

Report on the International Union of Immunological Societies (IUIS) meeting Budapest 2005

The IUIS expert committee on Primary Immunodeficiency Diseases met in Budapest for 3 days in June this year, to discuss the new findings in Primary Immunodeficiency Diseases. Prior to the committee meeting, scientists and physicians met to present the evidence relating to these findings so that there could be (and there was) far reaching discussion. There were 105 physicians and scientists from 21 countries including those in North America, Europe, Japan, Iran, Australia and Brazil, in addition to the eleven IUIS committee members from round the world.

The range of primary immune deficiencies discussed was very wide, from gene defects such as those resulting in autoimmune problems to molecular studies in diseases as diverse as IgA deficiency and SCIDs. The science included new genes discovered in common and rare forms of PID disease in humans as well as the diseases in mouse models in which specific genes had been “knocked out. Studies on immunity in the lamprey, a new animal to be studied from early in evolution, were of great interest and will help to understand how the immune system developed and identify new basic mechanisms that can go wrong.

The scientific sessions were divided according to the human disease group to which each talk was relevant. The meeting started with innate immunity. There is great excitement in the new area of interest, Toll-like receptors and the associated signalling pathways, involving a central molecule NF κ B. These responses relate to the most immediate response to infection and are proving to be very interesting and fruitful areas for new human diseases. It is already clear that defects in these pathways result in a wide range of immune problems. There was also news on potential gene therapy for chronic granulomatous disease, though as in gene therapy for SCID, these are early days. Two adults had their blood-forming stem cells harvested, and a correct copy of the gene was provided by a retrovirus. The corrected cells were re-infused after treatment; in the following year both men had unprecedented increases in neutrophil numbers and were able to clear long-standing, serious infections. In view of the recent reports of serious adverse events in gene therapy for X-linked SCID, careful monitoring of patients treated by gene therapy for CGD is mandatory; more work must be done to achieve safe as well as effective gene therapy treatments.

There was new information on regulation of immune cells. Whilst immune systems must be “activated “ in order to work, they must also be controlled to prevent inappropriate responses, such as autoimmunity or excessive proliferation. If there are defects in regulation, immune deficiencies may and do result.

Another new area was that on cell trafficking. In order to move to sites where they can be effective, all types of immune cells must not only be flexible but must respond to specific signals. Trafficking of cells depends on molecular structures (and therefore genes) for receiving signals, structural changes to squeeze through blood vessels and changing

shape to accommodate & assist other cells in the “immune team”. Defects in the genes for any of the structures or messengers involved cause a defective immune system.

The final session was devoted to antibody production and started with new exciting findings in B cell development. There is much interest in trying to sort out the myriad of primary immune deficiencies involving antibodies, not least to improve treatment & management of patients with these conditions. In order to switch on plasma cells to produce large amounts of antibodies relevant to a pathogen, factors with names like BLIMP-1 and Bach1 and Bach2 have been found to be needed in mice and these may be missing in some patients with antibody defects.

Complex issues involving enzymes, genetic transcription factors & signalling pathways are involved in the recognition of germs by B cells. Extrapolations from findings in mice have yielded exciting results in patients who fail to make antibodies. Laboratories in various parts of the world have independently found defects in several different genes responsible for B cell maturation in a small proportion of patients with the commonest forms of primary antibody deficiency (common variable immunodeficiency disorders). Patients have been found who are missing functional genes for B cell development; these include genes such as *TACI* and *BAFF R* and others are missing surface proteins such as CD19. The resulting defects cause a range of clinical diseases of varying age of onset and severity, indicating that these findings are not the whole story and that other genes will be found that modify these diseases. Furthermore, even the most optimistic only expect these defects to account for a very small proportion of the multiple genes involved in the various primary immune deficiencies involving antibodies. There may prove to be as many categories of antibody defects as there are SCIDs!

The need to continue to use animal models to indicate where to look in human immune systems, both adaptive (antigen specific) and innate (non-antigen specific), for potential gene defects was underlined by these presentations. The challenge of applying such findings from in-bred animals to out-bred humans, further compounded by the effects of the serious infections with which patients originally come to medical attention, will continue to encourage immunological scientists and clinicians for many years to come.

As ever, despite the fantastic surroundings, the delegates found the scientific sessions far too interesting to enjoy the delights of this beautiful city! A quick clamber up the hill on the gardens on the Buda side or a visit to the castle gave only a taste of the wonderful surroundings, but lively and friendly discussions more than compensated. We look forward to the ESID:INGID:IPOPI meeting in Budapest next year.

This meeting was organised by Luigi Notarangelo and Raif Geha with the Jeffrey Modell Foundation. We thank the following for their generous sponsorship: Baxter Healthcare, Octapharma, Talecris, Biotherapeutics, ZLB Behring and help from Correlagen, the US National Institute of Allergy & Infectious Diseases, National Institute of Child Health & Human Development and NIH Office of Rare Diseases.

Helen Chapel & Jennifer Puck
July 2005