Spreading the bad news: an update on the role of pathological proteins in neurodegenerative diseases

XXX OTTORINO ROSSI AWARD
NEW SERIES “THE PAVIA LEGACY”

IRCCS Mondino Foundation
Pavia, via Mondino 2, Berlucchi Hall

www.mondino.it
Ottorino Rossi was born on 17th January, 1877, in Solbiate Comasco, near Como, Italy. 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 was an intern pupil of the Institute of General Pathology and Histology, 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 continue his studies. At the same time, he continued to frequent the Golgi Institute which was the leading Italian centre for biological research. Having completed his clinical preparation in Florence under Eugenio Tanzi, and in Munich at the Institute directed by Emil Kraepelin, he taught at the Universities of Siena, Sassari and, from 1925, Pavia. In Pavia he was made Rector of the University (serving from 1925 to 1936), and during his tenure he was instrumental in getting the buildings of the new San Matteo General Hospital completed.

Ottorino Rossi made many important scientific contributions to the fields of 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, L’Arteriosclerosi dei Centri Cerebrali e Spinali (1906), which dealt with 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.

Since 1990, thanks to an initiative launched by the Scientific Director at the time (Prof. Giuseppe Nappi), the IRCCS Mondino Foundation has held an annual conference at which an award dedicated to the memory of Ottorino Rossi is presented to a scientist who has made an important contribution to research in the field of the neurosciences. Recent years have seen the introduction of a new Ottorino Rossi Award series, aimed at rewarding eminent researchers with cultural and scientific links with the city of Pavia. Having been informally started in 2017, on the occasion of the centenary of the Mondino Foundation, this new series was officially inaugurated in 2018, under the heading “The Pavia legacy”.

Ottorino Rossi / Historical notes
Adriano Aguzzi was born in Pavia in 1960. After graduating from high school, he moved to the University of Freiburg, Germany, where he obtained his MD degree in 1986. Following postdoctoral studies in Vienna, he received the *venia legendi* in neuropathology at the University of Zurich in 1993, where he is currently Full Professor of Neuropathology, Director of the Institute of Neuropathology and Chairman of the Interfaculty MD-PhD Committee.

Adriano Aguzzi has devoted his career to studying the immunological and molecular basis of human prion diseases, a group of fatal neurodegenerative conditions characterized by neuronal loss, vacuolation and glial activation. He is both founder and Director of the Swiss National Reference Center for Prion Diseases and has developed diagnostic and therapeutic methods in the field of transmissible spongiform encephalopathies. He invented the first *in vivo* model of microglia depletion, which helped to show the vigorous anti-prion activity of microglia. Aguzzi’s work led to the identification of the cell types and molecules that enable invasion of the brain by prions, and highlighted the role of follicular dendritic cells as the “prion factories” in extracerebral tissues. He identified plasminogen as a prion carrier in blood, and improved the process of differentiation of prion strains by fluorescence spectroscopy. Aguzzi’s lab also found that prion protein of neuronal origin prevents demyelination, thus highlighting a possible physiological role of this protein, and therefore the potential existence of new therapeutic targets.

Through his pioneering work, Adriano Aguzzi has made a highly original and fundamental contribution to research into prion diseases, and become a towering figure in the field of modern neuroscience. His studies have revealed the cells and molecules involved in prion neuroinvasion and the mechanisms that cause brain damage in these conditions, while critically analyzing whether and how such mechanisms may be shared by neurodegenerative diseases more frequent in the general population.

The Ottorino Rossi Award 2019 is therefore bestowed on Prof. Adriano Aguzzi in recognition of his relentless investigation into the most intimate mechanisms of neurodegeneration, and thus for his outstanding contribution to the advancement of neuroscience.
Previous Winners / Ottorino Rossi Award

1990
Vittorio Erspamer
Rome (Italy)

1991
Paolo Pinelli
Milan (Italy)

1992
Giovanni Di Chiro
Bethesda (USA)

1993
Clarence Joseph Gibbs
Bethesda (USA)

1994
David Zee
Baltimore (USA)

1995
Elio Lugaresi
Bologna (Italy)

1996
Michel Fardeau
Paris (France)

1997
Salvador Moncada
London (UK)

1998
Alain Berthoz
Paris (France)

1999
Ottar Sjaastad
Trondheim (Norway)

2000
John Timothy
Greenamyre
Atlanta (USA)

2001
Salvatore Di Mauro
New York (USA)

2002
Elio Raviola
Boston (USA)

2003
Michael Welch
Chicago (USA)

2004
François Boller
Paris (France)

2005
Jes Olesen
Copenhagen (Denmark)

2006
Stanley Finger
S. Louis (USA)

2007
Michael A. Moskowitz
Boston (USA)

2008
Patricia Smith Churchland
San Diego (USA)

2009
Stephen P. Hunt
London (UK)

2010
Vincenzo Bonavita
Naples (Italy)

2011
Cesare Fieschi
Rome (Italy)

2012
Giorgio Bernardi
Rome (Italy)

2013
Henry Markram
Lausanne (Switzerland)

2014
Emmanuele A. Jannini
L’Aquila (Italy)

2015
Roberto Crea
Hayward (USA)

2016
Richard Stanislaus
Joseph Frackowiak
Lausanne (Switzerland)

2017
Pierluigi Nicotera
Bonn (Germany)

2018
Gianvito Martino
Milan (Italy)
This conference will address the role of pathological proteins in the pathogenesis, pathophysiology and clinical evolution of major neurodegenerative diseases, such as Alzheimer’s disease, Parkinson’s disease and the clinical spectrum that includes amyotrophic lateral sclerosis and frontotemporal dementia. This is currently a key area of research in the field of neurodegeneration, sparked, in recent years, also by the groundbreaking work on the molecular basis and cell biology of prion diseases done by the winner of the 30th Ottorino Rossi Award. Distinct proteins — such as β-amyloid, tau, α-synuclein and TDP-43 — may follow similar patterns of cell-to-cell transfer and intracellular aggregation. By sowing the pathology among still unaffected neuronal populations, they have the effect of “spreading the bad news” throughout the areas of the central nervous system affected by the above-mentioned diseases. Gaining a deeper insight into the intrinsic mechanisms governing these dynamics, and learning how the spread of pathological proteins can affect the clinical manifestations and evolution of these diseases, is central to the development of innovative therapeutic strategies targeting these proteins. Equally crucial is the availability of reliable neuroimaging techniques able, for diagnostic purposes and for the monitoring of disease progression, to detect the presence and topographical distribution of these proteins in the brain. The conference format will reflect this conceptual framework. There will be three lectures per topic area, which will illustrate the state of the art with regard to pre-clinical research, clinical correlates and therapeutic implications, and advanced neuroimaging.
8.45  Registration and welcome coffee

9.30  Greetings from the Authorities

XXX OTTORINO ROSSI AWARD CEREMONY

9.45  Presentation of the Winner
Lecture by the Winner

10.00  The peculiar, fascinating biology of mammalian prions
Adriano Aguzzi (Zurich)

CONFERENCE

SPREADING THE BAD NEWS: AN UPDATE ON THE ROLE OF PATHOLOGICAL PROTEINS IN NEURODEGENERATIVE DISEASES

ALZHEIMER’S DISEASE

Chairpersons: Stefano Cappa (Pavia)
Fabrizio Tagliavini (Milan)

11.00  Oligomers: disease spreading and toxicity
Gianluigi Forloni (Milan)

11.35  Clinical relevance of neuropathological changes in Alzheimer’s disease
Alessandro Padovani (Brescia)

12.10  Tau, Aβ and network degeneration in Alzheimer’s disease
Rik Ossenkoppele (Amsterdam)

12.45  Lunch
**PARKINSON’S DISEASE**

*Chairpersons:* Fabio Blandini (Pavia)
Antonio Pisani (Rome)

13.45  **Alpha-Synuclein: a troublesome traveller**  
Donato A. Di Monte (Bonn)

14.20  **Clinical evolution in Parkinson’s disease and the spread of pathology: insights from the GBA story**  
Anthony H. Schapira (London)

14.55  **Body-first vs brain-first Parkinson’s disease: visualised by multi-modality imaging**  
Per Borghammer (Aarhus)

**AMYOTROPHIC LATERAL SCLEROSIS (ALS) AND FRONOTEMPORAL DEMENTIA (FTD)**

*Chairpersons:* Mauro Ceroni (Pavia)
Andrea Malaspina (London)

15.30  **Mechanism of aggregation, seeding and toxicity in ALS and FTD**  
Magdalini Polymenidou (Zurich)

16.05  **The clinical relevance of contact-dependent/independent cell-to-cell transfer of TDP-43 and SOD1 in ALS/FTD**  
Vincenzo Silani (Milan)

16.40  **A new perspective for advanced PET-based molecular imaging in FTD spectrum**  
Daniela Perani (Milan)

17.15  **CONCLUDING REMARKS**

Scientific Supervisor  
Fabio Blandini, Scientific Director IRCCS Fondazione Mondino (Pavia)

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- Assistente Sanitario
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- Tecnico di Neurofisiopatologia
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