新学術領域「転写サイクル」セミナー

Marking the X chromosome for global transcription regulation

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We study the phenomenon of dosage compensation in *Drosophila melanogaster* to uncover fundamental mechanisms of chromosome biology. In male fruit flies, a ribonucleoprotein Dosage Compensation Complex (DCC) doubles the transcription output of the X chromosome with exquisite selectivity. The DCC combines three enzymatic activities: the histone acetyltransferase MOF acetylates target chromait to activate transcription; the E3 ubiquitin ligase MSL2 is presumably involved in complex homeostasis and stoichiometry; the RNA helicase MLE incorporates the long.non-coding *roX* RNA into the complex, an early requirement for the assembly of the DCC.

A failure to discriminate the X from autosomes is lethal for the affected organism. Our recent discoveries provide a first molecular explanation for X chromosomal targeting. A genome-wide biochemical analysis revealed that MSL2, the male-specific DCC subunit, has the intrinsic ability to select X chromosomal binding sites from the vast excess of genomic DNA. Direct DNA binding requires the cooperative action of two distinct domains. Among those, the CXC domain is able to distinguish a subset of MREs termed 'PionX' sites, which are defined not only by additional sequence features, but by a distinct and critical DNA conformation (base roll). PionX sites are X chromosome-specific determinants involved in faithful dosage compensation. They are preferentially bound by an early intermediate of DCC assembly. They are the first to be occupied during *de novo* establishment of dosage compensation. Remarkably, the analysis of X chromosome evolution in *Drosophila miranda* suggests that PionX sites originate early during X chromosome evolution by neoX-specific deletion of a transposon-derived precursor sequence. This scebariomay serves as an instructive example for those who seek to explain how transcription factors coordinate the regulation of genetic programmes, which requires distinguishing a minority of functional DNA elements from a large pool of seemingly similar, but non-functional sequences.

Date : Monday, December 5, 2016, 4:00-5:00pm
Place: Biken Hall, 1st Floor, Main building, RIMD
Host : Dr. Hodaka Fujii (Combined Program on Microbiology and Immunology, RIMD)

*The Lecture will be given in English.

主催：新学術領域研究「転写サイクル」
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