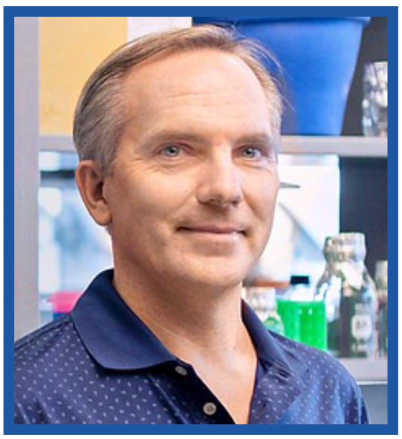
Serotonin Modulation of Spinal Circuits for Fexible Motor Control

May 21

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:



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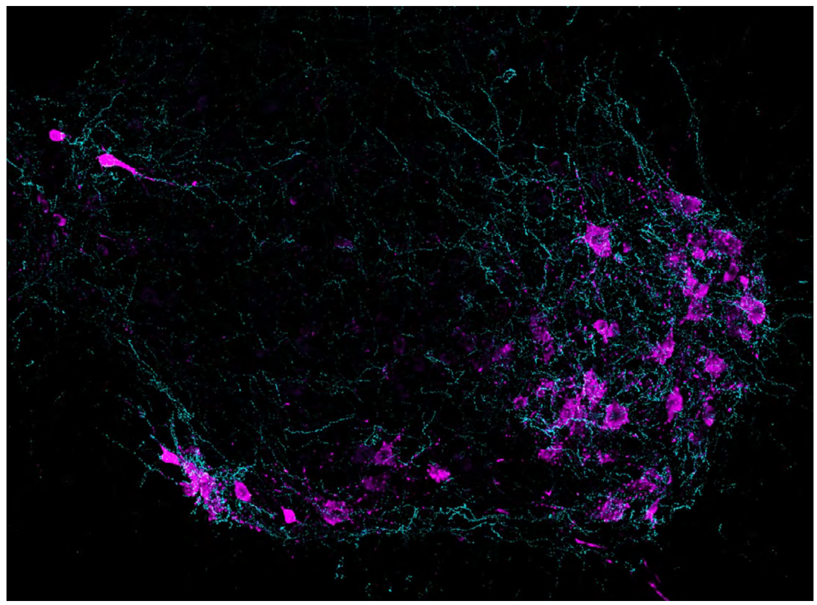
Abstract

Neuromodulators act throughout the central nervous system potently altering the dynamics of neural circuits. Neuromodulation by serotonin (5-HT) is intimately linked with control of mood and cognition, but its reach extends beyond these functions in the brain. The spinal cord is densely innervated by serotonergic fibers and the activity of spinal circuits is strongly influenced by 5-HT, yet the role of serotonergic modulation in motor control remains unclear. Interestingly, the 5-HT neurons that innervate the spinal cord are distinct from those targeting the forebrain, providing a separate and dedicated pathway for descending modulation of spinal motor circuits. Thus, our studies seeks to understand the role of descending genetically-defined serotonin neurons in control of movement. Using viral and genetic tracing strategies in mice, we find that spinal motor neurons receive direct input from three populations of brainstem 5-HT neurons: raphe obscurus, raphe pallidus, and the lateral paragigantocellularis neurons. In contrast, a distinct 5-HT population, raphe magnus, innervates the spinal dorsal horn. Therefore, unique descending 5-HT pathways exist for devoted modulation of locomotor networks. In vivo calcium imaging with fiber photometry shows that the activity of pre-motor serotonin neurons relates directly to the degree of motor activity. Perturbation studies are being performed to determine how the activity of pre-motor 5-HT neurons influences motor output, including muscle activity, limb kinematics, and locomotor speed. Interestingly, we find that sustaining the activity of 5-HT neurons prolongs the time that mice spend running. Finally, we find that pre-motor 5-HT neurons receive input from upstream midbrain locomotor control regions. These results suggest a model whereby higher motor control areas recruit descending systems in parallel, both neuromodulatory and instructive/command pathways, to coordinate precise activation of spinal circuits and muscles forproduction of motor behavior.



Publications

1. Baek M, Menon V, Jessell TM, Hantman AW, Dasen JS. (2019). *Molecular Logic of Spinocerebellar Tract Neuron Diversity and Connectivity.* Cell Reports 27, 2620-2635.

2. Shin MM, Catela C, Dasen JS. (2020). *Intrinsic control of neuronal diversity and synaptic specificity in a proprioceptive circuit.* Elife 18;9.

3. Sawai A, Pfennig S, Bulajić M, Miller A, Khodadadi-Jamayran A, Mazzoni EO, Dasen JS. (2022). *PRC1 sustains the integrity of neural fate in the absence of PRC2 function*. Elife. 7,11.