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Talk Title: **A serotonergic axon-cilium synapse drives nuclear signaling in the brain**

Abstract:
Chemical synapses between axons and dendrites mediate much of the brain's intercellular communication. Here we describe a new kind of synapse – the axo-ciliary synapse - between axons and primary cilia. By employing enhanced focused ion beam–scanning electron microscopy on samples with optimally preserved ultrastructure, we discovered synapses between the serotonergic axons arising from the brainstem, and the primary cilia of hippocampal CA1 pyramidal neurons. Functionally, these cilia are enriched in a ciliary-restricted serotonin receptor, 5-hydroxytryptamine receptor 6 (HTR6), whose mutation is associated with learning and memory defects. Using a newly developed cilia-targeted serotonin sensor, we show that optogenetic stimulation of serotonergic axons releases serotonin onto primary cilia. Ciliary HTR6 stimulation activates a non-canonical Gαq/11-RhoA pathway. Ablation of this pathway results in nuclear actin and chromatin accessibility changes in CA1 pyramidal neurons. Axo-ciliary synapses serve as a distinct mechanism for neuromodulators to program neuron transcription through privileged access to the nuclear compartment.