KN2

Comprehensive Characterization of Mammalian Brain N-Glycome: Isomer-Sensitive Nano-LC-MS/MS Analysis and its Application to Alzheimer's Disease Models

Dongtan Yin[1,2], Jong Hyuk Yoon[3], Doo Soo Chung[4], Hyun Joo An[1,2]

[1]Graduate School of Analytical Science and Technology, Chungnam National University, Daejeon, Korea, hjan@cnu.ac.kr

[2]Asia-Pacific Glycomic Reference Site, Daejeon, Korea

[3]Neurodegenerative Disease Research Group, Korea Brain Research Institute, Daegu, Korea

[4]Department of Chemistry, Seoul National University, Seoul, Republic of Korea

Summary

In the mammalian brain, over 70% of the proteome is known to be glycosylated, and a large fraction of this glycosylation is N-glycome. N-glycosylation plays an important role in neurobiology, including in the development of the nervous system and the regulation of neurotransmitter receptors. Particularly, aberrant glycosylation has garnered substantial interest due to its association with many brain diseases and disorders, including Alzheimer's disease. To understand the diverse functions of N-glycome at the molecular level, a comprehensive characterization is highly required. However, the heterogeneity of glycans in the biosynthetic process leads to the production of various isomers and hundreds of N-glycans, making it difficult to obtain in-depth structural insights due to this structural complexity. To overcome these challenges, we developed an analytical method using porous graphitized carbon nano-LC-MS/MS, an isomer-sensitive and reproducible analytical platform. The unique isomer selectivity of porous graphitic carbon underscores the importance of analyzing isomeric structures in glycomics, facilitating the clear identification of complex glycan structures that include bisected and hybrid-type glycans with novel features. Simultaneously, the use of MS/MS has defined the structure of brain-specific N-glycans including sulfated LacNAc, sialylated HexNAc, sialylated LacdiNAc, non-sulfated HNK-1, HNK-1, and phosphorylated mannose. As a next step, we applied this analytical platform to actual disease mouse model, specifically focusing on Alzheimer's disease. Subsequent statistical analyses based on our established database revealed differences in N-glycome composition across five key regions. Presently, further investigations are underway to understand the role of the specific molecular targets that have undergone changes.

Acknowledgement

This research was supported by the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (RS-2023-00267020) and the Korea Brain Research Institute (24-BR-04-02).