The role of N-acetylglucosaminyltransferase III in Alzheimer’s disease progression

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The pathogenic mechanism of Alzheimer’s disease (AD) has not been clearly defined, and many factors have been discovered to explain this multifactorial disorder. The alteration of glycoprotein glycans in AD has been highlighted recently. It has been reported that the bisecting N-acetylglucosamine (GlcNAc) levels were higher in the cerebrospinal fluid of most AD patients, which indicates that N-acetylglucosaminyltransferase III (GnT-III), a glycosyltransferase responsible for synthesizing a bisecting GlcNAc residue, may play an important role in the development of AD. In our previous studies, we demonstrated that the levels of GnT-III and bisecting GlcNAc were increased in AD models, and glucagon-like peptide-1 (GLP-1) receptor agonists could downregulate aberrant expression of GnT-III through the Akt/GSK-3β/β-catenin signaling pathway in neurons. Here, we further explored the role of GnT-III in AD progression. We overexpressed GnT-III in PC12 cells and found that the intracellular reactive oxygen species (ROS) was increased significantly in GnT-III overexpressing cells. The mitochondrial structure was damaged and the mitochondrial membrane potential (Δψm) tested by JC-1 probe was lower in GnT-III overexpressing cells, which indicated that the mitochondrial function might be damaged by aberrant GnT-III expression. Besides, we also tested the GLP-1 receptor signaling mediated by GLP-1 and found that overexpression of GnT-III disrupted the normal GLP-1 receptor signaling in neurons. In conclusion, our findings reveal that GnT-III could be a potential therapeutic target for AD.

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Biography

Ying Wang is a PhD student of Microbiology and Biochemical Pharmacy at the China Pharmaceutical University. She is investigating the molecular pathogenesis of Alzheimer’s disease, especially about the relationship between protein glycosylation and Alzheimer’s disease.

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