gustav / August 23, 2012 07:14PM

[Molecular Biology] Researchers at Academia Sinica Develop Mouse Model of Common Motor Neuron Disease Pinpointing TDP-43 Protein as Likely Cause

[Molecular Biology] Researchers at Academia Sinica Develop Mouse Model of Common Motor Neuron Disease Pinpointing TDP-43 Protein as Likely Cause (Chinese Version)

Academia Sinica Newsletter (2012/08/22) A research team led by Academician C-K James SHEN, a Distinguished Research Fellow at the Institute of Molecular Biology recently found that TAR DNA binding protein 43 (TDP-43) is a likely cause of the development of the motor neuron disease amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease. Using a mouse model, first author Ms. Lien-Szu WU and colleagues showed that mice with inactivation of the Tardbp gene (the gene that encodes TDP-43 protein) in spinal cord motor neurons exhibited progressive and male-dominant development of ALS-related abnormalities including spine curvature (kyphosis), motor dysfunctions, muscle weakness/atrophy, and motor neuron loss. The study was published in The Journal of Biological Chemistry on June 20, 2012.

Amyotrophic lateral sclerosis, the most common motor neuron disease, is a progressive, adult-onset degenerative disorder of motor neurons in the primary motor cortex, corticospinal tracts, brainstem and spinal cord, leading to paralysis of the voluntary muscles. Currently, the incidence of ALS is 1–2 per 100,000 worldwide each year and its prevalence is 4–6 per 100,000 of the total population, with a lifetime ALS risk of 1 in 400 to 1 in 1,000. Most incidences of ALS are sporadic (sALS) but approximately 10% of patients have a family history (fALS) of the disease. Mutations in the Tardbp gene have been identified in about 4% of fALS and less than 1% of sALS.

Interestingly, the TDP-43 protein is the major component of the ubiquitinated inclusions (UBIs) in the diseased cells of 80% of ALS patients. TDP-43 has been implicated in a number of cellular activities (such as transcriptional repression and alternative splicing). However, the physiological functions of TDP-43 in normal individuals and whether it causes neurotoxicity through gain-of-function or a loss-of-function in ALS are largely unknown. Currently, there is no effective cure for ALS, thus, suitable mouse models are urgently needed to further understand ALS and the development of drugs for ALS. The characteristics of this ALS mouse model also provide the foundation for design of other ALS mouse model(s)

This study establishes an important role of TDP-43 in the long-term survival and functioning of the mammalian spinal cord motor neurons, and also establishes that loss of TDP-43 function could be one major cause of neurodegeneration in ALS with TDP-43 involvement. This research was supported by the Frontiers of Science Award from the National Science Council and Academia Sinica.

Related Website:
http://www.jbc.org/content/early/2012/06/20/jbc.M112.359000

Media Contacts:
Dr. C-K James SHEN, Distinguished Research Fellow, Institute of Molecular Biology, Academia Sinica
(Tel) +886-2-2782-4188
Ms. Mei-hui LIN, Office of the Director General, Central Office of Administration, Academia Sinica
mhlin313@gate.sinica.edu.tw (Tel) +886-2-2789-8821 (Fax) +886-2-2782-1551 (M) 0921-845-234
Ms. Pearl HUANG, Office of the Director General, Central Office of Administration, Academia Sinica
pearlhuang@gate.sinica.edu.tw (Tel) +886-2-2789-8820 (Fax) +886-2-2782-1551 (M) 0912-831-188

Further Information:
Academia Sinica Newsletter 2012/08/22

Edited 1 time(s). Last edit at 08/23/2012 07:17PM by gustav.