LS17-003 - Elucidating sister chromatid structure by chemical DNA labeling and conformation capture

Abstract

Chromosomes extensively reorganize during the cell cycle to support regulated gene expression during interphase and to comply with mechanical genome segregation during mitosis. Following chromosome replication in S-phase, the two DNA copies co-localize within the same nuclear territory, but later in mitosis appear as separate rod-shaped structures. How sister chromatids fold during interphase and how they resolve to shape mitotic chromosomes has remained unclear. Recently developed chromosome conformation capture methods provide powerful approaches to probe the 3D organization of DNA within cells, yet available technology cannot distinguish between sister chromatids. Here, we will develop a chemical labeling-based methodology to selectively mark sister chromatids for detection by high-throughput DNA sequencing. We will use nucleotide analogues for in vivo pulse-labeling of one sister chromatid within each chromosome and develop high throughput sequencing methods to detect the labeled nucleotides. We will then use high-throughput chromosome conformation capture (Hi-C) to map intra- and inter-chromatid contacts based on the nucleotide analog label. With this technique, we will study synchronized cells to elucidate the dynamic reorganization of sister chromatids from replication until their segregation in mitosis. Our work will establish a novel technique of broad relevance and provide insights into fundamental mechanisms underlying chromosome segregation.

Scientific disciplines:
Chemical biology (50%) | Cell biology (25%) | Molecular biology (25%)

Keywords:
Chromosome, mitosis, cell cycle, sister chromatid resolution, chromosome conformation capture

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Status: Ongoing (15.06.2018 - 14.06.2023)

Further links to the persons involved and to the project can be found under
https://www.wwtf.at/funding/programmes/ls/LS17-003/