



The Department of Pharmacology

Proudly Presents the
Seminar Series:

Frontiers in Pharmacology

Signaling

Neuroscience

Genomics

Ricardo Dolmetsch, PhD

Department of Neurobiology
Stanford University

“The secret lives of calcium channels”

Calcium channels regulate almost every aspect of neuronal development and function by converting electrical signals into the activation of biochemical cascades in neurons. My laboratory studies how calcium channels are linked to biochemical pathways that control neuronal development and function and how mis-regulation of calcium signaling leads to neuropsychiatric disease. We have recently discovered a new family of transcription factors that is encoded by the CaV 1 family of calcium channels. The first member of this new transcription factor family, which we call CCAT, for calcium channel associated transcription factor, is associated with CaV1.2 and regulates the expression of gap junctions, potassium channels, NMDA receptors and other proteins that play a key role in neuronal excitability. We have also identified a new mechanism that regulates calcium channel levels on the surface of neurons. Using a combination of biochemistry and microscopy we have found that the oncogene, eif3E/int6, regulates calcium channel internalization in neurons in response to electrical activity. Using total internal reflection microscopy (TIRF) we studied small clusters of channels and found them to be highly motile and strongly regulated by the electrical activity of the cell. These results unveil an important mechanism by which neurons regulate their electrical excitability and plasticity. Finally we have studied how a mutation that is associated with autism alters channel signaling in neurons. We have found that mutant CaV1.2 channels from autistic patients with Timothy Syndrome are defective both in their ability to activate gene expression and to regulate the neuronal shape. The mutant channels prevent activation of the transcription factor CREB and thus cause profound retraction of the dendritic arbor. These studies help elucidate the mechanisms by which electrical activity regulates neuronal function and also provide insight into the molecular underpinnings of autism and other neurological diseases.”

Friday, March 14th

10:00 am

Auditorium (Room 1005)
in GBSF