Study Details Atomic Structure of Proteins Altered in Autism

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A new study by an international group of scientists describes in atomic detail a protein complex that is affected by genetic mutations implicated in autism spectrum disorders. The research team, including scientists from the University of California, San Diego (UCSD) Skaggs School of Pharmacy and Pharmaceutical Sciences (SSPPS), details the neuroligin family of proteins, which are encoded by genes known to be mutated in certain patients with autism. Their study will be published in the December 20 issue of *Neuron*.

"This goes beyond previous studies to show the individual atoms of these two proteins and how they interact," said Palmer Taylor, Ph.D., Dean of SSPPS and the Sandra & Monroe Trout Professor of Pharmacology. "We have described the mutations found in some people with autism; and we have identified where the altered amino acids are located in the protein, and how they impact the folding and cell adhesion properties of neuroligin and neurexin."

The research builds on earlier work that mapped the molecular structure of neuroligins and their partner proteins, neurexins – a protein complex involved in the junctions, or synapses, through which cells of the nervous system signal to one another. The new study, conducted with Pascale Marchot and Yves Bourne and their colleagues in Marseille, France, adds to a clearer understanding of how particular genetic mutations affect formation of this complex and contribute to the developmental abnormalities found in certain individuals with autism.

Normally, individual neuroligins interacting with specific neurexin partners are involved in synaptic adhesions, imparting 'stickiness' that enables them to associate and form synapses that have the capacity for neurotransmission. Incorrect partnering in these diverse protein families results when a mutant neuroligin fails to associate properly at synapses, preventing the normal transmission of brain cells.

The change in synaptic function may account for impairments in development, social interaction and communication displayed in individuals with autism spectrum disorders, according to the researchers.

Contributors include Pascale Marchot and Igor P. Fabrichny, Institut Fédératif de Recherche-Jean Roche, Université de la Mediterranée; Philippe Leone, Gerlind Sulzenbacher and Yves Bourne, Universités Aix-Marseille; and Davide Comoletti and Meghan T. Miller, UCSD Department of Pharmacology, Skaggs School of Pharmacy and Pharmaceutical Sciences.

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Media Contact: Debra Kain, 619-543-6163, ddkain@ucsd.edu