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TOHOKU MEDICAL MEGABANK ORGANIZATION

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Tohoku University
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High-accuracy whole genome sequencing of 1,000 healthy Japanese people: A base to search for the causes of diseases ~Collection of over 15 million new gene polymorphisms~

The Tohoku University Tohoku Medical Megabank Organization (ToMMo) has completed a whole genome sequencing of **1,000** healthy participants in the cohort studies of the Tohoku Medical Megabank project. This is the world's first high-accuracy whole genome sequencing of **1,000** people of the same nationality using independent facilities and equipment and identical protocols.

The sequencing has also presumed the existence of over **15 million** new gene polymorphisms. This information is anticipated to have a range of applications as a broad foundation for research in medical sciences from now on, such as through its application as a reference sequence in extracting the disease-associated genes of Japanese people.

【Background】

Following the completion of sequencing human genomes as a result of the 2003 International Consortium and other such initiatives, rapid progress in genome sequencing technology has given rise to an era where sequencing human genomes is an achievable reality. However as of the present date of November 2013, there is still no whole genome sequencing done to serve as a standard for the Japanese people.

The whole genome sequencing reported thus far has been a mixture of information on genome sequencing of people from several dozen ethnic groups and residents of a community in a foreign country, and so forth. Also, the genome sequencing of Japanese people to date has been a whole genome sequencing on an individual level, and a partial sequencing (only on sections that make proteins) at the group level.

【Method】

The Tohoku Medical Megabank project is carrying out large-scale cohort studies on a healthy group of Tohoku residents and building a biobank based on these studies. Using next-generation sequencers, the project has also conducted a whole genome sequencing on healthy people from some of the biological samples provided for these studies. This project is characterized by its use of the same facilities, equipment and protocols to obtain high-accuracy data to a depth of 30x.

【Current findings】

■ Completion of a whole genome sequencing of 1000 people ~ Creating a high-accuracy ToMMo whole genome reference panel

The Tohoku Medical Megabank Organization (ToMMo) has successfully completed the whole genome sequencing of 1,000 healthy people in half a year since the start of the cohort studies. This sequencing has enabled the detection of genome polymorphism in a healthy group of Japanese people, including persons that have a 5% frequency of rare mutations, as well as the estimation of frequency within the group.

These findings will form the foundation of medical sciences research in Japan from now on. The ToMMo Whole Genome Reference Panel will analyze the genes of people with diseases, and subsequently make this data widely available for use in medical and life sciences research as standard reference genomes. This data may also be used as a base for developing medicines and else, and is anticipated to play a crucial role in realizing next-generation medicine, such as preventative medicine and personalized medicine, through its application as a reference sequence when searching for disease-associated genes.

■ Collection of over **15 million** new gene polymorphisms

This is the first time that information has been obtained on the frequency and diversity of sequences seen in Japanese people for the entire region of human genomes. This sequencing searched for rare polymorphisms with a 5% frequency, which made it possible to estimate the existence of over 15 million novel gene polymorphisms not present in databases thus far. The data is characterized by a large number of polymorphisms with a rare frequency (rare variants) in the newly discovered polymorphisms.

【Significance】

The ToMMo Whole Genome Reference Panel is a reference genome sequence from Japanese people including those with polymorphisms, and can be used as a database of information on sequence variations and their frequency. The Panel will be integrated with data on blood and urine analysis as well as medical records and information on lifestyle habits, and will be built to serve as a database with a wide range of applications in research in Japan targeting next

generation medicine.

It is assumed that the over 15 million polymorphisms collected on this occasion include those with disease-causing mutations. The Tohoku University Tohoku Medical Megabank Organization will conduct further whole genome sequencing on the participants of cohort studies, and develop an optimal high-accuracy custom array for Japanese people, while also continuing to search for polymorphisms associated with disease susceptibility (disease causing) and working towards realizing personalized prevention and medicine. These current findings are a significant step in developing this array.

【Reference】

<Samples for genome sequencing>

This study was conducted based on biological samples provided from participants of cohort studies currently running in Miyagi Prefecture and Iwate Prefecture (Community Resident Cohort Study and Three-Generation Cohort Study). The Community Resident Cohort Study that started this May is a long-term health study aiming for 80,000 participants, who are adult residents (20 years or above) of Miyagi Prefecture and Iwate Prefecture. The Three-Generation Cohort Study (on expecting mothers and their families) that commenced this September is also aiming for 70,000 participants.

The objective of this project and study was explained to the residents in both cohort studies. Upon receiving the residents' consent, their blood, urine, and other health survey results, as well as information from questionnaires, were obtained. Over 10,000 residents have already provided cooperation for both the Three-Generation Cohort Study and Community Resident Cohort Study.

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