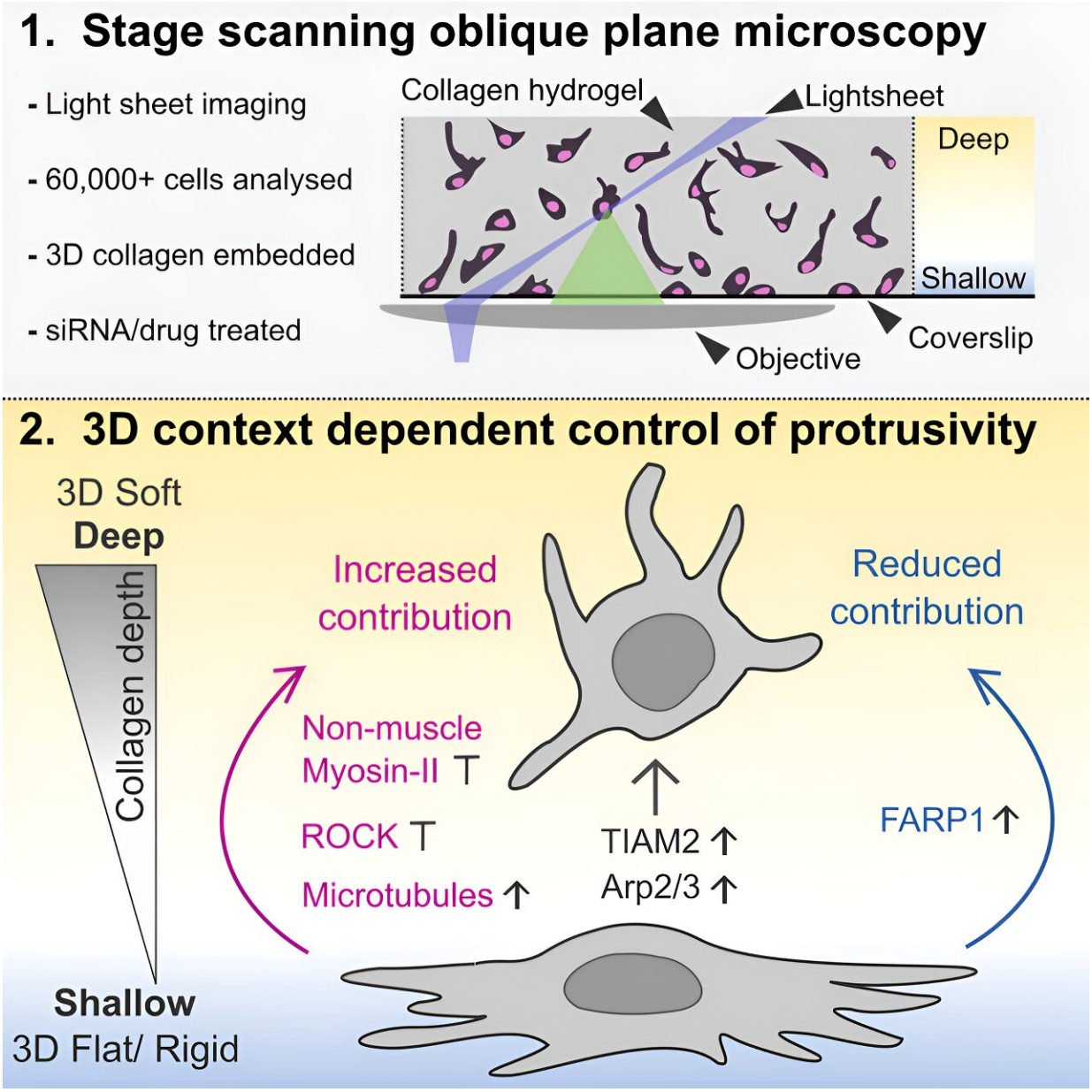
Shape-shifting cancer cell discovery reveals potential skin cancer drug targets

April 17 2024, by Hayley Dunning



Graphical Abstract. Credit: *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.114016

Cancer cells can change shape to travel around the body and spread (metastasize), but how they know when to do this has remained elusive.

Researchers have now used a new technique to identify two genes that control how melanoma skin cancer cells change shape in response to their environment—offering two potential drug targets to stop the cancer from spreading.

Cancer cells can change shape to move around the body, becoming drill-shaped to 'poke' through dense tissue like bone, or round and squishy to squeeze through soft tissues and get into the blood.

In a study published in *Cell Reports*, scientists at The Institute of Cancer Research, London, and Imperial College London have uncovered genes affecting how cells know what environment they are in and therefore which shape to choose.

Professor Chris Bakal, Professor of Cancer Morphodynamics at The Institute of Cancer Research, London, said, "Once cancer becomes metastatic and spreads to different parts of the body, it can be quite difficult to treat.

"This research has given us insight into the tricks that cancer cells are using to keep growing and spreading. We've identified two genes which could, in the future, be targeted to stop melanoma cancer from changing shape and metastasizing."

3D view

The team developed a new system to study cells in 3D environments—mimicking different parts of the body. Until now, most research has studied cells on hard 2D plastic surfaces.

A unique microscope called stage-scanning oblique plane microscopy (ssOPM) was used to take 3D images of melanoma cells—either stuck to a flat and rigid surface or embedded within a 3D soft collagen hydrogel.

By analyzing the 3D images taken of 60,000 cells when certain genes were 'switched off,' the researchers identified two genes that are important for melanoma cells to change their shape in response to their environment.

The researchers believe these genes, TIAM2 and FARP1, could be targeted to prevent melanoma cancer from metastasizing. These genes are good candidates for drug discovery as they have a structure similar to other proteins for which drugs are already in pre-clinical development.

Questions in cancer biology

Professor Chris Dunsby, from the Department of Physics at Imperial College London, said, "This study is the first to apply a new high-content microscopy technique called oblique plane microscopy to study many thousands of cells in 3D. In the future, we hope that the approach demonstrated here can be applied to address a wide range of questions in cancer biology."

The research team is currently creating AI-based technologies to make predictions about which drugs might be successful by using these 3D images of cells—which could reduce the time taken to develop new drugs.

Professor Kristian Helin, Chief Executive of The Institute of Cancer Research, London, said, "By using an innovative technique to study cells as if they were in a human, rather than in a laboratory, our scientists have uncovered a mechanism which cancer cells are using to move around the body."

"We know that most cancer deaths occur because cancer has spread from the original tumor to other parts of the body. I hope that further research will lead to the development of new treatments for metastatic melanoma."

More information: Environmentally dependent and independent control of 3D cell shape, *Cell Reports* (2024). DOI: 10.1016/j.celrep.2024.114016. www.cell.com/cell-reports/full … 2211-1247(24)00344-9

Provided by Imperial College London