Neuroscience Graduate Program

presents:

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IN A THESIS PROPOSAL

THURSDAY, 14 JULY 2016

10:00AM IN AUDITORIUM K-307 (3-6408)

Noradrenergic modulation of microglial dynamics and synaptic plasticity

Microglia, the innate immune cells of the central nervous system (CNS), respond rapidly and dynamically to homeostatic perturbations of the CNS milieu. In the healthy unperturbed brain, microglial processes make frequent contacts with neurons at synapses, impacting synaptic remodeling and turnover of dendritic spines. However, it remains unclear what receptors and signaling pathways govern microglial surveillance and synapse monitoring. Noradrenaline is a powerful signal that can affect many aspects of synaptic function and plasticity. Because microglia express high levels of **β**2 adrenergic receptors (AR) compared to other cell types in the brain, we asked whether noradrenergic tone could alter microglial behavior with respect to synapses through β2-AR signaling. Preliminary findings from our laboratory, along with published work, suggest that β_2-AR signaling inhibits microglial process motility and impairs experience-dependent plasticity in the visual cortex in mice. Based on this, ***I hypothesize that endogenous norepinephrine release alters microglial surveillance and microglia-synapse interactions through microglial β_2-AR signaling, leading to altered synaptic plasticity.*** To test this hypothesis, I will explore the effects of selectively ablating microglial β_2-AR signaling and altering endogenous norepinephrine release on microglial behavior and contributions to synaptic plasticity using the well-characterized model of ocular dominance plasticity during the visual critical period in mice. This study will be accomplished in three specific aims: I will selectively ablate the β_2-AR in microglia and evaluate changes in basic microglial physiology **(Aim 1)**. I will determine the effects of modulating endogenous norepinephrine pharmacologically on microglial physiology and synaptic interactions **(Aim 2)**. Finally, I will investigate how both changes in norepinephrine and ablation of the $\beta_{2\text{-AR}}$ in microglia impacts ocular dominance plasticity **(Aim 3)**. The results obtained from these complementary, but independent aims will greatly improve our understanding of the signaling mechanisms that govern microglial physiology and contributions to neural development and plasticity. Understanding the pathways that mediate microglial interactions with synapses will also provide novel therapeutic targets for neurodevelopmental and neurodegenerative disorders, where plasticity is affected.