



# Laudatio for Adrian Liston

Group leader at VIB Translational Immunology Lab, University of Leuven, Belgium Winner of the Eppendorf Award for Young Investigators 2016

**The laudatio was held by the Eppendorf Award Jury Chairman Prof. Reinhard Jahn (Director at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) at the prize ceremony at the EMBL Advanced Training Centre in Heidelberg on June 2, 2016.**

» Every living organism needs to survive and prevail in a hostile environment. In particular, our world is populated by an enormous diversity of microorganisms, invisible to the naked eye, that are fiercely competing for nutrients and that have pervaded every ecosystem of our planet. Complex organisms are continuously challenged by the microbial world. Their success in evolution critically depended on the ability to arrange themselves with microorganisms. This arrangement includes mechanisms to keep microbes out of cells, tissues and body fluids except of those where they are “tamed”, such as in the digestive system or in other specialized symbiotic relationships.

Considering the vast diversity of microbial attack mechanisms it is not surprising that the defense mechanisms evolved in higher organisms are of extraordinarily high complexity. Both plants and animals command over a sophisticated array of innate, i.e. genetically encoded, defensive weapons. However, it is only in vertebrates that the defense against foreign macromolecules and microorganisms advanced to an entirely different level. Vertebrates not only possess the standard weapons such as cytolytic peptides and phagocytotic cells to deal with attacks from noxious proteins and organisms. In addition, they possess a second and slower form of defense that is tailored to cope with each foreign

invader on a highly individual basis. This adaptive immune system has the capacity to mount a specific reaction to foreign proteins or organisms of which the attacked organism has no previous “knowledge”. (I should mention in parentheses that the distinction between innate and adaptive immune system is becoming blurred – for instance with the discovery of the CRISPR system it has been recognised that even bacteria possess elements of an adaptive defense). In principle, the main invention of the adaptive immune response in vertebrates consists of recognition molecules – so called immune receptors, more specifically B-cell and T-cell receptors. These receptors selectively recognize foreign structures, bind to them and thus “flag” them for the activation of the rather formidable defense machineries in our bodies. Everyone of us can generate tens of millions of different B-cell and even more T-cell receptors. This provides us with repertoire of enormous diversity that conveys unsurpassed efficiency in the defense against foreign cells and proteins.

The discovery of the mechanisms responsible for this amazing diversity belongs to the biggest achievements in molecular biosciences in the past decades. We now know that the diversity is achieved by directed somatic recombination events in which arrays of genes are randomly combined during lymphocyte development. This recombination creates a molecular complexity exceeding the number of genes in the genome by several orders of magnitude. Thus, many million of lymphocytes are generated, each of which having a specific receptor and thus being specific for a different structure (or epitope).

The randomness of this process has consequences that need to be dealt with. First, the organism must ensure that cells recognizing the body’s own molecules are eliminated before being commissioned to work. Otherwise they would mount attacks against its own organism. Second, it is in the nature of such a combinatorial approach that the number of cells specific for e.g. a certain pathogenic bacterium is very small. Thus, mechanisms are in place, termed clonal selection, that rapidly amplify those cells once the first contact with the enemy is established. Otherwise they would be rapidly overwhelmed by an army of millions or even billions of bacteria (or viruses). Third, there must be checks and balances fine-tuning the arsenal of weapons that are commissioned for a specific defense job. Too weak a response may cause an infectious agent to take over, too strong a response may go out of control and may attack unwanted targets within the body.

Research over the last decades has uncovered a network of interdependent regulatory events that govern these and many other functions of the immune system. I do not want to go into more details – the complexity exceeds that understandable to a neuroscientist like myself. If you ever think the brain is the most complex organ in your body, you may need to reconsider.... However, this is exactly the type of questions where this year’s winner of the

Eppendorf Young Investigator Award, Dr. Adrian Liston, is focusing on. Before Adrian tells you more about his work, I briefly want to introduce him to you.

Adrian is an Australian who graduated from Adelaide University and then moved to Canberra where he did his PhD work with Chris Goodnow at the Australian National University. During his PhD he became fascinated with autoimmunity and the regulation of the immune system, a fascination that he has maintained until today as a guideline for his scientific interests. In his thesis, he dealt with genetic factors contributing to autoimmune disease, and already then his focus was on T-cells. In particular, he worked on the early development of T-cells, a stage in which autoimmune T-cells must be eliminated. After completion of his PhD in 2006 he moved to Seattle in order to do postdoctoral work with Sasha Rudensky on regulatory T cells. In particular, he was interested in how these regulatory T-cells are generated and how they function in the control of disease.

In both his predoctoral and postdoctoral periods Adrian was extraordinarily successful, publishing a string of outstanding papers in the top immunology journals. For a rising star like him there were many career options. Interestingly, he did not want to remain in the US – he told me that he did not want to raise his kids in this country. Personally I can connect with this since I have had to make a similar decision in my career although at a somewhat later state. Thus, he applied for jobs in Europe, among others, and the offer he received from the VIB (Vlaams Instituut voor Biotechnologie) in Leuven was the best. In the year 2009 he moved to Leuven where he has been ever since, presently as a group leader at the VIB and a professor of Leuven University. He established a vigorous and highly productive research team. His interests have remained with T-cells that are the true drivers of the immune system. As explained, they are randomly generated, and thus each cell can be useful, useless, or dangerous. The screening mechanisms responsible for their selection and activation are still only understood in their basic outline, with many aspects still to be discovered, and I am sure he will tell you more about it in a few minutes.

The success Adrian has had in his scientific work is truly outstanding. His CV contains one of the most impressive lists of high-profile publications I have ever seen for someone at his career state, including numerous well-written reviews that are understandable even to me. He is a rising star, which is also increasingly being recognized by the community, resulting in an unusual cumulation of Awards. Thus, Adrian was successful in securing an ERC-Starting grant. After its expiration he applied for an ERC consolidator grant and again was successful – quite an achievement! Earlier in his career he was awarded the New Investigator Prize of the Australian Society for Immunology, and later the New Investigator Prize of the Australian Society for Medical Research, and he also obtained JDRF Career Development Award in the USA. Last year he has received the Dr. Karel Lodewijk Prize from the Belgian Royal Academy

of Medicine, meaning that he is now being even recognised by the “old boys network”. We had a nice chat about “old boys clubs” and National Academies in general that I do not wish to repeat here, as someone who was elected to three Academies last year, at the youthful age of 64.....

Before handing over the stage to Adrian, let me briefly comment on another side of his personality. Adrian is not only a terrific scientist, but he is also committed to education and to improving the quality of science. Thus, he has obtained a Graduate Certificate in Higher Education and an MS-degree in Public Health. He is interested in science policy and particularly in quality control in the granting and academic career systems and in academic appointments. Our scientific system depends on scientists of the quality of Adrian who are willing to take over responsibility in addition to leading outstanding research labs.

Without further ado, let us welcome the winner of the 2016 Eppendorf Young Investigator Award, Dr. Adrian Liston! «