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Press Release

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Identification of Autophagy Gene Regulation Mechanism Related to Dementia and Lou Gehrig's Disease

- An international Research Team led by Dr. Yun Ha Jeong at Korea Brain Research Institute has published the results of its research in 'Autophagy'.
- Expected to develop the treatment for neurodegenerative disease utilizing TDP-43 protein

□ Korea Brain Research Institute (KBRI, President Seo Pan-ghill) announced on **July 10** that **the international joint research team where Senior Researcher Yun Ha Jeong and John Hopkins School of Medicine collaborated, found that 'cell autophagy* gene' called ATG7 is related to the onset of frontotemporal dementia and Lou Gehrig's disease.**

* Autophagy: It refers to the phenomenon where a cell discomposes and recycles unnecessary organelles or components. It can be regarded as the self-cleaning taking place within the cell.

○ The research outcome was published in the July issue of 'Autophagy', which is an international journal and the name of the paper and authors are as follows.

* Paper: Upregulation of ATG7 Attenuates Motor Neuron Dysfunction Associated with Depletion of TARDBP/TDP-43

* Author: Aneesh Donde*, Mingkuan Sun*, Yun Ha Jeong* (co-first author), Xinrui Wen, Jonathan Ling, Sophie Lin, Kerstin Braunstein, Shuke Nie, Sheng Wang, Liam Chen and Philip C. Wong (corresponding author)

□ The research team **found that when the genes are manipulated to make sure that a certain protein called TDP-43* is not created in mice and fruit flies, then the activity of gene ATG7, which is essential for cell autophagy, was inhibited and neuronal degeneration occurred.**

* It is a transcriptional regulation protein and it is known as the major pathogenesis of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD).

* ATG7: Essential gene for autophagy

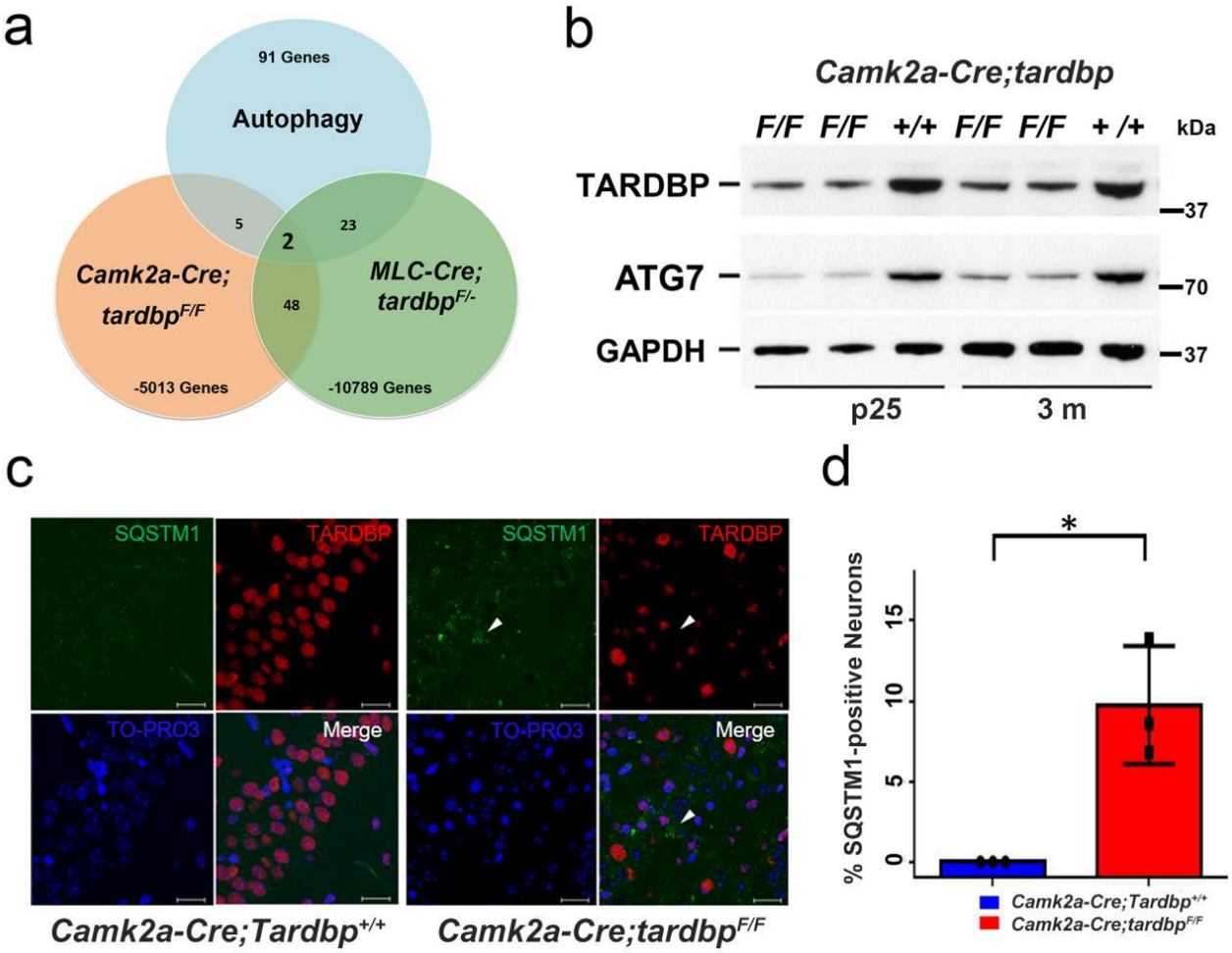
○ On the contrary, when the gene is manipulated to increase the ATG7 gene expression for activation of autophagy in fruit flies, for which the TBPH* gene expression is inhibited, it is found that neurodegenerative and ataxia symptoms were improved.

* TBPH: Gene of fruit flies that is equivalent to TDP-43 present in humans

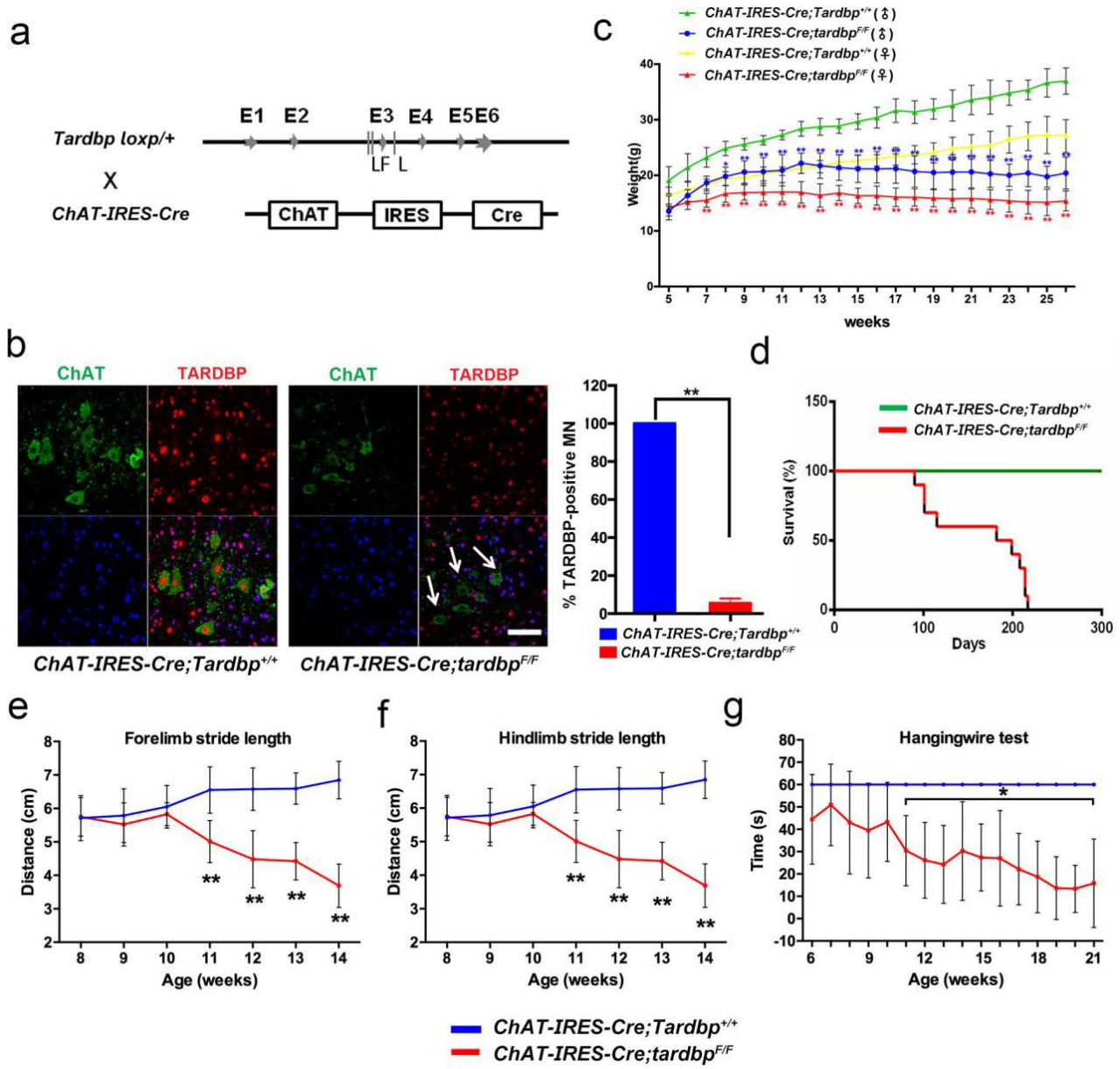
□ The result of this study is meaningful in that the study confirmed the fact that TDP-43 protein regulates the activation of ATG7, which is responsible for the autophagy of neurons as well as the specific process of neuronal degeneration at the gene level.

○ Cells improve the activity of overall cells by consuming damaged or old organelles or some structures (This is what we call autophagy). If the activity of gene ATG7, which is key to this process, is reduced, then the damaged and old organelles still remain, causing problems in the muscle cells and neurons.

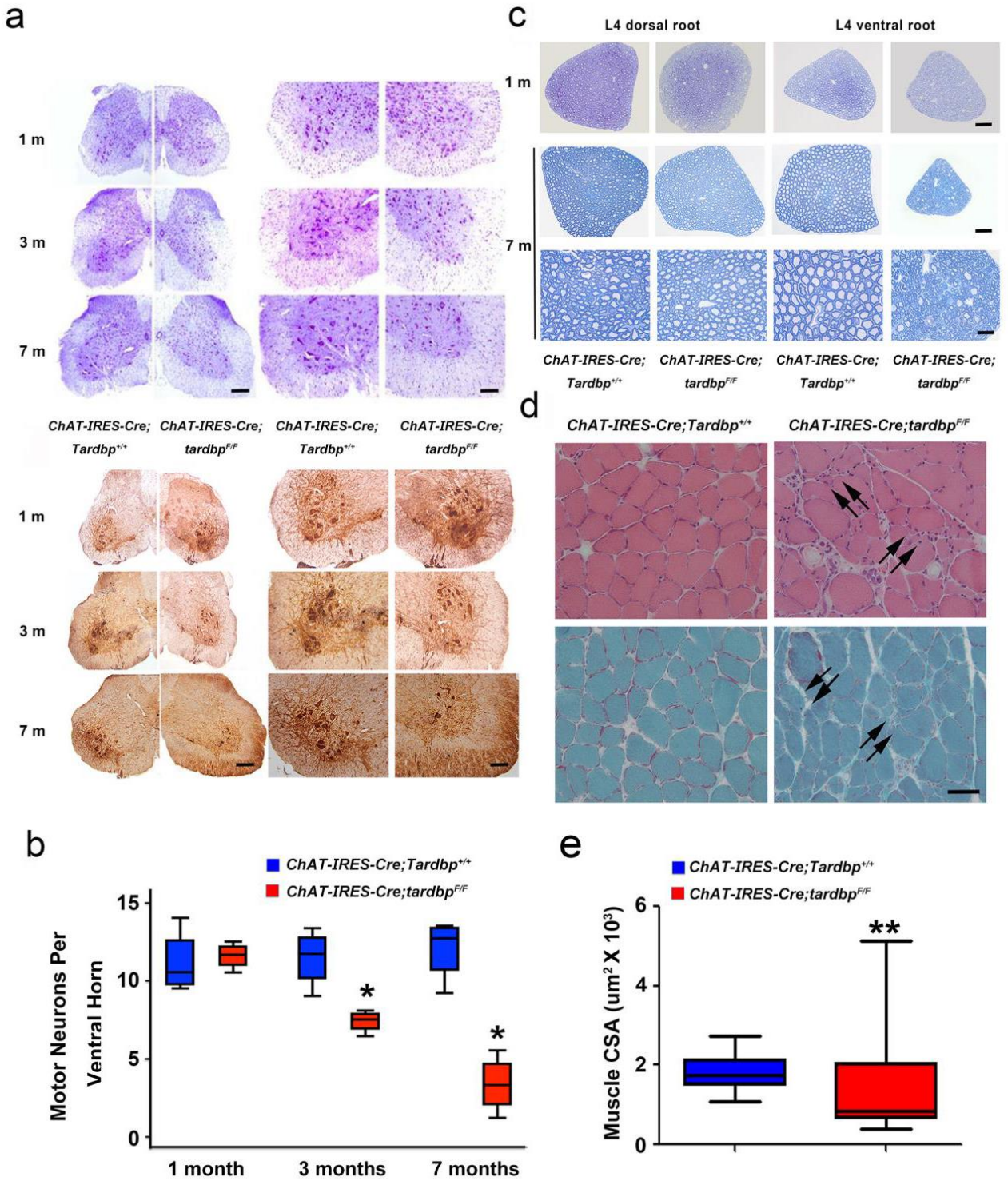
□ Dr. Yun Ha Jeong of the KBRI expected that “this research would contribute towards the development of a new treatment for neuro-degenerative diseases, aiming to activate the autophagy function of cell”.



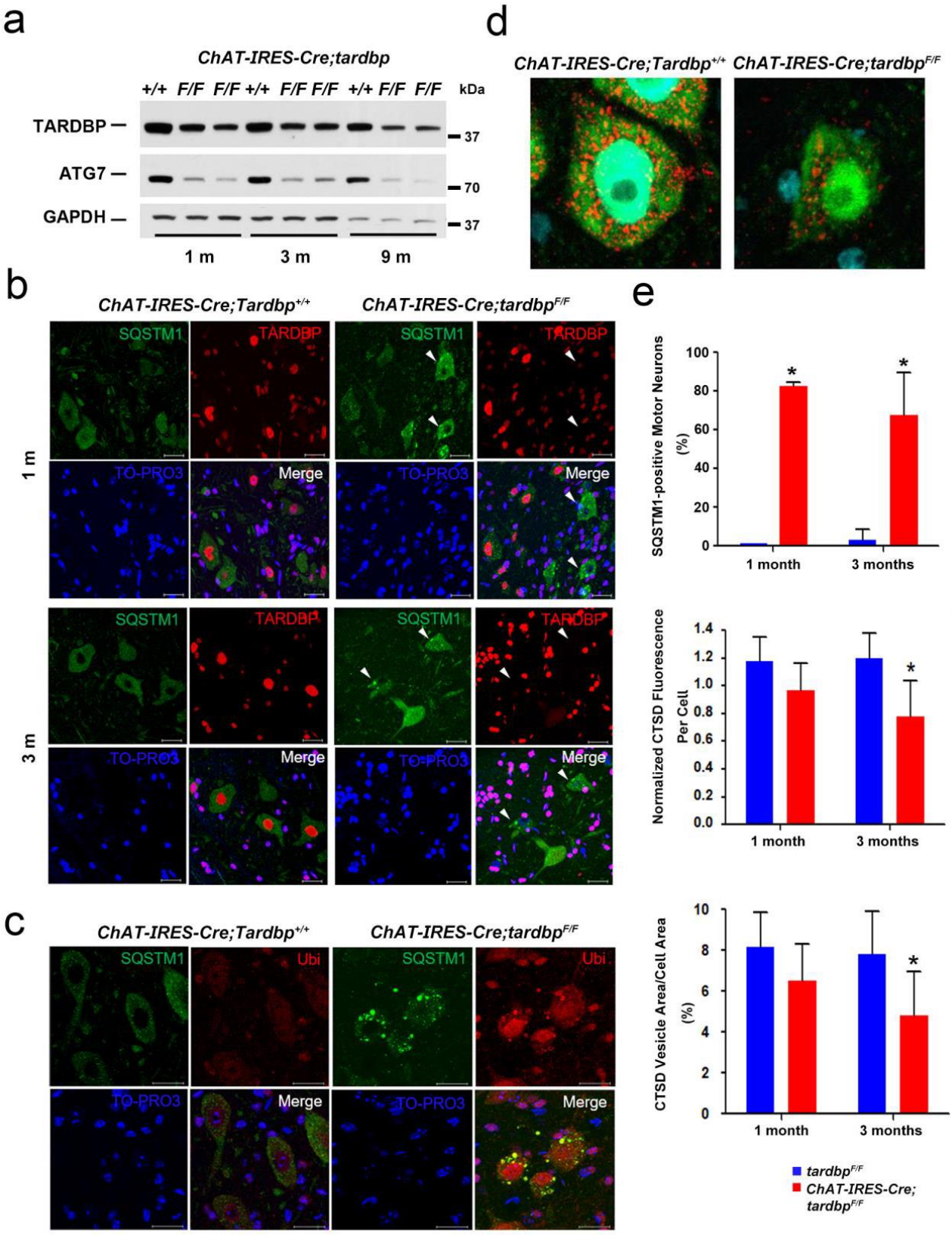
[Figure 1] If the TDP-43 protein expression is inhibited in neurons or muscle cells, then autophagy related genes are affected.



[Figure 2] After inhibiting TDP-43 protein expression in the motor neurons of a mouse, the symptoms of ataxia are observed as the mouse grows older.

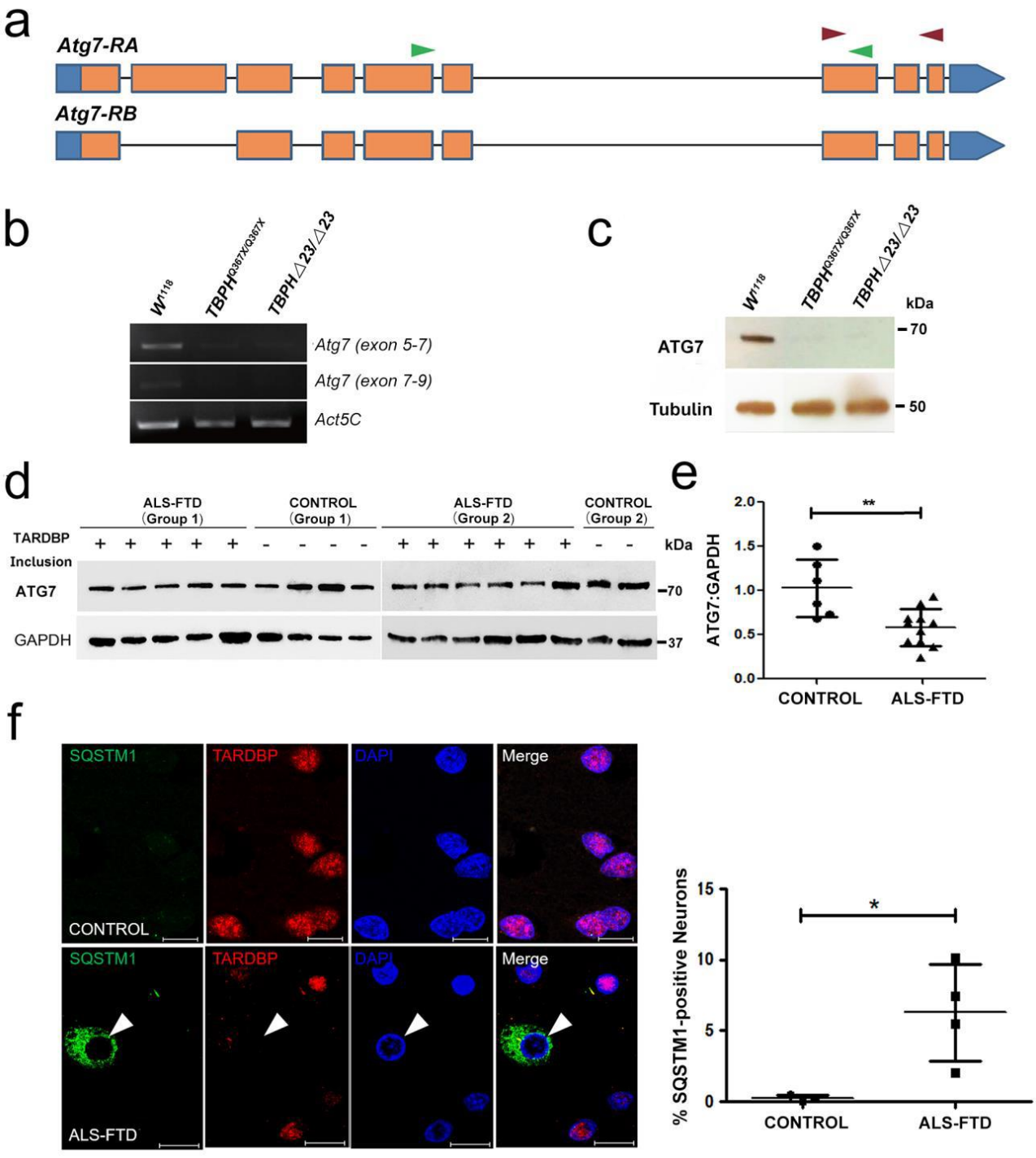


[Figure 3] After inhibiting TDP-43 protein expression in the motor neurons of a mouse, the symptoms of neural degeneration are observed as the mouse grows older.

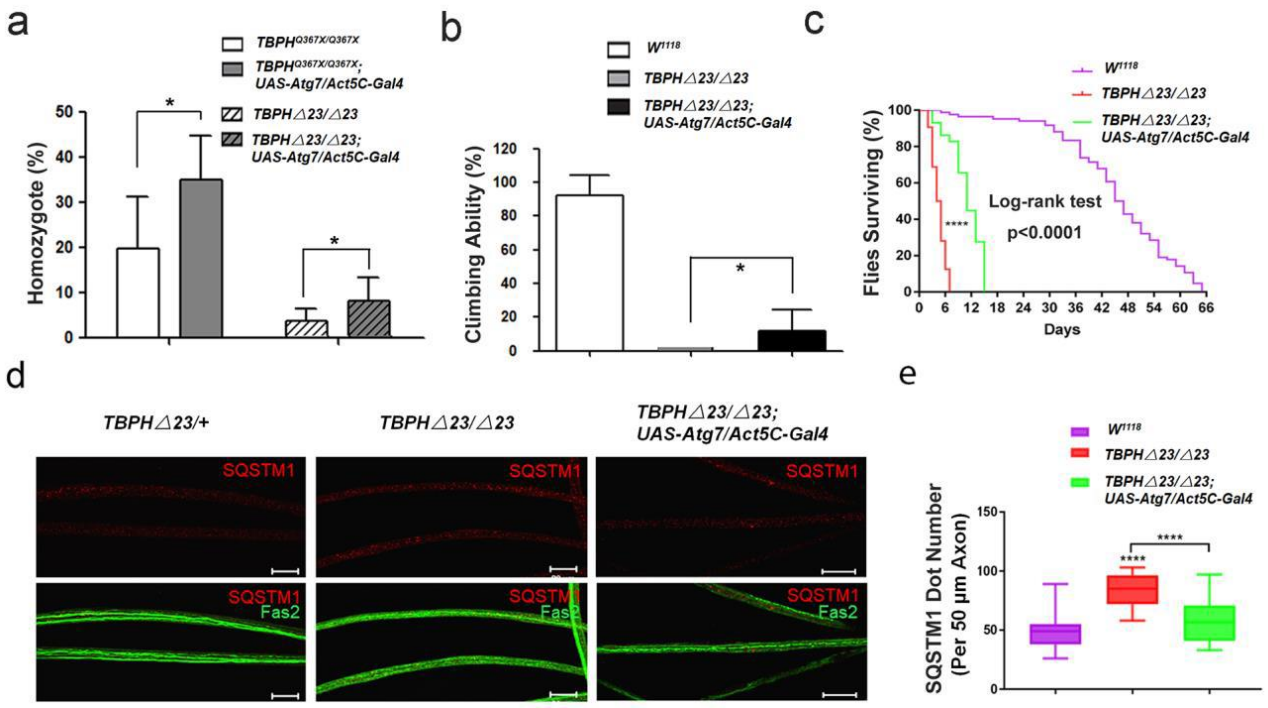


[Figure 4] After inhibiting the TDP-43 protein expression in motor neurons of a mouse, the

autophagy function weakened.



[Figure 5] After inhibiting TBPH protein expression in fruit flies, gene ATG7 expression was reduced and this reduced expression of ATG7 protein was found in patients with ALS-FTD.



[Figure 6] When the autophagy function was activated with an increased expression of the ATG7 gene in the fruit fly model for which TBPH expression was inhibited, the neurodegenerative and ataxia symptoms were found to have improved.