ÉCOLE NORMALE SUPÉRIEURE DE LYON

Master internship offer

Understanding the interplays between chromatin and condensin that shape human metaphase chromosomes

Key words: 3D genome organization, condensin, metaphase chromosome, chromatin, epigenetics,

Team: Chromatin dynamics in mitotic chromosome assembly

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Internship languages: French & English

Project

A fundamental principle in living organisms is that the folding of genomic DNA into dynamics loops underlies most if not all genomic functions. Mitotic chromosome assembly is a striking manifestation of such a tight connexion between 3D structure and function. In essence, mitotic chromosome assembly (or condensation) is the profound reorganisation of a long interphase chromatin fibre into a new 3D mega-structure, the metaphase chromosome, shaped for the accurate transmission of the genome during anaphase. When condensation is impaired, chromosome segregation is also impaired, with dramatic consequences for the cell and/or the organism (cancer). Although mitotic chromosome assembly has been described more than a century ago, we still do not fully understand the underlying mechanisms.

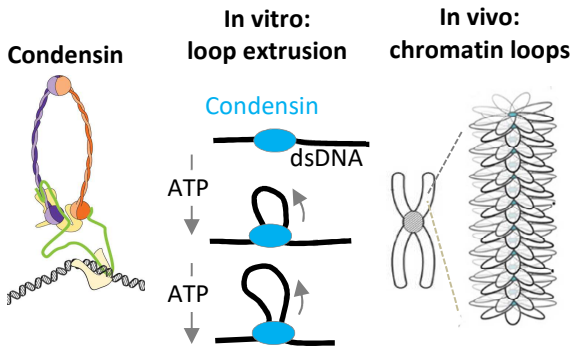

Figure. Condensin shapes mitotic chromosomes

The aim of the internship is to try to understand how a chromosomal complex named condensin reorganises chromatin into rod-shaped mitotic chromosomes.

Condensin is a universal genome organiser that is best characterised as the driver of mitotic chromosome assembly in eukaryotes. Current data indicate that condensin is a DNA motor that shapes mitotic chromosomes by directly binding to DNA and by extruding adjacent DNA into a loop of increasing size (Figure). What remains unknown, however, are the mechanisms by which condensin overcome the barrier formed by nucleosomes and chromatin-bound proteins to access DNA and to extrude DNA into a loop.

Using the fission yeast S. pombe as a model system, we provided evidence that histone post-translational modifications and nucleosome eviction by ATP-dependent chromatin remodelers allow condensin to load onto DNA during mitosis and to fold chromatin into mitotic chromosomes (Toselli-Mollereau *et al*, 2016; Robellet *et al*, 2017).

Further evidence in from the literature suggest that in human cells a similar chromatin-based nucleosome eviction mechanism might underpin the binding of condensin to DNA during

mitosis (Sutani *et al*, 2015), and that such mechanism might be linked to epigenetic marks that persist in chromatin during mitosis.

The overall objective of the internship is to assess this hypothesis in human culture cells by using fluorescent microscopy of isolated chromosomes and functional genomics approaches.

Interested applicants are invited to contact the internship supervisor by email. More information on background, research objectives and techniques will be obtained during informal interviews.

Techniques used during the internship

Culture and synchronization of human cell lines ● Transfection with the auxin-induced degradation system. ● ChIP-seq, MNase-seq and Hi-C. ● Immunofluorescence on human chromosome spreads

Bibliography

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Toselli-Mollereau E, Robellet X, Fauque L, Lemaire S, Schiklenk C, Klein C, Hocquet C, Legros P, N'Guyen L, Mouillard L, *et al* (2016) Nucleosome eviction in mitosis assists condensin loading and chromosome condensation. *EMBO J* 35: 1565–1581