Altered central nervous system (CNS) proteostasis, characterized by accumulation of extracellular or intracellular proteinaceous deposits, is thought to be a key trigger of many neurodegenerative disorders. There is considerable evidence that various assemblies of the aggregated proteins that form these inclusions can activate the innate immune system which, in turn, can contribute to the degenerative cascade. There is also growing evidence that alterations in innate immune signaling can play a key role in regulating proteostasis of key pathogenic proteins linked to neurodegenerative disorders. We term this complex interplay between the innate immune system and proteinopathy, immunoproteostasis. In a contextually dependent fashion, immunoproteostasis can have positive or negative effects on the proteinopathy and degenerative phenotype. Because of these effects and the plethora of therapeutic targets in the innate immune system, there is considerable interest in manipulating immunoproteostasis for potential disease modification in neurodegenerative diseases. We have numerous ongoing projects in the laboratory where we are using rAAV vectors, recombinant proteins or active vaccines to modulate immunoproteostasis in mouse models of neurodegenerative disease. Students can participate in various aspects of these projects. This experience can provide insights into the biology of neurodegenerative disorders and preclinical therapeutic discovery.