主　論　文　要　旨

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主 論 文 題 名

Phenotypic Insights Into Anti-IgLON5 Disease in IgLON5-Deficient Mice
（IgLON5ノックアウトマウスの解析によるIgLON5抗体関連疾患に関する研究）

（内 容 の 要 旨）

Anti-IgLON5 disease is an autoimmune neurodegenerative disorder which targets IgLON5. It has various phenotypes, including sleep and movement disorders, as well as tau pathology. Although it is known that the disease is related to IgLON5, little is known about the function of IgLON5. It is also unclear that whether the disease is caused by loss of function, activation of IgLON5 or inflammation-induced neuronal damage. Therefore, we generated IgLON5 knock-out mouse to investigate the function of IgLON5, and hence its role in anti-IgLON5 disease.

We subjected the mice to several behavioral tests. Histological analysis was also performed to determine whether tau aggregated in the mutant P301S tau transgenic background.

IgLON5-/- mice performed poorly in the wire hang test and the rotarod test, indicating poor motor function. The IgLON5-/- mice also showed reduced anxiety-like behavior and/or hyperactivity in behavioral tests. Moreover, IgLON5-/- mice showed poorer remote memory in the contextual fear conditioning test. However, IgLON5-/- mice did not show sleep disturbances in electroencephalogram or tau deposits in a mouse model of tauopathy.

Our results suggest that IgLON5 is related with hyperactivity/lower anxiety, poor motor performance and impaired contextual fear memory. Among the symptoms of the disease, loss of IgLON5 may be related to several phenotypes such as psychiatry and motor function; however, important phenotypes such as sleep disturbance and tau aggregation may be caused by gain of function of IgLON5 or inflammation-induced neuronal damage.