Under pressure: when tension builds up, the nucleus escapes

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Researchers at IBEC have discovered that epithelial tissues adapt to prolonged stretching by slowly reorganising their keratin cytoskeleton into large multicellular networks. Using advanced live imaging, engineered tissue models and computational simulations, the team found that this process eventually pushes the cell nucleus out of its surrounding keratin cage. The findings reveal a previously unknown mechanism by which tissues respond to sustained mechanical stress, with potential implications for development, organ physiology and diseases linked to defective keratin organisation.

Dome formed in response to pressure in the epithelial tissue. Left: a global view of a region of cells, including a dome (white dotted circle). Right: a zoomed view of squares 1, 2 and 3 from the image on the left (the top images are lateral views). Green: keratin; magenta: actin; blue: nucleus. We can clearly observe that, in bundled cells, keratin filaments reorganise into thick, star-shaped bundles that span neighbouring cells, forming supracellular networks across the tissue.

How do tissues cope with being stretched for hours or even days? A study led by researchers at the **Institute for Bioengineering of Catalonia (IBEC)** has uncovered an unexpected answer: cells radically reorganise their internal scaffolding and, in the process, release their nuclei from a protective keratin network. The work, published in *Nature Physics*, reveals a new way in which tissues adapt to long-lasting mechanical forces.

Keratin is one of the main structural components of the cytoskeleton, the network of protein filaments that gives cells their shape and mechanical resilience. Although keratin has long been known to protect tissues from large deformations, exactly how it responds to sustained stretching has remained unclear.

To investigate this question, the researchers combined engineered epithelial tissues, a custom-built microfluidic stretching device, live-cell microscopy and multiscale computational modelling. They observed that keratin does not react immediately when tissues are stretched. Instead, over several hours, individual filaments gradually reorganise into thick, star-shaped bundles that span neighbouring cells, forming supracellular networks across the tissue.

"Simulating the intracellular dynamics revealed that the same process that forms these striking bundles also generates forces that ultimately push the nucleus out of its cage," says **Marco Pensalfini**, Assistant Professor at **Queen Mary University of London, who developed the computational model together with Marino Arroyo**, Full Professor in the Department of Civil and Environmental Engineering at the UPC, principal investigator of the Soft and Living Material Interfaces research group at CIMNE. *"Computational modelling allowed us connect what we observed in experiments with the underlying physical mechanisms."*

The structural reorganisation begins at the junctions where three cells meet. Keratin filaments progressively disappear from these regions and accumulate into increasingly thick bundles. Remarkably, the process is collective: it starts in a few isolated cells and then spreads to their neighbours, creating expanding clusters of bundled cells connected by a shared keratin network.

Live imaging confirmed this prediction: as bundles grew thicker, the nucleus gradually detached from its surrounding keratin mesh until it separated completely, leaving it connected to only a residual amount of filament. This «nuclear uncaging» turned out to be one of the most striking findings of the study, tightly coupled to the formation of the keratin bundles themselves.

"One of the most intriguing questions raised by our study is whether this uncaging process ultimately protects the nucleus or makes it more vulnerable," says **Xavier Trepat**, ICREA Research Professor at IBEC, principal investigator of the Integrative Cell and Tissue Dynamics group, and co-lead author of the study. *"On the one hand, removing the keratin cage could expose the nucleus more directly to mechanical forces. On the other, and perhaps counter-intuitively, disconnecting the nucleus from a highly stressed cytoskeletal network may actually protect it by preventing force transmission. Understanding which of these effects dominates will require future studies examining how nuclei respond to prolonged mechanical stress."*

The researchers also identified an important role for actin, another major component of the cytoskeleton. Weakening the molecular links between actin and keratin accelerated the bundling process almost threefold, showing that interactions between the two filament systems are key regulators of how tissues adapt to stretching.

"These findings may help us better understand how tissues adapt to prolonged stretching in a wide range of biological contexts," says **Tom Golde**, postdoctoral researcher in Trepat's group and first author of the study. *"Similar mechanical conditions occur during embryonic development and in organs that repeatedly expand and contract, such as the bladder or the mammary gland. We also think that the mechanisms we uncovered could be relevant to diseases in which the keratin network is altered."*

As engineers often reinforce bridges and buildings to withstand repeated loading, this study shows that our own cells have evolved a remarkably similar strategy—continually rebuilding their internal scaffolding to keep tissues resilient in the face of everyday mechanical forces.

Xavier Trepat is also a professor at the University of Barcelona (UB) and a member of the Centre for Biomedical Research Network in Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN).

The study also involved the collaboration of the **Laboratori de Càlcul Numeric (LaCàN)**, **Universitat Politècnica de Catalunya-BarcelonaTech (UPC)**; the **Columbia University** in New York, the Faculty of Medicine in the **University of Barcelona (UB)**; the **University of Vienna**; the **University College London**; the **Centre Internacional de Metodes Numerics en Enginyeria (CIMNE)** in Barcelona.

Referenced paper:

Tom Golde, Marco Pensalfini, Nimesh Chahare, Pere Roca-Cusachs, Gerhard Wiche, Guillaume T. Charras, Marino Arroyo & Xavier Trepat. **Dynamics of supracellular keratin bundling and nuclear uncaging in stretched epithelia.** *Nature Physics* (2026).DOI: https://doi.org/10.1038/s41567-026-03371-8

https://ibecbarcelona.eu/es/under-pressure-when-tension-builds-up-the-nucleus-escapes