

## Editorial

# And the winner is ... 20 years of excellence in research on allergic disease!

**M. D. Chapman**

Indoor Biotechnologies Inc., Charlottesville, VA, USA

Martin D. Chapman  
Indoor Biotechnologies Inc.  
1216 Harris Street  
Charlottesville  
VA 22903  
USA

Accepted for publication 1 March 2006

The most prestigious prize for young scientists in allergy research is the annual award of the Pharmacia Allergy Research Foundation (PhARF). This award was conceived by *Pharmacia*, under the guidance of Professor S. Gunnar O. Johansson, in 1987 to celebrate the 20th anniversary of the discovery of immunoglobulin (Ig)E (1, 2). Without question, the award has been an outstanding success. Over the past 20 years, the PhARF award has recognized the achievements of scientists in the formative stages of their careers. The award is given to young scientists (aged under 40 years) who present the best research to cover a theme selected by the Scientific Committee of the PhARF each year. These themes have covered the gamut of basic and clinical allergy research: allergen structure and function; cellular regulation of IgE responses, effector cells (mast cells, basophils and eosinophils); asthma and allergic inflammation; allergy diagnosis and treatment. Past recipients of the PhARF award form a generation of scientists that has made substantive contributions to these key areas of allergy/immunology research (Table 1).

The topic for the award in 2005 was 'Advances in the understanding and treatment of allergic diseases'. Congratulations to Dr Omid Akbari of Harvard Medical School who is the 2005 recipient of the PhARF award! Dr Akbari's review of the identification of iNKT cells as a potential new target for asthma treatment is published in this edition of *Allergy* and the original data has just been published in the *New England Journal of Medicine* (3, 4). T cells, specifically CD4<sup>+</sup> Th2 cells, orchestrate allergic inflammation in the lung and are thought to be involved in the development of airway hyperreactivity (5, 6). Allergen-specific T-regulatory cells (Tregs) may

suppress allergic responses in normal individuals and the induction of Tregs producing interleukin (IL)-10 may be responsible for reduction in IgE antibody responses and for clinical improvement following allergen immunotherapy (5, 6). Over the past year, two studies have focused attention on an unusual class of T cells, CD1 restricted natural killer T (NKT) cells, in allergic diseases. These NKT cells recognize lipid and glycolipid antigens through the CD1 family of antigen-presenting molecules and are typically involved in host defense (innate) immune responses. The first paper, by Spinozzi and colleagues, showed that phospholipids isolated from cypress grass pollen-stimulated proliferative T-cell responses from cypress allergic patients with rhinitis/asthma through a CD1-dependant pathway (7). The second paper by Akbari showed that a high proportion of CD4<sup>+</sup> T cells in bronchoalveolar lavages (BAL) of asthma patients were NKT cells that expressed a highly restricted invariant T-cell receptor (iNKT cells) (3, 4). The prevalence of iNKT cells in BAL from patients with mild asthma, sarcoidosis or nonasthmatic controls was compared by flow cytometry, using a monoclonal antibody (mAb) specific for the invariant chain of NKT cells, and by using CD1d tetramers loaded with a glycolipid antigen. There was a remarkably high prevalence of iNKT cells in BAL from patients with asthma (13–71%), when compared with controls (<1%) and, strikingly, 60–85% of T cells in the BAL from asthma patients were iNKT cells. The results were supported by immunofluorescence and confocal laser scanning microscopy showing the presence of iNKT cells in endobronchial biopsies from a patient with asthma. In contrast, biopsies from a patient with sarcoidosis with

Table 1. Pharmacia Allergy Research Foundation Award Recipients, 1987–2005

| Year | Recipient(s)                                                                                             |
|------|----------------------------------------------------------------------------------------------------------|
| 1987 | Martin D. Chapman PhD, Charlottesville, VA, USA<br>Carla Bruijnzeel-Koomen PhD, Utrecht, the Netherlands |
| 1988 | Monique Capron-Dupont, MD, Lille, France                                                                 |
| 1989 | Patrick G. Holt MD, Subiaco, Western Australia<br>Donata Vercelli MD, Boston, MA, USA                    |
| 1990 | Tak Lee, MD, London, UK<br>Judah Denburg MD, Hamilton, ON, Canada                                        |
| 1991 | Michael Kemeny PhD, London, UK<br>Harald Renz MD, Denver, CO, USA                                        |
| 1992 | Shyam Mohapatra PhD, Bad Lippspringe, Germany                                                            |
| 1993 | Rafeul Alam MD, PhD, Galveston, TX, USA<br>Massimo Triggiani MD, Naples, Italy                           |
| 1994 | Thomas Bieber MD, Munich, Germany<br>David Lang MD, Philadelphia, PA, USA                                |
| 1995 | Hans C. Oettgen MD, Boston, MA, USA<br>Marc Benhamou PhD, Paris, France                                  |
| 1996 | Rudolf Valenta MD, Vienna, Austria                                                                       |
| 1997 | Paul Rothman MD, New York, NY, USA                                                                       |
| 1998 | Santa Ono PhD, Boston, MA, USA<br>Marc Rothenberg MD, PhD, Cincinnati, OH, USA                           |
| 1999 | David Dombrowicz PhD, Lille, France<br>Federica Sallusto PhD, Basel, Switzerland                         |
| 2000 | Stephan C. Bischoff MD, Hannover, Germany<br>Christof Ebner MD, Vienna, Austria                          |
| 2001 | Mark Larché PhD, London, UK                                                                              |
| 2002 | Anna Pomés PhD, Charlottesville, VA, USA                                                                 |
| 2003 | Gesine Hansen MD, Halle, Germany                                                                         |
| 2004 | Bart Lambrecht MD, PhD, Rotterdam, the Netherlands                                                       |
| 2005 | Omid Akbari PhD, Boston, MA, USA                                                                         |

elevated CD4<sup>+</sup> T cells in BAL, did not express the invariant chain and were not NKT cells.

Both the Spinozzi and the Akbari studies enrolled similar numbers of subjects (14–15 allergic adults) and show that CD1 restricted NKT cells occur in the BAL and in the peripheral blood. Akbari observed that iNKT cells in BAL produced IL-4 and IL-13, whereas those in peripheral blood produced IL-4, IL-13 and interferon (IFN)- $\gamma$  (where Spinozzi also observed IL-4 and IFN- $\gamma$  production). However, whereas Akbari's data demonstrates a major role for V $\alpha$ 24<sup>+</sup> iNKT cells in the BAL, Spinozzi and colleagues rarely found these cells involved in cypress phospholipid recognition in the peripheral blood. This appears to be a major difference between the two studies which, perhaps, may be explained by the vagaries of cloning or by a lower prevalence of V $\alpha$ 24<sup>+</sup>; NKT cells in the periphery. Like all exciting preliminary studies, these studies pose more questions than answers. Why is there such a high proportion of CD4<sup>+</sup> T cells in BAL in the lungs of asthmatics of the iNKT phenotype? How do they contribute to the pathogenesis of asthma, and do other allergenic sources that are more commonly associated with asthma (dust mites, animal danders, cockroaches) also contain similar phospholipids? Akbari's hypothesis that allergen-specific CD4<sup>+</sup> T cells somehow alter 'self-glycolipid antigens' within the lung, and that these modified self-antigens activate iNKT cells, is

worthy of further investigation. The identification of pulmonary iNKT cells as a potential therapeutic target for asthma is challenging and, in the nature of PhARF awards, forms the basis upon which to build a productive and satisfying career!

In recognition of his research achievements, Dr Akbari has received \$50 000 as the PhARF award and, more importantly, join a group of 28 previous recipients of the award who have greatly influenced allergy/immunology research over the past 20 years (Table 1). Kudos for the concepts behind developing the PhARF award go to Prof. Gunnar Johansson who not only chaired the Scientific committee for the first 3 years, but also played a major role in defining the ethos of this special prize. Prof. Johansson, ably assisted by the first Secretary of the Foundation, Hans Arrendal, had a vision that the award would raise scientific interest in allergy research, create an air of expectation, and encourage personal interactions and a sense of community through well-organized scientific and social events. One of the ways that this was achieved in the early years was (in the Swedish tradition) by maintaining secrecy of the award winner until the award ceremony itself. I can well remember being summoned to meet in private with Dr Johansson and Hans Arrendal at the American Academy of Allergy, Asthma and Immunology annual meeting in 1987, where they informed me that I had been awarded the prize, which was both shocking and exhilarating at the same time! The requirement to maintain secrecy, even from one's mentor, until the award was presented was an exciting dimension, which myself and Dr Carla Bruijnzeel-Koomen, as young scientists, eagerly embraced. We were both honored to receive the first award from Dr Kimishige Ishizaka at the European Academy of Allergy and Clinical Immunology annual meeting in Mallorca, Spain, in 1987. There were many surprised faces in the audience and the expectation effect had been overwhelmingly successful! This was maintained at subsequent award ceremonies where the identity of the award recipient was only revealed immediately prior to the presentation.

Highlights of the PhARF awards in the first 10 years were the lavish social events that accompanied the award ceremonies for award recipients, honorees, invited guest and Foundation members. These created a strong social ambience, strengthened academic ties and created lifelong friendships. There were several memorable boat rides, an evening train ride to Gstaad from Montreux, a dinner at a Japanese Ryokan, all of which served to enrich the sense of achievement. Much of the effort in organizing the award ceremonies fell to Hans Arrendal, who was recognized in a special presentation at the International Congress of Allergy and Clinical Immunology (now the World Allergy Organization) in Cancun, Mexico, in 1997.

In addition to the cash prize (for personal use!), a little known element of the award is that PhARF recipients also receive a cut glass model of the IgE molecule. The

first of these models were based on a large glass replica of IgE that was kept at the Foundation in Uppsala. In this replica, each constant region is represented by a different artistic 'motif' in the glass and each recipient received a separate model designed using one of the motifs (Fig. 1).

Over the past 10 years, the PhARF has been successively chaired by Prof. Allen Kaplan, Dean Metcalfe and Paul O'Byrne, and has involved leading allergist/immunologists who assess applications for the award each year. The Foundation has continued to maintain a high standard of scientific excellence in making the award. The Foundation has invested heavily in time, financial support and organization in making these awards over the past 20 years and is to be praised for such generous support of young scientists. The success of the PhARF award has stimulated other companies to become involved and to provide awards for young investigators. These include the Henning Lowenstein Research Award (ALK-Abello) and the Allergopharma Prize (Allergopharma Joachim Ganzer KG), as well as travel grants offered by smaller companies, including Indoor Biotechnologies.

The PhARF celebrates 20 years of its award in 2007, which will also be the 40th anniversary of the discovery of IgE. Doubtless, the Foundation has plans, and we can all look forward to further celebrations of research excellence in Allergy and Immunology.

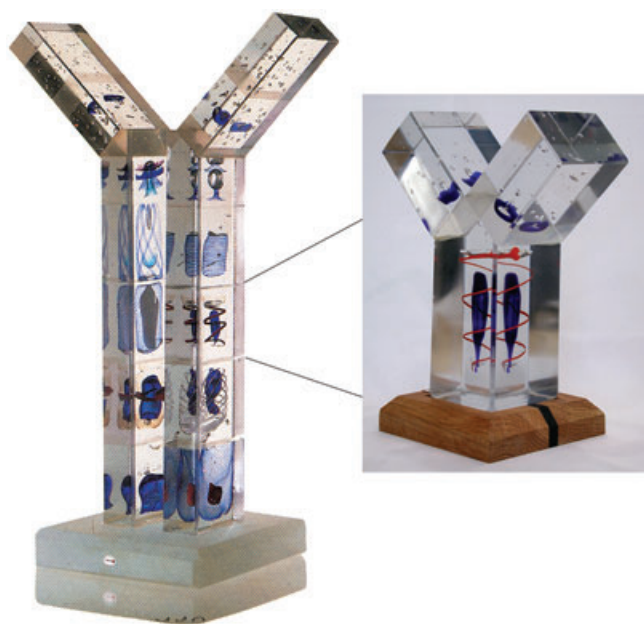


Figure 1. The Pharmacia (Phadia) Allergy Research Foundation Award. Right panel: original lead crystal glass replica of the immunoglobulin (Ig)E molecule, which is approximately 2 feet high. Inset: glass model of one 'domain' of the IgE replica, awarded to the author in 1987 (dimensions: 8" high  $\times$  6" wide; weight: 2.8 kg).

## References

1. Ishizaka K, Ishizaka T, Hornbrook MM. Physico-chemical properties of human reagenic antibody: IV. Presence of a unique immunoglobulin as a carrier of reagenic antibody. *J Immunol* 1966;**97**:75–85.
2. Johansson SGO, Bennich H. Immunological studies of an atypical (myeloma) immunoglobulin. *Immunology* 1967;**13**:381–394.
3. Akbari O. The role of iNKT cells in development of bronchial asthma: a translational approach from animal models to human. *Allergy* 2006;**61**:962–968.
4. Akbari O, Faul JL, Hoyte EG, Berry GJ, Wahlstrom J, Kronenberg M et al. CD4<sup>+</sup> iNKT cells; new target for treatment of asthma in human. *New Engl J Med* 2006;**354**:1117–1129.
5. Robinson DS, Larché M, Durham S. Tregs and allergic diseases. *J Clin Invest* 2004;**114**:1389–1397.
6. Kay AB. Allergy and allergic diseases. *N Engl J Med* 2001;**344**:30–37.
7. Agea E, Russano A, Bistoni O, Mannucci R, Nicoletti I, Corazzi L et al. Human CD1-restricted T cell recognition of lipids from pollens. *J Exp Med* 2005;**202**:295–308.