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Thomas Christian Südhof was born in Göttingen in 1955, and obtained his M.D. and doctoral degrees from the University of Göttingen in 1982. He performed his doctoral thesis work at the Max-Planck-Institut für biophysikalische Chemie in Göttingen with Prof. Victor P. Whittaker on the biophysical structure of secretory granules. From 1983-1986, Südhof trained as a postdoctoral fellow with Drs. Mike Brown and Joe Goldstein at UT Southwestern in Dallas, TX, and elucidated the structure, expression and cholesterol-dependent regulation of the LDL receptor gene. Subsequently, Südhof served on the faculty of UT Southwestern in Dallas until 2008, where Südhof among others served as the founding chair of the Department of Neuroscience. Südhof moved to Stanford University in 2008, and holds the position of Avram Goldstein Professor in the School of Medicine. In addition, Südhof has been an Investigator of the Howard Hughes Medical Institute since 1986.

Südhof's research interests focus on the molecular mechanisms underlying synapse formation and function, in particular on how synapses transmit signals from one neuron to the next, and how they become abnormal during disorders such as autism and schizophrenia. His studies have identified and functionally characterized key molecules in synapses, such as synaptotagmins, RIMs, Munc13s, Munc18s, complexins, neurexins, and neuroligins, and studied the role of these molecules in the information processing capacity of the brain. Among others, Südhof's laboratory found that synaptotagmins generally function as the calcium sensors for exocytosis, including synaptic vesicle exocytosis mediating neurotransmitter release, that RIMs function as central organizers of presynaptic active zones that dock synaptic vesicles and recruit Munc13 priming factors and calcium-channels to active zones, and that α -synuclein normally functions as a chaperone in presynaptic terminals that prevents inappropriate SNARE complex formation. Moreover, Südhof's laboratory identified neurexins, neuroligins, and their various interactors and demonstrated that these proteins function as the central trans-synaptic cell-adhesion molecules at synapses that organize the assembly of synapses into signaling machines. Südhof's work has also been relevant for understanding schizophrenia and autism pathogenesis. Mutations in synaptogenic molecules Südhof discovered predispose to these neuropsychiatric disorders, and mouse models of these gene mutations that Südhof produced mimic features of these disorders.

Südhof is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. Südhof is the recipient of several awards, including the Alden Spencer Award (1993), the Bristol-Myers Award in Neuroscience (2004), the Passano Award (2008), the Kavli Award in Neuroscience (2010), the Lasker-deBakey Medical Basic Research Award (2013), and the Nobel Prize in Physiology or Medicine (2013).

The Neurexin Enigma – Towards an Understanding of the Neurobiology of Synapse Formation and Neuropsychiatric Diseases

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Dramatic recent advances in the genetics of autism, schizophrenia, and other neurodevelopmental psychiatric disorders have identified recurrent mutations in genes encoding neurexins and their ligands. More than 100 mutations have been identified. The neurexins and their ligands are trans-synaptic cell-adhesion molecules that are essential for synapse function, and that shape the properties of synapses such as short- and long-term plasticity. Neurexins are presynaptic cell-adhesion molecules that are encoded by three extraordinarily large genes, each of which generates longer α - and shorter β -isoforms that are in turn diversified into thousands of alternatively spliced transcripts. Neurexins bind to multiple postsynaptic ligands, including neuroligins, LRRTMs, and the complex of cerebellins with GluR δ 2. The various splice variants of neurexins and the various isoforms of their ligands exhibit strikingly different functional activities and binding affinities; their interactions are likely competitive, and contribute to determining the properties and nature of synapses. Accumulating evidence demonstrates that neurexins and their ligands perform central functions in the assembly and function of neural circuits, but their precise roles and mechanisms of action are only now beginning to emerge. Understanding these role and mechanisms of action will allow insight into how these genes are involved in the pathophysiology neurodevelopmental diseases. In my talk, I will describe our recent studies on how neurexins and their ligands shape synapse properties, and how dysfunction of neurexins and their ligands might predispose to neuropsychiatric disorders.