



Invitation to Seminar Talk

Endophenotype in the brain: A key concept for understanding the relationships between genes and behavior

Tsuyoshi Miyakawa

Division of Systems Medical Science, Fujita Health University

Host: Ryuichi Shigemoto

Genetic studies have revealed millions of polymorphisms in human genome, and theoretically, these polymorphisms can have infinite possible combinations. However, it is well-accepted that the human personality can be represented by a small number of traits and that extreme forms of personalities can be categorized into a limited number of psychiatric disorders. An interesting question is: how, despite such huge genomic variability, are there distinct categories of individuals showing similar behavioral patterns? We have been investigating the relationships between genes and behaviors by using a comprehensive behavioral test battery in genetically engineered mice. This test battery covers a broad range of behavioral domains, such as sensorimotor functions, emotionality, and cognition. So far, we have subjected more than 180 different strains of mutant mice to this test battery. Among them, α calcium/calmodulin-dependent protein kinase II heterozygous-knockout (α -CaMKII HKO) mice show several strong behavioral phenotypes, such as hyper-locomotion, abnormalities in social behavior, and a working memory deficit. Detailed molecular and electrophysiological analyses revealed that almost all neurons in their dentate gyrus are in a pseudo-immature status; we named this phenotype "immature dentate gyrus (iDG)." Surprisingly, this phenotype is observed in several other strains of mutant mice showing behavioral phenotypes similar to that of α -CaMKII HKO mice as well as in wild-type mice subjected to chronic anti-depressant treatment or having epileptic seizures. Moreover, molecular expression analyses of post-mortem brains suggest that the iDG phenotype exists in certain populations of patients with psychiatric disorders, such as schizophrenia and bipolar disorder. The iDG phenotype might be an intermediate phenotype or an endophenotype onto which many unique genetic and non-genetic features converge and through which a similar pattern of behavioral traits emerges. By using iDG as an example, I will discuss the impact of "endophenotype of the brain" concept on understanding the pathways linking genes to behavior and on investigations into the pathogenesis and pathophysiology of neuropsychiatric disorders.

Thursday, June 21, 2018, 4.00pm
Mondi 3, Central Building, 1st Floor