

東京大学大学院理学系研究科 生物化学専攻／GCOE セミナー

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演題：BioClock: From Molecule to Behavior

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Central clock resides in the suprachiasmatic nucleus (SCN) of the hypothalamus. Recent studies using genetic and molecular approaches have disclosed fundamental features of molecular circadian clockwork and the network of transcription-translation feedback loops of clock machinery functions not only in the SCN, but also in peripheral clocks in most peripheral tissues. I will discuss our recent findings with two different topics: 1) Adrenal peripheral clock: Adrenal gland has its own intrinsic clock and the peripheral clockwork is tightly linked to steroidogenesis by a StAR(steroidogenic acute regulatory protein). Examination with transgenic mice harboring the adrenal-specific disruption of clock machinery shows that the adrenal clock controls rhythmic StAR expression and glucocorticoid production. The adrenal local clock appears to play an important role in harmonizing circadian physiology and behavior. 2) Ultradian rhythm of GnRH (Gonadotropin-Releasing Hormone) gene expression: Although pulsatile GnRH secretion from the hypothalamus is reported to be associated with the oscillatory GnRH gene expression, the cellular and molecular mechanism underlying the so-called ‘GnRH pulse generator’ remains to be explored. We generated transgenic mice carrying the rat GnRH promoter-driven destabilized luciferase reporter (GnRH-dsLuc), and monitored the GnRH promoter activity in individual GnRH neurons derived from postnatal hypothalamic slices by using a real-time bioluminescence recording system. GnRH gene expression is quite irregular, but shows robust ultradian oscillation in a cell-intrinsic manner. *In vitro* administration of kisspeptin, a potent neuropeptide of GnRH neurons amplifies pulsatile GnRH gene expression by augmenting the pulse amplitude. More importantly, rhythmic treatment of the kisspeptin synchronizes the regular oscillatory GnRH gene expression in the hypothalamus.

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