



ISI Newsletter

IRISH SOCIETY FOR IMMUNOLOGY

April 2005



Joanne Lysaght and Padraig Ross from the Immune Regulation Research Group at Trinity College Dublin.

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OUR YOUNG IRISH IMMUNOLOGISTS AT THE BRITISH SOCIETY OF IMMUNOLOGY 2004

Our young Irish Immunologists did us proud at the recent British Society of Immunology 2004. Joanne Lysaght and Padraig Ross were both shortlisted for the Award of Young Immunologist of the Year 2004. They both gave excellent presentations which were indicative of the quality of Immunology research being carried out in Ireland at present. Joanne's talk was focused on the site-specific roles of T cells in anti-tumour immunity in a lung metastasis model and a subcutaneous

tumour model. Her research demonstrated how the anti-tumour immune response can be modulated in these models using the bacterial derived molecules, CpG and cholera toxin. She demonstrated that CD4⁺ T cells have a regulatory role in the lung as their depletion resulted in significantly reduced tumour number, whereas depletion of CD4⁺ T cells did not affect the growth of the subcutaneous tumour. Th1-inducing CpG enhanced anti-tumour immunity in both models whereas Th2/Tregulatory-inducing CT significantly enhanced tumour growth in the subcutaneous model but it does not have a significant effect on tumour numbers in the lung metastasis model.

Work presented by Padraig Ross focused on the adenylate cyclase toxin (CyaA) from *Bordetella pertussis*, the causative agent of whooping cough. His work has shown that this protein has immunomodulatory function and synergises with Toll-like receptor ligands to modulate dendritic cells into a phenotype, which promotes the induction of antigen specific IL-10 secreting regulatory T-cells *in vivo*. The Immune Regulation Research Group led by Prof Kingston Mills at TCD are developing methods of exploiting such immunomodulators as therapeutic agents in immune mediated disorders and CyaA shows great promise in this regard. However, it can be cytotoxic at high doses and this would represent a block in its approval in clinical trials. To address this they have developed a derivative of CyaA, which lacks a particular post-translational modification, the lack of which ablates the protein's cytotoxic effects. This non-toxic derivative retains the ability to modulate both the innate and adaptive immune response and represents an excellent potential immune therapeutic agent.

The ISI would like to congratulate both Joanne and Padraig on their fantastic achievements.

IRISH SOCIETY FOR IMMUNOLOGY ANNUAL AWARD & PUBLIC LECTURE 2005

The mission of the Irish Society for Immunology is to contribute to better health in Ireland and worldwide through improved understanding of immunology.

The ISI has committed to promoting Public Understanding of Immunology in Ireland by making an award each year to an Irish Immunologist in recognition of major contribution to the understanding of Immunology and its role in improved health. The dual aims of the award are (a) to promote Irish Immunology and (b) to provide a vehicle for bringing immunology and immunological debate to the general public. Thus, a major component of the Award Ceremony is a Public Lecture by the Awardee on his or her work and how it pertains to better health. Ideally, the Public Lecture focuses on some immunological issue of interest and relevance to a general audience and also provides insight into the research process contributing to its better understanding.

This year Professor Denis Reen was nominated for the ISI Annual Award and Public Lecture. He has accepted this award and the public lecture will be held in the RDS on Thursday 28th April 2005 (7.30pm-8.30pm; doors open 7.00pm). The title of his talk will be "How well are we protected against infections and allergies in early life?" (*See flyer attached*)

Cliona O'Farrelly
President, Irish Society for Immunology

**IRISH SOCIETY FOR
IMMUNOLOGY AND THE
ULSTER IMMUNOLOGY GROUP
- JOINT MEETING.**

**16th-17th September, 2004
National University of Ireland,
Maynooth.**

I think everyone will agree that the recent Irish Society for Immunology Annual Meeting which was held jointly with the Ulster Immunology Group in Maynooth last September was a huge success. The sessions included Infectious Disease, Immune Regulation and Novel Genomic and Proteomic Approaches in Immunology so there was definitely something for everyone. The line-up of invited speakers was fantastic and included Brian Adair, Kingston Mills, Grace Mulchahy, David Wraith, Massimo Gadina, Marlene Rose, Steve Pennington and Mike Dunn. The standard of open papers and posters was extremely high and generated lots of interesting discussion. The prize for best open paper went to Geraldine Maloney from the Department of Biochemistry, Trinity College Dublin and the prize for best poster went to Jane Kelly-Rogers from NUI, Maynooth. Well done to the both of them. Even though the scientific programme was packed there was still time for a lovely dinner in the Glenroyal Hotel and a few drinks afterwards to catch up with fellow immunologists. All in all it was a huge success and a big thank you to all the hard-working committee members for organising it – in particular to Michelle Armstrong, Louise McCormack and Patricia Johnson. Looking forward to the next one!!!! Here are some photos of some of the immunologists who attended.



**The Venue – National University of
Ireland, Maynooth**



**Prof Cliona O'Farrelly and Sharon
Wilson.**



**Dr Massimo Gadina, Dr Karim Dib
and Dr James Burrows.**



**Prof Mike Dunn, Prof Marlene Rose
and Prof Cliona O'Farrelly.**



**Jane Kelly Rogers, Prof Denis Reen
and Geraldine Maloney.**



**Dr Michelle Armstrong, Louise
McCormack and Dr Patricia Johnson.**

ISI TRAVEL BURSARIES

The ISI will be awarding **3 travel bursaries** of **€300 each** to ISI members whose work has been accepted for presentation at an international meeting. In the last year only a small number of applications were received and we would like to encourage more people to apply. The applications received and bursaries awarded are summarised below.

ISI Bursary Applications 2004

Bursaries awarded	2
Bursaries not awarded	1
Bursary applications ineligible due to non-ISI membership	2
Bursaries application withdrawn	2
Total number of bursary Applications in 2004	7

Applications for consideration should be submitted to Dr Michelle Armstrong (ISI secretary), Department of Medicine & Therapeutics, The Conway Institute, UCD, michelle.armstrong@ucd.ie by the 30th May 2005 for review to include the following:

1. Copy of your abstract.
2. Proof that your abstract has been accepted (an email or a letter from the meeting organiser)
3. A letter from your PhD supervisor supporting your bursary application.

Only current ISI members may submit applications and no retrospective applications will be considered. Please make sure to send in applications in plenty of time, as the deadline will be strictly adhered to. All those who receive a bursary will be expected to write a short meeting report for publication in the ISI newsletter.

MEETING REPORTS

Cytokines in Cancer and Immunity: 5th Joint meeting of the International Cytokine Society (ICS) and the International Society for Interferon and Cytokine Research (ISICR)

Julieanne Stack, Trinity College Dublin.

San Juan, Puerto Rico was the setting for the Cytokines 2004 conference, which attracted some of the foremost researchers in the field of cytokines and interferons from around the world. It was a privilege to hear such eminent scientists as Dr Douglas Golenbock (University of Massachusetts, USA), Dr Tom Maniatis (Harvard University, USA) and Dr Tadatsuga Taniguchi (University of Tokyo, Japan), speak about their work and latest theories. Attending this conference was an invaluable learning opportunity and I acquired many fresh ideas for future research. I was extremely honoured to be awarded the ICS Outstanding Scholar Award (First Place). As a condition of accepting this prize, I had to make an oral presentation. This allowed me to share my theories and discoveries with the scientific community, to receive feedback from my peers and to promote both Irish immunology and Trinity College Dublin as a research institution. My research is focussed specifically on a Vaccinia Virus immunomodulatory protein, A46R, which has been found to specifically inhibit some Toll/Interleukin-1 receptor homology (TIR) domain-dependent intracellular signalling pathways. The Toll/Interleukin-1 Receptor (TIR) Superfamily is a Type 1 transmembrane receptor family that is characterised by an intracellular TIR domain. This family plays an important role in host defence against a wide range of pathogens including bacteria, fungi and viruses. Members of this family include IL-1R, IL-18R and the TLRs 1-10. Important signalling molecules in their mechanisms of action include the TIR adapter proteins MyD88 Mal/TIRAP, TRIF and TRAM, which are cytoplasmic members of the TIR Superfamily. A fifth TIR adapter molecule, SARM has recently been identified, but has as yet not been

implicated in TLR signalling. Vaccinia virus is a poxvirus. Members of the poxvirus family can infect mammals, birds and insects. There are only two human poxviruses, Variola Virus, the causative agent of smallpox (Vaccinia virus is used to vaccinate against Variola Virus), and Molluscum Contagiosum Virus. Poxviruses circumvent the host immune response by encoding proteins that can antagonise host defence mechanisms. A46R is one such protein, which was identified based on sequence similarity to the Toll/Interleukin-1 receptor homology (TIR) domain. We previously showed that A46R could down-regulate IL-1 induced activation of the transcription factor NF κ B, while having little or no inhibitory effect on TNF-induced NF κ B activation (Bowie et al., 2000). I have found that A46R inhibits multiple signals emanating from the IL-1R and TLR4 in a dose-dependent manner, including NF κ B activation, MAP kinase activation and p65 phosphorylation, but did not inhibit TNF induced signals. Given the fact that A46R has a TIR domain, we tested whether it could associate with other TIR proteins, and found that it was capable of co-immunoprecipitating with MyD88, Mal/TIRAP and TRIF and TRAM. However, it did not interact with SARM. Activation of NF κ B and MAP kinases by MyD88 and Mal were sensitive to inhibition by A46R. Other TLR pathways to NF κ B that utilise MyD88 (i.e. TLRs 2, 5, 7 and 9) were also sensitive to A46R inhibition. A46R has been found to block MyD88-independent signalling events such as TRIF induced NF κ B and IFN- β , as well as TLR3 and TLR4 induced IRF-3, IFN- β , ISRE and RANTES activation. These results show that A46R is a viral antagonist of TIR-dependent signalling pathways. Recently, I have been trying to determine exactly how A46R interacts with the various TIR adapters by carrying out interaction studies using A46R and mutants of the TIR adapters. Using purified recombinant Mal, I demonstrated that A46R directly interacts with this protein. Future work will involve the creation of A46R mutants and determining the portions of the protein that are required for its function as an inhibitor. It is hoped that this work will further

understanding of the IL-1R/TLR system, establish which particular components of it are involved in host anti-viral mechanisms and eventually provide a novel therapeutic tool for modulating the innate and inflammatory responses.

*Geraldine Maloney, Trinity College
Dublin*

An early start was had by all on the morning of October 19th 2004 as we embarked on our journey to the Cytokines and Cancer 2004 conference – destination Puerto Rico. This was the fifth joint meeting of the International Society of Interferon and Cytokine Research (ISICR) and the International Cytokine Society (ICS). The focus of this meeting was to provide a global overview of the most recent outcomes in cytokine research, to promote the exchange of information and reinforce the connection between academia and industry. Among scientists active in the interferon and cytokine fields this conference is regarded as one of the leading international forum, as it offers the opportunity to present and discuss the latest advances in basic science triggering the onset of new ideas. The keynote address entitled Cell Survival Signals of Cytokine Receptors was given by Professor Tak Mak from the University of Toronto, Canada. This was followed by the presentation of the Milstein Awards. These were awarded to Keiko Ozato (Bethesda, Maryland) and Ernest Borden (Cleveland Clinic Foundation, Ohio) for their outstanding contribution to the field of cytokine research. An extremely detailed programme of events had been put together which had scheduled talks from 8.00a.m. - 7.00p.m. each day. The day was divided into two plenary sessions comprising of three talks. This was followed by four workshops all running concurrently. The range of topics on offer in these workshops was varied and diverse encompassing the vast area of both cytokine and interferon research. Each of the workshops was given a theme, for example signal transduction, interferons or gene regulation. The workshops were extremely well organised and friendly, a more relaxed atmosphere was created as people came and

went depending on which presentation they were interested in. The most noteworthy talks included Human Interferon- β gene regulation given by Tom Maniatis (Harvard University, MA) and From Interferons to Interleukins to Chemokines and to Alarmins by Joost Oppenheim. Joost Oppenheim also known as the “father of cytokines” received the ICS lifetime achievement award. Dr. Oppenheim obtained his M. D. degree from the Columbia College of Physicians & Surgeons, New York, trained as a Clinical Associate at the National Cancer Institute, Bethesda, Maryland. He was a post doctoral fellow at the University of Birmingham, England, in immunology. He returned to the National Institute of Dental Health and subsequently headed the Section of Cellular Immunology there. Since 1983 he has been head of the Laboratory of Molecular Immunoregulation, National Cancer Institute, at the Frederick Cancer Research and Development Center. Three poster sessions were held over the five days. The theme of the day’s talks was the focus of the poster sessions. These sessions facilitated the opportunity to promote scientific contacts and highlighted the importance and relevance of international cooperation. My research involves investigating the effect of Vaccinia Virus protein A52R on IL-1R and Toll Like Receptor signalling under the supervision of Dr. Andrew Bowie at Trinity College Dublin. I presented a poster highlighting the ability of A52R to differentially modulate TLR signalling. A52R targets two key signalling molecules IRAK2 and TRAF6 and antagonises multiple TLR induced NF κ B activation. However, the effect of A52R on signals other than NF κ B has not been determined. In this study we show that A52R can activate the MAP Kinases p38 and JNK in a TRAF6 dependent manner. In addition, A52R leads to enhancement of the TLR induced p38 dependent gene IL-10, while inhibition of the TLR induced NF κ B dependent genes IL-8 and RANTES is observed. The conference ended on Monday afternoon and we bid our farewells to the people we had met, the collaborations that had been made and the promises to meet again next year in South Korea for the ICS 2005 meeting

DATE FOR YOUR DIARY: UP-COMING MEETINGS

Molecular Pathogenesis of Virus Infections.
4-8th April 2005, Heriot-Watt University,
Edinburgh.

Clinical Applications of Regulatory T Cells.
7-8th April 2005, Novartis, Horsham.

**Identifying T Cell Subset Phenotype and
Function.**
22nd April 2005, Birkbeck College, London.

**Irish Society of Immunology Annual Award
and Public Lecture – Prof Denis Reen**
28th April 2005, RDS, Dublin.

**6th Annual Immunogenicity for Protein-
based Therapeutics Conference.**
23-25th May 2005, San Francisco, CA.

**Genetic Control of T Cell Activation –
Implication for autoimmunity and cancer.**
18-22nd August 2005, Lofoten, Norway.

**3rd European Congress of Reproductive
Immunology.**
11-15th September 2005, Colchester, England.

**Joint Meeting of the Irish Society for
Immunology and the Royal Society of
Medicine.**
20-21st October 2005, Croke Park, Dublin.

**British Society for Immunology, Annual
Congress 2005**
6-9th December 2005, Harrogate, UK.

DAY OF IMMUNOLOGY EUROPEAN FEDERATION OF IMMUNOLOGICAL SOCIETIES

The first Day of Immunology will take place on the 29th April 2005 all over Europe. All national member societies of EFIS have been requested to organize an event around this date to contribute to this day. The aim of this day is to develop a joint strategy for advocating immunology all over Europe. The ISI will be participating by holding our Annual Award and Public Lecture at the RDS on the 28th April 2005.

A NOTE FROM THE EDITOR

Hi all. I hope you enjoyed this edition of the ISI newsletter. It has been a very successful year for the Newsletter, which is now published three times per year. The job of the editor is a difficult one –my time is spent convincing people to write articles and then constantly bombarding them with emails begging them to actually submit the agreed article for publication!!! The next issue of the newsletter is due for publication in the summer of 2005 so I'm giving you all plenty of notice to get your writing heads on and come up with something. I welcome any article as long as it will be of interest to our readers. Those of you attending conferences could write a meeting report and young researchers are encouraged to submit articles highlighting their area of research. Illustrations and cartoons are particularly welcomed. All articles should be emailed to me at Christine.Loscher@dcu.ie . I look forward to hearing from you all soon (of your own free will!!!!).

**2005 Joint Meeting of the
Irish Society for Immunology (20th Anniversary) and
the Royal Society of Medicine.**

**20th-21st October, Hogan Mezzanine, Conference Centre,
Croke Park, Dublin.**

Provisional line up of sessions (as of 12th April 2005)

Thursday, 20th October

09:30 – 11:00 Registration & Trade Exhibition

10:00 – 11:00 Coffee

11:00 – 11:10 Welcome from the President of the Irish Society for Immunology, Cliona O'Farrelly & John Axford (Royal Society of Medicine).

Session 1: *Innate Immunity*

11:10 – 11:50 Keynote Address: Luke O' Neill (Dublin), "Innate Immunity a source of Novel Therapeutic Targets for Autoimmune Disease."

11:50 – 12:05 Short presentation

12:05 – 12:45 Christine Biron (Rhode Island), "Innate Immune Mechanisms in Viral Disease."

12:45 – 13:25 Andrew MacPherson (Sweden). Dendritic cells/Commensal bacteria.

13:30 – 14:30 Lunch, Posters and Trade Exhibition.

Session 2: *Immunomodulation*

14:30 - 15:10 Nils Lycke (Sweden). Mucosal adjuvants/Nasal vaccines.

15:10 – 15:25 Short presentation

15:25 – 15:40 Short presentation

15:45 - 16:15 Tea

16:15 - 16:55 Neil Williams (Bristol). AB toxins/Intervention in inflammatory disease.

16:55 - 17:10 Short presentation

- 17:10 - 17:25** **History of the ISI by Denis Reen: 20th Anniversary**
- 17:30 - 19:30** **Wine Reception, Posters and Trade Exhibition.**
- 19:30 - late** **Banquet Dinner, Hogan Mezzanine, Croke Park.**

Friday, 21st October.

Session 3: ***Autoimmunity&Immunotherapy***

- 09:00 – 09:30** **Breakfast**
- 09:30 - 10:10** **Ian McInnes (Glasgow/RSM). Immunotherapy/inflammatory synovitis.**
- 10:10 – 10:25 Short presentation
- 10:25 – 11:00** **Cornelis Metlief (Leiden). T regulatory cells/Tumour Immunology.**
- 11:00 – 11:30** **Tea**
- 11:30 - 12:10** **Patrick Venables (London/RSM), “Immunotherapy for Rheumatoid Arthritis.”**
- 12.10 – 13:00** **Short Presentations from Selected Student Posters**
- 13:00 – 14:00** **Lunch, Posters and Trade Exhibition.**

Session 4: ***Session title to be confirmed***

- 14:00 – 14.40** **Plenary Lecture: T.B.A.**
- 14:40 – 14:55 Short presentation
- 14:55 – 15:10 Short presentation
- 15:10 – 15:25 John Axford (London/RSM).
- 15:30 –16:00** **Tea**
- 16:00 – 16:10** **Awarding of student prizes for best oral presentation and best poster presentation (€350 EACH!!)**
- 16:10 – 16:30** **Irish Society for Immunology, Annual General Meeting.**
- 16:30** **End of Conference**



The Irish Society for Immunology

in conjunction with

The Irish Times

Present a Public Lecture by:

Professor Denis Reen

*Children's Research Centre, Our Lady's Hospital for Sick Children,
Crumlin and The Conway Institute, University College Dublin.*

**"How well are we protected against
infections and allergies in early life?"**

The Concert Hall, RDS, Ballsbridge, Dublin 4.

Thursday 28th April 2005.

7.30pm – 8.30pm (Doors open 7.00pm).

*Professor Reen is the 2005 recipient of the annual award of the
Irish Society for Immunology.*