PARKINSON’S DISEASE: A TALE OF TWO DOMINANT GENES

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**WHEN:** Thursday, March 2, 2017
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**WHERE:** Room 2226
Veterinary Medicine Building

**HOST:** Dr. Anumantha Kanthasamy

PIZZA SERVED!

Parkinson’s disease (PD) is a chronic neurodegenerative movement disorder of unknown etiology. While typically occurring as an idiopathic disease, 5-10% of PD is inherited. Mutations in at least 13 genes are known to unambiguously cause familial forms of PD whereas genome-wide association studies implicate certain familial genes as risk factors for idiopathic PD. Despite the preponderance of genetic evidence in explaining many cases of PD, the mechanism(s) by which mutations in each of these gene products precipitates selective neurodegeneration remains largely enigmatic. In most cases, the physiological function of these PD-linked proteins and the molecular basis of familial mutations remain obscure, whereas the anticipated interplay amongst these proteins in common pathological pathways leading to PD is poorly defined. In this talk, we describe our recent efforts in dissecting the molecular and cellular basis of mutations in the dominant PD-linked gene products, LRRK2 and VPS35. We will focus on LRRK2 and describe the impact of familial mutations on the two enzymatic activities of this protein (i.e. kinase and GTPase), the intramolecular regulation of these activities, and how they contribute to neuronal toxicity. Furthermore, we will discuss the development of novel cellular and rodent models for exploring the pathogenic effects of LRRK2 and how we are beginning to utilize such models for the identification of key enzymatic activities, molecular targets and cellular pathways that are important for LRRK2-dependent neuronal damage. Finally, we will briefly discuss the PD-linked gene product, VPS35, and the strategies we are employing to understand the molecular basis of neurodegeneration in PD. Our studies are important for the identification and validation of novel molecular targets and pathways that can be exploited for the development of new therapeutic agents to treat PD.