

Long-range enhancer-promoter interactions during *Drosophila* embryogenesis

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Project description:

In multicellular organisms, embryonic development is governed by the highly orchestrated expression of genes in both a temporal- and tissue-specific manner. The regulatory networks that control these expression patterns are thus essential for metazoan development and can have drastic functional impact when perturbed. Such networks are controlled by the binding of transcription factors to enhancers, which in turn interact with the promoter of their target gene via the formation of a chromatin loop.

Enhancers can be located at great linear distances from the gene that they regulate. Indeed, our recent work shows that enhancer interaction distances in *Drosophila* can span up to hundreds of kilobases. Importantly, the enhancers' target genes are not necessarily the closest genes. Only 27% of the enhancer-promoter interactions identified in human cell lines are between neighboring elements, and this number increases only up to 47% when considering solely the nearest active promoter. The reasons for enhancer-promoter interaction specificity, that is why an enhancer interacts with a distant promoter, but not necessarily with one in its direct (linear) neighborhood, are still largely unknown.

In this context, we want to establish what determines the specificity of promoter-enhancer interactions in a complex genome by systematically perturbing enhancer-promoter interactions in a controlled manner.

Methods used in the lab:

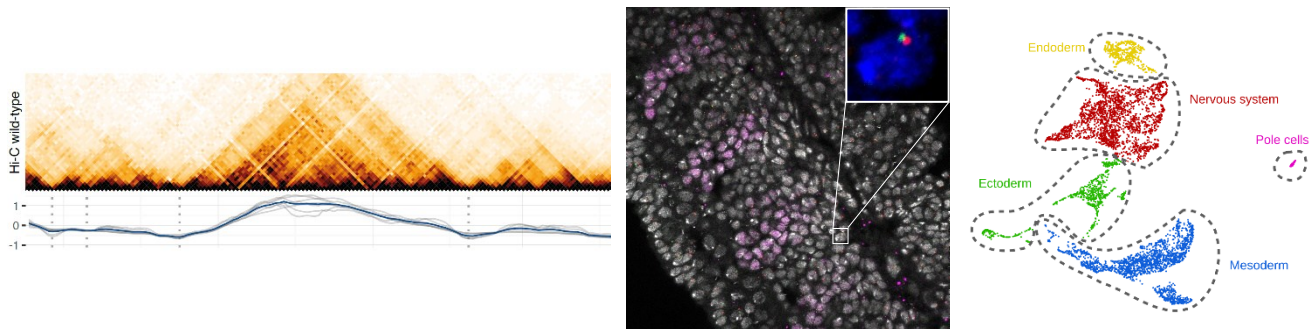
Genomics: RNA-seq, ChIP-seq, Chromosome Conformation Capture, single-cell OMICs

Drosophila genetics. Generation of transgenic flies using CRISPR-Cas9.

FACS sorting

In situ hybridization, confocal imaging, Spatial Transcriptomics

Bioinformatics



Selected publications:

Masoura M et al. Promoter-proximal gatekeepers restrict pleiotropic enhancer inputs to achieve tissue specificity. **BioRxiv**. 2024. doi: 10.1101/2025.09.23.678065v2

Balasubramanian D et al. Enhancer-promoter interactions can form independently of genomic distance and be functional across TAD boundaries. **Nucleic Acids Research**. 2024. doi:10.1093/nar/gkad1183

Ghavi-Helm Y et al. Highly rearranged chromosomes reveal uncoupling between genome topology and gene expression. **Nature Genetics**. 2019. doi:10.1038/s41588-019-0462-3.

Ghavi-Helm Y et al. Enhancer loops appear stable during development and are associated with paused polymerase. **Nature**. 2014. doi: 10.1038/nature18962.