Long-term nuclear regulation of cancer cells under confinement

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The physical properties of the tumor microenvironment are strongly modified during tumor growth and participate in the development and invasion of cancer cells [1], including not only stiffness, but also compression [2].

In particular, the nucleus is critically affected during compression [3] and is appearing as an important mechanosensor of deformations [4,5]. Nevertheless, most studies focus nowadays on short-term cell response (from minutes to few hours). New questions are open on the long-term adaptation to deformations and the mechano-sensing mechanism involved. We have recently developed a new agarose-based microsystem copping with media renewal impediment to investigate cell response to prolonged confinement [6].

We used this device to apply a tunable and controlled 1D confinement on the colorectal cancer cell line HT-29 up to several days. We evidenced a decrease of the nuclear volume after 24 hours under confinement. The overall nuclear shape is also dynamically regulated with the apparition of transient nuclear blebs. We are currently analyzing the mechanisms and consequences of such adaptation on cell division, transcription activity and protein expression. Such long-termed adaptation to mechanical constrains may be of importance for cancer cell plasticity and play a role in their resistance to treatments.

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