The 7th International Congress of Neuroimmunology

Nagoya, Japan, 15-19 October 2006.

For five days, on alternate years, the International Society of Neuroimmunology (ISNI) brings together research groups from all over the globe that are dedicated to understanding the relationship between the central and peripheral nervous system and the immune system in both health and disease. This year the conference was held in Nagoya - Japan's fourth largest city located on the Pacific coast; one of Japan's major ports. The newly opened conference centre housed some 2000 delegates attending distinguished review talks, plenary sessions, workshops, seminars, poster sessions and satellite symposia. There were many highlights; a handful of which are described below. I cannot however fail to applaud the traditional Japanese folk music 'minyo', to which the delegates were treated on the penultimate evening (compelling most to learn some new moves on the dance floor). Singers were accompanied by the 3 stringed lute known as the shamisen, taiko drums and a 13 stringed zither known as the koto.

IL17/23 cells

The breaking story of T cell immunology over the last two years has been the discovery of a new type of helper T cell, called the Th17 cell. (It is called this not because Th1 through to Th16 have already been defined, but because these secrete interleukin-17). In fact, like Helicobacter, these cells were always there, but their presence has been misunderstood. All the exciting news about this cell are summarised in Claire Helliwell's immunology primer in this issue of ACNR (page 8).

Now this scheme has to be redrawn. It turns out that a key experiment was flawed. The IL-12 receptor subunit knock-out in these animals also forms part of the IL-23 receptor. So, both IL-12 and IL-23 function was being neutralised. IL-23 stimulates a new kind of cell which secretes high levels of IL-17 and low levels of IFN-γ or IL-4. It is these cells, called 'Th17 cells', which drive EAE, not IFN-γ secreting Th1 cells. Animals that truly lack IL-12, but retain IL-23 and IL-17, still get EAE. Daniel Cua from Shering-Plough showed that Th17 cells secrete IL-22 as well as IL-17; but IL-22 lacks this feature. IL-22 has been used effectively as a treatment for paroxysmal nocturnal haemoglobinuria. Willison and colleagues are attempting to secure funding for a trial of echuzimab in Guillain-Barré.

Predicting who needs treatment in MS

The factors that determine the localisation of multiple sclerosis lesions are far from understood. It was interesting, therefore, to hear Michael Pender present data suggesting that proteolipid protein (PLP) reactivity drives the development of brainstem and cerebellar lesions.

His group performed HLA-DR and HLA-DQ typing and examined T cell reactivity (proliferation assays) to myelin proteins in 121 patients with MS, 71 healthy controls and 47 patients with other neurological disorders. Patients were assessed clinically by a blinded assessor and gadolinium enhanced MRI scans were performed. They found that nearly 50% of patients with brainstem and or cerebellar disease had increased T cell responses to the immuno-dominant region of myelin PLP.214-226, but not to other myelin proteins, compared to 10% of MS subjects without brainstem or cerebellar lesions, 11% of healthy controls and 19% of patients with other CNS disease.

They also found that 79% of patients with brainstem and or cerebellar lesions carried the HLA-DR4, DR7 or DR13 alleles compared to 29% of patients with disease elsewhere. In addition, the majority of patients with HLA-DR4, DR7 or DR13 alleles had increased T cell reactivity to PLP.214-226. Compared to only 12% of patients not carrying these alleles.

They concluded that reactivity to PLP.214-226 drives the development of brainstem and cerebellar lesions and suggested that patients carrying the susceptibility alleles HLA-DR4, DR7 or DR13 may benefit from therapy with altered peptide ligands based on PLP.214-226.

How the immune system protects against autoimmunity - a step closer.

The demands on our immune system are great: the system must defend against incoming pathogens, repair damaged tissue, recognise and remove abnormal cells, all without causing disease (autoimmunity). Naturally occurring regulatory T cells (Tregs) play an essential role in the maintenance of peripheral self-tolerance. Tregs express elevated levels of the high affinity interleukin-2 (IL-2) receptor alpha subunit (CD25); neutralisation of IL-2 reduces the size of the CD4+CD25+ compartment inducing autoimmunity in mice. Tregs also express FoxP3, a transcription factor which is critical in the development and function of Tregs. Transduction of FoxP3 into effector T cells results in these cells differentiating into Tregs, however, the mechanism by which FoxP3 prevents the emergence of autoimmune diseases have remained unsolved until now.

Shimon Sakaguchi has shown that FoxP3 interacts with acute myeloid leukemia 1 (AML1 also known as Runx1). AML1 regulates the expression of a variety of haematopoietic genes and is a critical regulator of haematopoietic development, including T cell development. A variety of post-translational modifications can modulate AML1 activity and these determine whether AML1 acts as a transcriptional repressor or activator of gene expression.

AML1 binds to the IL-2 promoter upon T cell receptor (TCR) stimulation. Sakaguchi showed that FoxP3 binds to AML1 and suppresses AML1 enhanced IL-2 production. T cells that do not express AML1 fail to bind wild type FoxP3, do not suppress IL-2 production and fail to up-regulate CD25, CTLA-4 and GITR, markers of Tregs; these cells were also shown to be less suppressive than those that could bind AML1 in a functional assay. Sakaguchi also demonstrated that single nucleotide polymorphisms (SNPs) affecting the AML1/FoxP3 interaction resulted in susceptibility to rheumatoid arthritis, systemic lupus erythematosus, psoriasis and other autoimmune diseases.

A new treatment for Guillain-Barré

Huw Willison’s group in Glasgow have studied the neuromuscular effect of the anti-ganglioside antibody, anti-GD1a, that is normally produced in the motor axonal form of Guillain-

Barré. They showed this antibody destroys the motor nerve endplate, by a process that is dependent upon the presence of complement.

Very happily, there is now a drug that can block complement in humans. A monoclonal antibody against complement, C5, (ecluzimab) has been used effectively as a treatment for paroxysmal nocturnal haemoglobinuria. Willison and colleagues are attempting to secure funding for a trial of echuzimab in Guillain-Barré.

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This work is crucial in our understanding of the regulation of self-tolerance and the mechanisms that control the critical balance that our immune system has to strike between defense, repair and autoimmunity. Importantly, it offers a possible target for future treatments that can hope to prevent autoimmunity without causing immunosuppression.

The enhancement of neurogenesis post stroke - a new role for rosiglitazone?
The formation and maintenance of central nervous system circuit integrity has been a focus of Theo Palmer’s work for over ten years. Now as assistant professor in Neurosurgery at Stanford University, he presented recent data examining the roles of inflammation on neurogenesis. He showed that in a post-stroke rat model, neurogenesis is enhanced, and microglial activation is suppressed, by non-steroideal drugs such as indomethacin. However, these results were overshadowed by the superior results seen with rosiglitazone. This peroxisome proliferator-activated receptor gamma agonist, used clinically in diabetics to enhance glycaemic control, is emerging as a new neuroprotective agent. How it does this remains to be defined, but is sure to involve modulation of pro-inflammatory cytokines and attenuation of an otherwise activated immune system.

Amanda Cox, Alasdair Coles
Dr Jo Jones, Dr Vicki Robertson and Dr Ben Wright.

PREVIEW: 75th Anniversary Celebrations of the Association of British Neurologists

The Association of British Neurologists will visit Cambridge on April 11-13th 2007 and this will form part of the 75th anniversary celebrations of the Association.

The main symposium on the Thursday will outline the history of Neurology in the United Kingdom during the 20th century, focusing on activities of the Association. The programme for Thursday also includes a guest lecture on spinal cord injury and repair by Professor James Fawcett. One of the meeting highlights will be the unveiling of the ABN Coat of Arms on the Thursday evening.

The Conference Dinner is at Kings College with music from members of the College Choir. Our principal guest is Baroness Onora O’Neill – Reith lecturer in 2002, and an authority on bioethics.

We shall be building upon the previous success of the case presentation competition and again putting greater focus upon poster presentations. The scientific events close with a debate with the motion ‘Modernising Medical Careers for patients, trainees and the practice of neurology,’ proposed by Chris Clough, and opposed by Professor Compston.

We are looking forward to seeing everyone in Cambridge and hope to make this an enjoyable, memorable and instructive meeting of the Association, fit for our 75th anniversary.

Association of British Neurologists.

PREVIEW: 17th Meeting of the European Neurological Society

The ENS 2007 scientific programme includes 4 symposia featuring lectures by experts discussing new advances in neurology and clinical neurosciences. The first symposium on Monday is the presidential symposium on axonal protection in chronic inflammatory neurological disorders, chaired by G Comi. This symposium will include lectures on mechanisms between inflammation and axonal degeneration, the implication of stem-cells for regeneration as well as new therapeutic avenues.

On Tuesday, two symposia will run in parallel. The first symposium deals with mitochondrial diseases and will be chaired by P Chinnery and includes lectures on the clinical investigation of mitochondrial disorders, the discovery of novel nuclear genes, the management of mitochondrial disorders and the implication of mitochondrial dysfunction in common neurological disorders.

The other symposium - chaired by V Dietz - is devoted to the contribution of repair of brain and spinal cord injuries and includes lectures on neuronal plasticity of the spinal cord injury, achievements in basic research on regeneration and advances in experimental spinal cord injury.

On Wednesday, the symposium focussing on stroke prevention will be chaired D Leys and includes lectures on preventing early recurrences after cerebral ischaemic event, new development in antiplatelet therapy, stroke prevention in women and stroke prevention in young adults.

This will be followed by the best of free communications 2007 which will give a summary of the best papers presented during the meeting.

In addition to the symposia, the scientific programme includes 5 poster sessions and 16 oral sessions of free communication. There will be an integrated programme on the management of MS patients, on the treatment of acute stroke and of motoneuron disease. After the successful introduction of poster walks last year, we will once again have these to display the posters in a more lively and interesting format. Experts will lead a review of selected posters promoting discussion with the authors.

Prof A Steck, Executive Committee.

Visit the ENS 2007 website www.ensinfo.com featuring:
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