CDB SEMINAR

Masako Tada

Chromosome Engineering Research Center, Tottori University, Japan

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16:00~17:00 Seminar Room A7F

Cyclic conversion of 5-methylcytosine to 5-hydroxymethylcytosine during the cell cycle in mouse embryonic stem cells

Summary

5-Methylcytosine (5mC) is an important epigenetic marker and is indispensable for mammalian embryonic development. Members of the Ten-eleven translocation (Tet) family of enzymes (Tet1–3) have dioxygenase activity and convert 5mC to 5-hydroxymethylcytosine (5hmC). The maintenance-type methyltransferase Dnmt1 cannot methylate newly synthesized cytosine at hemi-5hmC sequences, leading to cell cycle-mediated loss of 5mC inheritance in a passive manner. The 5mC-to-5hmC conversion initiates demethylation in early preimplantation embryos but not in wild-type mouse embryonic stem cells (ESCs), in which an extensive range of euchromatic regions remains 5-hydroxymethylated. Thus, we anticipated that DNA in euchromatic regions might be continually poised to be remethylated for the next 5-hydroxymethylation. To analyze which DNA methyltransferases are involved in active remethylation in genomic regions at which DNA modifications cyclically change in mouse ESCs, we analyzed 5hmC distribution patterns on mouse chromosomes in ESCs lacking both Dnmt3a and Dnmt3b or just Dnmt1. We show that not only Dnmt3a and Dnmt3b but also Dnmt1 are involved in the remethylation of newly synthesized double-stranded DNA following cell cycle-mediated loss of 5hmC. The detailed mechanisms underlying this are currently under investigation.

Host:
Shigehiro Kuraku
Genome Resource and Analysis, CDB
shigehiro-kuraku@cdb.riken.jp
Tel:078-306-3048 (ext:4232)

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