**Two tunable inhibitory systems govern the activity of neocortical layer 1 (L1).** *Bernardo Rudy, Ben Schuman, Rob Machold, Darpan Chakraborty, Shlomo Dellal, Hector Zurita, Illya Kruglikov, Chiung-Yin Chung. Neuroscience Institute, NYU Grossman School of Medicine, New York, NY, USA*

Neocortical 1ayer 1 (L1), the main cortical layer receiving contextual information carried by corticocortical and thalamocortical "feedback" connections, contains the distal "tuft" dendrites of pyramidal cells located in deeper layers. All resident L1 neurons are GABAergic interneurons (IN). In the adult mouse, neuron derived neurotrophic factor (NDNF) expression is largely limited to L1, where it is found in about 70% of L1 INs. The availability of mouse lines expressing Cre recombinase under control of the NDNF promoter has allowed studies exploring the role of these cells on a variety of cortical functions. Studies using up and/or down regulation of NDNF cell activity have suggested, among others, that these neurons terminate neocortical Up states and thus mediate the Down state. On the other hand, another study found that the activity of these INs increases with arousal. How do we reconcile these, and other, seemingly contradictory results?

Inhibition in L1 is thought to mediate the impact of long-range projections on PC tuft dendrites, powerfully controlling PC output. There are two types of NDNF-expressing INs in L1, neurogliaform and canopy cells, that differ in morphology, intrinsic electrophysiological properties, input and output connectivity, and their response to neuromodulators. Furthermore, L1 contains two types of non-NDNF-expressing INs and the dendrites of several IN subtypes with somata in L2/3, which have access to the axonal projections arriving in L1. An additional inhibitory influence arises from ascending axons of SST-expressing Martinotti cells in deeper layers that project to L1. Our studies investigate how these various inhibitory sources and neuromodulation regulate arousal, attention, sensory perception and learning.