Understanding the role of innate immune cells in synucleinopathies

My research programs have been geared towards understanding the mechanism of inflammation in the CNS and the periphery modulating neurodegenerative diseases. The long-term goal of my lab is to understand the relationship between innate immunity and proteinopathy and provide a novel immunotherapeutic strategy.

I developed a novel research program investigating the role of natural killer (NK) cells in the context of Parkinson's disease (PD). For that, I have established the relevant in vivo animal model, preformed fibril (PFF) alpha-synuclein (a-syn)-induced PD mice, which exhibit many clinically relevant hallmarks of PD including dopaminergic cell loss, behavior deficits, and synucleinopathies. By utilizing this model, I propose to investigate whether NK cells are neuroprotective or neurotoxic in PD. Both in vitro studies demonstrated that human NK cells efficiently clear extracellular a-syn and the systemic depletion of NK cells resulted in the exacerbated disease phenotypes in synucleinopathies in vivo. Currently, we are investigating the precise mechanism(s) by which NK cells reduce α-synuclein burden, modulate inflammation, and exert neuroprotection.

Another major research program in the lab is geared towards to determine whether microglia contribute the onset and/or progression of neurodegenerative diseases. Age-related changes in inflammation and metabolism in peripheral tissues and the brain have been implicated as risk factors for neurodegenerative diseases. However, the detailed mechanisms of how age-related inflammation and associated-metabolic changes affect the onset and/or progression of neurodegeneration have not been elucidated. Previously, I have identified a novel regulator of microglia activation and neuroinflammation, Regulator of G-protein Signaling (RGS) 10, and its neuroprotective effect on the nigrostriatal pathway. We showed the level of RGS10 in microglia significantly decreased with age. Our current research goal is to demonstrate that RGS10 enrichment in microglia restores microglia homeostasis, enhances amyloid fibril clearance, and exerts neuroprotection for amyloid fibril-induced neuronal death.