Title of Project : Exploring molecular basis for brain diseases based on personal genomics

Term of Project : FY2010-2014

Shoji Tsuji
(The University of Tokyo Hospital, Professor)

【Purpose of the Research Project】

The mission of this Scientific Research on Innovative Areas, "Exploring molecular basis for brain diseases based on personal genomics" is to establish the new research paradigm to explore molecular basis of brain diseases based on personal genomics. This projects consists of three areas; 1. Development of technologies to enable personal genome analyses with high accuracy, 2. Development of "cutting-edge" informatics for analyses of personal genome, and 3. Identification of molecular basis of brain diseases including Alzheimer disease, Parkinson disease, amyotrophic lateral sclerosis, spinocerebellar degeneration and schizophrenia based on personal genome analyses. Integration of the above three disciplines will be the key for the innovative research fields.

Genome-wide association studies (GWAS) employing common SNPs with minor allele frequency usually larger than 0.05 have recently revealed numerous variants associated with diseases. Such variants, however, usually have limited effect sizes, hence we are yet to understand the entire molecular basis for brain disease. Previous clinical genetic analyses suggest involvement of strong genetic factors. To identify the "missing heritability", we need to focus on rarer variants based on comprehensive personal genome analyses. Given the enormous information obtained by next-gen sequencers, analyses of personal genome are a challenging mission in terms of sequencing, informatics and genetics. Integrating the three disciplines of sequencing, informatics and genetics, this project will explore the molecular basis of brain diseases based on personal genomics.

【Content of the Research Project】

The project consists of 3 parts.

A01. Development of technologies for personal genome analyses
A02. Identification of molecular basis of brain diseases
A03. Genome Informatics

A01 focuses on development of various technologies for personal genome analyses, which are essential for application of next generation sequencers for identifying molecular basis of brain diseases. A02 will apply technologies of next generation sequencers for exploring molecular basis of Alzheimer disease, Parkinson disease, amyotrophic lateral sclerosis (ALS), and schizophrenia. A03 will focus on genome informatics to process massive amount of data generated by next generation sequencers and, furthermore, to identify variations involved in the pathogenesis of brain diseases.

【Expected Research Achievements】

The project will apply massively parallel sequencing technologies of next generation sequencers to identify variations involved in the pathogenesis of brain diseases based on common disease-multiple rare variants hypothesis. Identification of these disease-related alleles will contribute to better understand the molecular mechanisms of the brain diseases, and, furthermore, to develop new therapeutic strategies for the brain diseases.

【Key Words】

next generation sequencers, personal genome, genome informatics, brain diseases, common disease-multiple rare variants hypothesis.

【Homepage Address】

http://www.personal-genome.jp/en/