The Neuroscience Graduate Program

presents:

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Advisor:

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in a PhD Thesis Defense

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10:00am in Auditorium K-307(3-6408)

The Role of Microglia and Fractalkine Signaling in Experience-dependent Synaptic Plasticity

The remodeling of circuitry is a fundamental aspect of brain function, contributing both to the initial wiring of the brain during development and to critical processes such as learning and memory in the adult. Changes to neural network function rely on structural and functional changes at synapses, and the mechanisms which modulate these synaptic changes critically contribute to cognitive function throughout the life span. Recently, microglia have come into the spotlight as regulators of synapses. These immune cells have been shown to display dynamic interactions with synapses in the non-pathological brain, although their contribution to synaptic plasticity is still poorly understood. My work has characterized microglial contributions to experience-dependent plasticity in the visual cortex *in vivo*. I show that manipulations of visual experience elicit a remarkably rapid behavioral response in microglia which is distinct from their inflammatory behavior. This response corresponds to the early phase of plasticity in this model when synapses are lost and when microglia increase their synaptic interactions, implicating microglia in the process of dynamic synapse removal. To determine the underlying mechanism behind this response, I examined the role of the chemokine fractalkine. Fractalkine signaling is a pathway well studied in neuroinflammation, where it allows for specificity of signaling between neurons and microglia and initiates chemotaxis of microglial cells. These functions could also be critical in the physiological process of synaptic rearrangement. I report that in the visual system, removal of fractalkine signaling does not alter microglial density, morphology, or process motility - key baseline microglial characteristics regulating their physiological functions. Removal of fractalkine signaling also fails to impact the dynamic microglia-neuron interactions thought to underlie their role in synapse remodeling. Additionally, unlike other systems where fractalkine signaling is necessary for circuit remodeling, it is not required for normal plasticity in either early or late forms of plasticity in the visual system. Our findings suggest that microglia play an important role in synaptic plasticity, and use a subset of their pathological molecular repertoire in a time- and region-dependent manner to implement plastic changes in the non-pathological brain.