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Cohesin degradation effect on mechanical properties of human colon tumor cells

Kabirova E.[1, 2]*, Yunusova A.[1], Khabarova A.[1], Battulin N.[1, 2]

[1] *Institute of Cytology and Genetics, SB RAS, Novosibirsk, Russia*

[2] *Novosibirsk State University, Novosibirsk, Russia*

* *e.kabirova@g.nsu.ru*

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Motivation and Aim: Cohesin mediates chromatin loop extrusion forming topologically associated domains which establish promoter-enhancer interactions. That way cohesin contributes to fulfill one of the primary genome functions – gene expression. In addition, cohesin-mediated chromatin extrusion can facilitate DNA repair by restraining DNA strands after the break, thus contributing to genome stability. Since cohesin influences the genome through its spatial structure, it is of interest whether cohesin provides mechanical stability to the nucleus. We aimed to assess cohesin influence on mechanical properties of a cell, in particular cell resistance to mechanical stress.

Methods and Algorithms: Obtaining a cell line lacking cohesin is essential to determine the cohesin role in the process (to compare the effects with and without cohesin). However, it is associated with a limitation: cohesin is necessary for a normal cell division, thus creating a cohesin knockout is difficult. The issue can be overcome by a protein degradation system induced by the plant hormone auxin. Utilizing the approach, we were able to disrupt the assembly of the cohesin complex, caused by degradation of the RAD21 subunit (RAD21 degron). This model allows us to study the rapid effect of the cohesin absence, just one hour after auxin introduction to the system. We carried out work on a human colon tumor cell line (HCT116) with RAD21 degron [1] and HCT116 without degron as a control. To determine the ability of a cell nucleus in an absence of cohesin to resist mechanical deformations, we performed (a) "scratch wound" assay for analyzing cell migration on flat surface, (b) transwell assay for analyzing active cell migration in a serum gradient.

Results: Comparison of wound healing by cohesin-depleted and control HCT116 revealed no differences in efficiency and rate between the groups. For transwell, HCT116 cells migration through 8 um pores was more efficient than through 5 um pores (4 hours of migration through 8 um resembled 24 hours of migration through 5 um). But the difference of migration efficiency between cohesin-depleted and control HCT116 was mild.

Conclusion: Thus, we can conclude that cohesin depletion does not affect the migratory properties of cells when moving along a flat surface or migrating in a gradient of serum. Though there is a possibility that cohesin influence on mechanical properties of a nucleus is low relative to other features such as cytoskeleton or nuclear lamina. To further study the nucleus mechanical properties we are planning to distinguish contribution of each of the elements (cohesin, cytoskeleton, lamina).

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References

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