This year’s public lecture “Bugs or Us: Immunology and the Battle for Survival” by Professor Cliona O’Farrelly marked the ISI’s contribution to the “Day of Immunology” which was hosted on April 29th, 2008. The “Day of Immunology” event is organized by The European Federation of Immunological Societies in an effort to promote the public understanding of immunology in Ireland.

Prof O’Farrelly delivered an engaging talk to the gathered lay audience in the RDS. Her enthusiasm for science and her effervescent inquisitive mind were very evident as she walked us through her research years in Trinity, Harvard University, Sussex, and St Vincent’s hospital and on her return to Trinity. Cliona’s presentation was sprinkled with humorous anecdotes throughout. Overall, the lecture was very enjoyable and gave the public an insight to the exciting advances being made by Irish immunologists today.
The 2008 ISI meeting opens with a key note address from Prof. Luke O’Neill. The major focus of his group is to provide a molecular understanding of innate immunity and inflammation. The Cytokine Research Group are interested in receptors involved in innate immunity, such as Toll-like receptors and Nod-like receptors, and also signals activated, including NFκB, IRF family transcription factors and MAP kinases. The Trinity Researchers examine the role played by this system in inflammatory conditions such as sepsis and rheumatoid arthritis.

**Session 1: Immunoregulation**

“Signalling during innate immunity and Inflammation”

Luke O’Neill
Trinity College Dublin

“Interplay between pathogenic Th17 and protective T-regs in regulation of autoimmunity”

Vijay Kuchroo,
Havard Medical School

Dr. Kuchroo’s major research interests include studying the autoimmune diseases, particularly the role of co-stimulation, genetic basis of EAE, type 1 diabetes and cell surface molecules and regulatory factors that contribute to susceptibility and resistance to autoimmune diseases. Dr. Kuchroo’s laboratory has made several transgenic mice that serve as very useful animal models for human disease.

Professor Grencis’s research interests focus on the immune mechanisms operating during intestinal infection. A particular focus is the cytokine mediated control of intestinal helminth infection, especially roundworms. These parasites are extremely prevalent in man and animals and responsible for considerable ill health worldwide. He also researches into the genetic control of resistance and susceptibility and control of intestinal pathology following infection.

“Helminth parasites and modulating the immune system: Are worms really good for you?”

Richard Grencis
University of Manchester, UK
Session 2: Molecular mechanisms of Immune-mediated Disease

“Novel regulatory pathways in immune cells signalling”

Massimo Gadina

Dr. Gadina’s group has recently identified using microarray a new PDZ-containing scaffold protein, Cybr, which is up regulated by IL-2 and IL-12. Cybr binds and regulates the enzymatic activity of Cytohesin-1, a guanine nucleotide-exchange factor for ARF GTPases. Cytohesin-1 also binds and regulates the activation of the β2 integrin LFA-1. His research is aimed to establish the physiological role of the Cybr-Cytohesin pathway in the control of leukocyte activation, adhesion and migration. In addition his research activity includes the study of the signalling pathway downstream of the IL-2 and IL-12 receptors.

“Harnessing NKT cells in cancer vaccination strategies”

Vincenzo Cerundolo
Oxford University, UK

Studies have shown that several human tumours can be recognised in vivo by tumour-specific cytotoxic T lymphocytes (CTL). Dr Cerundolo’s research focuses on the study of the molecular mechanisms that control the generation of several defined melanoma CTL epitopes. The group is currently concentrating studies on the role of the multisubunit cytosolic protease proteasome and on the effect of its subunit composition on antigen presentation.

Session 3: Neuroimmunology

“Immune and innate signals in CNS inflammation”

Trevor Owens
University of Southern Denmark

Dr Owens’ laboratory focuses on animal models of multiple sclerosis and specifically on interactions between immune cells and glial cells in the brain and spinal cord.

“Interleukin-27 in CNS autoimmune inflammation”

Denise Fitzgerald
Jefferson University, USA

Denise Fitzgerald, a postdoctoral research fellow at Jefferson Medical College. Her research focuses on dissecting the mechanisms of how immune responses damage the myelin sheath and axons in the brain. Dr. Fitzgerald’s research identified that IL-27 could suppress IL-17 and inflammation. She has identified that IL-27-induced production of IL-10 by effector T cells contributed to the immunomodulatory function of IL-27.
“A role for neuroinflammation in age-related synaptic dysfunction”

Marina Lynch
Trinity College Dublin

Professor Marina Lynch’s research focuses on the analysis of neuronal signal transduction in synaptic plasticity, in particular on changes, which are associated with deficits in long-term potentiation (LTP) in the hippocampus with ageing and with experimental neuroinflammation. Her research programme explores synaptic dysfunction which has been linked with increased activation of microglia and consequently increased IL-1 β concentration which results in upregulation of IL-1 β-induced signalling; these changes have been identified in hippocampus of the aged brain and following treatment with LPS or A β.

“Non-CNS aspects of multiple sclerosis pathology”

Daniel Anthony
Oxford University, UK

Dr. Anthony’s research focuses on how mediators of the inflammatory response contribute to the outcome of spinal or brain injuries. His research examines how events in others organs, such as the liver, contribute to the outcome of brain injury or disease. In collaboration with other groups, the mechanisms that give rise to the reactivation of a Multiple Sclerosis-like lesions by a systemic inflammatory response and how brain injury contributes to the outcome of disease elsewhere in the body with a focus on how hepatic NFκB activity contributes to the acute phase response after CNS injury.

Session 4: Immunotherapy and Drug Discovery

“Do we need biotherapeutics? Novel approaches to drug development”

Doug Veale
St. Vincent’s Hospital, Dublin

The clinical research focus of Dr. Veale’s group is early inflammatory arthritis – RA, psoriatic arthritis and related psoriasis. Studies in the group are based on well-defined inflammatory arthritis cohorts. The translational research focus of his group is on angiogenesis and vascular biology. In collaboration with other groups, Dr Veale’s research examines the role of hypoxia on joint inflammation, mitochondrial bioenergetics, tissue perfusion and genomic instability.

“Polyclonal activation of regulatory T-cells with CD28 superagonists”

Thomas Hunig
University of Wurzburg, Germany

Prof. Hunig’s research examines the role that regulatory CD4 T cells play not only in the control of autoimmunity and overshooting immune responses to foreign antigens, but also in obstructing effective anticancer therapies. The homeostasis and activation of these
regulatory T cells (Treg cells) is tightly connected to that of effector CD4 T cells via the costimulatory receptor CD28 and the cytokine IL-2: Both subsets require costimulation to be activated by antigen, and Treg cells additionally depend on IL-2 produced by effector CD4 T cells in a costimulation-dependent fashion. Depending on the therapeutic aim, blockade, or stimulation of CD28 with monoclonal antibodies (mAb) can therefore profoundly affect the size and activity of the Treg compartment.

Poster Presentations:

Poster Boards:

Poster boards will be available at the RDS, which will accommodate posters in PORTRAIT FORMAT ONLY and up to A0 in size (91cm x 122cm).

Best Poster Competitions & Prizes!!

A total of €1,100 will be awarded in prizes for various poster competitions at the meeting. These will include prizes for: “Best Post-doctoral Poster” (& “Runner-up”) and “Best Student Poster” (& “Runner-up”). Judges will select 4 post-docs and 4 students to give short presentations of their posters (3 min talk & 2 min Qs). For this, you will be allowed to present 2 PowerPoint slides of your poster, to include a maximum of 2 pieces of data/graphs. Please do not include a “title” slide, as time will be at a premium at the meeting. All PowerPoint slides should be PC-formatted.

For further details, please find the 2008 ISI meeting programme on pages 12-15.

“From paediatric infectious diseases to novel primary immunodeficiencies”

Jean-Laurent Casanova
Inserm, France

Jean-Laurent Casanova’s research focuses on the potentially fatal condition known as herpes simplex encephalitis, which, for an unknown reason, develops from herpes simplex virus-1 in a small percentage of infected children. His search for a candidate gene and an understanding of the underlying immunodeficiency of this disease in families may have important medical and biological implications.
After your degree in Immunology, what drew you into the world of patent law?

During my final year at University, I spent time at the Roslin Institute, near Edinburgh. Dolly the sheep has just arrived onto the scene and there was a great amount of interest in the commercial possibilities based on the science behind Dolly. Moving into the business world interested me, so I took the plunge and moved away for academia.

“...a background in Immunology has never been more relevant!”

Describe a typical work day.

My job is split between being in the office drafting and prosecuting patent prosecutions and being out of the office visiting clients and attending business development events. As your career develops, you spend less time at your desk and more time visiting clients to build up a better picture of what your clients do.

What are the highlights of your job?

My client base ranges from Ireland and the UK to the US and Japan. I’m fortunate in that I work for one of the larger firms in Europe. This brings with it its own challenges and opportunities. One of the main benefits is the opportunity to travel. Also working with a variety of companies all of whom focus on different areas of the market helps keeps the job interesting.

Have you found that your background in Immunology has served you well as in your profession?

When I left University, journals such a Nature Immunology were in their infancy. Now their circulation is huge, in some cases more than Nature. This is evidence of the growing importance of Immunology. Virtually every major pharmaceutical company is now looking at developing some form of biologic, rather than traditional small molecule therapeutics – a background in Immunology has never been more relevant!

Have you any advice for PhD students/Postdocs who wish to follow a similar career path?

Entry into the profession can be difficult. Many patent attorney firms are quite small, so they do not have structured recruitment intakes. This means that opportunities can arise on an ad-hoc basis. A bit of luck will see you applying to the right company at the right time. Once you have an interview, some basic knowledge of the patent field and the role it plays can be helpful for impressing during interviews. Once part of the profession, 15 exams spread over 4-5 years lie ahead of you. Although you train on the job, studying has to be done in your own time, so my advice to postdocs in particular is to think this through,
because taking on the exams and giving up so much personal time is not to be taken on lightly.

If a researcher believes that they have an innovative finding with commercial potential, what are the first steps they should take?

The main thing is to not disclose the idea to anyone outside your immediate lab. Seek assistance from your organisation’s research and innovation department. Being an inventor on a patent application is a great way to get first hand experience of the job which a patent attorney does, so this can be very useful in helping decide whether this may be the career for you.

Many thanks to Gordon for giving us such a valuable insight into a career in patent law.

If you have any suggestions for the Career focus section please contact the Editor.

Report on the 6th International Symposium on Pneumococci and Pneumococcal Diseases

8-12 June 2008, Reykjavik, Iceland

Introduction
The 6th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD-6) was held from the 8th to the 12th of June this year in Reykjavik, the capital city of a country full of natural wonders and amazing sights. The meeting attracted many of the world’s experts on pneumococcal disease including delegates from industry, academia and state organisations. This year’s symposium was highly informative and interesting and covered a diverse range of topics.
relevant to pneumococcal disease including epidemiology, immunology, anti-microbial resistance and the development of novel vaccines. The downside of such a large conference was the absence of parallel sessions, which may have allowed more time for questions and in-depth discussions. This report will present an overview of talks that focused on immunity to pneumococci and to pneumococcal proteins as well as on the development of novel pneumococcal vaccines.

More than two million children less than 5 years of age die of pneumonia worldwide each year, making it the single biggest killer of children. *Streptococcus pneumoniae* is responsible for the majority of these deaths. This pathogen is also a major contributor to other invasive diseases and respiratory tract infections such as septicaemia, meningitis, otitis media, sinusitis and community acquired pneumonia. A highly efficacious seven-valent pneumococcal polysaccharide-conjugate vaccine (PCV7) was introduced in the USA in 2000 and since then in many other countries world-wide. This vaccine protects against seven of the main serotypes that cause disease. Throughout the ISPPD-6 conference many speakers highlighted the efficacy of the PCV7 vaccine in dramatically reducing the burden of pneumococcal disease in countries where universal vaccination has been introduced. Furthermore, new vaccine formulations, which offer protection against additional serotypes of *S. pneumoniae*, are in the final stages of development and are expected to be introduced in the next few years.

**The development of novel pneumococcal vaccines:**

Pneumococcal diseases may be caused by a large number of serotypes. Indeed, in some developing countries the PCV7 capsular polysaccharide vaccine only covers about one third of all disease-causing strains. Furthermore, since the introduction of the PCV7 vaccine there has been an unfortunate occurrence of strain replacement disease by non-vaccine serotypes. Therefore, there is a requirement for the development of protein-based vaccines that provide capsular-independent and serotype-independent protection. Protein vaccine candidates include well-characterised enzymes and toxins of *S. pneumoniae* such as detoxified derivatives of the toxin pneumolysin (pneumolysoid or PdT) and adhesins such as pneumococcal surface protein A (PspA) and pneumococcal surface adhesin A (PsaA). More recently, novel antigens are also being investigated as potential vaccine candidates including membrane-anchored proteins such as the
pneumococcal histidine triad proteins, PhtB and PhtE, and serine/threonine protein kinase (StkP).

Carmen Giefing from Intercell AG, Austria spoke about the method the company uses to identify putative vaccine antigens by screening sera from both healthy adults and patients with invasive disease. This genomic technology led to the identification of two lead vaccine candidates, StkP and the hydrolase PcsB. Giefing briefed delegates on their findings that subcutaneous immunization with these two antigens, which are highly conserved among clinical isolates, offer protection against challenge of mice with pneumococcal bacteria in models of sepsis and pneumonia. Ying-Jie Lu from The Children’s Hospital Boston, USA presented data showing that a vaccine based on a fusion conjugate of three streptococcal components, cell wall polysaccharide, the nonhemolytic variant of pneumolysin (PdT) and PsaA, protected mice against pneumococcal colonization following intranasal immunization with cholera toxin as adjuvant. He stated that TLR4 played an important role in protection as TLR4 defective C3H/HeJ mice were not protected against colonization compared to wild-type mice. Furthermore, mice immunized with the fusion conjugate showed increased IL-17A production in peripheral blood compared to mice that were immunized with a mixture of antigens.

Abiodun David Ogunniyi from the University of Adelaide, Australia stressed the absolute necessity of rigorously and robustly comparing protein vaccine candidates both singly and in combination, against an agreed benchmark, in various animal models and using multiple challenge strains of bacteria. He concluded that the best pneumococcal protein vaccine for pre-clinical testing should be a mixture of proteins that contribute to pathogenesis rather than a single antigen. Michele A. Barocchi (Novartis Vaccines, Italy) maintained this theme by re-emphasizing the importance of combining antigens to achieve optimal protection against disease. She explained the three-fold approach the company uses to select proteins as vaccine candidates. This method relies firstly on reverse vaccinology to identify all genes coding for pneumococcal surface proteins, followed by library immunoscreening of sera of patients with disease in order to identify proteins recognized by the human immune system and finally gene variability studies to give priority to proteins that are conserved among various clinical isolates. This combined approach has resulted in the identification of a host of antigens which
were screened for protection in various mouse models of pneumococcal infection. Two proteins of the pneumococcal pilus, RrgA and RrgB, were among the best vaccine candidates. Barocchi presented data showing that intraperitoneal (i.p.) immunization of BALB/c mice with these pilus antigens resulted in subsequent protection from i.p. challenge with *Streptococcus pneumoniae*. She stated that it may be important to include pili antigens, such as RrgA and RrgB, in future vaccines as emerging clones of serotype 19A of *S. pneumoniae* which are multi-drug resistant are also pilus positive.

**Host pathogen interactions and immunology of pneumococcal infection**

Marco Oggioni from Siena, Italy spoke about the influence of gender on the susceptibility of mice to infection with *Streptococcus pneumoniae*. He showed how male C57BL/6 mice were less able to control infection than their female counterparts. This susceptibility correlated with a more pronounced increase in cytokines such as IL-1alpha, IL-1beta, IL-6 and IL-12 in male mice following infection. Several presenters showed data relating to host immunological responses to pneumococcal proteins, in particular immunity to pneumolysin. Adam Finn (University of Bristol, UK) presented findings on T cell immunity to pneumococcal proteins in peripheral blood mononuclear cells of children undergoing adenoidectomy. He demonstrated that pneumolysin induces the proliferation of both naïve and memory CD4 T cells, but its effects are mediated through TLR4. He also presented more recent data showing the upregulation of chemokine (CCL2, CCL5 and CXCL8 among others) mRNA expression by recombinant pneumolysin in human myeloid dendritic cells. He stated that these findings may suggest that pneumolysin has adjuvant, in addition to antigenic, properties. This adjuvant activity of pneumolysin was demonstrated in a poster presentation by Kirsty Ross, University of Glasgow, UK. She presented data showing that intranasal immunization of mice with pneumococcal surface adhesin fused to the N terminal of pneumolysin generated a potent IgG antibody response that was not found when the proteins were mixed together and administered to mice. Several presentations by the group of Richard Malley, Boston, USA, focused on the emerging role of IL-17A in mediating immunity to pneumococcal infections. His group have found that protection against pneumococcal colonization following intranasal immunization of mice with an unencapsulated killed whole cell vaccine is dependent on IL-17A. Resistance to colonization correlated with the ability of cells from immunized mice.
to express IL-17 in response to stimulation with killed pneumococci in vitro. Importantly, his group have also shown that IL-17A enhanced human neutrophil-dependent killing of S. pneumoniae in a surface phagocytosis assay.

There were also many presentations in the conference that I have not covered in this report. In particular, many talks were dedicated to the epidemiology of pneumococcal disease pre- and post- PCV7 vaccination. The current status of antimicrobial resistance of pneumococci was also covered eloquently by several presenters throughout the conference and information was provided on how the increasing resistance may be contained.

-Edel McNeela,
Adjuvant Research Group, TCD

Visit our website: www.irishimmunology.ie

Cartoon Corner

Note from the Editor

***Calling all ISI members for suggestions, comments and articles***

Do you have a scientific meeting you’d like to tell us about? A suggestion for our career focus piece? Any suggestions/comments for any other article that you think would interest our members? Don’t be shy, email us, we would love to hear from you!

See you all on the 15th and 16th of September for what promises to be our best meeting yet!

Sarah Higgins.
Editor, ISI Newsletter.
Email: irishimmunology@gmail.com
Joint Meeting of the Irish Society for Immunology (ISI) & the Ulster Immunology Group (UIG)

15th & 16th September 2008,
The Concert Hall, RDS, Dublin 4, Ireland.

MONDAY, 15TH SEPTEMBER

09:15 – 10:15  Registration, Trade Exhibition & Tea/Coffee

10:15 – 10:20  Conference Open/Welcome
Aideen Long (St. James’s Hospital, Dublin & Trinity College, Dublin), President, Irish Society for Immunology.

Session 1: Immunoregulation.
Chair: Kingston Mills (Trinity College, Dublin)

10:20 – 11.00  Keynote address:
“Signaling during innate immunity and inflammation.”

11:00 – 11.30  “Helminth parasites and modulating the immune system: Are worms really good for you?”
Richard Grencis (University of Manchester, UK).

11.30 – 12.00  Tea/Coffee.

12:00 – 12:15  S001: “Cellular mechanisms of innate activation of Type 2 cytokine responses.”
Hendrik Nel (St. James’s Hospital & Trinity College, Dublin).

12:15 – 12:30  S002: “Helminth infection attenuates autoimmunity by induction of TGF-β expressing regulatory T cells.”
Kevin Walsh (Trinity College, Dublin).

12:30 – 13:00  “Interplay between pathogenic Th17 and protective T-reg cells in regulation of autoimmunity.”
Vijay Kuchroo (Harvard Medical School, USA).
13:00 – 13:15  **S003:** “CD39+ FoxP3+ Regulatory T cells suppress pathogenic Th17 cells and are reduced in multiple sclerosis.”
Jean Fletcher (Trinity College, Dublin).


**Session 2:** Molecular Mechanisms of Immune Mediated Disease.
Chair: Paul Moynagh (National University of Ireland, Maynooth).

14:15 - 14:45  “Novel regulatory pathways in immune cells signalling.”
Massimo Gadina (Queen’s University, Belfast & National Institutes of Health, USA).

14:45 - 15.00  **S004:** “Ro52 Negatively Regulates IFN-β induction by Degrading IRF3: A possible role in lupus?”
Rowan Higgs (Royal College of Surgeons, Dublin).

15:00 – 15:15  **S005:** “Pyrophosphate-stimulated VγVδ2 T cells induce dendritic cell maturation with Th1 bias.”
Margaret Dunne (National University of Ireland, Maynooth).

15:15 -15:45  Tea/Coffee.

15:45 – 16:00  **S006:** “Elevated osteoprotegerin (OPG) secretion by monocyte derived dendritic cells (MDDC) isolated from individuals with chronic Hepatitis C virus (HCV) infection.”
Elizabeth Ryan (Trinity College, Dublin).

16:00 – 16:15  **S007:** “Adenovirus E3/19K promotes evasion of NK cell recognition by intracellular sequestration of the NKG2D ligands, MICA and MICB.”
Brian McSharry (University of Cardiff).

16:15 – 17:00  “Harnessing NKT cells in cancer vaccination strategies.”
Vincenzo Cerundolo (University of Oxford, UK).

17:00 - 19:30  Poster Session & Wine Reception - sponsored by Abbott Laboratories.

17:00 - 19:30  Sponsors Trade Exhibition.

TUESDAY, 16TH SEPTEMBER

Session 3: Neuroimmunology.
Chair: Tom Connor (Trinity College, Dublin).

09:00 - 09:30  “Immune and innate signals in CNS inflammation.”
Trevor Owens (University of Southern Denmark).

09:30 – 09:45  S008:  “Inhibition of ERK attenuates IL-23-IL-17 induced autoimmune disease.”
Corinna Brereton (Trinity College, Dublin).

09:45 – 10:00  S009:  “Cell migration through the blood brain barrier (BBB) in feline immunodeficiency virus infection is significantly influenced by the pre-existence of virus and TNF-alpha within the CNS: studies using an in vitro feline BBB model.”
Nicola Fletcher (University College Dublin).

10:00 – 10:30  “Interleukin-27 in CNS autoimmune inflammation.”
Denise Fitzgerald (Jefferson University, USA).

10:30 - 11:00  Tea/Coffee.

11:00 – 11:30  “A role for neuroinflammation in age-related synaptic dysfunction.”
Marina Lynch (Trinity College, Dublin).

11:30 – 11:45  S010:  “Psychological stress suppresses the innate IFN-γ response via glucocorticoid receptor activation: reversal by the anxiolytic chlorodiazepoxide.”
Niamh Curtin (Trinity College, Dublin).

11:45 – 12:15  “Non-CNS aspects of multiple sclerosis pathology.”
Daniel Anthony (Oxford University, UK).

12.15 – 13:15  Short Presentations from Selected Posters
Chair: Cliona O’Farrelly (Trinity College, Dublin).
8 Presenters  (4 Post-docs & 4 students): 3 min talk + 2 min questions.


Session 4: Immunotherapy & Drug Discovery.
Chair: Jim Johnston (Queen’s University, Belfast).

Doug Veale (St. Vincent’s University Hospital, Dublin).

14:45 – 15:00  S011:  “A novel mimetic of the plant lectin Ulex europaeus agglutinin I (UEA-I) is an effective targeting agent for mucosal immunization.”
Edel McNeela (Trinity College, Dublin).

15:00 – 15:30  “Polyclonal activation of regulatory T-cells with CD28 superagonists?”
Thomas Hünig (University of Würzburg, Germany).
15:30 – 15:45  **S012:** “A multi-parameter image analysis strategy to identify morphology changes in migrating lymphocytes in high content screens.”
Dara Dunican (St. James’s Hospital & Trinity College, Dublin).

15.45 – 16:15  *Tea/Coffee.*

16:15 – 16:50  **State of the Art Lecture:**
Chair: Con Feighery (St. James’s Hospital & Trinity College, Dublin).

“No paediatric infectious diseases to novel primary immunodeficiencies.”
Jean-Laurent Casanova (Inserm, France).

16:50 – 17:00  **Awarding of Prizes:**

**Oral Presentation Prizes:**
Best oral presentation prize: €350
(Sponsored by Medical Supply Company)

Best oral presentation Runner-Up prize: €200.
(Sponsored by Abbott Laboratories)

**Poster Presentation Prizes:**
Best Post-Doctoral poster presentation prize: €350
(Sponsored by Opsona)

Best Post-Doctoral Runner-Up prize: €200.
(Sponsored by Abbott Laboratories)

Best Student poster presentation: €350 prize
(Sponsored by Randox)

Best Student Poster Presentation Runner-Up prize: €200.
(Sponsored by Mason Technologies Ltd).

*** Several additional merit prizes will also be awarded at the meeting ***

17:00  Close of Conference.
17:05  Irish Society for Immunology, AGM.