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CaMKII-dependent control of sleep duration in mammals

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The sleep-wake cycle is regulated through circadian clocks that drive the near-24 hrs rhythmicity of many physiological processes and sleep homeostasis that determines the sleep duration required per day. The discovery of core circadian clock components was initiated by the finding of *period* gene that controls the clock speed bidirectionally. On the other hand, it is still unknown whether there is a single gene that controls sleep duration bidirectionally. We focused on the role of Ca2+/calmodulin-dependent kinase II (CaMKII) in the regulation of sleep duration. We reported this enzyme as a sleep-promoting kinase by showing that the knock-out of *Camk2a* or *Camk2b* results in the significant reduction of sleep duration in mice (Tatsuki et al. Neuron 2016). CaMKII α/β dodecamer is activated by Ca2+/CaM and undergoes a large scale conformational change. The conformational change exposing the kinase domain affects the protein-protein interaction between CaMKII α/β and other binding partners. The exposure of the kinase domain also triggers the auto-phosphorylation that stimulates or suppresses the kinase activity of CaMKII α/β, depending on the phosphorylation sites. In this presentation, we will introduce our recent study aiming to understand what biochemical property of CaMKII α/β is most prominent to control the sleep duration and to create a gain-of-function mutant of CaMKII α/β that can, contrary to the phenotype of *Camk2a/b* knock-out, lengthen the sleep duration.