

博士論文(要約)

**The Molecular Cell Biology of KIF4 in the Brain: Analysis of
KIF4 Mutation Mouse**

(脳神経に於ける KIF4 の分子細胞生物学的研究: KIF4 変異マ
ウスの解析)

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Abstract

Kinesin superfamily proteins (KIFs) are the molecular motors that play critical roles in intracellular cargo transport, cellular morphogenesis, neuronal plasticity, cell fate, and so on. The superfamily contains 45 *Kif* genes in mouse, and the *in vivo* studies showed loss of their functions induced various disorders and even mortality. In this thesis, I focused on a chromokinesin, KIF4. A point mutation of the KIF4 is reported to be related to the neurological disorders such as developmental delay, intellectual disability, and epilepsy. Recently, it was reported that the cell division was regulated by the phosphorylation state of KIF4 and that the KIF4 is involved in controlling the midzone formation. Another publication described that KIF4 has a role to modulate cell apoptosis through binding/releasing to its binding partner PARP1. However, the role of KIF4 in brain functions and its related molecular mechanisms are still to be elucidated. In this present study, I succeeded in demonstrating the KIF4 mutant (*Kif4^{Mut/Y}*) mouse as a patient mimic model, which exhibited developmental delay, intellectual disability, and epilepsy. I have successfully demonstrated the association of dysfunctional KIF4 with the abnormal phenotype of neurons through cell biological and *in vivo* experiments. Based on the results, I want to address that KIF4 is engaged in the basic mechanism regulating epilepsy.