Changes in the size of cell nuclei in response to SMC proteins degradation in mammalian cells

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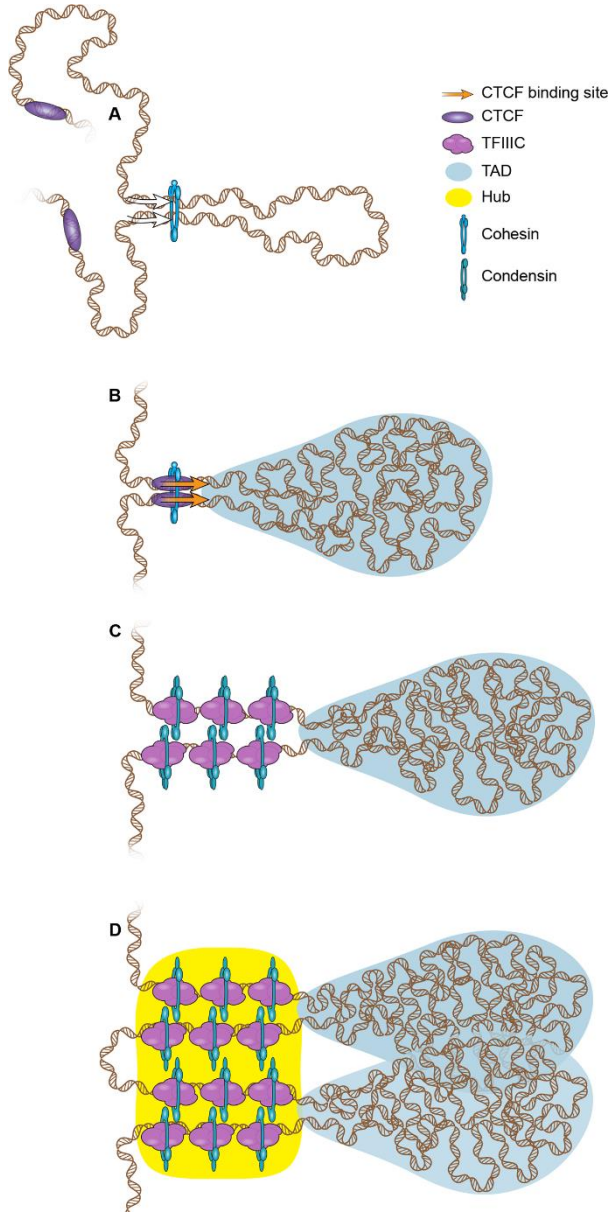
Motivation and aim

SMC complexes condensin and cohesin are essential for the three-dimensional organization of genome and cell division: besides the well-known mediation of sister chromatid cohesion and chromosome condensation in mitosis, recent findings prove their role in forming topologically associating domains.

However, a lot about the SMC complexes' function remains unknown. We apply a proteasomal degradation approach to these complexes in order to examine the knockout phenotype in mouse and human cells.

During these experiments, we have noticed a notable enlargement of the cell nuclei. We decided to inspect this phenomenon and perform an experiment that can prove the effect of enlargement.



Topologically associating domain (TAD) formation mediated by cohesin and condensin complexes. *Image: Yuen, Gerton, 2018.*

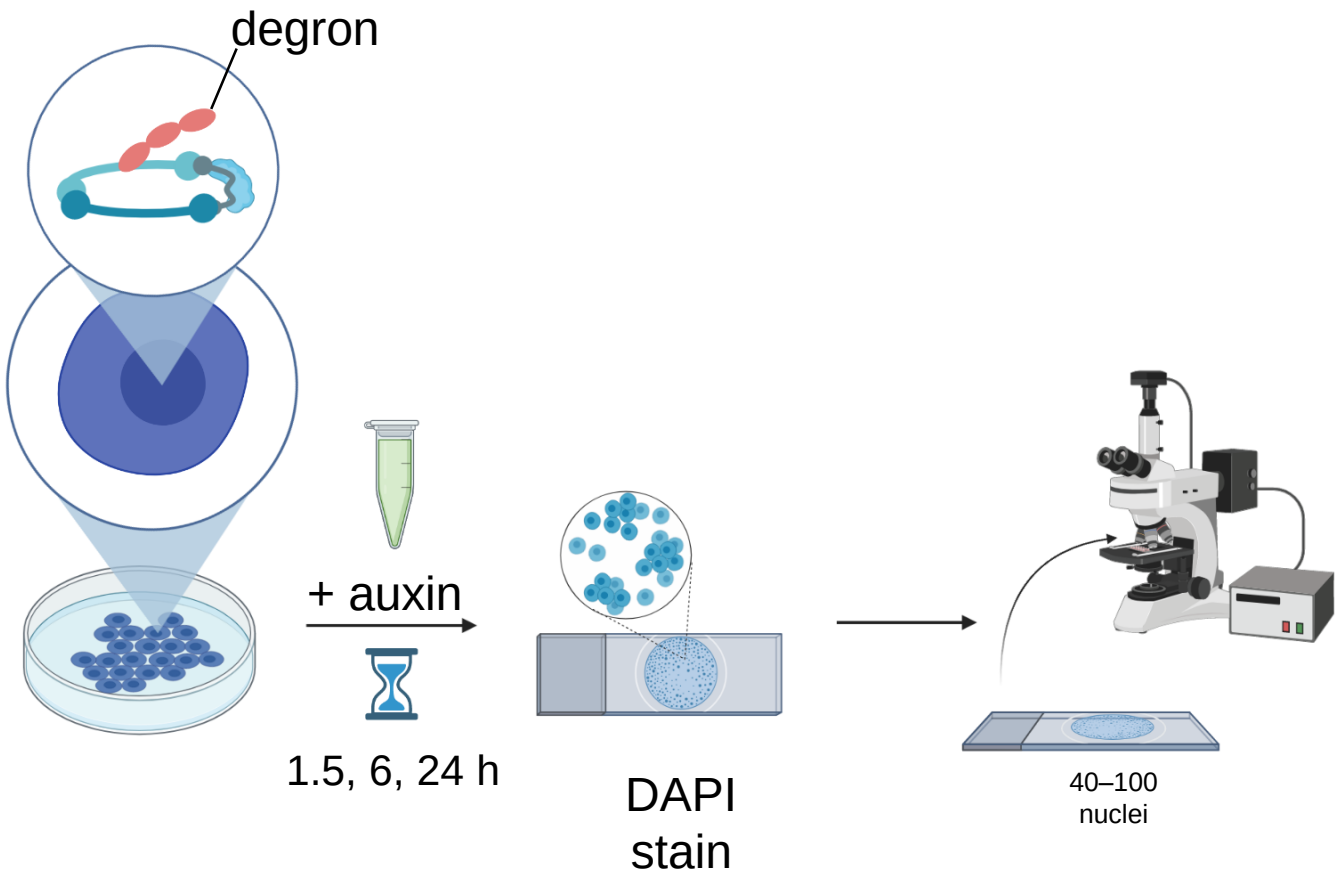
Methods

We performed the experiment on modified mouse and human cells, in which particular condensin and cohesin subunits are fused with an auxin-inducible degron system. We created these cell lines during previous experiments.

We exposed cell nuclei to auxin for different periods, stained them with DAPI, and captured them by the fluorescent visualization system.

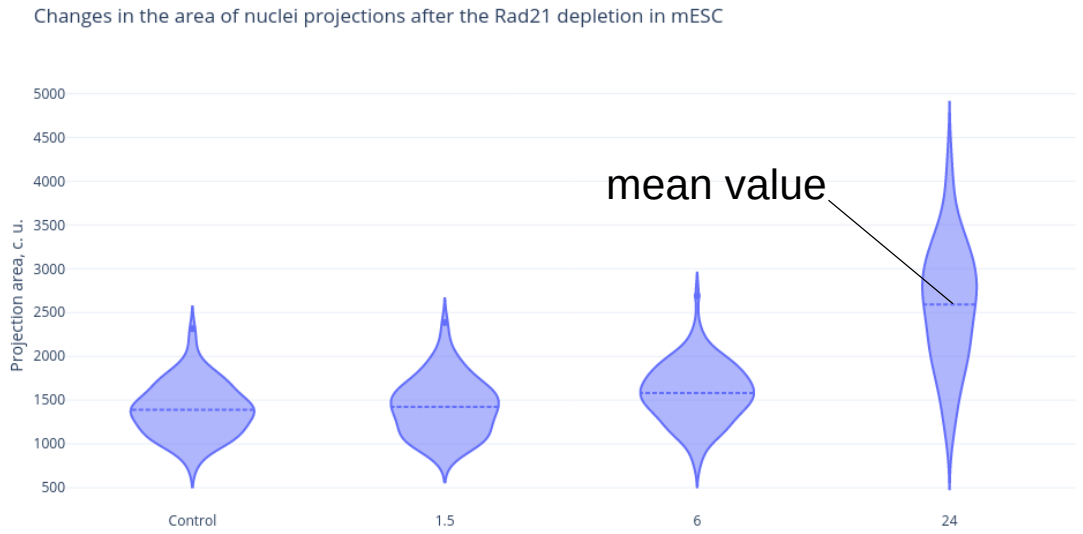
Cells without auxin were stained and captured as the negative control.

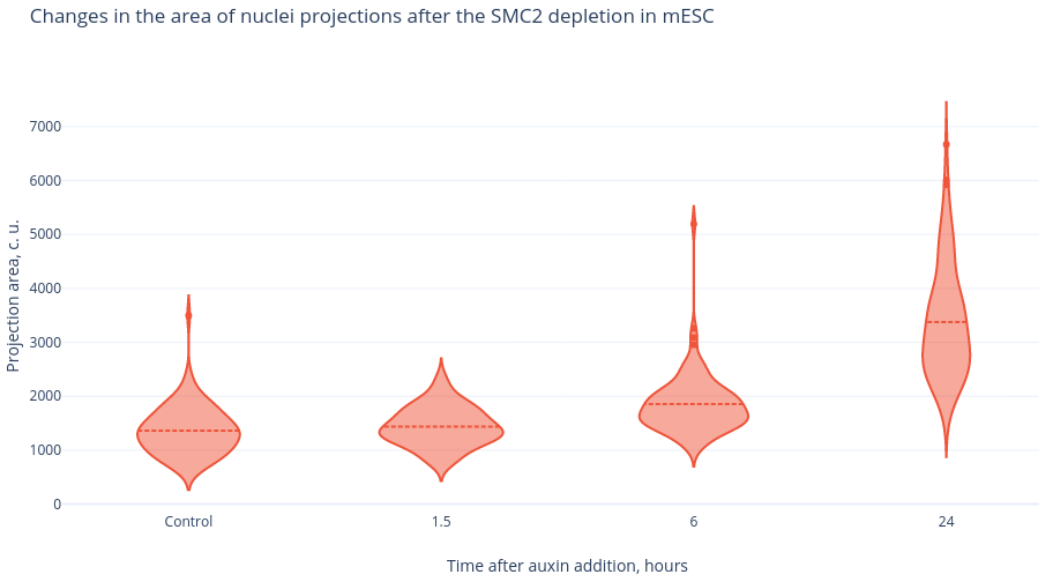
The area of the projection of the nucleus was calculated on received photographs using the ImageJ program with 40–100 nuclei taken in the sample.



Results

We observe an increase in the area of nuclei: the mean value increases with time, reaching a maximum value 24 hours after the addition of auxin, ranging from 132 % to 247 % of the original projection area.





Conclusion

Obtained results confirm the fact of a significant increase in the size of the cell nucleus in response to the depletion of condensin and cohesin complexes.

This effect might be explained with the mechanistic model: a compacted chromatin has physical properties of a compressed spring. While cohesin and condensins are depleted, the spring expands and stretches the nucleus from the inside that leads to the phenotype observed in our experiment. Development of the suitable mathematical model may help to prove this hypothesis.

Issues with SMC complexes and enlargement of nucleus are observed in cancer cells. Further research in this area may help to understand cancer pathogenesis and find a new insight into the regulation of chromatin and nuclear structure.