

Investigation of novel biomarkers for Alzheimer's disease using lipid-coated nanoparticles

Hitoshi Sohma^{1,2}, Mami Yamaguchi¹, Michitoshi Kimura¹, Shin-ichi Imai¹, Kayo Matsumoto¹, Norio Takei¹ and Yasuo Kokai¹

¹Department of Biomedical Engineering, Sapporo Medical University School of Medicine, Japan

²Department of Educational Development, Sapporo Medical University Center for Medical Education, Japan

Objective: Alzheimer's disease (AD) differs from other forms of dementia in its relation to amyloid beta peptide (Abeta42). Abeta42, a proteolytic product of amyloid precursor proteins (APP), has a toxic effect on neuronal cells. This effect implies that protein expression is changed in neuronal cells by Abeta42, which provides a molecular marker for this disease. In the present study, we used the mice primary culture neurons and investigated the proteins in the supernatant after incubation with or without Abeta₄₂.

Methods: In view of the appearance of an acidic phospholipid (phosphatidylserine (PS)) on the outer plasma membrane of an apoptotic cell, we used PS as a probe and proteins bound to PS-coated magnetic nano-beads in a Ca²⁺-dependent manner were identified using a proteomic approach.

Results: Of a number of proteins identified, we focused on annexin A5 and milk fat globule-EGF-factor 8 (MFG-E8) that is involved in the clearance of apoptotic cells. Both annexin A5 and MFG-E8 were found to be increased significantly in the culture supernatant by Abeta42. Tg2576 mice (AD mouse model), which overexpress mutant human APP, showed significant increase of annexin A5 in both the brain cortex and plasma, compared with control. The level of annexin A5 significantly increased in a greater proportion of AD patients as compared to that in a control group (*p*-value of less than 0.0001 in the logistic regression analysis).

Conclusions: Both annexin A5 and MFG-E8 are novel plasma biomarker candidates for AD.

Biography

Hitoshi Sohma completed his Ph.D. in biochemistry at Hokkaido University, Japan, focusing on Ca²⁺-signaling in cell-cell communications, and his postdoctoral studies at the National Institute of Mental Health, NIH. He is a professor in the Department of Educational Development, Sapporo Medical University Center for Medical Education, Sapporo, Japan. He is now involved in both pathobiochemical research and the management of medical education at the university. He has published more than 50 papers in the biomedical field.