Smilagenin represents a new approach for treating neurodegeneration disease

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Erxi Wu, assistant professor of pharmaceutical sciences, and Shuang Zhou, a doctoral student in Wu's lab, co-wrote the article, "Smilagenin Attenuates Beta Amyloid (25-35)-Induced Degeneration of Neuronal Cells via Stimulating the Gene Expression of Brain-Derived Neurotrophic Factor," which will be published by *Neuroscience*. They collaborated with Yaer Hu lab at Shanghai Jiaotong University, China, for the publication.

According to the authors, the development of drugs that weaken neurodegeneration is important for the treatment of Alzheimer's disease. They previously found that smilagenin, a steroidal sapogenin from traditional Chinese medicinal herbs that improves memory in animal models, is neither a cholinesterase inhibitor nor a glutamate receptor antagonist, but can significantly elevate the declined muscarinic receptor (M receptor density). In this paper, to clarify whether smilagenin represents a new approach for treating neurodegeneration disease, they first demonstrate that smilagenin pretreatment significantly attenuates the neurodegenerative changes induced by beta amyloid 25-35 (Aβ25-35) in cultured rat cortical neurons, including decreased cholinergic neuron number, shortened neurite outgrowth length and declined muscarinic receptor density. Brain-derived neurotrophic factor protein in the culture medium was also decreased by Aβ25-35 and significantly elevated by smilagenin.

Parallel experiments revealed that when the trk receptors were inhibited by K252a or the action of brain-derived neurotrophic factor was

inhibited by a neutralizing anti- brain-derived neurotrophic factor antibody, the effects of smilageninon the Aβ25-35 induced neurodegeneration in rat cortical neurons were almost completely abolished. In the all-trans retinoic acid-differentiated SH-SY5Y neuroblastoma cells, the brain-derived neurotrophic factortranscription rate measured by a nuclear run-on assay was significantly suppressed by Aβ25-35 and elevated by SMI, but the brain-derived neurotrophic factor degradation rate measured by half-life determination was unchanged by Aβ25-35 and smilagenin. Transcript analysis of the SH-SY5Y cells using quantitative RT-PCR showed that the IV and VI transcripts of brain-derived neurotrophic factor mRNA were significantly decreased by Aβ25-35 and elevated by smilagenin.

“Taken together, this study concludes that smilagenin attenuates Aβ25-35-induced neurodegeneration in cultured rat cortical neurons and SH-SY5Y cells mainly through stimulating brain-derived neurotrophic factor mRNA transcription implicating that SMI may represent a novel therapeutic strategy for Alzheimer’s disease,” Wu said. “Collaborating with Dr. Hu at Shanghai Jiaotong University, China, we together would like to find better therapeutics and elucidate the mechanisms of the potential novel therapy for Alzheimer’s disease,” Wu said.

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