Brandeis University
Waltham, MA
Susan Birren, Sacha Nelson
$1,000,000

Homeostatic plasticity describes the capacity of a neuron to increase its synaptic density or excitability under conditions of low activity and to decrease them under conditions of high activity. It allows brain circuits to adapt to changes in the internal and external environment while maintaining brain function within a normal range. Now four collaborators at Brandeis University will test for homeostatic plasticity in the autonomic nervous system, which regulates the physiological function of the peripheral organs. The team will genetically manipulate the activity of rat sympathetic neurons to study plasticity mechanisms and their role in controlling peripheral functions such as blood pressure. They will identify gene expression patterns associated with different plasticity states and use imaging and electrophysiological recordings in intact sympathetic ganglia to test their models for this simple, but crucial neural circuit.

Weill Cornell Medicine, Cornell University
New York, NY
Simon Scheuring
$1,000,000

A research team composed of biologists, engineers and physicists at Weill Cornell Medicine will develop the next generation high-speed atomic force microscope (NG-HS-AFM) to take single molecule movies of rare and transient conformational states of proteins at unprecedented spatiotemporal resolution. The temporal resolution of the planned instrument aims to outperform commercially available instruments by roughly two orders of magnitude, accessing the millisecond regime where many essential biomolecular processes take place. Current structural biology methods (Xray, cryo-EM) solve the structures of major conformational states of proteins through ensemble-averaging of thousands of molecules. Consequently, these techniques are blind to detect individual,

University of California, Irvine
Irvine, CA
Chang Liu, Ahmad Khalil
$1,000,000

Two investigators at UC Irvine (CL) and Boston University (AK), will develop a platform to create biomolecules that enable the systematic study of the basis of biased signaling by G-Protein Coupled Receptors (GPCRs). GPCRs are the largest family of cell membrane-bound proteins in humans and function to receive and transduce signals like hormones, neurotransmitters, and immunomodulatory molecules into the cell. In recent years, the classical on/off model of GPCR signaling has been fund t 3 t

W. M. Keck Foundation

rapid, selective aggregate clearance by small molecule drugs to reveal their direct effects on organismal health. Achieving these two goals could lead to a breakthrough in understanding cellular responses to protein misfolding and treating associated neurodegenerative diseases.

University of Washington
Seattle, WA