MICRORHEOLOGY OF ASTROCYTES AND GLIOMA CELLS AND CONTRIBUTION OF INTERMEDIATE FILAMENTS TO THEIR MECHANICS.

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Abstract:

Several studies show that cancerous tissues are stiffer than normal tissues, and the extracellular matrix seems to play a central role in this stiffening. However, at the scale of the individual cell, tumor cells appear to be softer than normal cells in a number of cancer types among which breast, pancreas, colon, and bladder cancers.
Here, we use two different microrheology techniques allowing us to probe the mechanical properties of cells at two different scales. The scale of the whole cell is probed with a single cell uniaxial rheometer, while the intracellular scale is probed with a set-up combining micropatterning and optical tweezers. These two techniques enable us to compare and correlate the internal visco-elastic properties with the mechanics of the entire cell.

We focus our study on the mechanics of astrocytes, the major glial cell type in the brain, and gliomas, brain tumors derived from astrocytes. We use two different grades of gliomas: an astrocytoma (grade III) cell line, and a glioblastoma (grade IV) cell line representing the most common and aggressive form of gliomas.

We first discriminate astrocytes and both types of gliomas based on their mechanical properties. We show that rat primary astrocytes are stiffer than glioma cells from both human and rat grade III and grade IV cell lines at both scales. Moreover, we bring out that mechanical differences exist between glioma cells grades, and that these differences depend on the probed scale. We explain the observed differences by changes in cytoskeleton composition and intracellular organization.

Next, since intermediate filaments (IFs) have been involved in the migration of glial cells and since the expression of IF proteins is modified in gliomas, we evaluate the contribution of IFs to the mechanics of gliomas and astrocytes. Focusing on three IF proteins (vimentin, nestin and GFAP), we show that the level of IF proteins correlate with the mechanical properties of the cells and that down-regulation of IF proteins lowers cell rigidity. Finally, using our intracellular technique, we are able to measure the force-deflection curve and the bending rigidity of IF bundles *in cellulo*.