January 15, 2008

Opening of the RIKEN Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies

Accelerating Identification of Causative Genes in Primary Immunodeficiencies and Understanding the Pathogenesis of these Diseases

RIKEN (President: Ryoji Noyori) Research Center for Allergy and Immunology ("RCAI", Director: Dr. Masaru Taniguchi) in conjunction with 13 universities including the University of Toyama (President: Tokuso Saito) and Kazusa DNA Research Institute (Director: Dr. Michio Oishi), and with the support of the Jeffrey Modell Foundation (JMF), a United States non-profit organization, on January 15 established the RIKEN Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies1 to promote comprehensive basic research in areas such as identifying causative genes in primary immunodeficiency diseases and understanding their pathological mechanism.

After signing a joint research agreement with 13 universities which specialize in clinical research into primary immunodeficiency diseases (PID) and Kazusa DNA Research Institute, RIKEN RCAI has been accepting the DNA of patients suffering from PID, performing genetic analyses, and building a database containing the analytical results. Recognition of the above research framework led to the establishment of the RIKEN Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies with Dr. Toshitada Takemori (RCAI Coordinator and Group Director) appointed as the center's director.

The opening of the first Jeffrey Modell Diagnostic and Research Center in Japan will focus the collective efforts of domestic organizations specializing in the diagnosis and treatment of PID. The long term goal of this strategy is to enable the prompt diagnosis of PID, allowing early decisions concerning appropriate treatment options, thereby resulting in a direct improvement in the quality life of patients.

Through its cooperation with other Jeffrey Modell Diagnostic and Research Centers, the RIKEN center is expected to become an important scientific base in promoting basic research into the treatment of PID, as well as increasing the understanding of the development of the human immune system.

1. Background

   RIKEN Research Center for Allergy and Immunology (RCAI) has formed a collaboration with 13 universities from all over Japan which belong to the research team for Investigative Research on Primary Immunodeficiency Disease Syndrome,2 ("Ministry of Health, Labour and Welfare Survey Research Team", Research Leader: Dr. Toshio Miyawaki, Director, Faculty of Medicine, University of Toyama), a research program of the Ministry of Health, Labour and Welfare for overcoming intractable diseases. This team, in cooperation with Kazusa DNA Research Institute, has been promoting research on the immunological analyses and identification of causative genes in anonymized3 PID patients (See August 9, 2007 press release).

   RCAI has been in the process of building a general diagnostic and therapeutic database which integrates clinical information and basic analytical data and a system for providing this information to specialists. In addition, to build a database for predicting the onset of pathological conditions and treatment results, Dr. Sujatha Mohan of the Bioinformatics Institute □iFounder and Director: Akhilesh Pandey, an institute in Bangalore India renowned for its achievements in this field, has also been engaging in joint operations through her participation as an RCAI unit leader. Through this platform, RCAI has also succeeded in developing a model mouse where human primary immunodeficiencies have been reproduced using a humanized mouse technology and, utilizing this system, is currently promoting basic research for identifying pathogenetic mechanisms and pathological conditions and discovering curative treatments

2. The current state of PID

   According to a report on PID syndromes compiled by the blood systems investigative research team, it is estimated that about 10,000 people in Japan suffer from PID,. The immune functions of individuals with these disorders are defective due to congenital abnormalities, making these patients susceptible to infection by pathogens such as bacteria, viruses, and fungi. These are extremely serious disorders, which at times are accompanied by malignant tumors at a young age, autoimmune diseases, and allergies. At present more than 120 causative PID genes have been identified, but there are many varieties of PID for which the cause has not yet been determined.

   In cases where the causative gene has been identified, treatments such as haematopoietic stem cell transplants and gene-repair therapy may be

administered, resulting in the cure of some disorders. However, because there is often a delay in diagnosis, there are many cases where patients become afflicted with serious infectious diseases and die as a result. Particularly in cases where the causative gene has not been identified, diagnosis and adequate treatment methods have not been established.

In Japan, cases of PID have been dispersed and no central database, which could amass clinical information or results of genetic analyses, has existed in the past, making it difficult to identify causative genes.

3. The opening of the RIKEN Jeffrey Modell Diagnostic and Research Center for Primary Immunodeficiencies

   The work of the RCAI to date has been highly regarded by the Jeffrey Modell Foundation (JMF), an American NPO established in 1987 to prevent PID and to promote its diagnosis and treatment throughout the world, and a decision was by made by RIKEN and JMF to jointly engage in a project to build a diagnostic research and clinical data platform. The establishment of the RIKEN Jeffrey Modell Research Center for Primary Immunodeficiencies with the cooperation of the RCAI and the Kazusa DNA Research Institute as well as 13 universities across Japan will not only contribute to the study of basic immunology but is also expected to play a major role in speeding up the diagnosis of PID and the selection of more appropriate approaches to treatment.

   To open the new center, the RCAI will hold an inaugural dedication ceremony which will be attended by JMF founders Mr. Fred and Mrs. Vicki Modell, President of CSL Behring LLC Peter Turner, and the Tsubasa no Kai (a Japanese advocacy group for PID patients and their families).

   The RIKEN Jeffrey Modell Immunodeficiency Research Center will begin its work to build a database on immunodeficiency diseases based on a three-year plan. The location of the center will be within RIKEN RCAI and initially is expected to have a staff of seven. In addition to recording PID clinical data, which will be collected from all over Japan, the center will perform immunological diagnostic analyses including DNA and RNA analyses and research on the onset of pathologic conditions in order to build a comprehensive data base. Through this endeavor the center, with the cooperation of universities, will promote research including the development of new diagnostic and therapeutic methods, which it can then provide to PID patients and their physicians.

4. Overview of each company

(1) Jeffrey Modell Foundation（JMF）

Fred and Vicki Modell established the Jeffrey Modell Foundation in commemoration of their son Jeffrey, who died at the age of 15 due to pneumonia resulting from PID. The objective of the foundation is to establish early appropriate diagnosis and effective methods of treatment for PID. In addition to the center established in Japan, 36 Jeffrey Modell Diagnostic and Research Centers have been established in locations all over the world. Location: New York

Established: 1987 (Fred and Vicki Modell serve as founders.)

(2) CSL Behring LLC

CSL Behring is one of the main sponsors of the JMF and is a global leader in blood plasma products made by extracting and purifying proteins found in blood plasma. The founding of the company dates back to 1904, when Behringwerke company was established by Dr. Emil von Behring of Germany, who won the first Nobel Prize for Physiology or Medicine. Headquarters: Pennsylvania, United States

President: Peter Turner

(3) Kazusa DNA Research Institute

A research institute founded in 1991, Kazusa DNA Research Institute promotes the creation of new business areas, the upgrading of industrial structures, and the development of scientific technology. Its objectives are to contribute to the welfare of humanity through analytical research into the structure of DNA, which houses all genetic material, research relating to the analytical technology of DNA structure, research relating to the functions of DNA and its applications, and the collection and provision of data relating to DNA.

Location: Kisarazu, Chiba

Director: Dr. Michio Oishi

(4) Kazusa DNA Research Institute

Tsubasa-no Kai began as an advocacy group for PID patients and their families in November 1991 after one mother of a PID patient wrote into a newspaper appealing to others like herself associated with the same disease with whom she

could share conversation. Providing mutual support and collective strength, the group has continued its activities aimed at seeking society's understanding of PID syndromes and improving and further developing systems for research and treatment and the social security system in Japan.
Representative: Ms. Keiko Nagai

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Notes (supplementary information):

1. Jeffrey Modell Diagnostic and Research Centers
   Altogether 36 centers have been established in locations all over the world. Stars on the map below mark their locations.

2. Investigative research team for Investigative Research on Primary Immunodeficiency Disease Syndrome, a research program of the Ministry of Health, Labour and Welfare for overcoming intractable diseases
   Dr. Toshio Miyawaki, Director of the Medical Studies, University of Toyama is the team leader.
   At present, the following 13 universities are participating as members of the research investigation group in the joint research project in addition to RCAI and Kazusa DNA Research Institute: University of Miyazaki, Gifu University, Nagoya

University, Kyushu University, Hiroshima University, Kanazawa University, University of Toyama, Tokyo Medical & Dental University, Tohoku University, Hokkaido University, Kyoto University, Shinshu University, National Defense Medical College.

3. Anonymization of patients

   Anonymization is the process whereby any and all information that might lead to the identity of an individual such as the full name, address, telephone number, hospital patient ID, etc. is eliminated

http://www.info4pi.org/referralcenter/index.cfm?section=referralcenter&content=jmfcenters&CFID=25683978&CFTOKEN=40555336