Cell biology of Lamina associating chromatin

Department: Cell Biology – RIMLS/IMM
Internship type: Master
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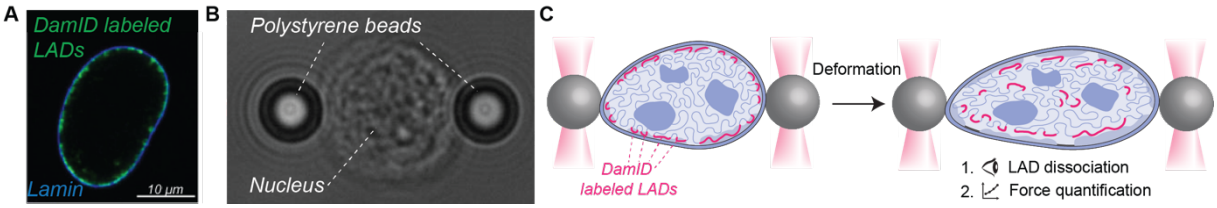
Aim: Design system for disrupting genome-nuclear lamin interactions

Background: To metastasize, cancer cells must squeeze through compact body tissue to enter the blood stream or lymph system. This squeezing subjects them to mechanical stress. Furthermore, cancer cells exhibit spatial rearrangement of their genetic material. This includes displacement of Lamina-associated domains (LADs), regions commonly associated with the nuclear periphery. These alterations in chromatin structure directly contribute to malignancy. **We hypothesize that this reorganization of LADs is caused by mechanical stress**.

Research plan: We want to test this hypothesis by visualizing the displacement of LADs while applying controlled mechanical forces to nuclei using optical tweezers. Our optical trap is equipped with brightfield illumination and confocal microscopy, allowing simultaneous visualization and force measurements. We thus need to set up a system that will allow us to visualize LAD-chromatin interactions, for which we will use DamID (Figure A). In this project, we will incorporate the DamID system into mouse embryonic stem cells. We will furthermore explore other visualization tools such as direct read out of transcription, repair, and signalling.



Techniques: cell culture, cloning, PCR, gel-electrophoresis, confocal microscopy, data and image analysis.

Lab environment: We are an interdisciplinary group that fosters a supportive environment in which there is a lot of room for creativity. This project is best suited for a student who wishes to expand their knowledge and skillset towards different fields. Independency and new ideas are encouraged.

References: https://doi.org/10.1007/s12551-019-00599-y, https://doi.org/10.1016/j.cell.2013.02.028