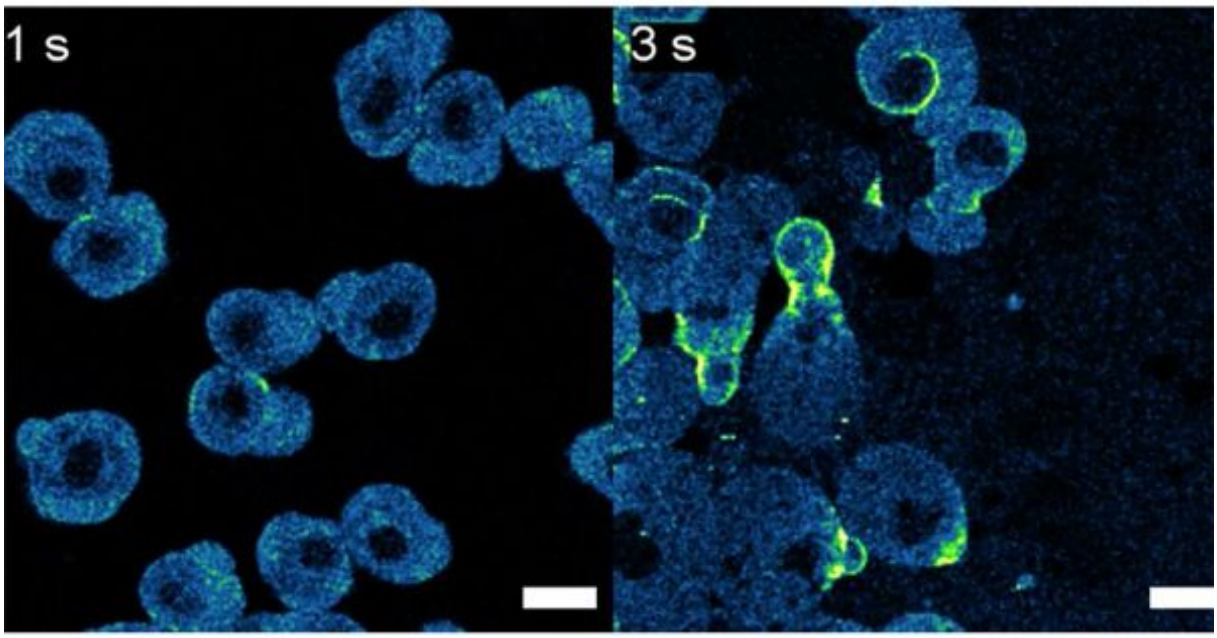


When feeling the pinch, nuclei instigate cells to escape crowded spaces

Scientists from CRG, ICFO, FHOO and UPF report on this new finding in a study published in the journal Science.

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The threat of serious deformation triggers a rapid escape reflex that enables cells to move away and squeeze out of tight spaces or crowded tissues.

In a new study published today in the journal Science, researchers reveal that squeezing a cell to the point where its nucleus starts to stretch triggers the activation of motor proteins which in turn transform the cell's cytoskeleton so that it can flee a packed environment.

Each cell has a nucleus, and each nucleus has a membrane that separates the chromosomes from the rest of the cell. At a rest state, the nuclear membrane is saggy, akin to a loose shopping bag. Now researchers at the Centre for Genomic Regulation (CRG) and ICFO - The

Institute of Photonic Sciences - have found that when the nuclear membrane is squeezed, the wrinkles on its surface iron themselves out, instigating a cascade of events that transform the cytoskeleton and eventually aid the cell in escaping its crowded environment.

i¿½Our work represents a paradigm shift where the nucleus itself is not simply a static-container of genetic material but rather a dynamic sensor that cells can use to ma e sense of the environment around them,i¿½ says Valeria Venturini, a PhD student with ual affiliation at ICFO - The Institute of Photonic Sciences - and the CRG. i¿½The intens ty of nuclear stretching predicted the intensity of the response, shedding new light on this fight or flight' reflex at the single cell level. Understanding this ability to sense deform tion, measure it and react accordingly may have important implications in underst nding processes like cancer growth and homeostasis.i¿½

It is the first time researchers have been able to explain how single cells measure and respond to acute shape deformation, a real threat to their survival. The reflex is activated in less than a minute, reversing when cells have escaped their packed environment.

i¿½We are all familiar with the traditional senses of sight, hearing, smell, taste and touch, b t we also depend on the lesser known ?sixth sense' - proprioception - our ability to percei e changes in our body posture and movement,i¿½ says Verena Ruprecht, Principal Investig tor at the Centre for Genomic Regulation (CRG) and last author of the study. i¿½It is rema kable that this sense also exists at the single cell level. Here we show for the first time th t the nucleus helps cells measure changes to their shape and adjust their behaviour to mech nical challenges in variable tissue niches.i¿½

The researchers used primary cells from the zebrafish embryo to study this cellular reflex. An accompanying study published today in the same issue of Science by researchers at the Institut Curie Paris (France), ETH Zurich (Switzerland), King's College London (UK), and Children's Cancer Research Institute Vienna (Austria) identified the same reflex in immune and cancer cells, suggesting it is conserved across species and in adulthood.

The human body is composed of trillions of cells which similarly require multiple sensations to fulfill their task in specific tissues. From a single cell's perspective, its environment is a crowded place with many types of physical constraints and mechanical forces.

These conditions induce changes in cell shape that can threaten a tissue's integrity. Cells need to be able to respond to these physical challenges during embryonic development and in adulthood, but how they measure their own shape and adapt their behavior to their surroundings has been an open question.

The study is a joint collaboration between the Centre for Genomic Regulation (CRG), ICFO, University of Applied Sciences Upper Austria (FH OO) and the Pompeu Fabra University (UPF). Researchers at ICFO that have co-authored the paper include the first author, Valeria Venturini, Valeria Venturini, Frederic Catala Castro, Mariona Colomer-Rosell, Monica Marro, Pablo Loza-Alvarez (SLN Chief), Michael Krieg (ICFO Group Leader of the Neurophotonics and Mechanical Systems Biology group), and Stefan Wieser (Team Leader @ SLN Facility).