

Japan-U.S. Brain Research Cooperation Program  
Information Exchange Seminar Program FY2016: Report

Research Field: Neurobiology of Disease

1. Seminar title:

The US-Japan Dominantly Inherited Alzheimer Network (DIAN) Collaborative Workshop

2. Dates, from/to (mm/dd/yyyy)

June 6-June 8, 2015

3. Location:

Kyoto

4. Coordinators

Japanese Coordinator

Name Takeshi Iwatsubo

Title Professor

Affiliation Department of Neuropathology, School of Medicine, University of Tokyo

U.S. Coordinator

Name John C. Morris

Title Friedman Distinguished Professor of Neurology, Director, Knight Alzheimer Disease Research Center

Affiliation Washington University, School of Medicine

5. Participants:

Japan: Invited participants \_19\_ people Others \_18\_\_ people

(Please give names, titles and affiliations of invited participants)

Hiroshi Mori (Professor, Osaka City University, Principal Investigator of DIAN-J)

Takami Tomiyama (Associate Professor, Osaka City University)

Takeshi Iwatsubo (Professor, The University of Tokyo, Principal Investigator of J-ADNI)

Mikio Shoji (Professor, Hirosaki University, DIAN-J clinical core leader)

Takeshi Ikeuchi (Professor, Niigata University, DIAN-J clinical core, biomarker core leader)

Masaki Ikeda (Assistant Professor, Gunma University, DIAN-J clinical core)

Hiroyuki Shimada (Associate Professor, Osaka City University, DIAN-J clinical core)

Etsuro Mori (Professor, Tohoku University, DIAN-J neuropsychology core leader)

Tomohisa Ishikawa (Assistant Professor, Kumamoto University, DIAN-J clinical core)

Akihiko Nunomura (Associate Professor, Yamanashi University, DIAN-J clinical core)

Etsuro Matsubara (Professor, Oita University, DIAN-J clinical core)

Shinobu Kawakatsu (Professor, Fukushima Prefectural University, DIAN-J clinical core)

Shigeo Murayama (Director, Tokyo Metropolitan Geriatric Hospital, DIAN-J neuropathology core leader)

Hiroshi Matsuda (Director, National Center for Neurology and Psychiatry, IBIC, DIAN-J MRI core leader)

Kenji Ishii (Director, Tokyo Metropolitan Geriatric Hospital, DIAN-J PET core)

Kyoko Takashima (Research Associate, Institute of Medical Sciences, The University of Tokyo, DIAN-J Neuroethics core leader)

Yoshiki Sekijima (Shinshu University, DIAN-J Neuroethicsl core)

Atsushi Iwata (The University of Tokyo, J-ADNI clinical core, deputy core leader)

Ryoko Ihara (The University of Tokyo, DIAN-J clinical core, J-ADNI clinical core, deputy core leader)

U.S.: Invited participants      \_10\_\_\_ people                      Others \_\_\_\_ people

(Please give names, titles and affiliations of invited participants)

John Morris (The Harvey A. and Dorismae Hacker Friedman Distinguished Professor of Neurology and Professor of Pathology and Immunology, Physical Therapy, and Occupational Therap, Washington University School of Medicine, Principal Investigator and Program Director of DIAN)

David Holtzman (Professor and Chairman, Department of Neurology, Washington University School of Medicine, Associate Director of DIAN)

Randy Bateman (Professor, Department of Neurology, Washington University School of Medicine, Clinical core leader of DIAN)

Chengjie Xiong (Neuroinformatics Research Group Washington University School of Medicine, Informatics Core Leader of DIAN)

Alison Goate (The Samuel and Mae S. Ludwig Professor of Genetics in Psychiatry, Washington University School of Medicine, Genetics Core Leader of DIAN)

Nigel Cairns (Research Associate Professor in the Departments of Neurology and Pathology & Immunology, Washington University School of Medicine, Neuropathology Core Leader of DIAN)

Tammie Benzinger (Washington University School of Medicine Imaging Core Leader of DIAN)

Virginia Buckles (Washington University School of Medicine, Executive director for DIAN)

Kristen Moulder (Washington University School of Medicine, Deputy Executive director for DIAN)

Jason Hassenstab (Associate Professor, Department of Neurology, Washington University School of Medicine)

#### 6. Seminar Outline and Significance:

One of the most important goals of neuroscience is to achieve effective methods for the treatment and prevention of dementia, especially Alzheimer disease (AD). As the mechanism-based therapeutics for AD are developed, Dominantly Inherited Alzheimer Network (DIAN) has been launched in United States, which aims to test the efficacy of the disease-modifying drugs in individuals who carry pathogenic mutations causative for familial forms of AD, at an asymptomatic stage. DIAN is now growing as an international clinical study, involving Germany, UK and Australia, and DIAN-Japan is being launched, supported by the grant-in-aid from the ministry of health, labor and welfare, by the efforts of a team headed by Professor Hiroshi Mori (Osaka City University) as the Principal Investigator. At this juncture, we propose to have a focused seminar discussing the cutting-edge of intervention into AD through the Japan-US collaboration on DIAN.

#### 7. Seminar Results and Future Implications:

Following four topics were covered. 1. "Establishing Registries of Dominantly Inherited Alzheimer Disease: Challenges in Japan versus the US". Mori and Shoji introduced the current status of familial AD research in Japan, and Morris discussed the cutting edge clinical data related to DIAN. 2. "The Relevance of Dominantly Inherited AD for Sporadic AD: DIAN and ADNI". Iwatsubo presented the latest data in J-ADNI and discussed the implication to familial AD research. Cairns discussed the genotype-phenotype correlation in neuropathological studies of DIAN and ADNI. 3. "Biological Consequences of Individual Pathogenic AD Mutations": Tomiyama discussed the unique phenotype of APP Osaka mutation, and Goate presented the overview of genotype-phenotype correlations. 4. "Barriers to Conducting Secondary Prevention Trials in DIAN": relevant problems were discussed by Matusbara and Bateman. On day 2, practical issues in establishing the DIAN-J protocol were discussed by Iwata, Hassenstab, Shoji and Morris. Technical and ethical problems in genetic, biomarker and imaging studies also were discussed in detail. Site visit to Osaka City University on June 8 was very effective in understanding the clinical study settings in Japan, and also to complete the scientific discussions between DIAN-US and DIAN-J members. Overall, the 3-day workshop was extremely helpful in fostering clinical studies on familial AD in Japan and US.

#### 8. Other (implementation issues, feedback, etc.)

None