Biosketch:

I am Srivathsa Magadi, a postdoctoral researcher at Linkoping University, Sweden. I obtained my PhD in Neuroscience at the Institute of Molecular Biology and Biotechnology, University of Crete, Greece, under the supervision of Prof Christos Delidakis. My research focuses on the intersection of neurobiology and molecular biology, particularly emphasizing the role of ribosomal proteins in neuroinflammatory processes. My work employs advanced translatome studies in mouse models to uncover new insights into the molecular mechanisms underlying neuroinflammation and neurodegenerative diseases. My current research has been recognized by the Hereditary Disease Foundation (HDF) and I was awarded a Postdoctoral Career Fellowship to study Huntington's Disease. I am passionate about translating basic science discoveries into potential therapeutic strategies for neurodegenerative disorders.

Abstract:

Ribosome heterogeneity is emerging as a crucial factor in regulating gene expression and cellular function, particularly in complex tissues like the brain. In this study, we investigated ribosomal protein (RP) expression patterns across different brain cell types and explored a small ribosomal protein isoform associated with neuroinflammation and neurodegenerative diseases. Using the RiboTag method combined with cell type-specific Cre lines, we isolated and analyzed translational profiles from astrocytes, microglia, and neuronal subtypes in mouse models. Our findings reveal distinct RP expression patterns across brain cell types, with microglia showing consistently lower levels compared to astrocytes and neurons. Reanalysis of existing datasets uncovered significant age-related increases in RP gene expression and alterations in response to inflammatory stimuli. These changes were consistent across both male and female mice, indicating conserved mechanisms in ribosome regulation during aging. Notably, we identified a ribosomal protein isoform that is differentially spliced in microglia compared to other brain cell types. This isoform is induced in Iba1-positive cells (microglia/monocytes/macrophages) during neuroinflammation and in neurodegenerative conditions. Further investigation revealed increased expression of this isoform in mouse models of Alzheimer's disease (AD), Parkinson's disease (PD), and Huntington's disease (HD), as well as in post-mortem human brain samples from these conditions. Intriguingly, the increased expression of this isoform correlates with the observed increases in RP expression in aging, suggesting a potential link between ribosome heterogeneity and neuroinflammatory processes in neurodegenerative diseases. These findings highlight the potential importance of ribosome heterogeneity and cell type-specific protein isoforms in aging and neurodegenerative diseases. This work opens new avenues for understanding the role of specialized ribosomes and microglial activation in neurological health and disease, potentially leading to novel diagnostic and therapeutic strategies.