



# 第 332 回 つくば分子生命科学セミナー

**TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR**

**演題 : THE CIRCADIAN CLOCK - DNA DAMAGE RESPONSE - CELL CYCLE CONNECTION**

**演者 : Gijsbertus T.J. van der Horst 先生**

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日時 : 2011 年 10 月 6 日 (木) 16:00-17:30

会場 : 医学学群棟 4A321

**要旨 :** Most organisms have developed an internal clock that drives circadian rhythms in metabolism, physiology and behavior, and allows them to optimally anticipate the momentum of the day. At the basis of circadian timekeeping lies a molecular oscillator, made up of auto-regulatory transcription/translation feedback loops, in which cyclically expressed clock gene products regulate their own expression with an approximate (circa) 24-hour (dies) periodicity. The mammalian circadian system consists of a light-entrainable master oscillator in the neurons of the suprachiasmatic nucleus (SCN) in the basal hypothalamus, and light-irresponsive peripheral oscillators in the cells of virtually all other tissues.

The importance of the circadian clock is well illustrated by the fact that some ten percent of the liver transcriptome displays robust mRNA cycling. Energy metabolism and xenobiotic metabolism are prominently controlled by the circadian clock, implying that the sensitivity of tissues to geno- and cytotoxic agents may well depend on the phase of the circadian clock. Moreover, the circadian system has been associated with control over DNA damage and cell cycle response pathways, while conversely we have shown that DNA damage can phase shift the circadian oscillator in an ATM/ATR dependent manner. This presentation will address the mechanism and biological/medical importance of the circadian clock, with emphasis on its impact on mutagenesis, carcinogenesis, and risk assessment of (non)genotoxic carcinogens.

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