



Introductory Remarks to Symposium 27

Neurodegenerative diseases: shaping neuronal circuits by membrane trafficking

Natalia Kononenko and Brunhilde Wirth, Cologne

The mechanism underlying cell death in neurodegenerative diseases (NDDs) is one of the most intriguing mysteries in neuroscience. Until recently, studies of molecular neurodegeneration were focused on the investigation of the synaptotoxic role of protein aggregates, such as amyloid- β peptides in Alzheimer's disease (AD) or polyQ proteins in Huntington's disease (HD). However, current data suggest that protein deposition per se may not be the primary cause of neurodegeneration but rather the result of the disease. What is then the molecular substrate of neurodegeneration? A growing body of evidence links the genes encoding endocytosis and autophagy proteins to the pathophysiology of NDDs. Both processes are part of the membrane trafficking machinery in the cell and are crucial for neuronal survival. Although defects in endocytosis and autophagy accompany the neuronal loss in NDDs, precise mechanisms by which these two pathways shape neuronal circuits to prevent neurodegeneration are currently unknown. By gathering world-leading scientists, whose research deals with the role of membrane trafficking in NDDs our symposium will provide the answers to this crucial question. The role of membrane trafficking in pathophysiology of HD will be highlighted by Michael Cousin, who is a world-leading researcher in the field of presynaptic physiology. Natalia Kononenko will present the data indicating that loss of the endocytic adaptor AP-2 can cause AD. Ira Milosevic will show how the tandem of autophagy and endocytosis can prevent Parkinson's disease (PD). Brunhilde Wirth, who is a pioneer in research dealing with the role of genetic modifiers in pathophysiology of spinal muscular atrophy (SMA), will present her work implicating defective endocytosis as a main cellular mechanism underlying SMA. Finally, Ferdi Kiral will identify autophagy as a process shaping neuronal circuits in flies.

NDDs are among the most serious health problems facing modern society. Some of these disorders, including the majority of AD and PD cases are sporadic in nature. Others, such as SMA and HD have clear genetic causes. In spite of this fact, all of these NDDs are characterized by an array of membrane trafficking defects, which are not yet fully understood. This symposium, thematically linked and financially supported by the the Cologne Research Training Group "Neural Circuit Analysis on the cellular and subcellular level" (DFG-RTG-1960), will provide latest insights into the research dealing with the role of endocytosis and autophagy in NDDs and offer a potentially novel approach for NDD therapy.

Symposium 27

Friday, March 22, 2019
14:30 - 16:30, Lecture Hall 9

Chairs: Natalia Kononenko and Brunhilde Wirth,
Cologne

- 14:30 **Opening Remarks**
- 14:35 Michael A. Cousin, Edinburgh, UK
LOSS OF FUNCTIONAL HUNTINGTIN CAUSES
ACTIVITY-DEPENDENT PRESYNAPTIC DEFECTS
IN HUNTINGTON'S DISEASE (S27-1)
- 15:00 Natalia Kononenko, Cologne
ONE-WAY TICKET FOR A RIDE: HOW ENDO-
CYTIC PROTEINS PREVENT NEURODEGE-
NERATION IN THE BRAIN (S27-2)
- 15:25 Ira Milosevic, Göttingen
ENDOCYTOSIS AND AUTOPHAGY DYSFUNC-
TION IN NEURODEGENERATION (S27-3)
- 15:50 Brunhilde Wirth, Cologne
PROTECTIVE MODIFIERS UNVEILED IMPAIRED
ENDOCYTOSIS IN SPINAL MUSCULAR ATROPHY
AND OPENED NEW THERAPEUTIC OPTIONS
(S27-4)
- 16:15 Ferdi Ridvan Kiral, Berlin
DECREASED FILOPODIAL DYNAMICS AT
AUTOPHAGY-DEFICIENT PHOTORECEPTOR
AXON TERMINALS LEAD TO ECTOPIC SYNAPSE
FORMATION AND NEURONAL MISWIRING
(S27-5)
- 16:25 **Concluding Remarks**