The Neuroscience Graduate Program

presents:

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IN A PHD THESIS DEFENSE

WEDNESDAY, 28 SEPTEMBER 2016

10:00AM IN WHIPPLE AUDITORIUM (2-6424)

The transcription regulator Lmo3 is required for correct cell fate specification in the external globus pallidus.

The external globus pallidus (GPe), a core component of the basal ganglia, can powerfully influence the processing of motor information due to its widespread projections to almost all basal ganglia nuclei. Aberrant activity of GPe neurons has been linked to motor symptoms of a variety of movement disorders, such as Parkinson's Disease, Huntington's disease and dystonia. While several decades of work had suggested the existence of heterogeneity within GPe GABAergic projection neurons, it is not until recent years that multiple molecular markers have been established to unambiguously define and distinguish between two main GPe neuronal subtypes: the prototypic and arkypallidal neurons. This demarcation is also based on their unique projection patterns, membrane properties and ion channel expression, and consequently, distinct electrophysiological profiles, in both healthy and diseased (Parkinsonian) states. As a result of this, we now have an improved understanding of how these neurons function and encode motor behavior in both healthy and diseased states.

A few studies have established some of the basic aspects of GPe development- such as the parts of the developing forebrain from which GPe neurons originate and the embryonic time points during which they are born. However, specific molecular factors required for the development of GPe neurons remain unexplored. For my thesis project, I studied the role of the transcription regulator, Lmo3, in the specification of subsets of external globus pallidus neurons. My work has shown that Lmo3 is required at the embryonic stage for the development of the medial ganglionic eminence (MGE) derived $Nkx2.1^{+}$ and PV^{+} prototypic GPe neurons, but not the lateral ganglionic eminence (LGE) derived $FoxP2^{+}$ arkypallidal neurons. Consequently, *Lmo3*-null mice have a reduced pallidosubthalamic input, as well as alterations in connectivity of GPe neurons with the striatum. Our data from the analysis of embryonic *Lmo3*-null tissue suggests that Lmo3 regulates the development of prototypic GPe neurons through mechanisms that are distinct from earlier mechanisms that have been shown to control the development of MGE derived PV^{+} neurons. Future directions of this project could involve analysis of potentially compromised GPe and subthalamic nucleus neuronal function in *Lmo3*-null mice in the healthy and Parkinsonian (dopamine depleted) states.