Translational modulation of neuronal homeostasis

Growing evidence indicates that neurons are particularly reliant on the spatial and temporal regulation of mRNA translation for their function and survival. In agreement, mutations in numerous components of the translational machinery have been linked to neurological disorders. Using a phenotype-driven approach in mice, we have identified several novel translational pathways that when disrupted can lead to loss of neuronal homeostasis. Recently, we found that loss of function of a novel ribosome rescue factor combined with a hypomorphic mutation in a brain-specific tRNA leads to neurodegeneration. Here I will present evidence that loss of other ribosome rescue factors or of tRNA function induces alterations of neuronal function that are accompanied by widespread reprogramming of translation. Our work highlights the exquisite sensitivity of the nervous system to even subtle disruption of cellular homeostasis, and demonstrates that the regulation of tRNAs and other factors involved in translation elongation play a critical role in complex neuronal processes.

Biography

Dr. Ackerman is the Steven W. Kuffler Chair of Biology and a professor in the Neurobiology Section in the Division of Biological Sciences at the University of California, San Diego; she is also a Professor in the Department of Cellular and Molecular Medicine in the School of Medicine and an Investigator of the Howard Hughes Medical Institute. Dr. Ackerman focuses on the mechanisms involved in the maintenance of neuronal homeostasis during aging. Her studies combine mouse genetic screens, genomics, cell biology, and biochemistry to identify novel molecular pathways in this process, including those involved in mRNA translation and RNA homeostasis.

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