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Molecular Mechanisms of Synaptic and Circuitry Development and Psychiatric Disorders

Synapses are fundamental units of neuronal connectivity in the brain. It is at these specialized cell junctions that neurons communicate with one another. Many neuroscientists now look to the synapse for principles of learning and memory, for processes underlying behavior, and for pathological mechanisms of various neurological and psychiatric disorders. Our long-term goal is to understand the mechanisms regulating the development and function of synapses and to probe the roles of synaptic and circuitry dysfunction in certain abnormal behaviors and their relevance to psychiatric disorders.

There are currently three major aspects of research in the lab. First, we are interested in the molecular mechanisms regulating the assembly and function of the postsynaptic complex. Although hundreds of proteins have been identified at the postsynaptic complex, little is known about their in vivo functions at synapses. Using genetic approaches in mice we are dissecting the roles of some key synaptic proteins in the assembly, maintenance and plasticity of the postsynaptic complex.

The second aspect of our research is focused on using genetic approaches in mice to dissect the molecular and cellular basis of behaviors. We are particularly interested in how changes in synaptic and circuitry function may lead to abnormal behaviors related to OCD, autism and bipolar disorder. We apply a variety of mouse molecular genetic methods, such as regional and cell type-specific knockout and transgenic mice, to elucidate the molecules, the types of neurons, and the circuits involved in generating specific behaviors.

The third line of research in the lab is to develop cutting-edge genetic tools for probing synaptic and circuitry function and dysfunction in mice. These include transgenic mice expressing GFP in single neurons in the brain for long-term live imaging; single-neuron labeling with inducible cre-mediated knockout (SLICK) in transgenic mice for combined genetic manipulation and imaging in single neurons in the brain; transgenic mice expressing Channelrhodopsin-2 and Halorhodopsin for cell type-specific manipulation of neural activity and circuit function in living mice; and transgenic mice expressing genetically encoded activity sensors for monitoring neuronal activity in vivo.

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Additional Publications

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