CDB SEMINAR

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15:00~16:00 A7F CDB Conference Room

Genetic analysis of neuronal migration in cerebral cortex

Summary

Haploinsufficiency of 17p13.3 results in the human neuronal migration disorders, isolated lissencephaly sequence (ILS) and the more severe Miller-Dieker Syndrome (MDS). ILS results from only dysfunction of *Lis1*. On the other hand, MDS patients have larger deletion of 17p13.3 region involves *Lis1* and other genes, but it has been unknown which genes in 17p13.3 region are responsible for more severe migration defect in MDS patients. Here we report that *14-3-3ε* deficient mice show neuronal migration defects in cerebral cortex and 14-3-3ε protein protects phosphorylated NDEL1 from PP2A-mediated dephosphorylation. *Lis1/14-3-3ε* double heterozygotes indicate more severe migration defects than single heterozygotes. These data strongly suggest that 14-3-3ε is important for the neuronal migration in cerebral cortex and is one of responsible genes for MDS. In addition, the analysis of *Ndel1* deficient mice show that the signaling pathway involves LIS1, NDELl, 14-3-3ε and the effector molecule, cytoplasmic dynein, is crucial for neuronal migration. In this signaling pathway, the phosphorylation and dephosphorylation of NDELl play a pivotal role and phosphorylated-NDEL1 regulates the localization of the microtubule severing protein, Katanin p60.

Taken together, these studies provide new findings that LIS11, NDELl1, 14-3-3ε, Katanin p60 and cytoplasmic dynein function in the same signaling pathway and play an important role for neuronal migration through regulating microtubule array.

In this seminar, I present the following data which we have found.

(1) Analysis of *14-3-3ε* deficient mouse
(2) Analysis of *Ndel1* deficient mouse

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