Form 1-5-2

Japan-U.S. Brain Research Cooperation Program
Report of Researchers Dispatched to the U.S. for the 2010 Fiscal Year

Field: (4) Others

1. Name/Title/Affiliation: Takeshi Yoshimura / Project assistant professor /
Division of Neurobiology and Bioinformatics,
National Institute for Physiological Sciences

2. Project Title: Identification and determination of N-glycan structures involved in myelination

3. U.S. host researcher's Name, Title, and Affiliation: Dr. Bruce D. Trapp / Professor /
Neurosciences, Cleveland Clinic

4. Term of Research: From 2010 Yr. July Mo. 14th Day to 2010 Yr. August Mo. 14th Day (1 mo.)
(Elimination period: July 18th, 2010 - July 26th, 2010)

5. Abstract, Results, and Research Significance (300 Words):

Myelin is a multilamellar, tightly compacted membrane that surrounds axons of neurons. Myelination is essential for saltatory conduction of neuronal action potentials. However, the molecular machinery involved in myelination remains unclear. N-glycans are crucial for the folding, intracellular transport, stability, and secretion of glycoproteins. N-glycans on cell surface glycoproteins are involved in various cellular functions including cell-cell and cell-matrix interactions. In this study, we analyzed N-glycans on myelin proteins, especially myelin protein zero (P0). P0 is the major myelin protein expressed by Schwann cells, comprising approximately 50% of all peripheral nervous system (PNS) myelin proteins, and is necessary for normal myelin function and structure. P0 contains a single N-glycosylation site and heterogeneity in its glycosylation pattern has been reported. It was thought that the glycan heterogeneity on P0 might be regulated by alterations in physiological conditions. Dr. Trapp and his colleagues reported that transgenic mice in which myelin proteolipid protein in central nervous system (CNS) was replaced by P0, displayed hypomyelination (Yin et al., J Cell Biol., 2006). During the research period, myelin was purified from the transgenic mouse brains by sucrose density gradient centrifugation, and purified myelin was lyophilized after acetone precipitation. N-glycans from lyophilized samples were purified, tagged with a fluorophore, 2-aminopyridine, and analyzed by three-dimensional HPLC system. Several sulfated N-glycans were detected in porcine PNS myelin, but not in CNS myelin. Six main N-glycan structures on purified porcine P0 were identified. One N-glycan was a neutral sugar chain, and the others were sulfated glycans, including those with the HNK-1 carbohydrate epitope containing a terminal sulfoglucuronyl residue. Interestingly, sulfated N-glycans were not detected in CNS myelin from the transgenic mice in which P0 was expressed in CNS. These results suggest that sulfated N-glycans on P0 are essential for its normal function.

6. Other (Any concerns regarding the research or special instructions):
This study was suspended from July 18th to July 26th, because I obtained my J-1 visa.

(Please attach reference materials.)