oregon and a PhD in biochemistry from Harvard University. As a graduate student and postdoctoral fellow in Don Wiley's laboratory, she solved the crystal structure of a human histo-compatibility molecule. She continued her postdoctoral training at Stanford with Mark Davis, where she worked on T cell receptors. Prof. Bjorkman is a member of the National Academy of Sciences and the American Philosophical Society. She has received the William B. Coley Award for Distinguished Research in Fundamental Immunology from the Cancer Research Institute (shared with Don C. Wiley and Jack L. Strominger), the James R. Klinenberg Science Award from the Arthritis Foundation, the Gairdner Foundation International Award for achievements in medical science (shared with Don C. Wiley), and the Paul Ehrlich and Ludwig Darmstaedter Award (shared with Jack L. Strominger and Hans-Georg Rammensee). Prof. Bjorkman's laboratory is interested in protein-protein interactions, particularly those mediating immune recognition. The laboratory uses X-ray crystallography and biochemistry to



study purified proteins, and is beginning to include confocal and electron microscopy (EM) to examine protein complexes in cells. Some of the work focuses upon homologs and mimics of class I MHC proteins. These proteins have similar three-dimensional structures, but different functions including immune functions (IgG transport by the neonatal Fc receptor, FcRn; evasion of the immune response by viral MHC mimics), and non-immune functions (regulation of iron or lipid metabolism by HFE and ZAG). Prof. Bjorkman's laboratory is also comparing the structures and functions of host and viral Fc receptors with FcRn.

Dr Thomas Blankenstein (Berlin)

Thomas Blankenstein received his PhD from the Institute of Immunology in Cologne, Germany. He analyzed the molecular evolution of immunoglobulin variable region



genes such as gene duplications, gene conversion and genomic organization. Since 1988 when he joined the Institute of Immunology of the Free University of Berlin, he worked in the field of cancer immunology. He analyzed whether and under which conditions cytokines contribute to tumor rejection. Currently, he is group leader at the Max-Delbrueck-Center for Molecular Medicine (since 1994) and head of the Institute of Immunology of the Charite, Berlin (since 2000). Some discoveries over the last 5-10 years are: (1) B cells inhibit the generation of tumor immunity; (2) The tumor stroma is a critical target for tumor rejection by T cells; (3) IFN- γ inhibits tumor-induced angiogenesis; (4) Tumors do not lose their intrinsic immunogenicity, while growing in immune-competent hosts. Further work is on T cell engineering for more effective adoptive T cell therapy.

Professor Ian Frazer (Queensland)

Ian Frazer is Director of the Centre for Immunology and Cancer Research, a research centre of the University of Queensland at the Princess Alexandra Hospital in Brisbane. He was trained as a renal physician and clinical immunologist in Edinburgh, Scotland before emigrating in 1981 to Melbourne, Australia to continue



his clinical training and to pursue studies in viral immunology and autoimmunity at the Walter and Eliza Hall Institute of Medical Research with Prof. Ian Mackay. In 1985 he moved to Brisbane to take up a teaching post with the University of Queensland, and he now holds a personal chair as head of the Centre. His current research interests include immunoregulation, and immunotherapeutic vaccines for Papillomavirus associated cancers, for which he holds research funding from several Australian and US funding bodies. Dr Frazer teaches immunology to undergraduate and graduate students of the University. He is on the board of and chairs the Medical and Scientific advisory committee of the Queensland Cancer Fund. He is vice president of the Cancer Council Australia.

Associate Professor Fabienne Mackay (Sydney)

A/Prof Mackay obtained her PhD in 1994 at the Louis Pasteur University in Strasbourg. Co-supervision: Dr Werner Lesslauer (Hoffmann La Roche, Basel Switzerland) and Prof. Diane Mathis. In 1994, A/Prof Mackay joined Biogen/Idex Inc in Boston where she dissected the role of lymphotoxin-alpha/beta in autoimmunity and cancer. This work led to many patents and the development of two new treatments currently tested in the clinic. In 1998, A/Prof Mackay's lab cloned a new member of the TNF family, named BAFF, and discovered the role of this new molecule in B cell-driven autoimmunity. In 2000, A/Prof Mackay joined the Garvan Institute in Sydney as a Wellcome Trust senior research fellow and was awarded a NHMRC program grant. A/Prof Mackay's lab at Garvan discovered the role of BAFF as a key B cell survival factor essential for the maturation of B-lymphocytes and became one the leading group on BAFF research. In March 2006, A/Prof Mackay was appointed to director of a research unit on Autoimmunity. Her unit has a program studying BAFF, the role of B cell subsets in autoimmunity and neuro-immunology projects studying the role of stress hormones on immune functions. A/Prof Mackay has authored more than 40 articles/reviews/book chapters, many in high impact factor journal journals and she is a consultant for several biotech and pharmaceutical groups.



Professor Marc Feldman (Imperial College London) – Burnett Orator 2006



Professor Feldman is the Head of the Kennedy Institute of Rheumatology Division, Faculty of Medicine, Imperial College London. He gained his MBBS (1967), BSc Med (Hons) (1970) and PhD at the Walter & Eliza Hall Institute (with Sir Gus Nossal), all at the University of Melbourne (Australia) (1972). He went to London in 1972 to take up postdoctoral position with Professor N.A. Mitchison at the Institute of Cancer Research Fund, University College Hospital (now Cancer Research UK) where he gained a permanent senior staff position in 1974. He joined the Sunley Research Centre in 1985 as the Deputy Director and Head of the Immunology Unit, which amalgamated with the Kennedy Institute of Rheumatology in 1992 and from then until 2002 he was the Deputy Head of Division and Head of Cytokine Biology and Cellular Immunology Department. His chief interest is the molecular pathogenesis of inflammatory and rheumatic disease, with a special interest in the role of cytokines in rheumatoid arthritis. His major accomplishment has been to discover the important role of TNF α in the pathogenesis of rheumatoid arthritis; this has led to the award, jointly with Professor Sir Ravinder Maini, of the Crafoord Prize of the Royal Swedish Academy of Sciences in 2000 and the Albert Lasker Clinical Medical Research Award in 2003 for the discovery of anti-TNF therapy as an effective treatment for rheumatoid arthritis and other autoimmune diseases.

Comments on ASI from Members

On the Membership Information Update form which accompanies the membership renewal, members are asked to comment on whether ASI meets the member's expectations for a Scientific Society. This year, a total of 46 comments were received from the 591 who had renewed at the time of preparing this newsletter. Of these, 23 simply said either *Yes* or *Meets my expectations*, or variations on that theme. The more substantive comments are listed below:

Doing well – 2005 meeting a great success

I would like to see publication of the annual ASI meeting abstracts – if not in *Immunology & Cell Biology*, then at least as a member-accessible PDF.

Yes. Good job done by many willing and friendly volunteers.

The scientific meeting in Melbourne in 2005 was excellent.

More attention to clinical immunology is urgently required.

Yes – active state committees, good conferences, good newsletters.

Mostly – not enough visiting speakers coming to NZ!

It would be great to have more ASI training/seminars in the area of Education – University level immunology - share ideas, etc.

I think ASI does a fine job with conferences, workshops and keeping us up to date on relevant news through the newsletter.

I would like to see some more emphasis on Veterinary Immunology.

More student bursaries for travel to overseas conferences.

Yes, I am satisfied with the services ASI provides me.

ASI 2005 was a fantastic conference.

I appreciate the regular emails which keep us up-to-date on seminars and visiting lecturers etc. Annual conferences are always well organised and worthwhile, newsletter is informative, therefore meets expectations.

Yes, I think ASI does a good job.

ASI is well organised and doing a great job.

Very happy.

ASI is excellent.

I think member services for students are limited. ASM provides grants for students to travel interstate to learn about new techniques and fosters inter-lab collaboration better.

I am enjoying my time as a Student Representative and also ASI has been valuable in organizing conferences and workshops.

Really great society! Wouldn't change it.

ASI has met all of my expectations. Great work.

ASI does meet my expectations. I can't think of anything that may help to improve it.



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An Immunological Saga

Tony Basten

Professor Tony Basten retired as Director of the Centenary Institute earlier this year. Here he reflects upon a career in Immunology.

Early Years: 1958

My first inkling that there was a subject called immunology occurred in 1961 when I was in fourth year medicine at Adelaide University – my first teacher the newly appointed Professor Derrick Rowley. The most vivid recollection I have of him was his vintage blue Austin Seven which one day we took to pieces and re-assembled in his office in the lunch hour. Although this was a sore test for his Yorkshire temperament, he gracefully allowed the culprits, after exhaustively researching our identities, to pass at the end of the year.

My one foray into research during my undergraduate days was in the department of surgery where I measured sodium levels by flame photometry in bile collected from patients undergoing T-tube drainage post cholecystectomy – afar cry from immunology but a paper (my first) nevertheless in a journal, albeit with an unrecorded impact factor.

The Oxford Years: 1966 – 1969

My real career in Immunology began serendipitously when I arrived in Oxford on a Nuffield Clinical Assistantship in early 1966 just a few months after the new professor of Medicine, Sir Paul Beeson. In contrast to his haematological predecessor, Witts, with whom I was originally supposed to work, Beeson was one of America's renowned experts in infectious disease who by chance had previously collaborated with Derrick Rowley on the role of complement in renal disease – a small world indeed. He offered me two projects, one to study the effects of iodides on granulomas and the other on the mechanism of eosinophilia which appealed rather more. One reason for this was the fascination the eosinophil had held for many a scientist in the past. Thus by 1914 there were 2758 references in the literature compared to a few hundred for neutrophils and a handful for macrophages. As a greenhorn in the lab, I was set to work grinding up rat muscle to yield the parasite *Trichinella Spiralis* as a stimulus for eosinophilia. On reading about it, I discovered with some concern that not only were polar bears, pigs and stray cats

the animal reservoirs, but the standard form of suicide amongst Eskimos was ingestion of uncooked polar bear meat. Six months later, however, I was still standing, albeit intoxicated with ether and the rats had developed a substantial eosinophilia.

The next step was to isolate the eosinophilic factor from the parasite for which I was instructed to use a high voltage water cooled electrophoresis 'machine'. The instruction manual (dating back some 20 years) recommended running the machine over the weekend. This I did, but on Monday morning when I arrived in the lab I was met by a very short, very irate man whom I did not recognise. He took me, protesting, by the ear and conducted me downstairs to a lab which was flooded with water from the machine and contained a brand new gamma counter. From this was emerging roll upon roll of printout containing nothing but the words 'you dill Bill, you dill Bill ...' – Bill being the name of the chief technician as I gathered later. Being human I laughed, another serious mistake, and was then taken into this man's office. After taking down the Index Medicus, he asked me my name: 'Basten, A, sir'. Under that name he found six citations. Having handed me the tome, I was invited to turn to page 205 where

to my horror I found the name Krebs, H with citations going on for pages. 'When you have as many citations as I have young man, you may piss into my Nobel equipment as much as you please, but until then get out!' A week later he invited me back to use his equipment instead under Bill's guidance.

It was about this time in 1967 that lymphocytes were becoming fashionable and the discoverer of their functional capabilities, Professor Jim Gowans, was just down the road in the Dunn School where Florey had developed penicillin as a therapeutic. I told him that I had a bee in my bonnet that eosinophilia was T cell dependent and asked him to teach me thoracic duct cannulation. Not only did he do so, but met me in his lab every night to collect the lymph. Thanks to him I was able to prove the hypothesis and be awarded my D.Phil. The doctorate was presented in Christopher Wren's Sheldonian Theatre by Sir Peter Medawar who gave the occasional address in Latin and then in English. How fortunate I was that Witts had retired, presenting me with the opportunity to interact with such a stellar group of scientists and become an immunologist not a haematologist.



Tony Basten (left) with a young Mark Hogarth and Bob Raison at 1980 World Congress in Japan

Then followed a year of uncertainty. I was due to do my postdoc with John Humphrey at the National Institute of Medical Research in London's Mill Hill (where James Murray began his famous work on the Oxford English Dictionary). Humphrey, however, regularly smoked a pipe in his office and after falling asleep, burnt half his laboratory down. He and Gowans then put their heads together. Their solution was to put me in touch with Jaq Miller at the Walter and Eliza Hall Institute and what a great solution that turned out to be.

WEHI years: 1970 – 1972

I recall appearing for the first time in Jaq's lab when he was doing neonatal thymectomies with a technician who had the tiniest of mini skirts. On my arrival in the lab he asked 'Who are you?' he asked and when I replied he said, 'Oh good, come back in six weeks – I am busy'. Fortune favoured me again and I found solace next door with Jon Sprent who had 30 mice cannulated on old jam tins and with whom I have remained firm friends ever since.

In those days, WEHI under Gus Nossal's directorship was amongst the most exciting and dynamic immunological centres anywhere in the world. Even for young scientists there were so many experiments just waiting to be done. Jon and I thought we would solve immunological memory by determining whether it was a quantitative or qualitative phenomenon. The primed mice yielded 20% antigen binding cells in thoracic duct lymph versus <1% in controls – QED I thought but was unable to repeat the experiment. Eventually the penny dropped: the primed mice of course had made antibodies which adhered loosely to Fc receptors on the B cells and could be washed off before addition of antigen but not afterwards. The moral: always put the number of centrifugations in one's day book. The discovery of the Fc-receptor was therefore pure luck or serendipity. A bonus for me was working with Noel Warner (now a Vice President and head of R&D at BD) to establish the heavy chain binding specificity of the FcR.

The early 70s was also the time when T cell derived soluble factors and suppressor T cells first emerged on the

immunological horizon. In the Miller Unit the focus was on the latter and we established them as a fail safe mechanism in tolerance just after Peter McCullagh at ANU and Dick Gershon in USA published the initial reports on their existence. Our suppressor cells were CD 8+ as well as expressing the elusive MHC related IJ molecule. T cell derived soluble factors were the province of Marc Feldmann, then a PhD student in the Nossal Unit and my squash partner. By using the then famous Diener/Marbrook double chamber culture vessel we demonstrated the existence of antigen specific and non-specific factors by placing T cells above and B cells below what we believed to be a cell impermeable membrane. Some years later it was shown that T cells could in fact migrate through the membrane but Marc had moved on and begun his seminal work on the role of TNF in inflammation which formed the basis of his and Tiny Maini's use of anti-TNF monoclonals in treatment of rheumatoid arthritis.

This era completed my training and the acquisition of an array (range) of wonderful colleagues and mentors who have continued to enrich my career. It was at this time that I was greatly buoyed by coming across Burnet's wittiest aphorism. In answering the question of why support research, he wrote: 'Rulers of any ideology have always found it dangerous to have a considerable group of unemployed intellectuals and professionally trained men'.

University of Sydney/Royal Prince Alfred Hospital era: 1972 – 1982

When my Fellowship at the Hall Institute finished, I had three options: to stay on as Jaq's second in command, to apply for a senior lectureship at Sydney University in the departments of Bacteriology and Medicine with Professor Pat de Burgh (the BSc. Med. Supervisor of Metcalf, Nossal and Miller) and Professor Ruthven Blackburn respectively, or to accept an offer from Derek Rowley to return to Adelaide. The latter proposal was most flattering as Rowley informed me that I had improved significantly since my days as a rather 'mischievous' undergraduate. The problem, however, was that I would have to find a salary – no easier then than it is now! Although a hard decision at the time to pick between Sydney and Melbourne, I decided on Sydney, a choice I have never regretted.

Sydney in those days was very different from Melbourne: clinical medicine was

exceptionally strong thanks to Ruthven Blackburn, whereas there were great opportunities to develop research oriented units. My first lab was located in David Nelson's section of de Burgh's department. My office had the unique feature of being the preferred location for the largest and most sluggish blow flies in Australia. Nevertheless it was possible to work on suppression in tolerance and immunity and to add the now forgotten Transfer Factor (TF) to the menu. This low molecular weight leucocyte extract according to New Yorker, Sherwood Lawrence could transfer DTH to naïve recipients. In the absence of a T cell receptor or any known cytokines, this intrigued a number of immunologists, among them a student of James Watson who fraudulently claimed that TF contained low molecular weight mRNA – a cause celebre at the time. In collaboration with Chris Parish, we subsequently showed it in fact contained fragments of antigen and low molecular weight Ia, thereby explaining its apparent specificity. On the other hand, TF was side effect free and we used it to treat immunodeficient patients, including those with APECED, with anecdotal success as well as conducting a two year controlled trial in multiple sclerosis where patients with relapsing disease appeared to benefit due, it seemed, to a reduction in the number of febrile episodes and consequent relapses. TF has now sunk into obscurity and unlike suppressor cells has not been resurrected. Ironically, however, it did more to promote our image in the community than all our Nature papers put together!

During the late 70s, T cell dependent suppression remained in vogue and was widely accepted by the immunological community to the extent that it was a guaranteed ticket to Brook Lodge and Cold Spring Harbor Symposia. The 1976 CSH symposium was particularly memorable with suppression being interwoven with the discovery of MHC restriction by Doherty and Zinkernagel. While our host, JW, was selecting his postdoc for the night, Peter Doherty was standing on the table setting up a new research centre. My appointed task was to act as the medical officer since suppression, in his view, was 'a load of old cobblers'. What led to its temporary demise was the failure to identify a gene for IJ and development of impossibly complex circuits linked by suppressor factors which existed only *in vitro*. Now suppressor cells have been reinvented as Tregs and the old literature

conveniently forgotten.

At the same time I was tasked with the responsibility of setting up a clinical immunology service at nearby Royal Prince Alfred Hospital. In those halcyon days all one had to do was write a one page letter to the hospital General Superintendent and a secretary followed by two scientific officers materialised. The next 8–10 years were among the happiest of my professional life because at that time it was still possible to combine competitive basic research with clinical medicine. I was privileged to work alongside a cadre of great physicians and resident staff the first two of whom were Graeme Stewart and Paul Gatenby, now of course distinguished in their own right. Rarely did a week go by without an immunological case being presented at Grand Rounds: ‘if the cause of a disease was unknown then it must be immunological’ – a view which was very good for our image! Because of its intrinsic importance in pathogenesis of many diseases, immunology became a recognised specialty in the Colleges of Physicians and Pathologists in 1974 with the first training centres in Sydney being located at Royal Prince Alfred and St Vincent’s Hospitals under the direction of myself and Ron Penny respectively. Consequently our unit became a focus for combined clinical and research training for those aspiring to be immunologists/allergists *per se* and aspirants from the many other related disciplines. When trying to seduce PhD students to join the lab, I always enjoyed quoting Peter Medawar’s definition of clinical immunology: *‘It bears upon every branch of medicine and every organ system in the body.’*

The CIRCUS: 1982 – 1989

1982 was the year when the immunology unit became the Clinical Immunology Research Centre University of Sydney (known as the CIRCUS), one of the first 10 Centres of Excellence to be set up by the Federal Government. The Medical School could not accommodate us so that we moved into a picturesque 19th century ‘classic’ building which was formerly the morgue, the residents’ quarters and Dermatology ward before being declared uninhabitable by patients (but not by immunologists). The building was shared with the hospital department with which close ties have existed ever since.

As suppression waned, transgenesis was introduced to the centre by Chris Goodnow

and the HEL/anti-HEL pizza eating mice were born. The choice of B cells not T cells to study was a tactical masterstroke of the type for which Chris has now become famous. He worked in close association with Jeff Crosbie and Rob Brink, both of whom remained part of the home team while Chris has gone on to achieve great things, first at Stanford and more recently at the John Curtin School in Canberra. To be part of the early days of transgenic models was for me an absolute delight and real compensation for the drudgery of administration. The editor of this Newsletter will remember the CIRCUS when he worked there as a BSc Med student with a square foot of bench space and a place on the conduit for the tie he never wore.

HIV AIDS Years: 1987 – 1989

Early in 1987 I received an unexpected phone call from the then Federal Health Minister, Neal Blewett, inviting me to take over the Chairmanship of the AIDS Task Force with Ian Gust, the Founding Director of the Burnet Institute as Deputy. This proved to be a fascinating challenge as HIV/AIDS and its management were still in their infancy. I came to meet and work with not just the Bruce Shepherds of this world, but the gay community, IV drug users, the Prostitutes Collective – all much better educated about the disease than the population at large and other groups like the Breast Feeding Mothers Association. The latter in a sense epitomised the issues raised by AIDS, their stance at the time being that pregnant women should not be tested for the virus which to me implied that the unborn had no rights. The Task Force was subsumed into the Australian National Council on AIDS (ANCA). The new council was chaired by Professor Peter Karmel, formerly chairman of the AUC, a distinguished economist and father of seven with Ron Penny and myself as the Chief Advisers on Education and Medical and Scientific Aspects of AIDS respectively.

Fronting up to the media as one of the ‘three wise monkeys’ (a Karmel term) was quite an experience, but we had good backup since ANCA contained some of Australia’s top research brass including not just Ian Gust but Fiona Stanley, Peter McDonald and John Chalmers. At my interview with the press on my resignation to become the Centenary’s Director, I recall making three points. On the positive side of the equation were: (a) the creation of the first multi-disciplinary grants committee (CARG) where virologists and immunologists sat

cheek by jowl with behavioural scientists and epidemiologists and; (b) the fact that AIDS had been taken off its artificial pedestal and reinstated into mainstream medicine – very much to the benefit of the patients. On the negative side was the stultifying effect on decision making of the bureaucracy and army of government consultants. Nevertheless the first White Paper on AIDS was a credit to this country and the disease has continued to be managed sensibly ever since.

Centenary Years: 1989 – 2005

The origins and early history of the Centenary Institute of Cancer Medicine and Cell Biology are summarised in a 1999 paper published in the Medical Journal of Australia. In practical terms it is one of the second generation of independent institutes originally created around the CIRCUS in the image of the major Melbourne institutes, the goal being to co-ordinate research in NSW, to act as a beacon for attracting back from overseas outstanding young Australian scientists and to obtain block grant funding from the NHMRC. Since its creation, Centenary has been best known for its immunology, although in recent times outstanding molecular biologists like John Rasko, Chris Semsarian and John Allen have joined the staff and expanded the research base. Thanks to the magnificent efforts of the management team, particularly Denyse Bartimote (General Manager) and Jeff Crosbie (Operations Manager), as well as key members of the Board like Dr Bernie Amos (then Director General of State Health), we secured the 21 million dollars needed to commission a new building which was officially opened by John Howard in 1997. The opening ceremony was a great success despite being overshadowed by Pat Rafter winning the US Tennis Open just as the PM took to the podium.

What was the highlight for me during my 15 years as Director was the number of talented young men and women who chose to work at Centenary and on whose performance its track record is now firmly based. In addition, Centenary of today has one of the best flow cytometry and transgenic animal facilities in the country as well as a diversified research staff which augurs well for the future be it in immunology, cancer or some other field. The challenge for the new director will as



Tony Basten with Prime Minister Howard and Professor Peter Doherty AC at official opening of new building in 1997 (you can see we are celebrating Pat Rafter's victory)

always be to secure the resources needed to preserve what is a very valuable asset for NSW and Australia.

Colleagues and Friends

Personal friendships are one of the bonuses of doing research, often overlooked in a life of grant deadlines, meetings and student responsibilities. I have already mentioned some of the senior immunologists responsible for shaping my career particularly Jacques Miller who, in my book, is as multi-talented as the likes of Edward Jenner. The latter, in addition to pioneering smallpox vaccination, was an oboist, ornithologist and curator of the British Museum, while Jaq is not just the discoverer of the thymus but an accomplished artist, French chef and an authority on Dante's *Inferno*. However, it is also timely to acknowledge the friendship and support of my peers. Jon Sprent, Peter Doherty and Marc Feldmann have been life long colleagues and a source of many stimulating hours of discourse on virtually every topic known to man. Likewise the 2005 Burnet Orator, Ian McKenzie, whose generosity with reagents in the early days of the two cell system is legendary, his successor at the Austin Research Institute, Mark Hogarth who has made the FcR his own, and Mauro Sandrin whose expertise at snooker improves exponentially after midnight. A little farther afield have been

Chris Parish and Geoff Shellam, the former a wonderfully stimulating ideas and techniques man as well as a pioneer in biotechnology and the latter a great contributor to NHMRC and the Fellowships' scheme over the years. Finally I have been greatly privileged to be associated at the CIRCUS and Centenary with many talented students and colleagues like Barbara Fazekas, Chris Goodnow and Phil Hodgkin, all of whom have excelled in their own right. Indeed, 16 of them now head their own research enterprises or departments and even faculties across Australia. By way of acknowledgement I would be so bold as to quote from Isaac Newton: *'If I have seen further on occasions, it is by standing on the shoulders of giants'*.

In Peter Doherty's eminently readable book entitled *'The Beginners Guide to Winning the Nobel Prize'*, he lays down 18 criteria for being a successful scientist. On running my career past them, I score well for choosing an appropriate field (Immunology!), working with the right people, being prepared to fail and enjoying my fair share of luck. On the other hand, I have done less well in my attempts to avoid what he termed 'prestigious administrative roles' and being a dilettante, i.e. working on both T and B cells.

The Future

Having attended the 2005 ASI meeting in Melbourne, I can say without fear of contradiction that the immunological legacy

of Burnet, Lafferty, Miller and Nossal is alive and well. What was particularly impressive was the depth and variety of the scientific presentations. In addition to those of the usual high fliers, there were a number of outstanding presentations from students, postdocs and research fellows. To try and keep up with these young stars, I plan to spend 6–12 months at the Laboratory of Molecular Biology in Cambridge brushing up on my pipetting, annealing and thinking with Greg Winter, Michael Neuberger and Doug Fearon. The real challenge, however, for an ex Oxford man will be punting from the wrong end of the boat!

I do sometimes wonder what is the long term future for immunology and its tool box of vaccines, cytokines and monoclonals. The more effective these tools become, the more likely is it that the burden of infectious disease and cancer will diminish – will the world cope with the resultant increase in population? Being a born optimist I think it will. I agree with Gus Nossal's view of immunology expressed as long ago as 1982: *'The overwhelming impression is one of tremendous growth in knowledge and power; of a discipline that has reached full maturity and independence; of a future with possibilities.'*

UPCOMING CONFERENCES

17th Annual Meeting – ASCIA
September 7–10, 2006
Sydney
incorporating ASCIA Primary Care
Allergy & Immunology Update,
September 10
Website: www.allergy.org.au

International Conference of
Immunogenomics and Immunomics
October 8–12, 2006
Budapest, Hungary
Website: www.bcii2006.org

3rd International Congress on Healthy
Ageing and Longevity
October 13–15, 2006
Melbourne
Website: <http://www.longevity-international.com/>