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The role of cohesion in providing the physical properties of the nucleus and DNA breaks repair

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Motivation and Aim: The cohesin protein complex ensures the packaging of chromatin in the nuclear space in the form of loops—topologically associated domains. It is known that this level of packaging is involved in the implementation of genome functions—gene transcription, establishing and maintaining the interaction of the enhancer with the target gene and isolating the regulatory contexts of different genes. At the same time, cohesin-mediated chromatin looping contributes to genome stability because it can facilitate the repair of double-strand DNA breaks by restraining DNA strands after the break. By structuring chromatin, cohesin contributes to the mechanical properties of the nucleus. However, it remains unknown how significant the contribution of cohesin is to this process, and in particular in response to mechanical stress.

Methods and Algorithms: The solution to this issue is associated with a limitation: cohesin is necessary for normal cell division, that is, obtaining a cell line with deletion of the cohesin complex proteins is difficult. This problem can be overcome by a protein degradation system triggered in response to the plant hormone auxin. With this approach, we are able to disrupt the assembly of the cohesin complex, causing degradation of the RAD21 subunit just one hour after auxin addition. This model allows us to study the rapid effect of the absence of cohesin. We carried out work on HCT116 tumor cells with RAD21 degron.

Results: In this work, we ask the question of the contribution of cohesin to cell resistance to mechanical stress. As a first step in studying this issue, we assessed the ability of the cell nucleus in the absence of cohesin to resist mechanical deformations that occur during normal cell activity. To do this, we used the scratch wound assay: we disrupted the integrity of the cell monolayer ("wound") and, using time-lapse microscopy, observed the healing of the "wound" by cells within 24 hours. Comparison of efficiency and rate of wound healing showed no differences between groups of cohesin-depleted cells and control HCT116 cells.

Conclusion: Thus, we can conclude that cohesin depletion does not affect the migratory properties of cells when moving along a flat surface. Interestingly, according to the literature, when cohesin is depleted, predominantly normal gene expression occurs.

It can be assumed that under normal conditions, the loss of cohesin does not lead to serious disruptions in the functioning of the cell until the moment of division. In continuation of our work, our model will allow us to study how the absence of cohesin affects the resistance of cells to mechanical stress and DNA repair.

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