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# SIK family regulates sleep/wakefulness in mice

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Sleep is a behavior conserved from invertebrates to vertebrates, and tightly regulated in a homeostatic manner. The molecular and cellular mechanism determining the amount of sleep remains unknown. We established Sleepy mutant pedigrees through EEG/EMG-based screening of randomly mutagenized mice. The causative mutation for Sleepy mutant was a splicing mutation of Sik3 gene. The mutant SIK3 protein lacks a region containing a well-conserved protein kinase A-phosphorylated site, S551. We further investigated the molecular basis of sleep need using quantitative phosphoproteomic analysis of the sleep-deprived and Sik3 mutant mouse. The brain proteome of Sik3 mutant mice exhibits hyperphosphorylation, similar to that seen in that of sleep-deprived mice. The substitution of S551 into alanine residue resulted in a decreased time spent in wakefulness as original Sleepy mutant mice. I will present several on-going projects.