School of Life Sciences
Seminar Series

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Three-dimensional genomics and its applications

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학력

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Abstract

The 3D genome structure is highly ordered by a hierarchy of organizing events ranging from enhancer-promoter or gene-gene contacts to chromosomal territorial arrangement. I have employed the 3D genomic tools methods such as in situ Hi-C and ChIA-PET approaches to comprehensively identify genome-wide association in yeast and human cells.

I examined the 3D organization of fission yeast genome throughout the cell cycle. I demonstrate that during mitosis in fission yeast Schizosaccharomyces pombe, large domains of 300 kb–1 Mb are formed by condensin. This mitotic domain organization does not suddenly dissolve, but gradually diminishes until the next mitosis. By contrast, small domains of 30–40 kb that are formed by cohesin are relatively stable across the cell cycle. This study describes the different functions of condensin and cohesin in cell cycle-dependent genome organization.

Epstein-Barr virus (EBV) genomes persist in latently infected cells as extrachromosomal episomes that attach to host chromosomes through the tethering functions of EBNA1, a viral encoded sequence-specific DNA binding protein. I employed circular chromosome conformation capture (4C) analysis to identify genome-wide associations between EBV episomes and host chromosomes. I found that EBV episomes in Burkitt's lymphoma (BL) cells preferentially associate with cellular genomic sites containing EBNA1 binding sites enriched with B-cell factors EBF1 and RBP-jK, the repressive histone mark H3K9me3, and AT-rich flanking sequence. These attachment sites correspond to transcriptionally silenced genes with GO enrichment for neuronal function and protein kinase A pathways. Depletion of EBNA1 led to a transcriptional de-repression of silenced genes and reduction in H3K9me3. EBV attachment sites in lymphoblastoid cells (LCLs) with different latency type show different correlations, suggesting that host chromosome attachment sites are functionally linked to latency type gene expression programs.

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