Dr. Wan-Chen Lin

University of California, Berkeley

Special Seminar

"Optogenetic manipulation of neural inhibition: from tool development to *in vivo* photo-control"

Tuesday
Jan. 17, 2017

11:00 a.m.

Seminar Hall
(1315 Chemistry)

Optogenetics is a hybrid approach that integrates optical and genetic manipulations of a protein target to control the physiology of a cell. It is a revolutionary technique for functional investigations of signaling and circuitry in the nervous system. The use of light allows remote control of protein function with high spatial and temporal precision. I will present a chemical-genetic method for photo-sensitizing $GABA_A$ receptors, the major mediators of inhibitory neurotransmission in the brain. Each light-regulated $GABA_A$ receptor (LiGABAR) was engineered by conjugating an azobenzene-based photoswitch ligand nearby the agonist-binding site of the receptor. In concert with azobenzene photo-isomerization, a LiGABAR can be rapidly and reversibly switched between normal and antagonized states by two different wavelengths of light. This approach has been applied to confer light sensitivity onto six subtypes of $GABA_A$ receptors individually, providing photo-control with refined biochemical specificity. LiGABARs have been successfully implemented *ex vivo* in brain slices and *in vivo* in the cerebral cortex of awake behaving mice, enabling optical manipulation of inhibitory synaptic transmission, neuronal firing, and sensory-evoked cortical activities. The LiGABAR toolkit thus offers a powerful means for optogenetic interrogations of GABAergic signaling in the complex nervous system.