Tumor cell expansion challenges current physics

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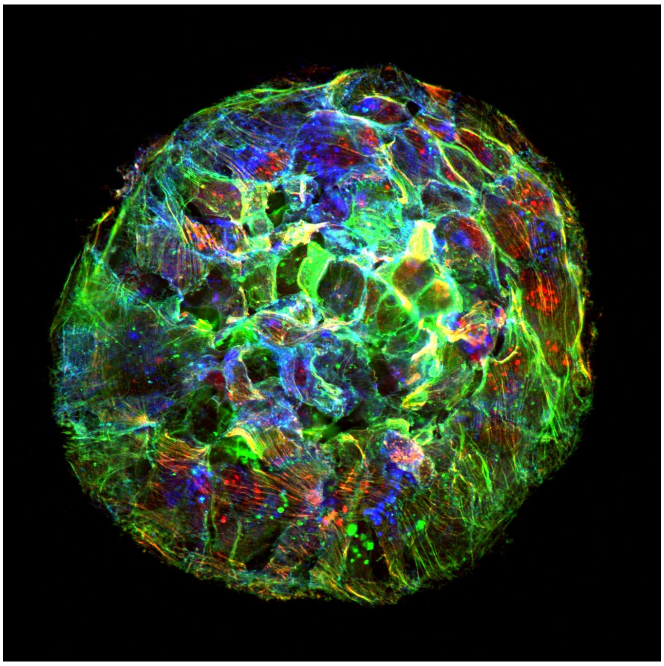
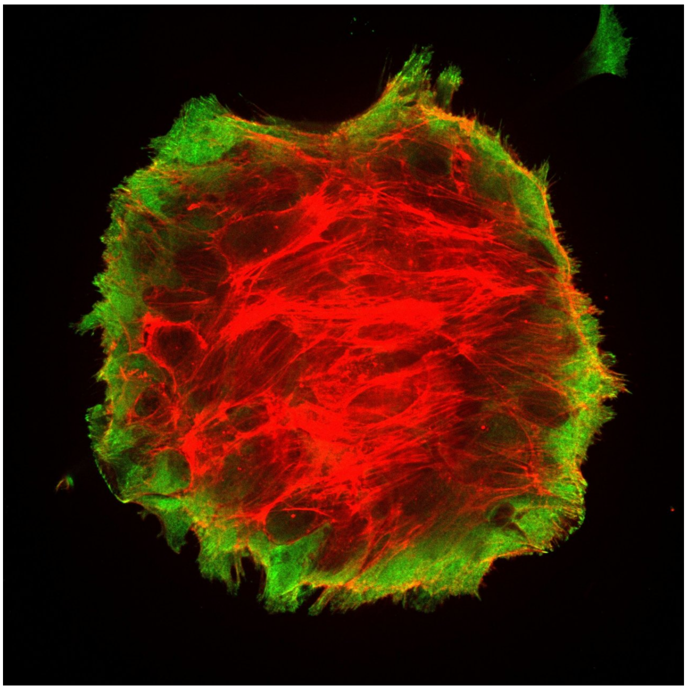


Breast cancer cells attached to a surface rich in collagen. The actin cytoskeleton can be seen in green, coated with active myosin (ppMLC) in red, and the cell-cell junctions (E-cadherin) in blue. Credit: X. Trepat/IBEC

A malignant tumor is characterized by the ability to spread. To do so, tumor cells stick to the surrounding tissue (mainly collagen) and use physical forces to propel themselves. A study published in *Nature Physics* by a team led by Xavier Trepat, lecturer at the Department of Biomedicine, University of Barcelona (UB), and Jaume Casademunt, professor of Physics at the UB, reveals the forces these tumor cells use to spread.

Researchers put breast tumor cells on a collagen-rich surface and observed how they expanded. The technology Trepat's group developed allowed them to measure the physical forces used by the cells during the process, which has not been observed before. They report that tumor metastasis depends on a competition between forces: cells stick to each other and are kept together, and at the same time, they adhere to the environment in order to escape. Depending on the predominant force, the tumor will keep its spherical shape or it will spread around the tissue surface. "It is a similar process to placing a drop of water on a surface. In some surfaces, the drop will spread out, for example on a brick, while the drop will remain spherical on waterproof fabric, for example," says Carlos Pérez, IBEC researcher, intern at 'la Caixa' and first author of the article.

Despite the similarities between tumors and liquids, the physics in these two phenomena are very different. "Wetting in surfaces is a core problem in classical physics we understand, but tumors seem to follow very different laws," notes Ricard Alert, UB researcher, intern at 'la Caixa' and co-author of the article. Unlike passive fluids, cells can create forces and move on their own. This turns biological tissues into active fluids, and in particular, tumors into active drops. Therefore, understanding tumor expansion on a surface requires developing a new physical theory that researchers have named "active wetting."



Breast cancer cells beginning to detach from a surface to form a spherical aggregate. In red, the actin cytoskeleton stretching the adhesions to the substrate (paxilina, in green). Credit: IBEC

"When we think about states of matter, we usually think about solids, liquids or gases. Our results and other laboratory results point out that living cells do not fit into this scheme and behave like another state of matter, which we call active matter," says Jaume Casademunt. When a tumor appears, cells accumulate mutations and their mechanical properties change. In general, tumor cells lose the connection between one another and join with their environment. During tumor growth, the own environment changes too, increasing the amount of collagen and rigidity. "Our experiments show that these changes are enough to put the balance of forces out of order, causing cells to spread around," says Xavier Trepat.

These findings show the importance of physical forces in metastasis, opening the window to the development of therapies to alter the mechanics of tumors as a potential treatment.

More information: Carlos Pérez-González et al, Active wetting of epithelial tissues, *Nature Physics* (2018). DOI: 10.1038/s41567-018-0279-5

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