Targeting RNA metabolism for drug discovery in ALS/FTD

Rukayat Aromokeye, Isarel Aispuro, Chase Kappel, Tahsin Reaz Ahmed, Phyo Han Thwin, Lei Wang, Chunlong Ma, Haining Zhu

Department of Pharmacology and Toxicology, R Ken Coit College of Pharmacy, University of Arizona, Tucson, AZ, USA

RNA binding proteins and RNA metabolism have been implicated in multiple neurodegenerative diseases including amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Fused in Sarcoma (FUS) is a DNA/RNA binding protein and mutations in FUS cause a subset of familial ALS. The role of FUS in neurons under physiological and pathological conditions remains to be better understood. Our laboratory has characterized the wild-type and disease-causing mutants of FUS using a variety of approaches including proteomics, biochemistry, cell biology and genetic models. We recently found that pos-translational modifications of FUS play a critical role in regulating its subcellular localization, RNA binding, and formation of protein-RNA condensates. We recently discovered an extended cohort with family members carrying FUS mutation who do not develop ALS. New progress on the potential resilience factors will be presented. Related drug discovery studies will also be discussed.

This work was funded in part by NIH grants R01NS115507 and R21NS122169, and Department of Veteran Affairs awards I01BX002149 and IK6BX006316-01 to H.Z.

Presenter Name and contact information:
Haining Zhu, Ph.D.
Department of Pharmacology and Toxicology, R Ken Coit College of Pharmacy, University of Arizona, Tucson, AZ 85721
Email: haining@arizona.edu