A new hope in treating neurodegenerative disease

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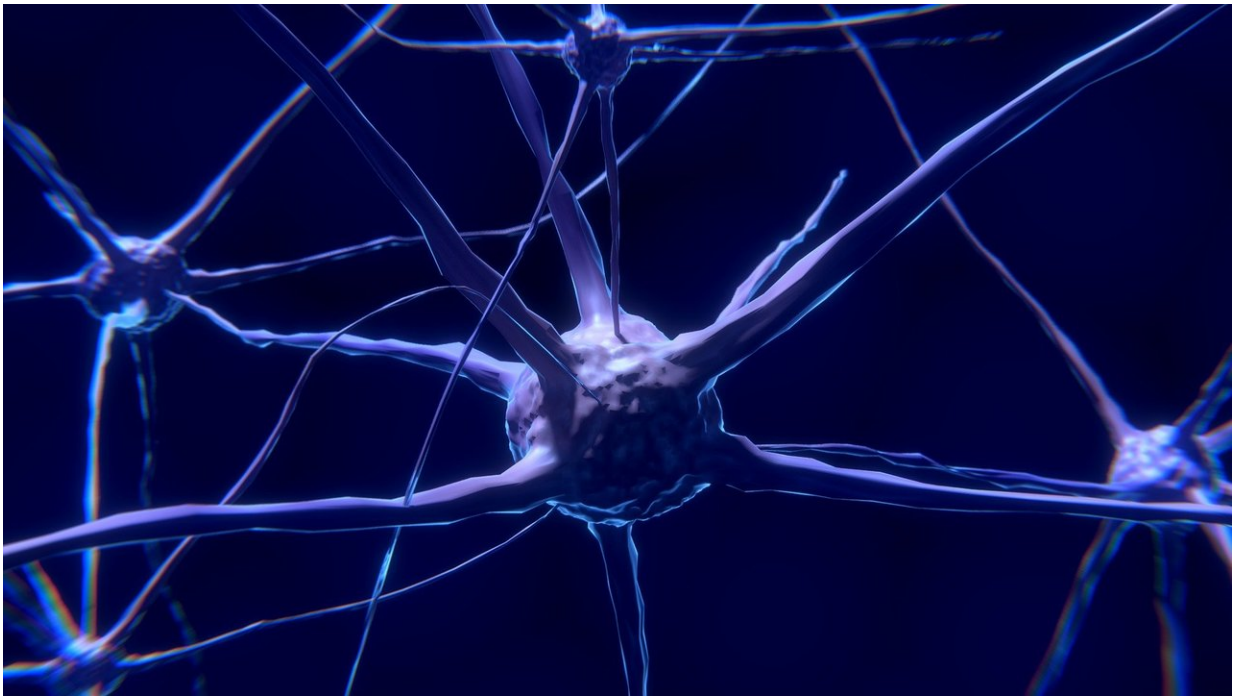

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Korean researchers have identified the inhibition of autophagy in microglia, brain immune cells. It is expected to help develop treatments for Alzheimer's disease which occur due to the inhibition of autophagy.

Alzheimer's disease (AD) is the most representative degenerative brain disease, accounting for 60 to 80 percent of all dementia cases. In search

for new mechanism for AD, the research team led by Professor Seong-Woon Yu of Brain and Cognitive Sciences paid attention to the autophagy of microglia, brain immune cells, is suppressed by inflammation.

'Microglia' are phagocytic immune cells which are resident in the central nervous system and share many characteristics with macrophages. They act as brain janitors that eliminate harmful materials accumulated in the brain tissue. Autophagy plays an important role in removing pathogens such as mycobacteria or toxic materials inside cells, for which Professor Ohsumi Yoshinori received the Novel Prize in Physiology in 2016.

Professor Yu's team identified that PI3K/Akt signal transmission routes are activated inside cells if inflammatory materials combine with TLR4 (Toll-like receptors) which exist on the microglia surface, inhibiting autophagy. The team verified for the first time that the suppression of autophagy leads to decline of the ability to decompose amyloid β, which causes Alzheimer and aggravates the disease even further.

While researches have been continuously conducted to show that inflammation and brain cell autophagy are related with degenerative brain diseases, there has been a lack of understanding on its process. Also, it has been known that autophagy becomes more active in other immune cells in our bodies by inflammation, in contrast to microglia. Thus, this research of brain cell autophagy is expected to suggest an important clue for brain disease treatment by understanding how the problems of autophagy would affect brain functions.

Professor Yu said "Though nerve inflammation always increases if one contracts a degenerative brain disease, it has not been known that an autophagic effect is suppressed in microglia which is related to inflammatory increase. If we focus on brain tissue cells and keep researching the relationship between nerve inflammation and autophagy,

we will be able to take a step closer to developing treatments and new strategies for curing brain diseases."

This study has been published in *Autophagy*, the most-renowned journal on autophagy, on December 7. It was conducted with the funding of the Brain Science Source Project and the Project supported by the Ministry of Science and ICT and the National Research Foundation of Korea, as well as convergence research project of Rehabilitation Mechanism and Technique based on Cerebral Nerve Plasticity at DGIST.

More information: Ji-Won Lee et al. TLR4 (toll-like receptor 4) activation suppresses autophagy through inhibition of FOXO3 and impairs phagocytic capacity of microglia, *Autophagy* (2018). DOI: 10.1080/15548627.2018.1556946

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