NU Tech
Technology Partnership of Nagoya University, Inc.

(A-67)

A new animal model and therapeutic agent for synaptic dysfunction, FTLD and ALS

Background

Frontotemporal lobar degeneration (FTLD) is the second *most common* cause of *dementia* next to Alzheimer's disease, and is characterized by disturbances in personality and social interaction deficits. Amyotrophic lateral sclerosis (ALS) causes muscular atrophy, resulting in severe motor impairment characterized by muscle weakness. While FTLD and ALS are apparently two different symptoms, RNA-binding proteins, including Fused in Sarcoma (FUS) and another RNA-binding protein TDP-43, are common causative factors in these two diseases. A number of studies have suggested that aberrant RNA metabolism of these proteins inhibits normal neuronal functions and affects disease symptoms. However, to date, no treatment has been developed for these devastating progressive neurodegenerative diseases.

Technology Overview

Researchers at Nagoya University have identified a potential therapeutic agent by developing a novel knockout mouse that presents the symptoms mimicking FTLD patients.

FUS depletion significantly reduced the level of SynGAP α2 protein that is the major factor to regulate synaptic maturation. Moreover, FUS binds directly to the mRNA encoding for SynGAP α2 and protects it from degradation. To elucidate whether SynGAP α2 is responsible for synaptic dysfunction upon the loss of FUS, the FUS-knock-down mice showing abnormal synaptic maturation and behavior that mimic those of FTLD patients has been successfully generated. Interestingly, gene therapy based on supplementation with SynGAP α2 ameliorated the symptoms of the knockout mice, which indicates SynGAP α2 as a potential major therapeutic target for FTLD and ALS. The findings could be useful for developing a new treatment for FTLD and also ALS.

Applications:

Developing a new treatment for FTLD/ALS

IP Status:

Patent application submitted

Seeking:

Licensing

Further Details:

Satoshi Yokoi *et al.*, 3'UTR Length-Dependent Control of SynGAP Isoform α2 mRNA by FUS and ELAV-like Proteins Promotes Dendritic Spine Maturation and Cognitive Function. Cell Rep. 2017 Sep 26;20(13):3071-3084. doi: 10.1016/j.celrep.2017.08.100.

Contact

Rena Shimizu, Ph.D., TEL: 919-535-8724 Email: rshimizu@tpnu.org
Technology Partnership of Nagoya University, Inc.
One Copley Parkway, Suite 305, Morrisville, NC 27560

名古屋大学
NAGOYA UNIVERSITY

Figure:

Figure 1: Immunocytochemistry of mouse primary cultured neuron (blue; nucleus, red; dendrite, green; post-synapse/spine). Researchers analyzed the morphology of spines which were stained with green.

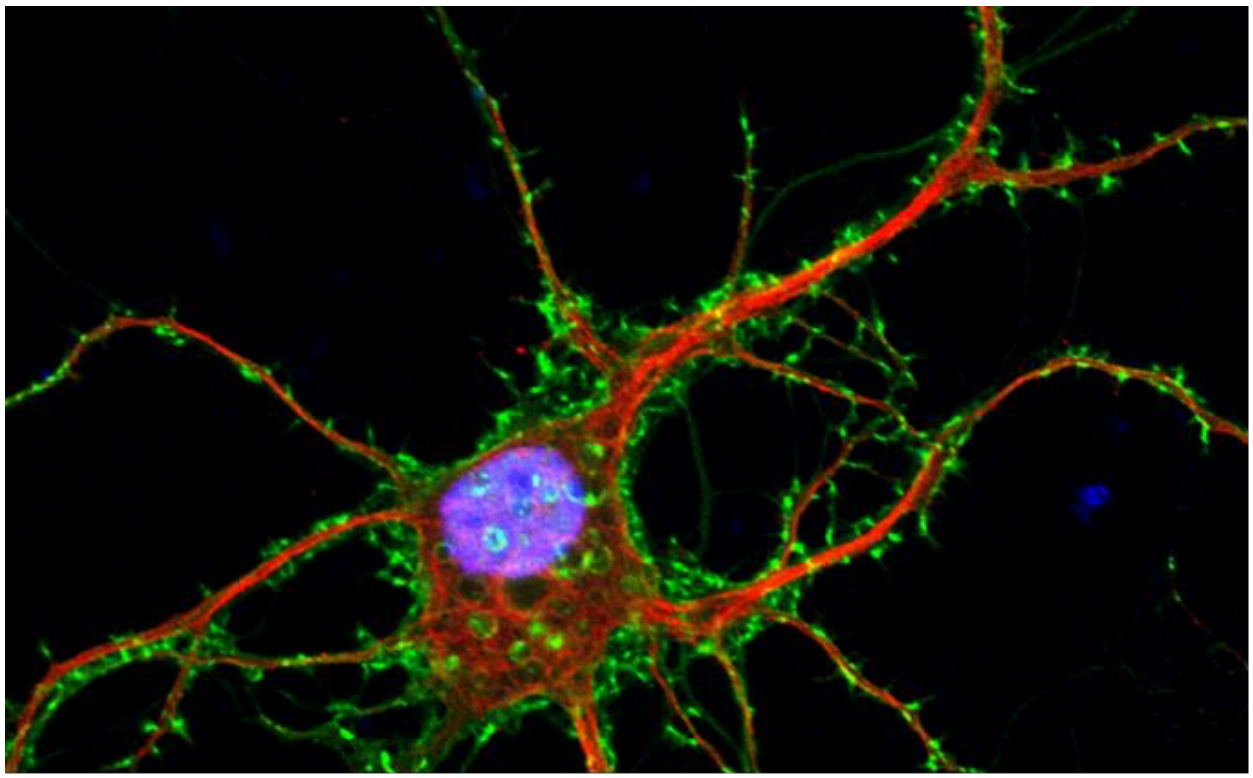
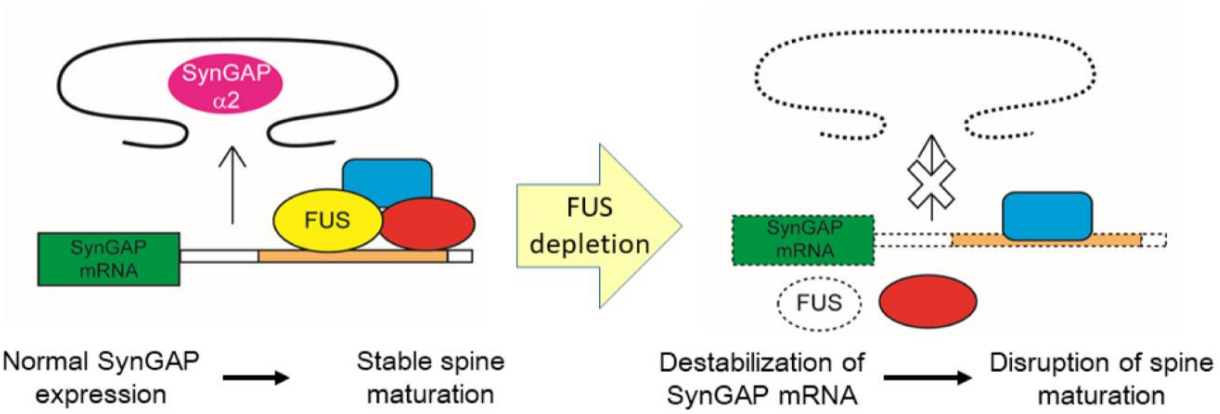


Figure 2: The graphical summary of the findings



Contact

Rena Shimizu, Ph.D., TEL: 919-535-8724 Email: rshimizu@tpnu.org
Technology Partnership of Nagoya University, Inc.
One Copley Parkway, Suite 305, Morrisville, NC 27560

名古屋大学
NAGOYA UNIVERSITY