

THE  KAVLI PRIZE

THE KAVLI PRIZE IN
NEUROSCIENCE 2010

*The Norwegian Academy of Science and Letters has decided
to award the Kavli Prize in Neuroscience for 2010 to*

RICHARD H. SCHELLER
Executive Vice President, Genentech, US

THOMAS C. SÜDHOF
Professor, Department of Molecular and Cellular Physiology
Stanford University School of Medicine, US

JAMES E. ROTHMAN
Professor and Chairman, Department of Cell Biology at Yale University, US

*“for discovering the molecular basis of
neurotransmitter release”*

The question of how nerve cells communicate with one another has been a central problem in modern neuroscience since the pioneering studies of Cajal, Dale and Sherrington. By the 1980s, it was well established that nerve cells communicate through the process of chemical synaptic transmission at specialized contacts called synapses. Electron microscopic studies revealed that the presynaptic terminal of the neuron transmitting the information is filled with synaptic vesicles, small organelles containing thousands of molecules of a chemical neurotransmitter. During an action potential, calcium influx into the presynaptic terminal triggers the fusion of synaptic vesicles with the plasma membrane, leading to the release of transmitter through the process of exocytosis. Over the past thirty years, Richard Scheller, Thomas Südhof, and James Rothman, have used a creative multidisciplinary set of approaches to

elucidate the key molecular events of neurotransmitter release. Moreover, their work demonstrates that neurotransmitter release represents a special case of the fundamental cell biological process of membrane trafficking.

Richard Scheller has used a combination of biochemistry, molecular biology and cell biology to identify several key synaptic vesicle and plasma membrane proteins involved in fusion of the neurotransmitter-containing vesicles with the membrane of the presynaptic terminal. In particular, he characterized the first synaptic vesicle membrane associated protein, v-SNARE or VAMP, and the first plasma membrane associated target proteins, t-SNAREs or syntaxin and SNAP-25. Using physiological assays, Scheller demonstrated the importance of these proteins for exocytosis.

Thomas Südhof used powerful biochemical and molecular biological approaches to identify other important synaptic vesicle proteins. He discovered that one of the vesicle membrane proteins, synaptotagmin, had separate calcium and phospholipid binding domains, suggesting it had a key role in transmitter release. Südhof then made use of the emerging power of mouse genetics to delineate the functional role of a number of these vesicle proteins including the role of synaptotagmin, which he demonstrated to be the critical calcium sensor for rapid neurotransmitter release.

James Rothman developed a cell-free assay system to analyze the basic cell-biological processes that mediate membrane trafficking. He identified two soluble proteins (NSF and SNAP) that are important for vesicular transport and membrane fusion in non-neural cells. Remarkably he found that these proteins,

**The Norwegian Academy of
Science and Letters**

Drammensveien 78, 0271 Oslo, Norway

Phone +47 22 12 10 90

Fax +47 22 12 10 99

www.dnva.no

See also:

The Kavli Prize

www.kavliprize.no

The Kavli Foundation

www.kavlifoundation.org

when exposed to brain extracts, formed a complex with the vesicle protein VAMP and two plasma membrane proteins, syntaxin and SNAP-25, precisely the proteins that Scheller had identified earlier. The tertiary complex of one vesicle protein, or v-SNARE, with two target membrane proteins, or t-SNAREs, is fundamental not only to transmitter vesicle fusion but to all forms of membrane fusion.

Together these revolutionary insights have given us a fundamental understanding of the molecular basis of neurotransmitter release.

