GENOME INTEGRITY and CONTROL

生物物理学セミナー

GIC seminar

今泉 結 博士

Institute of Molecular Genetics (IGMM)
CNRS and University of Montpellier

Role of DNA methylation in asynchronous replication timing at imprinted gene domains

Across almost the entire mammalian genome, the timing of DNA replication is similar between the paternal and the maternal genome. At some genomic loci, however, including certain imprinted gene domains and X-linked genes, asynchronous replication has been described, with one parental allele replicating earlier than the other. Nevertheless, the precise regions that show asynchronous replication and the underling mechanisms and roles remain unknown. By carefully comparing replication timing between androgenetic and parthenogenetic mouse ES cells, and by using newly derived naïve hybrid mouse ES cells, we mapped allelic replication timing along the genome. We identified the strongest replication asynchrony within the imprinted Dlk1-Dio3 domain on chromosome 12. This large chromosomal domain plays diverse roles in development and disease through the mono-allelic expression of several of its genes. Analysis of mutant hybrid ES cell lines with genetically/epigenetically altered DNA methylation patterns indicate that the allelic DNA methylation at the domain's ICR ('Imprinting Control Region') plays a predominant role in the asynchronous replication at the Dlk1-Dio3 domain. Our ongoing CRISPR-based studies explore whether there is a direct effect of the ICR, or, rather, whether the replication asynchrony could somehow be linked to parental-specific chromatin interactions mediated by the ICR. As concerns its possible functionality, the replication synchrony between the parental chromosomes may contribute to the faithful somatic maintenance of differential chromatin organization and gene expression at critical early stages of development.

BP1（106号室）

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