Study shows cells respond quickly to small light-induced micro-environment movements

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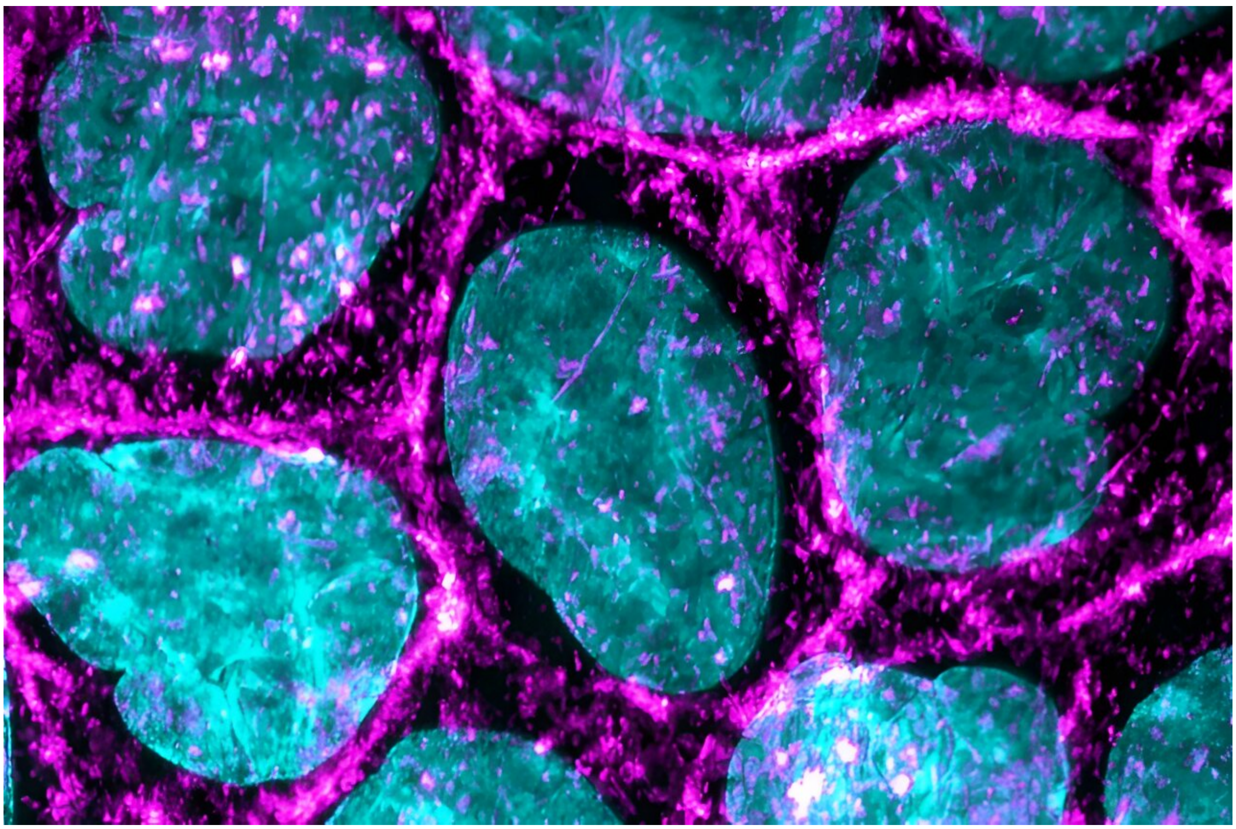


Microscopy image of the epithelial cells used in the study, the cytoskeleton (magenta) and nuclei (cyan) of the cell are fluorescently labeled, allowing the detailed studies of the structures. Credit: Heidi Peussa

Life sciences and photonics researchers at Tampere University have made a remarkable discovery in studying superficial cells' response to mechanical stimuli. By simulating the deformation of the extracellular matrix below the cells, researchers have shown that the cells quickly sense even minor changes in their environment, and their response is more complex than expected. The discovery may help to better understand, for example, the processes related to cancer metastasis formation.

Three research groups investigated in this joint project how epithelial cells sense small changes in their environment through ion channels. The study was conducted using light-responsive materials developed by the Smart Photonics Materials research group led by Professor Arri Priimägi, which can be used as a substrate for cell culturing. These materials allow precise and controllable movement of the cell substrate using light stimulation.

"The cells had a marker protein for intracellular calcium, so we were able to draw small grooves on the substrate surface on a confocal microscope and at the same time monitor how living cells respond to these changes in the environment with the help of calcium," says Teemu Ihalainen, Senior Research Fellow at Tampere Institute for Advanced Study (IAS) and leader of the Cellular Biophysics research group at the Faculty of Medicine and Health Technology.

"We found that even the movement of a few tens of nanometers of material opened mechanically gated calcium channels in the cells, through which the cells were able to change their calcium levels."

Calcium is needed in cells for a wide variety of processes, so even small changes in the amount of calcium can have large effects on cellular functions. The study shows, perhaps for the first time, that cells are able to sense minute movements in their environment and these movements are detected by changing the flow of calcium ions through the cell membrane, i.e. electrically via ionic currents.

The study focused on intracellular calcium changes during the first seconds of the mechanical stimulus. An article titled "Light-induced nanoscale deformation in azobenzene thin film triggers rapid intracellular Ca^{2+} increase via mechanosensitive cation channels," which is a key part of Doctoral Researcher Heidi Peussa's dissertation, was published in the journal *Advanced Science.*

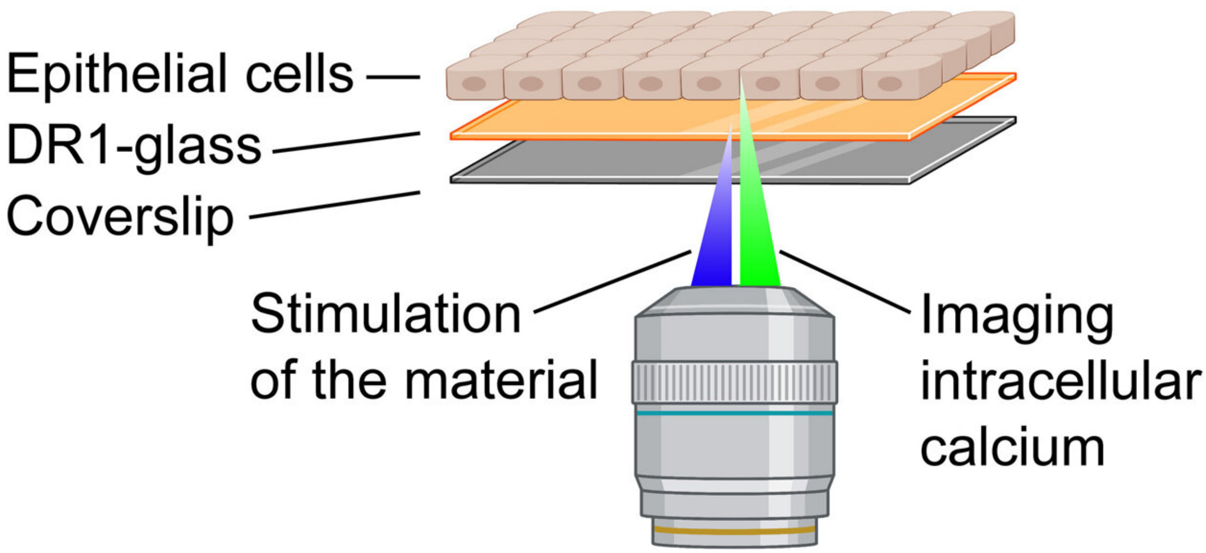
Mechanically gated ion channel as a key

In the body, epithelial cells are tightly attached to the extracellular matrix, allowing mechanical strain of the environment, for example, to be transmitted to the cells. Mechanical stimuli are important in the normal functions of cells. Disruption of cell attachment often causes disease or other problems.

Cells sense changes in their environment in a variety of ways, for example, by mechanically gated PIEZO1 ion channels. The channels can be understood as cell membrane pores that are closed in a mechanically relaxed state, but open as the cell membrane stretches. The opening happens in thousandths of a second and leads to calcium influx into the cell. The process has a key role in many physiological functions, e.g., in touch sensation. The discovery of mechanically gated ion channels was awarded the Nobel Prize in 2021.

The study showed that PIEZO1 channels are crucial for sensing rapid changes in the cell's microenvironment.

"We discovered that cells are capable of sensing deformations as small as 40 nanometers (0.000040 mm) that occur in thousandths of a second. For the first time, we were able to monitor how the PIEZO1 channel opens as a result of a physical change in the local, extracellular environment," Ihalainen says.



In the study, calcium signals from cells grown on top of photosensitive DR1 glass were monitored under a microscope using green light and at the same time mechanical stimuli with blue light were induced on the basal side of the cells. Illustration: Heidi Peussa. Credit: Heidi Peussa, Tampere University

New possibilities to study cellular processes of the eye

The method used by the researchers is new and allows studying the mechanical stimulus of the extracellular matrix in particular and simultaneously monitoring cell responses. Further research addressing the PIEZO01 channel functioning is already on the way. In addition, the researchers' aim is to study and develop new light-responsive materials.

"Our next steps are to study the regulation and regulating factors of these mechanically gated ion channels. The goal is also to gain a broader understanding of what happens after the first few seconds in the perception of force sensation," says Soile Nymark, Associate Professor of Biosensor technology and leader of the Biophysics of the Eye research group at the Faculty of Medicine and Health Technology.

"We are developing new transgenic cell lines to further study calcium signaling at different locations in the cell. These transgenic cell lines also allow us to extend the studies to underlying retinal pigment epithelium of the eye and to study the role of PIEZO1 channels in retinal maintenance,"

More information: Heidi Peussa et al, Light-Induced Nanoscale Deformation in Azobenzene Thin Film Triggers Rapid Intracellular Ca^{2+} Increase via Mechanosensitive Cation Channels, *Advanced Science* (2023). DOI: 10.1002/advs.202206190

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