Spatial coordination between cell and nuclear shape within micropatterned endothelial cells

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Changes in cell morphology play a crucial role in the microarchitecture of many human tissues and are commonly associated with alterations of nuclear shape. In this work, we investigated the mechanism of nucleus regulation by cell shape. To achieve this, we shape-engineered single endothelial cells to quantitatively and non-invasively assess the nuclear morphology and the intracellular force balance in response to cell shape changes.

Our study reveals that nuclear orientation and large deformations observed when cells elongate are regulated by actin stress fibers and actomyosic contractility. We showed that cell elongation results in the formation of tensed stress fibers aligned with the long axis of the cell and we demonstrated that nuclear deformation results from the action of an increased tension in these lateral actomyosin filaments. We devised a simple physical model that relates the spatial organization of actin stress fibers to the lateral compressive forces imposed on the nucleus. These lateral compressive forces induce significant changes in the three dimensional nuclear morphology. We show that this important nuclear remodelling during cell elongation leads to a decrease of nuclear volume up to 50 % and a reorganisation of chromatin inside the constrained nucleus. In order to assess the biological implication of these forces deforming the nucleus, we compared the ability of various shaped-engineered cells to enter S phase and to proliferate. Interestingly, our results show a highly decreased rate of proliferation for highly elongated cells.