ISI Newsletter
Irish Society for Immunology

April 2003 Issue

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ICS and ISI conference dates: Coincidence… or not???

Is it a coincidence that the prestigious International Cytokine Society Annual meeting to be held in Ireland from 20th-24th September, 2003 falls back to back with the annual ISI meeting? ***Of course not***, it was planned to make attendance by ISI members even easier!!!!

Trinity College will provide the backdrop for one of the most exciting scientific programmes seen locally, or internationally, in recent years. A wide range of topics will be covered – from cytokines and disease to signal transduction; T cell regulation, chemokines, inflammation, specialized sessions on both known and novel cytokines and of course, cutting edge presentations on TLRs (not surprising given that Luke O'Neill is chairman of the organising committee!!) – there's something for everyone with an interest in the basic biological sciences. Guest speakers include Alberto Mantovani, Joseph Schlessinger, Shizuo Akira, Joost Oppenheim, John O'Shea, Charles Dinarello, Nancy Rothman, Richard Flavell, Nancy Ruddle, Warren Leonard and our own Kingston Mills. A number of awards and fellowships are hosted by the ICS and local post-docs and graduate students are especially encouraged to apply (CASH PRIZES). Entertainment (included in the registration fee) includes Welcome Reception, State Reception in Dublin Castle and a Banquet Irish night in historic TCD. Additional tours (additional cost!) will also be available.

All details, including the on-line registration form can be found at www.ics2003.net. The abstract deadline is June 11th, 2003 so remember to put the dates in your diaries and plan to attend the conference of the year, 2003 - the ICS (after the ISI.)

Membership

!!!!!! Tell your friends about the ISI !!!!!!!!

Annual Membership: € 40 (full) €20 (postgrads)

Benefits: Reduced registration for ISI meetings
Free admission to ISI events (public lectures, workshops, etc.)
Reciprocal membership : Ulster Immunology Group
Access to ISI directory
Free subscription to ISI newsletter
Postgrads - Ellegibility for travel bursaries
- Oral & poster prizes at ISI meeting

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BSI 2002 Report :

Antimicrobial peptide mediators of host defence : bridges between the innate and adaptive phase of the immune response

Colin Murtagh,
Innate Immunity Group,
Education and Research Centre,
St.Vincent's University Hospital

The BSI conference was an excellent experience for me, especially the Thursday session entitled 'Antimicrobial Peptides and the Innate Immune Response'. This session included talks from some of the most influential researchers in this field, e.g. Tom Ganz, Chuck Bevins, Yash Mahida, etc. The overall impression I got was that this is an area of research which is becoming increasingly important and hence popular. Deborah O'Neill explained her delight in organising a whole day devoted to AMPs and innate immunity in a week which was predominantly focused on adaptive immunity. This set the tone for the day as most speakers steered clear of adaptive processes or apologised for briefly mentioning them!

Tom Ganz gave an excellent talk on Hepcidin, which is essentially LEAP-1. He suggested that hepcidin limits iron availability during infection. As iron is essential for microbes, iron sequestration via hepcidin is a human defence strategy. However, this does leave infected patients in an anaemic state. Mice lacking hepcidin develop iron overload in the liver whilst mice over-expressing hepcidin die of anaemia, therefore hepcidin is a key regulator of iron metabolism. Interestingly, he briefly commented on the amino acid sequence which contains 8 cysteines, including three pairs which create kinks that are important for the folding properties of the protein. I was encouraged when listening to this as the first mismatch in my LEAP-2 sequence creates a pair of cysteines. Initially we ruled it out as an error but it may not be as unlikely as we first thought.

The ISI Logo Competition is still running (prize €200), but here are some sample entries :

€200 Prize for winning logo

all by John Curtin, Dept of Microbiology NUI Galway

by Michael Welsh, Vet. Sciences Division, Stoney Rd, Belfast

by Christian Coates, St. James' Hospital, Dublin

by Graham Donnelly, TCD

Send entries to derek.g.doherty@may.ie or any ISI committee member

M Bajaj-Elliott gave an interesting talk on beta-defensins in the GI tract. Her studies suggest that infecting microbes may develop diverse strategies in regulating the expression and function of epithelial beta-defensins, thus allowing them to colonize and persist in the gut mucosa. She talked about *Heliobacter pylori* as an example of such a microbe. It has a long association with the human stomach but peptic ulcer disease is relatively new, therefore the pathogenicity has evolved. This type of microbial resistant may be taking part in *Eimeria*-infection in our chicken model. The parasite itself may have developed a mechanism for down-regulating pro-inflammatory mediators.

There were many other interesting talks during the day, most of which focused on defensins. Other highlights of the week included a talk on stress-induced inflammation by M H Perdue from Canada.

This talk leapt up at me from the page when flicking through the programme as we thought this might be occurring in our chicken model. Their studies suggested that psychological stress in rodents can initiate intestinal inflammation by decreasing epithelial barrier function and allowing enhanced uptake of antigens. This suggested to me that the outcome of stress on our chickens would be an increase in inflammatory mediator production and not the down-regulation that we have observed. In short, I don't think that stress is causing our results.

All in all, it was an very well organised week which I believe I got a lot out of, in particular the AMP session which underlined for me the importance of this area of research.

Colin Murtagh.

Up-coming Meetings

Inaugural Symposium
Institute of Immunology

NUI MAYNOOTH
Ollscoil na hÉireann Má Nuad

The inaugural symposium of the Institute of Immunology at NUI Maynooth will be held on Friday April 11th from 1 to 6 pm. Nobel laureate, Professor Peter Doherty, will deliver the keynote address. Unfortunately seating is limited to 100 persons so a **reply by e-mail before April 3rd** to bpmahon@may.ie

Time	Event & Location
1.00 pm	Reception in Foyer of Institute of Immunology (Venue: New Bioscience Research Building). Transfer to Arts lecture theatre 2 (Th2)
2.00- 2.45	Keynote address: Nobel Laureate Peter Doherty
2.45- 2.55	Presentation and awards
2.55- 3.20	Dr Shirley O'Dea: "Immunity and repair in the airways"
3.20-3.45	Coffee
3.45- 4.00	Postdoctoral Presentation: Dr David Casey "siRNA silencing of immune mediators"
4.00- 4.25	Dr Derek Doherty: "Non-classical T cell populations in the Liver"
4.25- 4.35	Postgraduate presentation:
4.35- 5.00	Dr Patricia Johnson: "Immune modulation by Influenza"
5.00- 5.25	Dr Bernard Mahon: "*B. pertussis*, asthma, and the hygiene hypothesis"

17th Annual Meeting of the European Federation for Immunogenetics
May 6th-9th 2003
Baden-Baden, Germany
Website : www.efiweb.org

2nd Annual Irish Society for Immunology Award Public Lecture
May/June 2003 (Date TBC)
RDS, Ballsbridge

Hepatitis C – Past, Present, Future
25-17th June 2003
International Conference
Trinity College Dublin .
Topics: Current and new treatment modalities; Immune responses to Hep C; Transplantation for Hep C; Liver Immunology; Immunogenetics.
Website: www.hepc2003.com

British Society for Histocompatability & Immunogenetics
Sept 3rd-5th 2003
Newcastle
Website : www.bshi.org.uk

"Flexibility of mouse classical and plasmacytoid-derived dendritic cells in directing Th1 and Th2 cell development: dependency on antigen dose and differential Toll-like receptor ligation"
Dr Anne O'Garra, Head of the Laboratory of Immunoregulation, The National Institute for Medical Research, London
16th April 2003 at 5.00pm in lecture theatre LTEE2, East End Building (under Smurfit Institute for Genetics) Trinity College, Dublin
AND
17th April 2003 at 5.00pm in the Postgraduate Lecture Theatre, Belfast City Hospital

(Title TBC)
Prof Koen Vandenbroeck, Lecturer in Biomolecular Sciences, School of Pharmacy, Queen's University, Belfast
Thursday 1st May at 5.00pm in the Sir Samuel Irwin lecture theatre at the Royal Victoria Hospital Belfast.

"Cytokine signalling, from the membrane to the nucleus and back"
Dr Massimo Gadina, Senior Lecturer, Department of Microbiology and Immunology, Queen's University, Belfast.
Tuesday 3rd June at 1.00pm in the Common Room, Microbiology & Immunobiology Building, Royal Victoria Hospital, Belfast.

International Cytokine Society Annual Meeting 2003
Trinity College Dublin
Sept 20th – 24th, 2003
register on-line www.ics2003.net
Abstract deadline June 11th 2003

The 19th Annual Irish Society for Immunology Meeting on Immunity and Disease
18th-19th Sept, 2003
Topics: Autoimmunity; Innate Immunity and Disease
Abstract deadline June 30th 2003

BSI Annual Congress
December 2003
Website : www.immunology.org

PAPER ALERT

Peripheral Neuropathies and Anti-glycolipid Antibodies.

H.J.Willison and N. Yuki. 2002. Brain **125:** 12, 2591-2625.

This wonderfully-written review charts the progress of anti-glycolipid antibodies in neuropathy, from their original discovery 20 years ago through to current discoveries. Antibodies to more than 20 glycolipids have been associated with a wide variety of clinically identifiable acute and chronic neuropathy syndromes such as Guillain-Barre syndrome, acute motor axonal neuropathy, acute inflammatory demyelinating polyneuropathy, Miller Fisher syndrome, Bickerstaff's brainstem encephalitis, acute ophthalmpparesis, anti-MAG IgM paraproteinaemic neuropathy, multifocal motor neuropathy and chronic sensory ataxic neuropathy. The paper acknowledges that placing the wealth of emerging data into a clinical and pathological framework is complex, and points out the shortfalls in this area of research. The authors ask whether there is any evidence to show a disease-specific correlation between peripheral neuropathies and ganti-glycolipid antibodies. The review explores this theme primarly using Guillain-Barre syndrome (GBS) as a model. GBS is a peripheral neuropathy which can result after infection with *Campylobacter jejuni*. It is currently hypothesised that glycolipids on the surface of the bacterium trigger the production of anti-glycolipid antibodies which cross- react with nerve tissue causing the neurological damage seen in GBS patients. The paper takes the reader through the literature from glycolipid structure, to origins and immunological characteristics of antibodies, to therapeutic considerations. This paper is a wonderful, non-intimidating, starting point for anyone interested in the area of the pathogenecity of anti-glycolipid antibodies.

Classic Papers in Immunology: The Impact of Zinkernagel and Doherty

B.P. Mahon. Institute of Immunology, NUI Maynooth, Co. Kildare

It is almost thirty years since Rolf Zinkernagel and Peter Doherty published two papers that transformed our understanding of how the immune system works (1,2). While both scientists have continued to make important contributions to the field, that anniversary, and the impending visit of Peter Doherty to the Institute of Immunology at Maynooth, signal a moment to review the impact of their discovery. My first appreciation of their work came as an undergraduate, when I sat in Ivan Roitt's Immunology 1.01 lectures. Ivan was an excellent teacher and to explain Doherty and Zinkernagel he went to earlier Nobel laureates. He described how our separation of humoral (antibody–mediated) and cell mediated immunity could be traced back to the different approaches of Paul Ehrlich and Elie Metchnikov at the beginning of the twentieth century. I think Ivan was correct in his assessment that by 1970 we had a reasonable understanding of B cell immunology and the chemistry of immunoglobulins, however, our understanding of the cell-mediated arm of the adaptive response was rudimentary. This was not through lack of scientific application; the terrible injuries encountered during World War II had prompted a renewed impetus to transplantation biology. It was known that T-lymphocytes could kill cells from an allograft after recognition of certain molecules - the major histocompatibility complex (MHC or HLA) antigens. The question was "Why?" To get an idea of the confused state of the discipline it is worth looking at a first edition of Roitt's "Essential Immunology" from the 1970s (you can probably find it lurking on the recent acquisition shelves of our underfunded University libraries!). The impression given was that a complicated set of HLA genes existed simply to make life difficult for transplantation and for undergraduates who had to learn the HLA rules. There seemed to be no evolutionary point to this diversity.

The two Nature papers clarified the whole issue, and redressed the Ehrlich- Metchnikov imbalance. Zinkernagel and Doherty were examining the role of T cells against Lymphocytic choriomeningitis virus (LCMV) in mice. Put simply, they showed that T cells from one mouse strain recognize and kill LCMV-infected cells from another mouse strain, only if the two strains cells are MHC matched; or to use a different terminology: CD8+ CTL recognition of specific antigen is MHC (class I) restricted. Roitt described this brilliantly, "at a stroke the immune system made sense. The MHC was not there to make the (in evolutionary terms) irrelevant aspect of transplantation tricky. Instead, it had evolved to bind and present molecules from viruses and other microorganisms, allowing the T cell to look within the target for lurking invaders, invisible to antibody"

The clarification of the recognition mechanisms of the T-cells within the cellular immune system has fundamentally changed our understanding of the development and normal function of the immune system. The tremendous polymorphism of the MHC now makes sense. Evolution has selected these large immunological differences between us as individuals and between species. This diversity means that as a species we are likely to survive even severe epidemics. The price we pay for this advantage is transplant rejection and an increased susceptibility to autoimmune diseases such as rheumatoid arthritis by certain individuals. Thirty years on, that advance in understanding is still inspirational.

1. Zinkernagel RM, Doherty PC. Restriction of in vitro T cell-mediated cytotoxicity in lymphocytic choriomeningitis within a syngenic and semiallogeneic system. Nature 248, 701- 702, 1974.

2. Zinkernagel RM, Doherty PC. Immunological surveillance against altered self components by sensitised T lymphocytes in lymphocytic choriomeningitis. Nature 251, 547-548, 1974

Positions for Immunologists

Postdoctoral Research Opportunities
Department of Pharmacology and Center for Pharmacogenetics
University of Pennsylvania School of Medicine

Two postdoctoral research positions are available immediately in the Center for Pharmacogenetics at the University of Pennsylvania School of Medicine. The mission of the Center is to apply cutting edge technologies to the analysis of pathogenic processes in human disease and the identification of genetic factors that determine individual responses to a range of drug therapies.

We have ongoing projects to define the genetic architecture of a number of developmental and adult conditions including spina bifida and cardiovascular diseases. The methods that are being used to explore the etiology of these conditions includes the evaluation of functional polymorphisms of known and novel candidate genes in family and population studies, and the molecular analysis of the underlying pathogenic processes in tissue culture systems.

Our current pharmacogenetic projects includes analysis of the impact of functional mutations in enzymes of folate and homocysteine metabolism on inter-individual variation in the toxicity and efficacy of a range of chemotherapeutic agents and anti-inflammatory drugs in cancer and rheumatoid arthritis patients respectively. This work has the potential to subdivide patients according to their genetically mandated drug responses and may bring about a radical improvement in patient care by facilitating rational drug choice and dosing strategies.

New or experienced postdoctoral researchers are invited to apply for the above positions. However, exceptional candidates with research training to Master's degree level will also be considered. Familiarity with molecular biology and molecular genetic approaches to biomedical research would be an advantage. The are particularly suited to those who wish to do basic biomedical research that may be translated into practice in the relatively short term. Informal inquiries and applications should be directed to:

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