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発表題目（※学会発表の場合のみ記載）	Nwd2 欠損による多動と社会行動異常の発現機構の解析

発表の概要と成果（抄録を公開している URL がある場合、「概要・成果」を記載した上で、URL を末尾に記してください。また、抄録 PDF は別途ご提出ください。なお、抄録 PDF は Web 上には公開されません。）

上記学会においてポスター形式にて発表を行った。

以下 Abstract を示す。

The habenula is a highly conserved brain structure across vertebrates, serving as a control center for monoamine neurons that regulate the firing of serotonin and dopamine neurons. Recent studies have implicated habenular dysfunction in the pathophysiology of mood disorders. However, the molecular mechanisms underlying the development and functional regulation of the habenula remain largely unclear. We previously demonstrated that the NACHT and WD repeat domain-containing protein 1 (Nwd1), a member of the STAND family, contributes to de novo purine biosynthesis during mouse brain development. Here, we identified Nwd2, a paralog of Nwd1, which is predominantly expressed in neurons of the medial habenular nucleus (MH). Through yeast two-hybrid screening, we identified Kv channel-interacting protein 1a (Kcnip1), also enriched in medial habenular neurons, as a potential binding partner of Nwd2. To investigate the in vivo role of Nwd2, we generated Nwd2 knockout mice using CRISPR-Cas9 genome editing. These mice exhibited hyperactivity with significantly increased total distance traveled in the open field test, and showed heightened social dominance in the social interaction assays. In contrast, no significant differences were observed in anxiety or depression-related behaviors compared to wild-type controls. Notably, both mRNA and protein levels of Kcnip1 were elevated in the brains of Nwd2-deficient mice. This increase may enhance neuronal excitability in the MH, contributing to hyperactivity and behavioral abnormalities. These findings suggest that Nwd2-deficient mice represent a new model for hyperactive behavioral disorders, including attention-deficit/hyperactivity disorder (ADHD).

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