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## Generation and characterization of brain-specific UBIAD1-deficient mice using a nestin promoterdriven cre/loxP strategy

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UBIAD1is a key enzyme of vitamin K2/menaquinone-4 (MK-4) biosynthesis in mammals. Both MK-4 and UBIAD1 distributeatrelatively high levels in brain. However, the roles of UBIAD1and MK-4 in brain functionare not fully understood. We generated mice completely lacking *ubiad1*, a homolog of human UBIAD1 by gene targeting; however, they were embryonic lethal. Therefore, to investigate the role of *ubiad1* in brain, we conducted a conditional, region-specific, genetic approach to target *ubiad1* using the Cre/loxP strategy with a nestin promoter-driven cre transgenic mouse line that will make possible to induce recombination in the central nervous system (CNS). The resulting *ubiad1* conditional knockout (CKO) mice were viable, but the size of *ubiad1*-CKO mice was significantly smaller than wild-type littermates. UBIAD1 expression and MK-4 concentration of *ubiad1*-CKO mice were severely decreased in all brainregions. Ubiad1-CKO mice can be useful for analysis of neuronal function of *ubiad1* and MK-4. To address the impact of loss of UBIAD1 signaling in brain, we subjected*ubiad1*-CKO mice to multiple behavioral tests. In the open field test, activity levels were higher in *ubiad1*-CKO mice than wild-type (WT) littermate. In the Y-maze test, *ubiad1*-CKO mice displayed a significantly lower working memory index but higher locomotion activity compared to their WT littermates. Ubiad-CKO mice exhibit decreased anxiety-like behavior. These results indicate that UBIAD1/*ubiad1* or MK-4 may play a critical role in the CNS. Future studies are required to clarify the neurochemical functions of UBIAD1 and MK-4 in brain.

## **Biography**

Kimie Nakagawa received a Ph.D. in Pharmaceutical Sciences from Kobe Pharmaceutical University in 2006 and she is serving as an Associate Professor of the Department of Hygienic Sciences at Kobe Pharmaceutical University since 2012. She has made significant contributions to the identification and characterization of the vitamin K2/MK-4 biosynthetic enzyme, UBIAD1. Her major interests are to generate various tissue-specific UBIAD1-deficient mice in order to explore the physiological and pathophysiological roles of UBIAD1.

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