

東京大学 グローバル COE 特別セミナー

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東京大学大学院 理学系研究科 生物化学専攻

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演題 :

HEXIM1 targets a repeated GAUC motif in the riboregulator of transcription 7SK and promotes base-pair rearrangements

日時 : 平成 23 年 3 月 2 日 (水) 15:00~16:00

場所 : 東京大学理学部 3 号館 3F 303 号室

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7SK snRNA, an abundant RNA discovered in human nucleus, regulates transcription by RNA polymerase II (RNAPII). It sequesters and inhibits the transcription elongation factor P-TEFb which, by phosphorylation of RNAPII, switches transcription from initiation to processive elongation and relieves pauses of transcription. This regulation process depends on the association between 7SK and a HEXIM protein, neither isolated partner being able to inhibit P-TEFb alone.

In this work, we used a combined NMR and biochemical approach to determine 7SK and HEXIM1 elements that define their binding properties. Our results demonstrate that a repeated GAUC motif located in the upper part of a hairpin on the 5'-end of 7SK is essential for specific HEXIM1 recognition. Binding of a peptide comprising the HEXIM Arginine Rich Motif (ARM) induces an opening of the GAUC motif and stabilization of an internal loop. A conserved proline-serine sequence in the middle of the ARM is shown to be essential for the binding specificity and the conformational change of the RNA. This work provides evidences for a recognition mechanism involving a first event of induced fit, suggesting that 7SK plasticity is involved in the transcription regulation.

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