Centre for Biological Timing
Seminar

1-2 pm, Friday 12th May, 2023. Smith Lecture Theater

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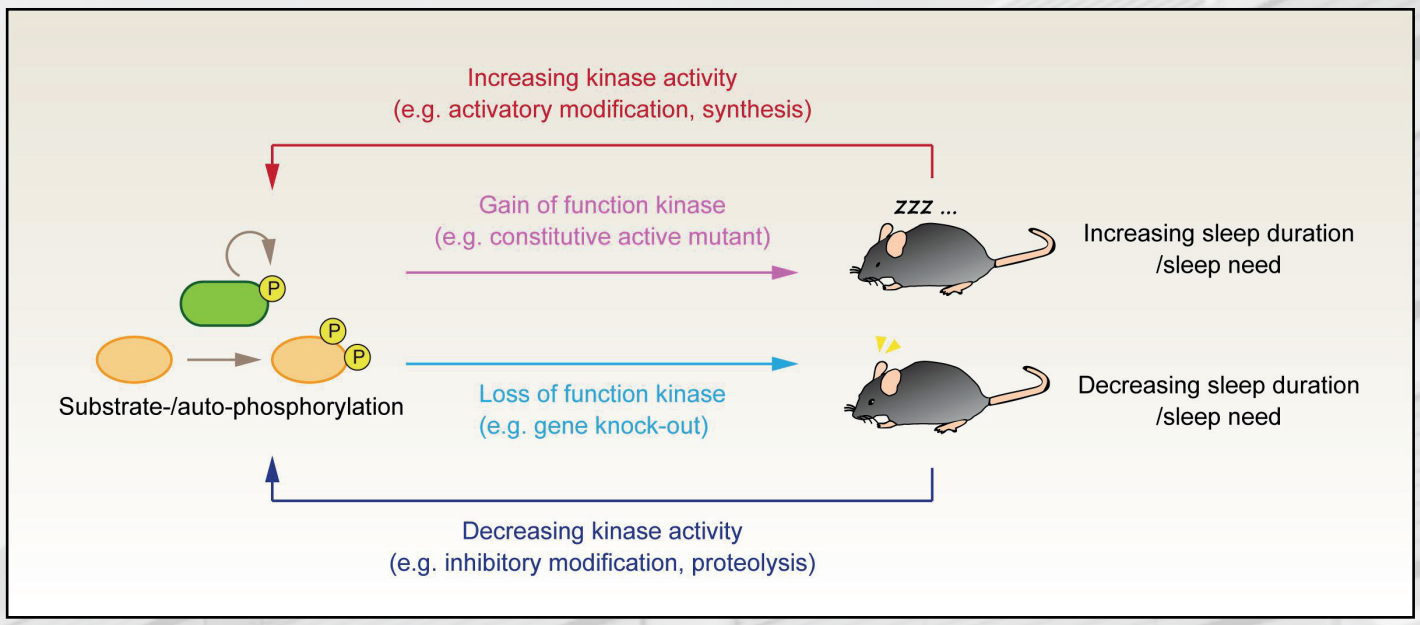
Towards Systems Biology of Human Sleep/Wake Cycles: Phosphorylation Hypothesis of Sleep



The detailed molecular and cellular mechanisms underlying NREM and REM sleep in mammals are elusive. To address these challenges, we constructed a mathematical model, Averaged Neuron Model (AN Model), which recapitulates the electrophysiological characteristics of the slow-wave sleep. Comprehensive bifurcation analysis predicted that a Ca2+-dependent hyperpolarization pathway may play a role in slow-wave sleep. To experimentally validate this prediction, we generate and analyze 26 KO mice, and found that impaired Ca2+-dependent K+ channels, voltage-gated Ca2+ channels, or Ca2+/calmodulin-dependent kinases (Camk2a and Camk2b) decrease sleep duration, while impaired plasma membrane Ca2+ ATPase increases sleep duration. Genetical and pharmacological intervention and whole-brain imaging validated that impaired NMDA receptors reduce sleep duration and directly increase the excitability of cells. Based on these results, we propose phosphorylation hypothesis of sleep that phosphorylation-dependent regulation of Ca2+-dependent hyperpolarization pathway underlies the regulation of sleep duration in mammals. In this talk, I will also present how we identify essential genes (Chrm1 and Chrm3) in REM sleep regulation as well as new projects on human sleep/wake cycle measurements for next-generation sleep medicine and on whole-body/brain profiling of cells in mammals.