Fondation Francqui-Stichting
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Ceremony of the Francqui Prize by his Royal Highness Prince Philippe at the "Palais des Académies" on June 8, 2011

Biography - Vanderhaeghen's research - Report of the Jury

Pierre Vanderhaeghen

Biography

Pierre Vanderhaeghen was born in Brussels on August 30th 1967. After primary and high school studies at the Athenée Robert Catteau, he undertook medical studies at the Université Libre de Bruxelles (ULB). Early on he was thrilled by basic life sciences, and worked as a student in several laboratories in Belgium and abroad. After graduating from Medical School, he started a PhD at ULB as a Fellow "Aspirant" of the Belgian National Fund for scientific research (FNRS), under the supervision of Professors Vassart et Parmentier at the IRIBHM Institute. He received his PhD thesis in 1996, focusing on the expression of olfactory receptor genes in sperm cells. He thus acquired a solid background in molecular biology, as well as the taste for risk-taking projects and discovery.

He then decided to shift to a completely different field that fascinated him for a long time: brain development. He joined the team of Pr. John Flanagan at Harvard Medical School, as a Fellow of the Francqui and Belgian American Educational Foundations. Combining genetic and embryology in the mouse, he and his collaborators at Harvard demonstrated the crucial role of a novel family of signaling factors, the ephrins, in the development of neuronal connections in mammals.

He then moved back to Belgium and started his own group at IRIBHM, appointed as a Research Scientist of the FNRS in 2001. With the support of the FNRS, the IUAP programme and the Queen Elizabeth Medical Foundation, he gathered a small team of young talented scientists, who developed a research programme centered round the cerebral cortex, an essential brain structure for which the developmental mechanisms had remained largely unknown.

They first discovered that ephrins played several roles in important mechanisms underlying cortical development, from the control of brain size through the regulation of apoptosis, to the patterning of cortical networks. In parallel, Pierre Vanderhaeghen started to become interested in another fascinating aspect of the cerebral cortex: its evolution. He developed a research programme in collaboration with clinical groups of Erasme Hospital, centered on gene expression in the human developing cortex. This approach resulted in the identification of a first series of genes potentially involved in human brain evolution, thanks to a fruitful collaboration with computational biologists D. Haussler and K. Pollard at the University of California.

More recently, his team was the first to report an entirely novel cellular model of cortical development from mouse embyonic stem cells. This breakthrough constitutes an important step for our understanding of brain development, and opens several perspectives for the development of innovative tools to study the mechanisms of brain diseases, and test novel treatments.

Since then Pierre Vanderhaeghen pursued his research following these discoveries, and was joined by a rich panel of scientists from all over Belgium and Europe, with additional support from the Walloon Region and European Union. He was elected a Member of the Royal Academy of Medicine and European Organization of Molecular Biology EMBO in 2009. He is the very happy father of two daughters, Julie and Marion. Pierre Vanderhaeghen's less known passion is music, and he performs occasionally as a singer in a Brussels-based rock band, the FCBs.

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Vanderhaeghen's research

The cerebral cortex is one of the most complex structures in our brain, controlling movements, perceptions, as well as higher cognitive functions. It is the target of many neurological and neuropsychiatric diseases, most of which remain without cure today, but the mechanisms undelying its development remain largely unknown.

On the other hand the cortex underwent striking changes during mammalian evolution, particulary in the human species. Homo sapiens's neural abilities are likely to be linked to specific programmes orchestrating its development, but the underlying mechanisms remain largely unknown.

Pierre Vanderhaeghen's research developed along these important questions, by focusing on the genetic mechanisms that control cortical development and evolution, from stem cells to neural circuits, from mouse to man.

Combining genetics and embryology in the mouse, Pierre Vanderhaeghen and his colleagues first identified the role of several crucial genes in cortical development, most notably the functions of ephrins in the control of brain size and apoptosis of neural progenitors, as well as in the patterning of neural networks in the cortex. On the other hand, through a series of pioneering studies centered on the human embryonic brain, he and his collaborators identified genes that display human-specific patterns of expression and evolution, which makes them attractive candidates to link cortical development and evolution in the human species.

Genes and mechanisms that were thus identified in mouse and human contribute in a very significant way to our understanding of the innate mechanisms of development of higher cognitive functions, and uncover some of the potential effectors of its rapid evolution in primates.

The complexity of the cortex is at the core of its higher functions, but also poses serious experimental challenges. Pierre Vanderhaeghen and his team thus attempted and succesfully developed innovative reductionist models of cortical development from embryonic stem cells. Most strikingly, their work demonstrated that embryonic stem cells can recapitulate in vitro the major milestones of cortical neuron generation. When grafted into the mouse cerebral cortex, these neurons develop patterns of axonal projections corresponding to genuine native cortical neurons. By building entirely new bridges between pluripotent stem cell technology and brain development complexity, these studies shed new light on the mechanisms of brain development, and provide important and novel opportunities for the rational design of brain repair by cell replacement, as well as for the cellular modelling of human neurological diseases.

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Report of the Jury (May 9, 2011)

The 2011 Francqui Price in Biological and Medical Sciences is awarded to **Pierre Vanderhaeghen** for his seminal contributions to our understanding of the formation of the mammalian brain. In the brain of humans and of other mammalian species, each neuron has to find its own specific place, and connect to other neurons in order to be able to perform their complex functions. The work of Pierre Vanderhaeghen is beginning to uncover how specific molecular signals orchestrate this development.

Through elegant experiments, Pierre Vanderhaeghen discovered that neurons use ephrin signals to guide the making of connections during embryogenesis. This work has important implications for our understanding of how the mammalian brain is formed, and in particular how specific nerve cells move to their appropriate position in the brain. The same pathway controls the number of neurons in the cortex, and thereby influences the size of the brain.

More recently, Pierre Vanderhaeghen performed groundbreaking work in which he demonstrated how mouse embryonic stem cells can be induced to differentiate into cells that resemble functional neurons. These engineered cells

develop the appropriate patterns of axonal projections when grafted into the cerebral cortex, with promise for the use of such cells for the correction of neurodegenerative diseases.

Collectively, the experiments of Pierre Vanderhaeghen provide insight into brain development and offer hope for the future development of therapies for diseases of the human brain.

Jury members :

Professor Sir R. Timothy Hunt FRS
(Cell Cycle Control Laboratory - **London Research Institute** - Clare Hall Laboratories – **United Kingdom**) Dr Tim Hunt recently retired from running a laboratory at Cancer Research UK, but continues to have an office at the London Research Institute. Dr Hunt won the Nobel Prize in Physiology or Medicine in 2001, together with Lee Hartwell and Paul Nurse, for "Their discoveries of key regulators of the cell cycle". Dr Hunt continues to study the control of cell cycle transitions. He is a Fellow of the Royal Society, a Member of EMBO, a Foreign Associate of the US National Academy of Sciences and a member of the Scientific Council of the European Research Council.

Chairman

and

Professor Han G. Brunner
(**University Medical Center St Radboud** - Department of Human Genetics **Nijmegen** – **Nederland**) Han Brunner is full professor and head of the department of Human Genetics at University Medical Center St Radboud in Nijmegen. He has initiated and conducted several research projects that use patient observations as the starting point for human molecular genetic investigations into such topics as human behaviour, skeletal development, brain development, neuromuscular disease, congenital malformations, and gonadal development and function.

Professor Richard Flavell PhD, FRS
(Chairman and Sterling Professor of Immunobiology at **Yale University** School of Medicine and Investigator of Howard Hughes Medical Institute, **New Haven - USA**). He is well-known for his early research on Mammalian gene structure and epigenetics and more recent studies on innate and adaptive immunity . He is a member of EMBO, the National Academy of Sciences of the United States and a Fellow of the Royal Society of London.

Professor Anne O'Garra
(**The MRC National Institute for Medical Research** - Division of Immunoregulation **London - United Kingdom**) obtained her Ph.D. at the MRC National Institute for Medical Research (NIMR), Mill Hill, London. At the DNAX Research Institute, California, USA (1987 – 2001), she defined key functions and mechanisms for cytokine expression and function in the immune response. She returned to the UK in 2001 and then formed the new Division of Immunoregulation at the NIMR, to interface the divisions of immunology and infectious diseases. She and her group are continuing research on immunoregulation and role and function of cytokines in the immune response, but now also with major emphasis on the immune response in tuberculosis in mouse models and in human disease. Anne O'Garra was elected as a Fellow of the Academy of Medical Sciences, UK. in 2005; as a Fellow of the American Association for the Advancement of Science, 2006; as a Fellow of the Royal Society, UK in 2008; and elected to EMBO membership, 2009. O'Garra has given numerous named lectureships at major academic institutions and conferences in the UK, the US and abroad. She serves as an Editor of the Journal of Experimental Medicine.

Professor Peter W H Holland FRS
(**University of Oxford** - Department of Zoology - **United Kingdom**) holds the Linacre Professorship of Zoology at the University of Oxford, UK. After a degree in zoology from Oxford, and a PhD in developmental genetics from London, he has held academic appointments at the Universities of Reading and Oxford. Peter Holland's scientific research on the evolution of genes and genomes has been recognized by award of the Genetics Society Medal, the de Snoo Medal,

the Zoological Society Scientific Medal and the Kowalevsly Medal, and election to Fellowship of the Royal Society.

Professor Jonathan C. Howard MA, DPhil. FRS
(**University of Cologne** - Institute for Genetics **Germany**) Graduated in Zoology at the University of Oxford in 1964 and spent the following year working on ecological genetics at the laboratory founded by JBS Haldane in Orissa, India. In 1969 he obtained a D.Phil. on cellular immunology in Oxford under ProfessorJ.L.Gowans. After post-doctoral work at the University of PennsylvaniaSchool of Medicine Howard joined the Immunology Department of theInstitute of Animal Physiology in Cambridge where he worked on the immunogenetics of antigen processing and presentation. In 1994 Howard became a Professor at the Institute for Genetics in Cologne, Germany, where he studies mechanistic and evolutionary aspects of host-pathogen interactions. Professor Howard was elected a member of EMBO in 1993 and Fellow of the Royal Society in 1995.

Professor Emeritus Sir Ravinder Maini FRS FMedSci FRCP
(**The Kennedy Institute of Rheumatology**, Imperial College London - **London** - **United Kingdom**) In his career, Sir Ravinder Maini, a clinician, has combined clinical and laboratory-based immunological research. Lately he was Scientific Director of The Kennedy Institute of Rheumatology (and is currently Emeritus Professor) at Imperial College, London. His research is focussed on mechanisms of autoimmunity and immunotherapy. For his research he has beenawarded honorary doctorates by the Universities of Glasgow and Paris, the Crafoord Prize by The Royal Swedish Academy of Sciences and The Lasker prize for Clinical Research. Sir Ravinder is Fellow of The Royal Society, Fellow of the Academy of Science (UK) and Foreign Associate of the US Academy of Sciences

Professor Anthony W Segal MBChB, MD, DSc, PhD, F Med Sci, FRS
(Charles Dent Professor of Medicine, Director, Centre for Molecular Medicine, **UCL**,**London** – **United Kingdom**) Born South Africa, Medical training at the University of Cape Town. Charles Dent Professor of Medicine at University College London (UCL) since 1986. Physician and scientist - expertise in infection and inflammation with particular expertise in neutrophil biology and the causes of inflammatory bowel disease (Crohn's disease and ulcerative colitis). Fellow of the Royal Society 1998.

from left to rigth : Prof. Richard A Flavell, Prof. Peter W H Holland, Prof. Sir Ravinder Maini, Prof. Sir Tim Hunt, Prof. Anne O'Garra, Prof. Anthony W Segal, Prof. Jonathan C. Howard, Prof. Han Brunner, Prof. Pierre Van Moerbeke