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The Competitive World of 'Synaptic Organizers' – Cell Surface Molecules Implicated in Neuropsychiatric Disease

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Dr. Rudenko received her PhD training at the Rijksuniversiteit Groningen (Netherlands) and University of Washington (USA) under mentorship of Professors Wim Hol and Alessandra d'Azzo. Subsequently, Dr. Rudenko carried out postdoctoral training at UT Southwestern Medical Center (USA) mentored by Professor Johann Deisenhofer collaborating with Professors Thomas Südhof, Michael Brown and Joseph Goldstein on the three dimensional structure of cell surface receptors and synaptic adhesion molecules.

Abstract: Dr. Gabrielle Rudenko's laboratory focuses on proteins that mediate synapse development, especially the growing class of so-called 'synaptic organizers'. Many synaptic organizers are implicated in neuropsychiatric disorders such as autism spectrum disorder, schizophrenia, and bipolar disorder. Typically, these proteins form trans-synaptic bridges that span the synaptic cleft, the space between two neurons connected by a synapse. There they mediate adhesion between the presynaptic and postsynaptic membranes, working to facilitate proper neural connections and connect groups of select neurons into discrete neural circuits. Specific synaptic organizers also play a critical role in developing and maintaining excitatory versus inhibitory synapses which are crucial for the excitation/inhibition balance that regulates overall neuronal excitability and communication through neural circuits. While previously, synaptic organizers were thought to simply promote cell adhesion, we now know that they guide the formation of complex protein interaction networks in the synaptic cleft and work as scaffolds to organize macromolecular assemblies that modulate synaptic function. Their laboratory is using a combination of structural biology, biochemical and biophysical methods, and proteomics, to study a portfolio of different synaptic organizers implicated in neuropsychiatric disease. By elucidating structure-function relationships of key molecules that selectively guide synapse development and uniquely impact specific neural circuits, they hope to identify novel therapeutic targets that can be leveraged to design better treatments for brain disorders in future.