

Orexin/hypocretin neurons specific control of gene expression reveals its physiological role *in vivo*

Orexin/hypocretin is a neuropeptide produced in neurons which are sparsely distributed in the lateral hypothalamic area (orexin neurons). Although specific ablation of orexin neurons results in sleep disorder narcolepsy, its physiological role on the regulation of sleep/wakefulness has not been completely understood. To reveal this, we generated transgenic mice in which orexin neurons specifically express tetracycline transactivator protein (tTA) (orexin-tTA mice). These mice enable to control the expression of specific gene in the orexin neurons *in vivo* since tTA induces gene expression to bind tetracycline response element (TetO). To confirm specific regulation of gene expression in the orexin neurons by tTA, orexin-tTA mice were bred with TetO red fluorescent protein (RFP) mice. In orexin-tTA; TetO RFP double transgenic mice brain, 85% of orexin-immunoreactive (ir) neurons expressed RFP. No ectopic expression of RFP other than orexin-ir neurons was observed throughout the brain. This result suggested that orexin-tTA mice enable to control the expression of gene in the orexin neurons just to breed with various TetO mice. Additionally gene expression could be temporally controlled since tTA lost its function to induce gene expression in the presence of doxycycline (DOX). Therefore, application of DOX in chow inhibits gene expression induced by tTA, but remove DOX from chow induces gene expression. These results suggest that orexin-tTA mice are useful tool to study its physiological role *in vivo*.