

**Deletion of PHD finger protein 24 (Phf24) causes elevated seizure sensitivity, emotional defects and cognitive impairment in rats.**

Naofumi Kunisawa<sup>1</sup>, Tadao Serikawa<sup>1,2</sup>, Masaki Kato<sup>1</sup>, Higor Alves Iha<sup>1</sup>, Hisao Nishikawa<sup>3</sup>, Yu Shirakawa<sup>3</sup>, Masashi Sasa<sup>4</sup>, Yukihiro Ohno<sup>1</sup>

<sup>1</sup>Dept. Pharmacol., Osaka Univ. Pharm. Sci., <sup>2</sup>Inst. Lab. Anim., Kyoto Univ., <sup>3</sup>KAC Co. Ltd., <sup>4</sup>Nagisa Clinic.

PHD finger protein 24 (Phf24), also known as G  $\alpha$  i-interacting protein (GINIP), was found to be absent in Noda epileptic rat (NER) (Behav. Genet., 47, 609, 2017). In this study, to explore the role of Phf24 in modulating CNS functions, we analyzed behavioral characteristics of Phf24-knockout (KO) rats, especially changes in seizure sensitivity, emotional responses and cognitive functions. Phf24-KO rats showed higher intensity and incidence of seizures induced by pentylenetetrazole (PTZ) and pilocarpine than F344 rats (control). Furthermore, PTZ-induced kindling was significantly facilitated in Phf24-KO rats. Anxiety-like behavior and cognitive function were analyzed by elevated plus maze and Morris water maze tests, respectively. Phf24-KO rats at old age exhibited reduced anxiety (impulsive) behaviors in the elevated plus-maze test compared with F344 (control) rats. In addition, Phf24-KO rats showed impaired learning behaviors in Morris water maze test. The memory retention ability was also disrupted in Phf24-KO rats. These results suggest that Phf24 negatively regulates epileptogenesis (seizure induction and development) and plays important roles in controlling emotion and cognition.