3D chromatin organization of lamin-depleted cells in Drosophila

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Chromatin in interphase nucleus is constrained by interactions with nuclear lamina – the network of proteins, such as lamin and lamin-associated proteins, lining nuclear envelope. Extended chromatin regions called lamin-associated domains (LADs) are involved in this interaction. Despite extensive studies, current knowledge of the mechanisms of chromatin tethering to nuclear lamina is still incomplete.

To explore the effect of chromatin detachment from nuclear lamina we used advanced high-throughput chromosome conformation capture (Hi-C) for the analysis of control and lamin Dm0-depleted *D. melanogaster* S2 cells.

We generated the interaction heatmaps with hiclib [1] and determined the topologically-associating domains (TADs) using Armatus software [2].

First, in order to capture the general properties of lamin-associated chromatin, we performed analysis of the control experiment. Recently, the partial correspondence of TADs to different chromatin types was revealed in *D. melanogaster* cell lines [3, 4, 5], but the direct comparison between TADs and LADs was not yet done. Comparison of TADs profile with LADs from previous studies [6] demonstrated that generally LADs are corresponding to

TADs.

We also compared TADs layout with 9-type and 5-type chromatin segmentations (so-called colors) [6, 7] and found that TADs with high levels of lamin-associated colors are longer and more compact than other TADs. We analysed scaling curves for TADs and found that the characteristic of chromatin folding (the slope of scaling curve) is more uniform for lamin-associated TADs.

We investigated the impact of lamin depletion on chromatin structure. The pattern of TADs has changed only slightly after lamin depletion allowing us to compare the compactness levels of TADs before and after depletion. We observed that TADs are becoming less compact in general. This effect was less prominent for lamin-associated TADs at short genomic distances (up to 140 Kb).

More thorough analysis revealed that peripheral parts of separate TADs are interacting more tightly while TADs interiors are decompacted upon lamin depletion. We also observed the increase of interaction frequency between different TADs.

Using comprehensive analysis of chromatin interaction data we have shown that chromatin in *Drosophila* cells is attached to nuclear lamina and this attachment makes chromatin more compact.

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