

(SD2018-312) Inhibition Of Stress Granule Formation Through Manipulation Of UBAP2L

Tech ID: 29546 / UC Case 2018-312-0

BACKGROUND

Stress granule (SG) formation has been suggested as a two-step process, with initial formation of a dense stable SG “core” followed by accumulation of proteins containing intrinsically disordered regions (IDRs) and low-complexity domains (LCDs) into a peripheral “shell” through a process involving liquid-liquid phase separation (LLPS). Recently, SGs have been associated with human neurodegenerative disorders characterized by the presence of toxic insoluble protein aggregates. This link is most compelling in the case of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), where numerous disease-causing mutations are purported to interfere with LLPS-dependent growth and dynamics of SGs.

TECHNOLOGY DESCRIPTION

Researchers from UC San Diego have developed a method to reduce stress granules (SG) and related protein aggregation by lowering expression levels or simply deleting a small portion of UBAP2L. UCSD bioengineers were able to deplete UBAP2L by small interfering RNA (siRNA) in HeLa cells and almost completely abolish NaAsO2-induced SG formation, establishing UBAP2L as an essential regulator of SG assembly.

APPLICATIONS

- ▶ Research tool for studying the molecular mechanisms of protein aggregation. Using this technology, researchers revealed that UBAP2L may be an excellent future candidate to study how protein aggregation might be regulated both in the absence or presence of cellular stress.
- ▶ Therapeutic for diseases. Lowering UBAP2L levels in patients with certain neurodegenerative diseases through one of many potential routes (RNAi, antisense oligonucleotides, CRISPR/Cas9) could prevent formation and buildup of potentially toxic protein aggregates.

ADVANTAGES

This is an improvement over similar attempts to reduce SG formation because previous approaches employed proteins with known disease-association and critical functions in neuronal cells. UBAP2L may be less functionally critical, as suggested by minimal effects on cell viability upon UBAP2L knockout. A second significant improvement over previous approaches is the technology’s ability to affect SG levels through targeted deletions within UBAP2L, thus not requiring a loss of function of the entire protein.

INTELLECTUAL PROPERTY INFO

Patent rights are pending and available for commercial development/licensing.

RELATED MATERIALS

- ▶ Markmiller S, Soltanieh S, Server KL, Mak R, Jin W, Fang MY, Luo EC, Krach F, Yang D, Sen A, Fulzele A, Wozniak JM, Gonzalez DJ, Kankel MW, Gao FB, Bennett EJ, Lécuyer E, Yeo GW. Context-Dependent and Disease-Specific Diversity in Protein Interactions within Stress Granules. Cell. 2018 Jan 25;172(3):590-604 - 01/25/2018

PATENT STATUS

Patent Pending

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OTHER INFORMATION

KEYWORDS

RNA-binding proteins; amyotrophic lateral sclerosis; granules; heat shock; motor neuron disease; neurodegeneration; phase separation; ribonucleoprotein; stress

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Disease: Central Nervous System
 - ▶ Research Tools
- ▶ **Research Tools**
 - ▶ Nucleic Acids/DNA/RNA

RELATED CASES

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