

Tuning bio-nano interactions through mechanobiology

Marco Cassani^{1,4*}, Soraia Fernandes^{1,4}, Jorge Oliver-De La Cruz², Margherita Morpurgo³, Frank Caruso⁴, Giancarlo Forte^{1, 5*}

¹International Clinical Research Center, St. Anne's University Hospital, Brno, Czech Republic.

²Institute for Bioengineering of Catalonia (IBEC), The Barcelona Institute for Science and Technology (BIST), Barcelona, Spain.

³Pharmaceutical and Pharmacological Sciences Dept (DSF), University of Padova, Via Marzolo, 5-35131, Padova, Italy.

⁴Department of Chemical Engineering, The University of Melbourne, Parkville, Victoria, Australia.

⁵School of Cardiovascular and Metabolic Medicine & Sciences, King's College London, London WC2R 2LS, UK.

*Email: mcassani@unimelb.edu.au; giancarlo.forte@kcl.ac.uk

Mechanosensing regulates the interactions between cell and extracellular space and accounts for the translation of the environmental mechanical stimuli into biochemical signals. In this regard, mechanobiology has emerged as a promising field to unveil the molecular pathways driving cancer progression.¹ Indeed, the mechanical properties of cells have been recently proposed as new prognostic factors in cancer growth and dissemination.¹⁻² In the context of nanomedicine, understanding the complex interactions between cells and nanoparticles has been one of the main objectives for the past decades.³ The physico-chemical properties of nanoparticles have been extensively studied for improving the delivery of therapeutic anti-cancer drugs.⁴⁻⁵ Nevertheless, the intrinsic cellular mechanisms driving bio-nano interactions remain elusive.⁶ By using nanoparticles with tunable size and surface coating, we demonstrate that the inhibition of mechanobiology pathways affects nanoparticles' internalization by cancer cells.⁷ This phenomenon occurs independently of nanoparticle's material properties, but relies on the activation or inhibition of specific cellular molecular markers. Our study shows that the internalization of nanoparticles by the cells might be controlled by tuning cell mechanosensing pathways, ultimately improving the specificity of a nanotherapy.

References:

- ¹ Septiadi D., Crippa F., Moore T. L. et al., *Advanced Materials*, **2018**, 30, 19.
- ² Northcott J. M., *Frontiers in Cell and Developmental Biology*, **2018**, 6, 17.
- ³ Wilhelm S. et al., *Nature Reviews Materials*, **2016**, 1, 16014.
- ⁴ Best J. P. et al., *Advanced Healthcare Materials*, **2012**, 1, 1.
- ⁵ Shimoni O. et al., *ACS Nano*, **2013** 7, 1.
- ⁶ Van der Meel R. et al., *Nature Nanotechnology*, **2019**, 14.
- ⁷ Cassani M. et al., *Advanced Science*, **2024**, 11, 2302965.