高次脳機能学セミナー
Advanced Brain Functions Seminar

Pogz deficiency leads to abnormal behavior, transcription dysregulation and impaired cerebellar physiology

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Genes implicated in autism spectrum disorder (ASD) are enriched with chromatin regulators, but the mechanisms leading to the abnormal behavior and cognition are still unclear. Animal models are crucial for studying the effects of mutations on brain function and behavior. We generated conditional knockout mice with brain-specific mutation in Pogz, a heterochromatin regulator recurrently mutated in ASD and other neurodevelopmental disorders, and demonstrated that these mice display phenotypes that resemble the human condition. Pogz deficiency led to smaller brain, growth impairment, motor learning deficits, and increased social interactions that mimic the human overly friendly phenotype. At the molecular level, reporter assay indicated that POGZ functions as a negative regulator of transcription through its interaction with HP1 proteins. In accordance, we found a significant upregulation of gene expression, most notably in the cerebellum. Furthermore, Pogz deficiency was associated with a significant reduction in the firing frequency of simple and complex spikes in cerebellar Purkinje cells with no changes in their intrinsic properties. Overall, our findings support a mechanism linking heterochromatin dysregulation to cerebellar circuit dysfunction and to motor and social abnormalities in ASD.

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16:00~17:00
蛋白質研究所1階講堂
(Lecture room @IPR 1F)

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