Effects of energy metabolism on the mechanical properties of breast cancer cells

Marina L. Yubero[1].
Priscila M. Kosaka[1], Álvaro San Paulo[1], Marcos Malumbres[2], Montserrat Calleja[1] & Javier Tamayo[1].

[1]*Bionanomechanics Lab, Instituto de Micro y Nanotecnología, IMN-CNM (CSIC), Isaac Newton 8 (PTM), E-28760, Tres Cantos, Madrid, Spain.*
[2] *Cell Division and Cancer Group, Centro Nacional de Investigaciones Oncológicas (CNIO), C/ Melchor Fernández Almagro, 3, E-28029, Madrid, Spain.*

jtamayo@imm.cnm.csic.es

Tumorigenesis induces actin cortex remodelling, which makes cancerous cells softer [1]. Cell deformability is largely determined by myosin-driven cortical tension and actin fibre architecture at the cell cortex [2]. However, it is still unclear what the weight of each contribution is, and how these contributions change during cancer development, and little attention has been paid to the effect of energy metabolism on this phenomenon and its reprogramming in cancer.
Here, we perform precise two-dimensional mechanical phenotyping based on power-law rheology to unveil the contributions of myosin II, actin fiber architecture and energy metabolism to the deformability of healthy (MCF-10A), non-invasive cancerous (MCF-7), and metastatic (MDA-MB-231) human breast epithelial cells. The results show marked differences in the nature of the active processes that build up cell stiffness, namely that healthy cells use ATP-driven actin polymerization whereas metastatic cells use myosin II activity. Non-invasive cancerous cells exhibit an anomalous behaviour, as their stiffness is not as affected by the lack of nutrients and ATP, suggesting that energy metabolism reprogramming is used to sustain active processes at the actin cortex.

References

[1] Salbreux, G., Charras, G. & Paluch, E., *Trends Cell Biol.* Actin cortex mechanics and cellular morphogenesis. (2012) 22, 536-545.
[2] Calzado-Martín, A., Encinar, M., Tamayo, J., Calleja, M. & San Paulo, A. *ACS Nano.* Effect of actin organization on the stiffness of living breast cancer cells revealed by peak-force modulation atomic force microscopy. (2016) 10, 3365-3374.

Figures

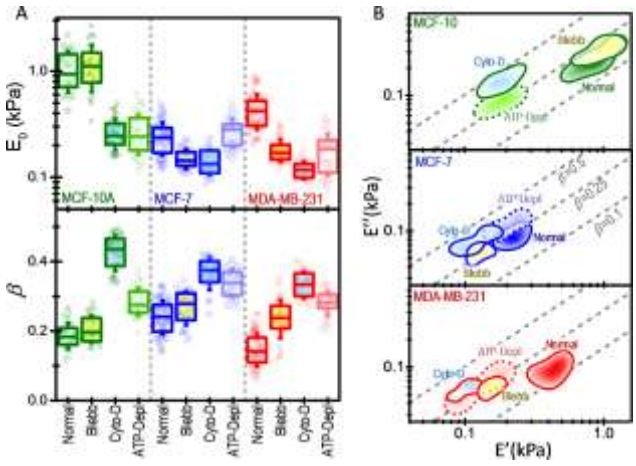

Figure 1: Power-law rheology parameters of the studied breast cell lines in normal conditions, treated with cytoskeletal drugs and in ATP-depletion conditions.

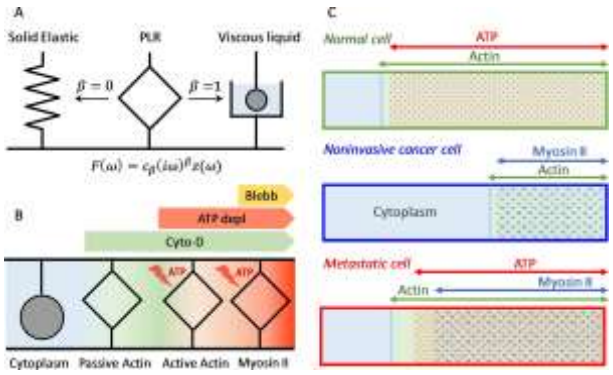

Figure 2: Sketch of uncoupling the effects of actin network, myosin II-driven contractility, and ATP hydrolysis on the cell stiffness.