Drug Discovery & Development

Mouse Models for Protein Granule Diseases

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partner interested in mouse models for protein granule diseases in patients.

Overview

Overload of protein granules in cells induces many forms of diseases, and is especially found in neurodegenerative diseases such as Alzheimer's disease and amyotrophic lateral sclerosis as well as very rare skeletal muscle diseases. Clinical studies also show that human patients with genetic mutations in a muscle specific splicing factor, RNA binding motif 20 (RBM20), can develop severe dilated cardiomyopathy as early as young adulthood, and they are at particularly high risk for sudden cardiac death.

The Invention

UW-Madison researchers have developed two mouse models with mutations found in human dilated cardiomyopathy patients. These mice display a similar phenotype to that observed in human patients, and manifest dilated cardiomyopathy at an early age (less than 2 months). Through further characterization of the phenotype, the researcher has discovered that the mutations are causing the protein to translocate out of the nucleus into the cytoplasm, where it aggregates into protein granules. These modifications to RBM20 affect downstream gene transcription, translation and other cellular activities.

Applications

- This model can be used to screen drugs that may modulate the buildup of toxic granules, with a timespan more tractable than the decades necessary for the natural development of clinical symptoms in humans.

Key Benefits

- Protein granules that form in cardiomyopathy are more accessible to study than in neurons and brain tissues.
- The mouse models accelerate drug discovery for protein granule degenerative diseases of the heart and nervous system.

Stage of Development

The researchers currently working to make a mouse model in which the RBM20 gene comprises a deletion of the entire domain from which the six known mutations arise.

Tech Fields

- Drug Discovery & Development : Disease models
- Research Tools : Animal & disease models

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