Epidemiological studies suggest that chronic use of non-steroidal anti-inflammatory drugs (NSAIDs) lowers the incidence of Parkinson’s disease (PD) in humans and implicate neuroinflammatory processes in the degeneration of ventral midbrain dopaminergic (DA) neurons, the pathophysiological hallmark of PD. As the brain resident macrophages, microglia are responsible for immune surveillance, becoming activated in response to injury, infection, environmental toxins, and other stimuli that threaten neuronal survival [1]. Thus, mechanisms that regulate microglia function and neuroinflammation are of relevance to our understanding of neurological diseases and in particular chronic and progressive neurodegenerative conditions like PD [2]. Previous work from our group has revealed that soluble Tumor Necrosis Factor (TNF) is a microglial-derived cytokine that exerts neurotoxic effects on nigral DA neurons [3-5]. Regulator of G protein Signaling 10 (RGS10), a microglia-enriched GTPase accelerating protein (GAP) for G alpha subunits, is an important regulator of microglia activation and RGS10-null mice display increased microglial burden in the CNS from birth and develop nigral degeneration in response to chronic systemic inflammation [6]. Together, these data suggest an important regulatory role in microglia activation responses and a neuroprotective role for RGS10 in the nigrostriatal pathway during chronic neuroinflammation. More recent progress from in vitro and in vivo studies has revealed clues regarding the molecular mechanisms and signaling cascades involved in RGS10 function. RGS10 may be a new therapeutic target in neurological conditions characterized by neuroinflammation [Funding by M.J. Fox Foundation for Parkinson’s Research Target Validation Program, NIH 1R01NS072467-01, and Emory Parkinson's Disease Collaborative Environmental Research Center Development Program P01-ES016731].

References