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PhD position – 3D structure and gene regulation in *C. elegans*

DNA is highly organized inside the nuclear space and understanding how genome packaging and folding regulates transcription is of great importance for cell fate manipulations. Recent studies have started uncovering the regulatory principles of chromosome folding using chromosome conformation capture, a technique designed to characterize nuclear genome organization. These studies led to the discovery of Topologically Associated Domains (TADs), three-dimensional structures effectively segmenting the genome into domains. In mammalian cells, these TADs are created by the combination of structural maintenance of chromosome (SMC) family complexes (cohesins and condensins) and boundary elements such as CTCF binding sites[1]. Beyond genome segmentation, the role of TADs, in particular TAD compaction in gene regulation remains unclear.

The research project aims at deciphering how TAD formation by SMC complexes regulates gene expression. We use a model system, the X chromosome in *C. elegans.* In nematodes, X-linked gene expression is regulated as a function of the number of X chromosomes present in the animal (one in males, two in hermaphrodites)[2]. This phenomenon, called dosage compensation (DC), occurs at least in part on both X chromosomes in hermaphrodite animals, on which a specific condensin is loaded. In contrast to most model systems, this loading of an SMC/condensin complex has a clear transcriptional output, moreover restricted to a single chromosome. Work in our laboratory has uncovered that the X chromosome forms sex-specific nuclear domains: in males, the X chromosome lies in a pore-proximal territory, while in hermaphrodites the DCC impairs this[3]. Other laboratories have shown that DCC loading leads to the formation of enhanced TAD structures[4,5]. It remains however unclear how DCC loading, TAD structure, subnuclear localization and gene regulation are mechanistically linked. This is the topic of this PhD project.

To understand how DCC modifies promoter structure to regulation gene expression, we developed in collaboration with the de Laat group in Utrecht a chromosome conformation capture protocol which makes use of new long molecule sequencing techniques (PacBio/nanopore). This adaptation allows capturing multiple contacts from a single promoter, thereby elucidating the structural changes induced by SMC loading at gene/promoter resolution.

Technically, the laboratory is specialized in the use of high resolution chromatin mapping techniques, classical and CRISPR-based genetic methods for gain- and loss-of-function experiments, as well as advanced microscopy approaches.

For more information about our Institute, please see: http://www.izb.unibe.ch/. Bern is the capital of Switzerland, the old city is UNESCO world heritage and located half an hour away from the major ski resorts of the Alps. The University, with almost 15'000 students and 1160 teachers delivers 500 PhD diplomas per year and is ranked among the best 200 Universities worldwide (Shanghai rating). The Institute of Cell Biology is a very dynamic place and has recently hired 5 new group leaders.

Please email, as a single PDF file, your cover letter, CV (including relevant courses and grades received), and contact information for three references to: peter.meister@izb.unibe.ch

References

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