Alteration of the chromatin structure in response to lamin depletion

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The development of chromatin conformation capture methods led to significant progress in the study of the spatial organization of chromatin. One of these methods is the Hi-C [1] method based on high-performance sequencing, which allows creating full-genome frequency maps of contacts between chromosomal loci. Analysis of the results of Hi-C and other methods has shown that the chromatin of eukaryotic cells forms topologically associated domains (TADs) [2]. On the other hand, it is known that the chromatin of eukaryotic cells comes into contact with nuclear lamina, a protein structure lining the inner surface of the nucleus. DNA sites that are constantly in contact with lamina form lamina-associated domains (LADs).

The purpose of this work is to study the changes in the three-dimensional structure of chromatin as a result of the depletion of the nuclear lamin B, leading to the destruction of the nuclear lamina. The data of sequencing of Hi-C S2 *D. melanogaster* cell lines with depletion of nuclear lamin B and without it was used. To study the displacement of the density of contacts within TADs as a result of lamin depletion, various computational approaches were developed and tested. It is shown that as a result of lamina depletion, chromatin folding changes: the frequency of contacts between peripheral regions of the same TAD increases, and the interior of TADs is loosened. The frequency of contacts between TADs is also significantly increased. In addition, TADs and LADs significantly overlap. Thus, the nuclear lamina is important for the proper formation of TADs.

This work was supported by the RSF (grant No14-24-00155).

1) van Berkum N.L. et al. (2010) *J Vis Exp.* 39, pii: 1869
2) Sexton T. T. et al. (2012) *Cell* 148: 458–472

3) Guelen L. et al. (2008) *Nature* 453: 948–951