

Hopewell M.I.N.D. Prize Finalists

Drs. Jiami Guo and Lizheng Wang

Project Title: Targeted Primary Cilia Protein Degradation for Neuroinflammation Modulation in CNS Diseases

There are more than 600 known diseases affecting the nerves system. Whether triggered by a pathogen, genetics, aging, or a physical impact, neuroinflammation—the immune response in the brain, plays a role in nearly all of them. Normally a guard against insults by promoting repair and healing, neuroinflammation can become a driver for pathology when chronic or excessive.

This dichotomy is caused by the complex and dynamic nature of immune cells and their intricate cell-cell crosstalk. Astrocytes are the brain resident immune cells and central players in this dichotomy by initiating and escalating neuroinflammation. Due to their different immune responses, astrocytes can exert either beneficial or detrimental effects on brain health and diseases. However, what drives their “protective” vs. “pathological” states remains poorly understood.

Our recent discoveries shed new light. We focused on primary cilia, underappreciated signaling sensors in almost all astrocytes. Using a mouse model where we can induce ciliary dysfunction specifically in astrocytes, we made an exciting finding: Mice with ciliary dysfunction in astrocytes show significantly improved functional outcome after an ischemic stroke attack and better cognitive performance in advanced age compared to controls. Our work suggests that this desirable outcome is due to the altered astrocyte immune reaction and their crosstalk with other cell types that collectively change neuroinflammation.

Taking advantage of the HOPEWELL M.I.N.D Prize, we propose to provide mechanistic insights into the cilia-driven modulation of neuroinflammation and take the next leap developing primary cilia control methods for therapeutic strategies for CNS diseases emerging from neuroinflammation.