Form 2-4-2

Japan-U.S. Brain Research Cooperation Program
Group Joint Study Project Report

Field: (2) Motor regulation

1. Principal Researcher
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2. Project Title:
Mechanisms of ion channel localizations in axon initial segments

3. Japanese Group
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4. U.S. Group
Names, Titles and Affiliations of Principal Researcher and Collaborating Research Members
Division of Neurology, Children's Hospital of Philadelphia（Present: Department of Neurology, Baylor College of Medicine）・Professor・Edward Cooper
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University of California at San Diego, Professor, Jack E. Dixon
Washington University, Professor, Jianmin Cui
Baylor College of Medicine, Professor, Matt Rasband

5. Research Period, from/to (mm/dd/yyyy) and total number of years.
From 04/01/2008 to 03/31/2011 (3 years)

6. Abstract, Results, and Research Significance (300 words):

Axon initial segment is the key place for generation of action potentials in mammalian neurons. It remains unknown how clustering of voltage-gated sodium channels and potassium channels are integrated at AIS and how it is different from that at nodes of Ranvier. Okamura group previously cloned mammalian Nav1.6 cDNA and ascidian Nav cDNA both of which exhibited ankyrin binding motif at the linker region between II and III domains. As one approach toward understanding these issues, we set out to address how clustering of sodium channels and potassium channels are split along evolution. This was done by bioinformatics search for voltage

gated sodium channel genes and KCNQ potassium channel genes from genomes of chordates, from ascidian to mammals. We found that KCNQ2/3 type potassium channel harboring ankyrin-binding motif is only present in vertebrates that contain myelin in their nervous system. Lamprey do not contain KCNQ2/3 channels nor myelin. However, reticulospinal neurons and motor neurons clearly exhibited AIS-like structure at the proximal part of axons showing intense immuno-positive stains of Nav channels. Therefore, AIS is evolutionarily more ancient than nodes, raising a possibility that regulatory mechanisms are partially distinct between AIS and nodes. We also studied biophysical properties of ascidian KCNQ1 channel in comparision with those of mammalian orthologs. In addition, molecular basis of interaction between Kv1 and Adam22 at juxta-paranode was studied in vitro studies including coimmunoprecipitation and RNAi method.

7. Other (Research-related concerns, particular points of note):

*Please attach any reference materials as necessary.