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Dissecting and Targeting mRNA Regulation in Brain Development

During development, neural stem cells reproduce continually while giving rise to a large number of neurons to build the brain. Perturbation in these processes frequently results in neurodevelopmental disorders. The balanced behaviour of neural stem cells relies on the precise control of gene expression at all levels of information flow from DNA to proteins. However, our understanding of how the regulation at the RNA level instructs neural stem cell fate decisions and brain development is still limited. We have recently identified an RNA-binding protein that can change its own location in neural stem cells to control where and when select mRNAs are translated into proteins. When this RNA-binding protein is mutated and consequently goes to where it is not supposed to be in cells, it causes a rare neurodevelopmental disorder. This project will focus on this RNA-binding protein and further explore the mechanisms that underlie its regulation of neural stem cell fate decisions and brain development. By uncovering how it orchestrates the translation of mRNA critical for cell fate decision and what controls its subcellular positioning in neural stem cells, this study will advance the mechanistic understanding of brain development and provide novel insights into approaches that can correct protein localization error as a potential therapeutic intervention for this rare disorder.