The 10th Brain Science Seminar

Molecular Basis of Normal and Disordered Brain Development: mouse cerebellar development transcriptome project, CAPS2-mdeiated BDNF secretion, and susceptibility to developmental disorders

Teiichi Furuichi, PhD

RIKEN Brain Science Institute Team Leader

Date: July 10th, ２００９ (Friday)
Time: １６：００ ～ １７:００

Place: Daigaku Kaikan 2F meeting room

Please join the get-together with **speaker** after the seminar (fee 300 yen; students free)

Inquiries: Takafumi Sakai (TEL 4308)

We will have the Brain Science Seminar once a month. Come out and join us.

セミナー要旨 **Abstract**

In the post-genomic sequencing era, genome-scale and genome-based approaches are important for comprehensive understanding the molecular mechanisms of brain development, function, and diseases. Our laboratory aims to elucidate the molecular mechanisms underlying normal brain development and its disorders by systematic identification and functional analyses of brain development genes. We focus on the genetic design for mouse cerebellar circuit development as a model system and have characterized the transcriptomic basis of mouse cerebellar circuit development by generating the Cerebellar Development Transcriptome Database (CDT-DB, http://www.cdtdb.brain.riken.jp). The CDT-DB project has opened a new door to elucidating cerebellar development from a transcriptomic standpoint and indicates that cerebellar circuit development is programmed by thousands of different genes that exhibit differential spatiotemporal expression patterns in the developing brain. In addition, we have been able to identify many brain development genes by CDT-DB mining. Deficits in the expression or function of brain development genes are likely to affect the development of neuronal circuits and may cause impaired brain function and behavior. We found that Ca2+-dependent activator protein for secretion 2 (CAPS2), one of the genes we identified, is involved in release of brain-derived neurotrophic factor (BDNF) and that CAPS2 knockout mice not only show reduced BDNF release activity but also exhibit autistic-like behavioral phenotypes such as decreased social interaction. Moreover, we identified increased expression of a rare splicing variant, which is never transported to axons, as well as single-nucleotide polymorphisms in some patients with autism, a developmental disorder characterized by qualitative impairments in social interactions and communications and by restricted interests and repetitive behavior. Taken together, we hypothesize that the disturbance of CAPS2-mediated BDNF release patterns is responsible for the onset of autism.