Exploring cancer cells through the lens of physics: the role of optomechanical technologies

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Historically, cancer has been regarded as a genetic disease, in which key mutations provide cells with the capability for uncontrolled growth and proliferation, the ability to avoid cell death in the primary tissue, and the potential to continuously mutate to achieve metastasis and drug resistance.
It is now recognized that tumorigenesis, tumor growth, and metastasis are closely linked to transitions in the mechanical properties and interactions of cancerous cells and their microenvironment [1].
Here, we will focus on two essential mechanobiological hallmarks that cancer cells undergo: i) continuous and dynamic cytoskeleton remodeling adapted to cancer progression, and ii) increased mechanical power linked to dysregulated metabolism in cancer.
These hallmarks are studied using a set of optomechanical technologies, including atomic force microscopy [2] , quantitative phase imaging [3] , and micromechanical sensing devices (**Fig. 1**). These techniques have been developed with distinguishing theoretical and computational methods, including denoising algorithms, image processing, and inverse problem methods. These methods enable the study of the mechanical properties of cancerous cells with enhanced specificity, visualize intracellular fluctuations with unprecedented sensitivity, and provide the first evidence of the existence of vibration modes in complex human living cells under physiological conditions.

The results shed new light on the roles of cytoskeleton remodeling and altered metabolism in cancer. Moreover, the technologies are well-suited to determine the functional impact of genetic variants in cancer, which is an unmet need in precision oncology. Additionally, the discovery of mechanical resonances in living cells opens fascinating avenues for mechanobiological therapies.

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] 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.
[4] E. Gil-Santos, J.J. Ruz, O. Malvar, I. Favero, A. Lemaître, P.M. Kosaka, S. García-López, M. Calleja, J. Tamayo, Optomechanical detection of vibration modes of a single bacterium, Nat. Nanotechnol. 15 (2020) 469–474.
[5] V. Puerto-Belda, J.J. Ruz, C. Millá, Á. Cano, M.L. Yubero, S. García, P.M. Kosaka, M. Calleja, J. Tamayo, Measuring Vibrational Modes in Living Human Cells, PRX Life 2 (2024) 013003.

Figures

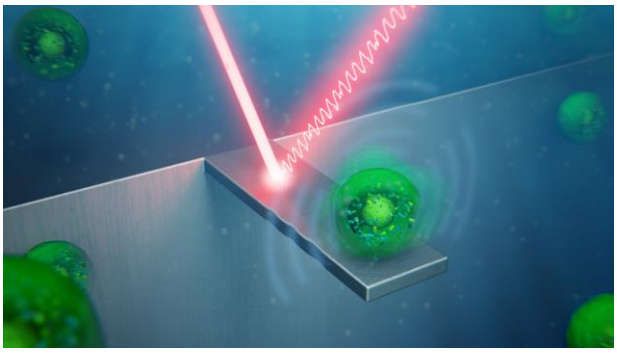

Figure 1. Schematic cartoon of a living cell attached to small microcantilever resonator.