Title: Neuronal Exosomes Can Eliminate Alzheimer's Amyloid Protein in Vitro and in Vivo Model Mouse

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Abstract

Exosomes are extracellular nanovesicles, which are released from a variety of cells including neurons. The neuronal exosomes were reported to be associated with several proteins in neurodegenerative disorders, including amyloid β-protein (Aβ) in Alzheimer’s disease (AD), α-synuclein in Parkinson's disease, and prion protein in Creutzfeldt-Jakob disease. In recent study, we found that the neuronal exosomes significantly enhanced Aβ amyloid formation through binding Aβ with glycosphingolipids on the exosomal surface, and then were incorporated into microglia together with Aβ amyloid fibrils. We also confirmed that secretion of neuronal exosomes was modulated by sphingolipid metabolism. Their release was largely decreased by inhibition of N-sphingomyelinase (SMase) activity, whereas increased by inhibition of sphingomyelin synthase (SMS) activity. And interestingly, SMS knockdown decreased extracellular Aβ levels in transwell culture system of neuronal and microglial cells. These results suggest that neuronal exosomes accelerate Aβ assembly on its surface and transports Aβ into microglia to degrade. In vivo study to confirm exosomal function of Aβ clearance has been presently carried out using AD model mice. The potential of exosomes to clear Aβ might be useful for AD therapy.

Biography

Dr. Igarashi is a lipid biochemist, graduated from Biochemistry Department, Faculty of Science, Tokyo University in 1968 and got Ph.D. from Tokyo University in 1975. He worked internationally after graduation: for Gunma University (1975-1982), Wayne State university USA (1982-1985), Grenoble CENG France (1986-1988). In 1988 he moved to University of Washington and Biomembrane Institute in Seattle, USA (1988-1998) as an institute head scientist and associate professor of UW. In 1998 he returned to Japan and became the professor of Graduate School of Pharmaceutical Science, Hokkaido University (1998-2006). In 2008 he established Graduate School of Advanced Life Science, Hokkaido University and worked as the first Dean. Since then he is also the director of Frontier Research Center for Post-genome Science and Technology, Hokkaido University. His research has been focused on sphingolipid biology, basic research and and applied research including the development of sphingolipid-based drugs and functional foods. Now he is mainly working on biology of S1P, ceramide and SMS2 and he is recognized as one of world leading scientists in this research field. He published over 230 papers and gave 60 invited lectures in various international conferences. He organized many international conferences in the field, and he was elected as the Chair of Gordon Research Conference, Sphingolipid and Glycolipid Biology which was held in 2012 in Italy, and the Chair of FASEB Summer Research Conference in 2013 in Sapporo.