Cytophysics: How cells migrate through gaps smaller than their nucleus

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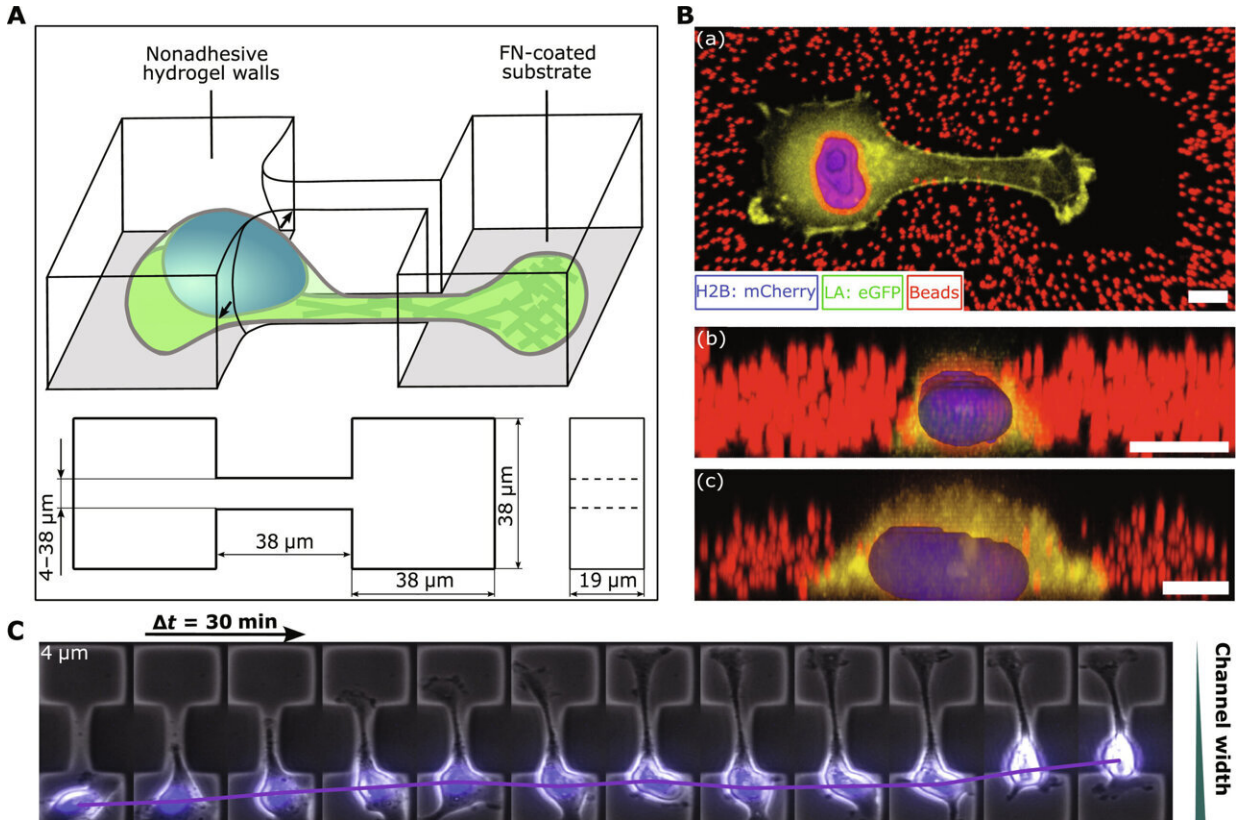

Synthetic hydrogel-based assay to study 3D confined cell migration. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.adm9195

Eukaryotic cells—that is, cells with a nucleus—possess an astounding ability to radically change their shape and their cytoskeleton, allowing

them to migrate through tiny pores and constrictions even smaller than their nuclear diameter. Yet how exactly the cell nucleus changes shape as a response to the surrounding structures, and what physical mechanisms are behind this deformation, have remained unclear.

The research group of LMU Professor Joachim Rädler from the Chair of Experimental Physics investigates the self-organization and dynamics of living cells. In a study published in *Science Advances*, the team analyzed the characteristics of cells that pass through tight spaces.

"Cells are active systems with elastic properties," explains Rädler, who wants to understand what determines their individual shape, speed, and orientation decisions. To this end, he and his team use synthetic microstructures as platforms for investigating cell motion and local forces.

"In this controlled environment, we employ scanning time-lapse microscopy to observe a large number of individual cells that move through the material," says Rädler. The cell motion is analyzed with data-driven models from the group of Professor Chase Broedersz (VU Amsterdam).

In this way, the researchers investigated the mechanics and dynamics of cancer cell nuclei that migrated through deformable 3D hydrogel channels. "Using confocal imaging and hydrogel bead displacement, we were able to track the nuclear deformation and corresponding forces during migration through the given constrictions," says doctoral candidate and lead author of the study, Stefan Stöberl.

The observations revealed that the nucleus reversibly deforms with a reduction of volume during the confinement.

Furthermore, the researchers discovered that as the channel width

decreases, the shape of the nucleus changes in two phases during the migration. They found a biphasic dependence of migration speed and transition frequency on channel width, revealing maximal transition rates at widths comparable to the nuclear diameter.

"The physical model we propose explains the observed nuclear shapes and transitioning dynamics in terms of the cytoskeletal force-generation adapting from a pulling- to a pushing-dominated mechanism with increasing nuclear confinement," says Rädler.

Armed with this knowledge, the researchers can now help identify the elements in the cytoskeleton that are relevant for the invasion of cancer cells.

More information: Stefan Stöberl et al, Nuclear deformation and dynamics of migrating cells in 3D confinement reveal adaptation of pulling and pushing forces, *Science Advances* (2024). DOI: 10.1126/sciadv.adm9195

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