Mechanical phenotyping of breast cancer cells based on stochastic intracellular fluctuations.

Álvaro Cano[1], Marina. L. Yubero[1], Carmen Millá[1], Verónica Puerto-Belda[1], Jose J. Ruz[1], Priscila M. Kosaka[1], Montserrat Calleja[1], Marcos Malumbres[2] and Javier Tamayo[1]

[1]Bionanomechanics Lab, IMN-CNM (CSIC), Tres Cantos, Madrid, Spain.

[2]Cancer Cell Cycle Group, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain

alvaro.cano@csic.es

Recently, it has been observed that cancer cells undergo changes in their mechanical properties during carcinogenesis [1]. Cellular stiffness has been the most studied mechanical property due to the existence of Atomic Force Microscopy [2], a well-established and universal technique.

A correlation exists between the amplitude of the fluctuations of intracellular particles at short time scales, in the range from tens of milliseconds to tens of seconds and cell malignancy [3]. Even though this is viable approach to study cellular mechanical properties, it has a limited throughput and it only provides very local information.

In order to improve the viability of intracellular stochastic fluctuations in these studies, we propose the use of Digital Holographic Microscopy (DHM) and three breast cancer cell lines with different degrees of malignancy, MCF-10A (Healthy), MCF-7 (Non-metastatic) and MDA-MB-231 (Metastatic). DHM has proven method to achieve label-free quantitative imaging of the whole intracellular dry mass fluctuations with unmatched sensitivity. DHM images of the cell lines are present in fig. 1a).

For these means we record 100 s videos of our cells, fig 1b), and posteriorly determine our regions of interest fig. 1c). In order to quantify the amplitude of this fluctuations we calculate their root mean square (RMS), fig 1d), which scale with the malignancy [4].

References

[1] H.T. Nia, L.L. Munn, R.K. Jain, Physical traits of cancer, Science 370 (2020) eaaz0868.

[2] M.L. Yubero, P.M. Kosaka, Á. San Paulo, M. Malumbres, M. Calleja, J. Tamayo, Effects of energy metabolism on the mechanical properties of breast cancer cells, Commun Biol 3 (2020) 1–9.

[3] Guo M. et al. Probing the Stochastic, Motor-Driven Properties of the Cytoplasm Using Force Spectrum Microscopy, Cell 158 (2014) 822-832

[4] Á. Cano, M.L. Yubero, C. Millá, V. Puerto-Belda, J.J. Ruz, P. M. Kosaka, M. Calleja, M. Malumbres and J. Tamayo. Rapid mechanical phenotyping of breast cancer cells based on stochastic intracellular fluctuations. iScience (2024), in press.

Figures

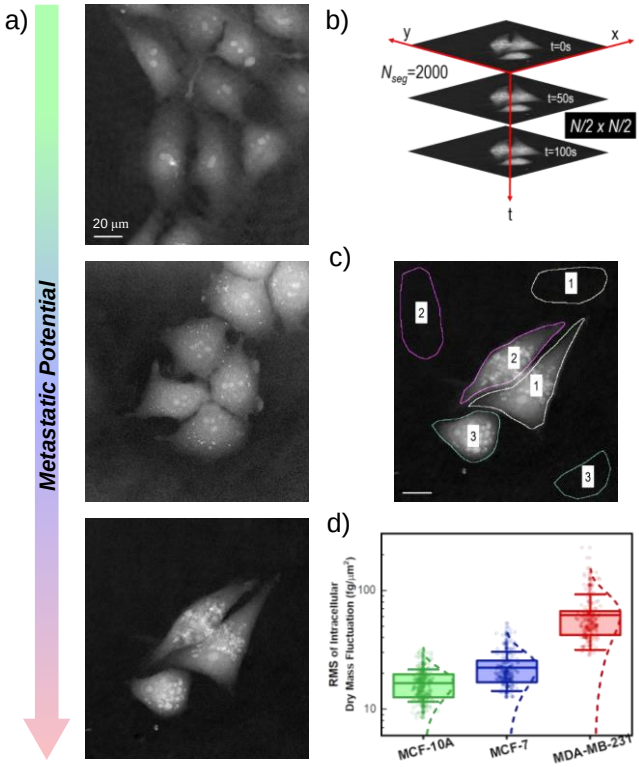

Figure 1. DHM fluctuation measurements. a) Morphology of the three cell lines. b) Schematics of image acquisition. c) Region of interest determination. d) Amplitude of stochastic intracellular fluctuations that scales with malignancy.