Proposition de stage de M2 et de thèse
2019-2020

Mechanics of the nucleus in cancer cells

The mechanical properties of the nucleus are critical for cell mechanics, in particular when a cell migrates in a confined environment and has to squeeze its nucleus to move through narrow pores. Cancer cells invade the surrounding tissues and can migrate long distances from the primary tumor. To facilitate this process, cells are thought to modify their mechanical properties and in particular nuclear stiffness. The project aims at testing this hypothesis by correlating **rheological measurements of the nucleus of cancer cells** with their invasive properties.

The candidate will focus on **glioblastomas**, the most aggressive form of brain tumors, using patient-derived cells form a glioblastoma bank (HGCC, University of Uppsala). First, the **morphology and dynamics** of the nucleus will be compared in the selected patient-derived cells (Figure A). Next, several biophysical techniques will be applied to measure the **rheological and mechanosensing properties of the nucleus** in living cells or of isolated nuclei: intracellular optical tweezers (Figure B), microplate rheometry, migration through microchannels, and cell stretching. Theoretical **models** (visco-elastic, power-law rheology, Hertz model) will be developed to analyze the data. Finally, the mechanical measurements will be correlated with the aggressiveness of the tumor estimated from the glioblastoma bank data (patient survival, proliferation, migration and invasion) and with the expression of genes associated with nuclear mechanics by **bioinformatics** approaches.

This project combines micromanipulation and live cell imaging to address both fundamental questions on **mechanotransduction** and clinical issues related to the diagnostic of glioblastoma by **mechanical phenotyping.**

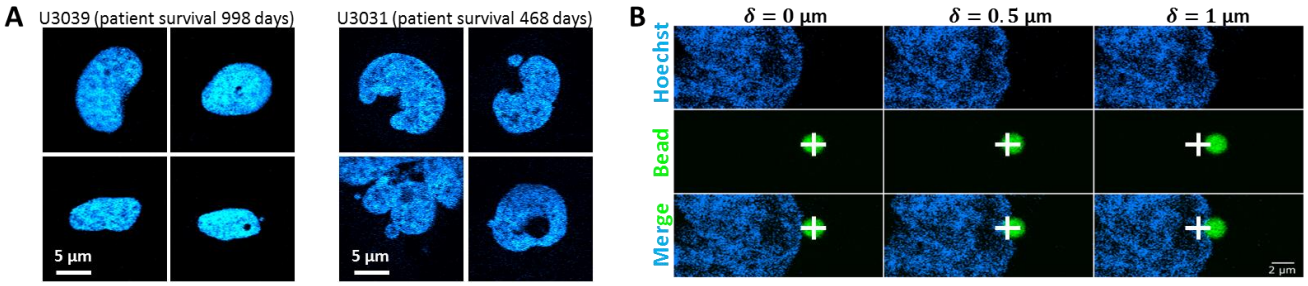

Figure: A. Examples of nuclear morphology in U3039 and U3031 patient-derived glioblastoma cells. B. Indentation experiment of the nucleus (blue) in a living cell using a 2 µm diameter bead (green) manipulated with an optical tweezers (indicated by the white cross). The indentation of the nucleus (δ) increases with the applied force.

Key words: optical tweezers, micropatterning, microfluidics, microplate rheometer, cell stretcher, bioinformatics, patient-derived cells, glioblastoma, microarray analysis, super resolution microscopy, correlative light-electron microscopy

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