

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

Research Field: 4

1. Seminar title:

US-Japan Brain Research Cooperative Program Workshop

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

From 06/09/2016 To 06/10/2016

3. Location:

TKP Tokyo Otemachi Conference Center

22F KDDI Otemachi building, 1-8-1 Otemachi, Chiyoda-ku, Tokyo. 100-0004

4. Coordinators:

Japanese Coordinator

Name Haruko Yamamoto MD, PhD

Title Director

Affiliation Dept. of Advanced Medical Technology Development,
National Cerebral and Cardiovascular Center

U.S. Coordinator

Name Yuko Y Palesch, Ph.D.

Title Professor

Affiliation Department of Biostatistics, Bioinformatics and Epidemiology,
Data Coordination Unit, Medical University of South Carolina

5. Participants:

Japan: Invited participants 15 people Others 5 people (※)

(※) Observers from AMED and Ministry of Health, Labour and Welfare are included.

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

Kazunori Toyoda	National Cerebral and Cardiovascular Center
Masatoshi Koga	National Cerebral and Cardiovascular Center
Toshimitsu Hamasaki	National Cerebral and Cardiovascular Center
Masafumi Ihara	National Cerebral and Cardiovascular Center
Manabu Inoue	National Cerebral and Cardiovascular Center
Sohei Yoshimura	National Cerebral and Cardiovascular Center

Akihiko Taguchi	Foundation for Biomedical Research and Innovation
Teruyuki Hirano	Kyorin University
Yasuhiro Hasegawa	St. Marianna University School of Medicine
Yoji Nagai	Kobe University Hospital
Nobuyuki Sakai	Kobe City Medical Center Central Hospital
Kentaro Sakamaki	Yokohama City University
Chin-Fu Hsiao	National Health Research Institutes, Taiwan
Shuheii Okazaki	National Cerebral and Cardiovascular Center
Mayumi Fukuda-Doi	National Cerebral and Cardiovascular Center

U.S.: Invited participants 11 people Others ____ people

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

Marc Chimowitz, MD.	Professor of Neurosciences, Medical University of South Carolina
Hooman Kamel, MD.	Director of Clinical and Translational Research, Weill Cornell Brain and Mind Research Institute
Joseph Broderick, MD.	Professor and Chair Department of Neurology, University of Cincinnati Principal Investigator, National Coordinating Center, NIH StrokeNet
Opeolu Adeoye, MD.	Associate Professor of Emergency Medicine and Neurosurgery, University of Cincinnati
Pooja Khatri, MD.	Professor of Neurology, Director of Acute Stroke, University of Cincinnati
Magdy Selim, MD.	Associate Professor of Neurology, Beth Israel Deaconess Medical Center
Jamey Frasure, PhD.	Director, NIH StrokeNet National Coordinating Center, University of Cincinnati
Judith Spilker, RN	Admin. Director NIH StrokeNet, University of Cincinnati
Wenle Zhao, PhD	Professor in Biostatistics, Medical University of South Carolina
Catherine Dillon, BS	Associate Director of Trial Operations, Medical University of South Carolina
Scott Janis, PhD	Program Director, National Institute of Neurological Disorders & Stroke

6. Seminar Outline and Significance:

As a collaboration with the stroke investigators of the NINDS StrokeNet and the Japan Network for Clinical Stroke Trials (NeCST), the US-Japan Brain Research Cooperative Program Workshop was held from 9 to 10, June, 2016 at Tokyo Otemachi Conference Center. Various stakeholders for clinical

trials, such as investigators, biostatisticians, project manager, data manager, monitors, government officials are involved in the workshop.

The main goal of this workshop is to exchange information about the opportunities and barriers for conducting collaborative stroke clinical trials, including differences in the culture, the patient care management and regulatory systems, and financial issues; and to explore the feasibility of collaboration on future clinical trials in stroke.

Dr. Palesch (PI of the StrokeNet National Data Management Center) provided a brief background of how the Workshop was realized, including the positive experience in ATACH II Trial, the investigator initiated international multicenter clinical trials, which was recently published in *The New England Journal of Medicines* (N Engl J Med 2016; 375:1033-1043). The participation of Japanese clinical sites in ATACH II Trial was the major accomplishments of the previous Workshop held in 2010 (Accepted US-Japan Brain Research Cooperative Program Workshop, 2010) , and nearly 30% of the study participants in this trial were registered in Japan.

Dr. Palesch and administrators of the NIH StrokeNet introduced its organization, aims, and responsibilities. The StrokeNet processes of moving clinical trial proposals forward and the logistics of implementing funded clinical trials in the network are also presented. Dr. Toyoda from National Cerebral and Cardiovascular Center, provided a summary of NeCST, the new organized network of stroke investigators throughout Japan for the purpose of conducting stroke clinical research. Dr. Yamamoto, presented the health insurance law and the pharmaceutical affairs law that are tied to the regulatory process for conducting clinical trials in Japan. The US and Japanese investigators exchanged information on some of the current and pending proposals for stroke clinical trials and discussed the feasibility of collaboration on these trials.

Stroke is a major global public health issue, also in both Japan and the US. It would be mutually beneficial for both countries to collaborate on large clinical studies that could yield higher precision and greater confidence in and broader applicability of the study results. The Workshop would enable open dialogue about potential clinical trials that can be jointly conducted in Japan and US. Subsequently, this collaboration would contribute to develop effective treatment & preventive strategies in stroke.

7. Seminar Results and Future Implications:

During the workshop, investigators exchanged information about the opportunities and barriers for conducting collaborative stroke clinical trials, including differences in the culture, the patient care management and regulatory systems, and financial issues. An understanding of special circumstances around “Chiken” and Universal health coverage which prohibiting the combination of insured and uninsured care in Japan was obtained. For future clinical trials, investigators from both countries should be involved from early phase of study planning so as to create feasible protocols which adapts medical systems and regulations in both countries.

In this workshop, the US PIs gave brief presentations of the NIH StrokeNet 4 clinical trials: ARC ADIA by Dr. Kamel at Cornell University, MOST by Dr. Adeoye at University of Cincinnati, PICASSO by Dr. Chimowitz at the Medical University of South Carolina, and SATURN by Dr. Selim at Beth Israel Deaconess Medical Center. Two clinical trial proposals were presented by the Japanese PIs: THAWS by Dr. Koga at NCVS and Cell Therapy for Subacute Stroke by Dr. Taguchi at Foundation for Biomedical Research and Innovation. After the presentation of each proposal, pros and cons of collaboration were dis

cussed, with main focus on the availability of patients.

The expected outcome from this Workshop was to identify specific projects that is considered to be of major clinical importance, and that is feasible to implement in both US and Japan. ARCADIA and PICASSO were most favorably received by the attending investigators as a scientifically important and logistically feasible study to conduct in both countries.

For these projects, it was decided to form small working group consisting of US and Japanese investigators to move the project forward with respect to assessing the required resources and addressing potential obstacles for conducting the collaborative clinical trials between Japan and US, such as differences in clinical guidelines, diagnostic criteria as well as regulatory and financial issues.

Although the PI of the currently ongoing DEFUSE 3 Trial (ClinicalTrials.gov: NCT02586415) was unable to attend the Workshop, he may be open to discussions about the possibility of Japanese sites to participate and financial implications of conducting DEFUSE 3 in Japan will need to be considered as well.

In summary, while the primary focus of the Workshop was on identifying specific projects to collaborate, the Workshop was also beneficial to create the investigators' network in order to establish future projects. The participants of the workshop agreed the need to continue discussions for the future collaborations.

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

In order to organize the collaborative workshop between Japan and US, travel cost (time, expense) can be a problem. To ensure the regular meeting in stroke research planning, remote meeting via internet should be considered. Face to Face meeting, however, is beneficial to encourage open discussion among several stakeholders of clinical trials and we would like to organize another workshop in near future.