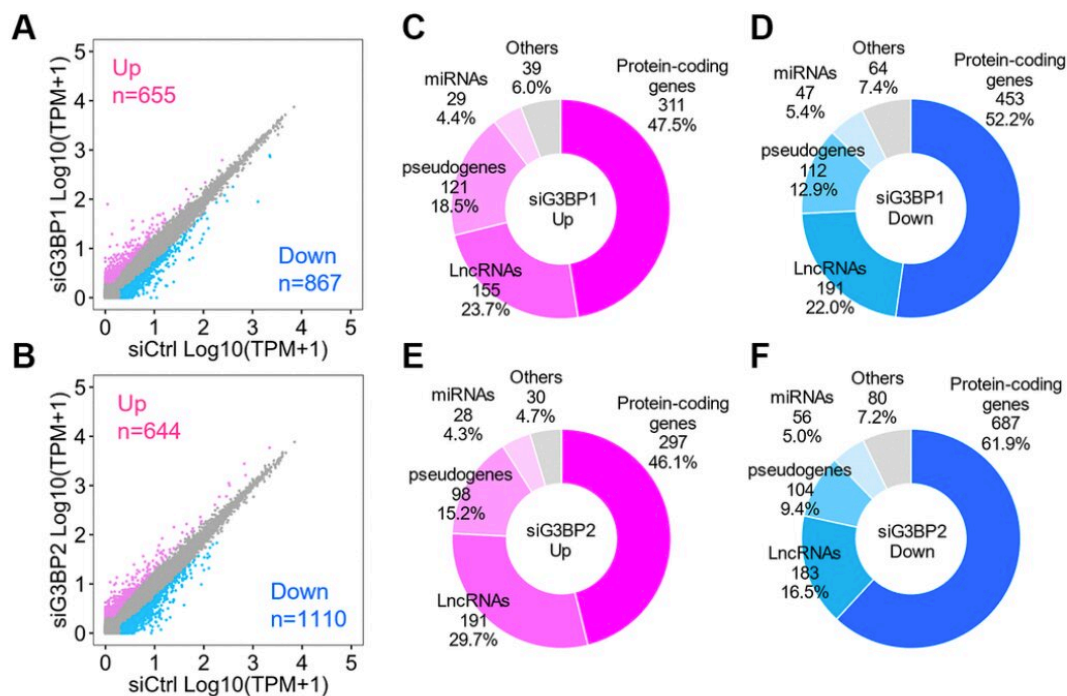


Study: Stress granules control Alzheimer's gene transcripts and neuronal proteostasis

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Changes in RNA levels after the depletion of G3BP1 and G3BP2, and AS-treatment in SH-SY5Y. Credit: 2023 Sato et al.

A new research paper was published on the cover of *Aging*, title "Stress granules sequester Alzheimer's disease-associated gene transcripts and regulate disease-related neuronal proteostasis."

Environmental and physiological stresses can accelerate Alzheimer's disease (AD) pathogenesis. Under stress, a cytoplasmic membraneless structure termed a stress granule (SG) is formed and is associated with various neurodegenerative disorders, including AD. SGs contain translationally arrested mRNAs, suggesting that impaired RNA metabolism in neurons causes AD progression; however, the underlying mechanism remains unclear.

In this new study, researchers Kaoru Sato, Ken-ichi Takayama and Satoshi Inoue from Tokyo Metropolitan Institute for Geriatrics and Gerontology identified numerous mRNAs and long non-coding RNAs that are directly targeted by the SG core proteins G3BP1 and G3BP2.

"In this study, we conducted a genome-wide investigation of the G3BP1- and G3BP2-bound RNAs using enhanced cross-linking and immunoprecipitation-sequencing (eCLIP-seq) in the human neuroblastoma (NB) cell line SH-SY5Y," say the authors.

G3BP1 and G3BP2 redundantly target RNAs before and after stress conditions. The researchers further identified RNAs within SGs, wherein AD-associated gene transcripts accumulated, suggesting that SGs can directly regulate AD development. Furthermore, gene-network analysis revealed a possible link between the sequestration of RNAs by SGs and the impairment of protein neurohomeostasis in AD brains.

"Together, our study provides a comprehensive RNA regulatory mechanism involving SGs, which could be targeted therapeutically to slow AD progression mediated by SGs," conclude the researchers.

More information: Kaoru Sato et al, Stress granules sequester Alzheimer's disease-associated gene transcripts and regulate disease-related neuronal proteostasis, *Aging* (2023). [DOI: 10.18632/aging.204737](https://doi.org/10.18632/aging.204737)

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