

東京大学グローバル COE 『統合生命学』 特別セミナー

東京大学 大学院理学系研究科 生物化専攻セミナー

演者：Dr. Steven A. Brown

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演題：Layers of Clocks:

Keeping Cellular Time in Different Frames

日時：平成 21 年 3 月 6 日 (金) 16:00 ~ 17:30

場所：東京大学理学部 旧 1 号館 3 階 350 号室

Human behavior is influenced by many genetic and environmental factors; it is therefore often difficult to study by reductionist approaches. However, in rare cases it can be linked directly to a biological process that can be understood at the cellular level. The circadian clock is one such instance: physiologically, it affects diverse processes such as sleep-wake time, activity patterns, body temperature, cardiac and respiratory rate, renal flow, and digestion. Molecularly, it is present in most cells of the body and modulates the transcription of about ten percent of our genes. Although this clock tells time at a daily level, recent research from my laboratory and others suggests that its mechanism is connected to biological clocks with other metrics. By directly controlling the transcription of some cell cycle genes, the circadian clock likely gates cell division, perhaps in order to segregate DNA replication from catabolic processes. Through shared components, it can be coordinately regulated with cellular senescence pathways. Finally, circadian clock function is itself governed by individual genetic differences and physiology, which explain its different behavior in ageing humans, and thus its subjection to each of our overall “lifetime” clocks. Together, this delicate interplay provides a mechanistic explanation for physiological timing in several frames.

Brown, S.A. *et al.* (2008) Molecular insights into Human Daily Behavior. *Proc. Natl. Acad. Sci. USA*, **105**:1602-1607.

Brown, S.A. *et al.* (2005) PERIOD1-associated proteins modulate the negative limb of the mammalian circadian oscillator. *Science* **308**:693-6.

哺乳類の概日時計は、中枢に存在する主振動体と末梢組織に存在する従属振動体群から構成されるが、Brown 博士は末梢組織である線維芽細胞の解析を通じて、ヒトの中枢組織における時計発振機構の理解を目指している。参考文献において Brown 博士はヒト線維芽細胞に内在する時計を可視化し、リアルタイムで観察する実験系を構築した。さらに、線維芽細胞における時計発振の性質が、ヒトの生活リズムの特徴をも反映していることを明らかにした。今回のセミナーでは、これらの成果と最新の研究について Brown 博士に講演していただく。

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