The XXIV Ottorino Rossi Award

Who was Ottorino Rossi?

Ottorino Rossi was born on 17th January, 1877, in Solbiate Comasco, a tiny Italian village near Como. In 1895 he enrolled at the medical faculty of the University of Pavia as a student of the Ghislieri College and during his undergraduate years he was an intern pupil of the Institute of General Pathology and Histology, which was headed by Camillo Golgi. In 1901 Rossi obtained his medical doctor degree with the highest grades and a distinction. In October 1902 he went on to the Clinica Neuropatologica (Hospital for Nervous and Mental Diseases) directed by Casimiro Mondino to learn clinical neurology. In his spare time Rossi continued to frequent the Golgi Institute which was the leading Italian centre for biological research. Having completed his clinical preparation in Florence with Eugenio Tanzi, and in Munich at the Institute directed by Emil Kraepelin, he taught at the Universities of Siena, Sassari and Pavia. In Pavia he was made Rector of the University and was instrumental in getting the buildings of the new San Matteo Polyclinic completed.

Ottorino Rossi made important contributions to many fields of clinical neurology, neurophysiopathology and neuroanatomy. These include: the identification of glucose as the reducing agent of cerebrospinal fluid, the demonstration that fibres from the spinal ganglia pass into the dorsal branch of the spinal roots, and the description of the cerebellar symptom which he termed “the primary asymmetries of positions”. Moreover, he conducted important studies on the immunopathology of the nervous system, the serodiagnosis of neurosyphilis and the regeneration of the nervous system. He was the author of major scientific works including an extensive investigation of arteriosclerosis in the brain, giving a new interpretation of the development of lesions of vascular origin. He died in 1936 at the age of 59, having named the Ghislieri College as his heir. Ottorino Rossi was one of Camillo Golgi’s most illustrious pupils as well as one of the most eminent descendants of Pavia’s medico-biological tradition.

Ottorino Rossi Award: previous winners

Since 1990, the IRCCS C. Mondino National Institute of Neurology Foundation has held an annual Ottorino Rossi Award Conference at which the award is presented to a scientist who has made an important contribution to research in the field of the neurosciences.

In previous years the Ottorino Rossi Award has been conferred upon: Vittorio Erspamer, Rome, Italy (1990); Paolo Pinelli, Milan, Italy (1991); Giovanni Di Chiro, Bethesda, USA (1992); Clarence J. Gibbs Jr, Bethesda, USA (1993); David S. Zee, Baltimore, USA (1994); Elio Lugaresi, Bologna, Italy (1995); Michel Fardeau, Paris, France (1996); Salvador Moncada, London, UK (1997); Alain Berthoz, Paris, France (1998); Ottar Sjaastad, Trondheim, Norway (1999); J. Timothy Greenamyre, Atlanta, USA (2000); Salvatore DiMauro, New York, USA (2001); Elio Raviola, Boston, USA (2002); Kenneth Michael A. Welch, Chicago, USA (2003); François Boller, Paris, France (2004); Jes Olesen, Copenhagen, Denmark (2005); Stanley Finger, St Louis, USA (2006); Michael A. Moskowitz, Charlestown, MA, USA (2007), Patricia Smith Churchland, University of California, San Diego, USA (2008); Stephen P. Hunt, London, UK (2009).
The period 2010-2012 was devoted to the *New Series - The Founders of Neurology* and saw the prize awarded to the founders of the most important Italian schools of neurology, namely: Vincenzo Bonavita, Naples, Italy (2010); Cesare Fieschi, Rome, Italy (2011); Giorgio Bernardi, Rome, Italy (2012).

Academic profile and scientific achievements of the XXIV Ottorino Rossi Award winner

Henry Markram was born in South Africa on 28 March 1962. In 1984, he obtained his **Bachelor of Science** (with Honors) from Cape Town University under the supervision of Rodney Douglas. He moved to Israel in 1988, where he obtained a PhD from the Weizmann Institute of Science, under the supervision of Menahem Segal. During his PhD studies he discovered a link between acetylcholine and memory mechanisms, showing that acetylcholine modulates the primary receptor linked to synaptic plasticity (the NMDA receptor, N-methyl-D-aspartate).

He spent 1992-1993 in the USA, where he did his **first postdoctoral** study as a Fulbright Scholar at the National Institutes of Health (NIH), National Institute of Neurological Disorders and Stroke. Working in the laboratory of Dr G. Ehernstein and Dr E.F. Stanley, he studied ion channels on synaptic vesicles.

He did his **second postdoctoral** study as a Minerva Fellow in the laboratory of Bert Sakmann at the Max Planck Institute, Heidelberg, Germany, where he discovered calcium transients in dendrites evoked by sub-threshold activity, and by single action potentials propagating back into dendrites. He also started exploring the micro-anatomical and physiological principles of the different neurons of the neocortex and of the monosynaptic connections that they form. He published a paper describing in great detail how layer 5 pyramidal neurons are interconnected. He was the first to alter the precise millisecond relative timing of single pre- and postsynaptic action potentials to reveal a highly precise learning mechanism operating between neurons. This mechanism has now been reproduced in many brain regions and is now commonly known as spike timing-dependent synaptic plasticity (STDP). Although it was preceded by some correlation-sensitive findings, this was the first study that manipulated single pre- and postsynaptic spike times to monitor the effect of synaptic changes.

Henry Markram was appointed **assistant professor** at the Weizmann Institute for Science, Israel, where he started systematically unraveling the neocortical column. At the Weizmann Institute, he discovered that synaptic learning, rather than merely changing the strengths of connections, can also involve a change in synaptic dynamics (called redistribution of synaptic efficacy). He also revealed a spectrum of new principles governing neocortical microcircuit structure, function, and emergent dynamics. Based on the emergent dynamics of the neocortical microcircuit he, together with Wolfgang Maass, developed the theory of liquid computing or high entropy computing. At the Weizmann Institute, he also uncovered the “tabula rasa principle”, which governs the random structural connectivity between pyramidal neurons and a non-random functional connectivity due to target selection.

He received early tenure as an **associate professor** at the Weizmann Institute and in 2002 moved to Lausanne, Switzerland where, at the age of 39, he was appointed **full professor** and founder/director of the Brain Mind Institute (BMI) at the Swiss Federal Institute for Technology (EPFL) and director of the Center for Neuroscience and Technology. At the BMI, Markram has continued to unravel the blueprint of the neocortical column at a greatly accelerated pace, building state-of-the-art tools to carry out multi-neuron patch-clamp recordings combined with laser and electrical stimulation as well as multi-site electrical recordings (up to 12 patch-clamp recordings) and chemical imaging and gene expression.

Markram has received numerous awards and published over 75 papers.

In April, 2005 the EPFL signed the agreement with the BMI to launch one of the largest single initiatives in neuroscience – the **Blue Brain Project** (BBP). The BBP used the BMI’s most advanced supercomputers to reconstruct a detailed computer model of the neocortical column composed of 10,000 neurons, more than 340 different types of neurons distributed according to a layer-based recipe of composition and interconnected with 30 million synapses (six different types) according to synaptic mapping recipes. The Blue Brain team built dozens of applications that now allow automated reconstruction, simulation, visualization, analysis and calibration of detailed microcircuits. This proof of concept completed, Markram’s lab is now working in the direction of whole-brain and molecular modeling.

With his in-depth understanding of the neocortical microcircuit, Markram set out to determine how the neocortex changes in autism. He found hyper-reactivity due to hyperconnectivity in the circuitry and hyperplasticity due to hyper-NMDA expression.

Markram is the coordinator of the **Human Brain Project** (HBP) and, with its Swiss team, is responsible for the development and operation of the project’s Brain Simulation Platform. The HBP is one of two ten-year one billion Euro Flagship Projects selected in January 2013 by the European Commission and it builds on the work of the Blue Brain Project which has already taken an essential first step towards simulation of the complete brain. The goal of the HBP is to pull together all our existing knowledge about the human brain and to reconstruct the brain, piece by piece, in supercomputer-based models and simulations. Federating more than 80 European and international research institutions, the HBP is scheduled to last ten years (2013-2023).