

## **Our Research Mission**

### **Molecular Psychiatry: Signaling in Neurons and Synapses**

All cells in your body, including your brain cells (neurons), depend on thousands of proteins encoded by the genes in your DNA to develop and function properly. Some of these proteins participate in biochemical communication (signaling) between cells. This includes signaling at synapses, a highly specialized type of electrochemical connection between neurons. Proteins are the fundamental building blocks of neurons and synapses, and neurons and synapses are the fundamental building blocks of your brain. By affecting the way that neurons and synapses are connected, proteins encoded by genes affect the way that your brain works. Since the mind is the product of the brain, proteins encoded by genes also affect the way that your mind works - including your perceptions (both inner and outer), emotions, thoughts, as well as your ability to learn (incorporate new information) and remember (retain and retrieve old information).

In the Cheyette Laboratory at UCSF we study the role of proteins implicated by human genetics in susceptibility to psychiatric illness. We specialize in proteins involved in signaling between cells. Because we are interested in how these proteins contribute to psychiatric symptoms (that is, to mental processes), we focus on how these proteins contribute to the assembly and function of neurons and synapses in the brain. We do most of our experiments in genetically modified laboratory mice that we have engineered ourselves or obtained from other scientists. We use these animals as models in which to probe and answer experimental questions that can lead to a better understanding of what is happening molecularly in the human brain as it develops and matures - and what goes wrong with these events on the road to mental illness.

Some of the proteins we study can also affect signaling between cells outside the brain; disruption of their function in these other cell types can sometimes lead to birth defects or to other important diseases, such as cancer.

### **Wnt Signaling**

Wnt signaling refers to one biochemical class of communication that occurs between cells in your body, including brain cells (neurons). Wnt signaling can be further subdivided into two broad varieties (biochemical pathways).

**Wnt/b-catenin pathway:** regulates levels of b-catenin, a protein that controls gene expression (whether another gene is "on" or "off") inside the cell nucleus. This pathway helps determine crucial cellular decisions such as how many times an immature cell divides to create more cells, when those cells should stop dividing, and what kind of mature cells they should become. This pathway therefore contributes to the numbers and types of neurons generated as our brains grow and mature. Because it was the first Wnt pathway to be scientifically described, it is sometimes referred to as the 'canonical' Wnt signaling pathway.

**b-catenin-independent Wnt pathway:** by definition this is any Wnt pathway that does not regulate b-catenin levels. In actuality this is many different pathways, because many different types of b-catenin-independent ('non-canonical') biochemical pathways have now been described in different cell types downstream of Wnt signals. Despite this diversity, a common output of these pathways is the regulation of cell shape and movement. In the brain these pathways therefore contribute to the location and shape of neurons, including the type and shape of the 'wiring' they form through their connections.

Notably, both **b-catenin-dependent** and **b-catenin-independent** forms of Wnt signaling are implicated in the formation, structure, and function of synapses - those special electrochemical connections between neurons that underlie all mental activity.

## Our Research

The Cheyette Laboratory is particularly interested in how these signaling pathways participate in brain development and behavior, especially as this may relate to the biological origins of mental illness.

Our research suggests that changes in the development and function of synapses caused by disruption of these pathways contribute to psychiatric disorders including autism, schizophrenia, and bipolar disorder.

## News Stories About Our Research

- Science Online <sup>[1]</sup>
- The Atlantic <sup>[2]</sup>
- Fox News <sup>[3]</sup>

Dept. of Psychiatry Main Site  
UCSF Main Site

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### Links

[1] <http://www.sciencemag.org/news/2016/10/new-clues-how-lithium-soothes-bipolar-brain-may-shed-light-other-mental-illnesses>

[2] <http://www.theatlantic.com/health/archive/2016/10/lithium/504746/>

[3] <http://www.foxnews.com/health/2013/06/25/genes-known-to-cause-birth-defects-may-also-lead-to-mental-illness/>