Cell 'stickiness' could indicate metastatic potential

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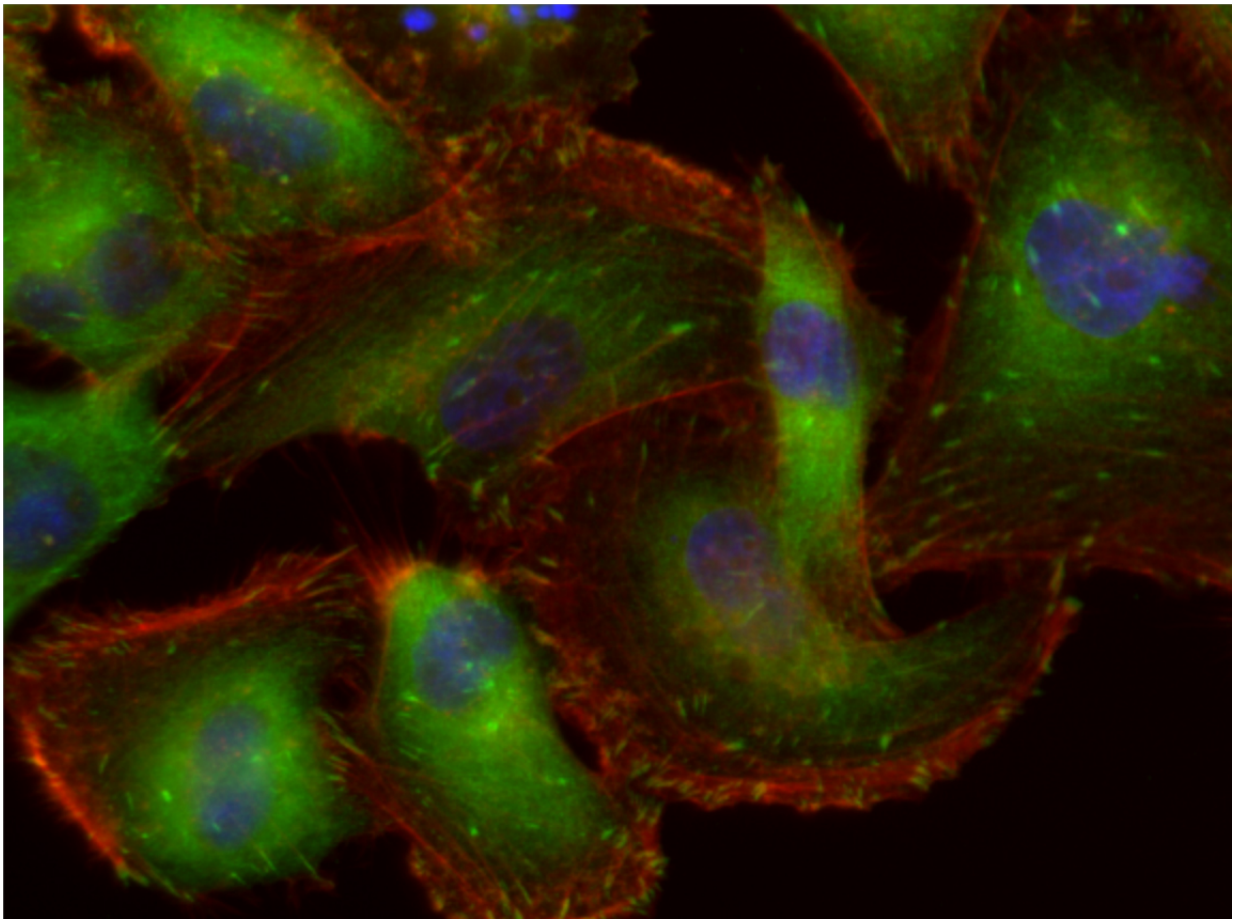


The adhesions (green) of strongly adherent and poorly migrating metastatic cancer cells. Credit: Alexander Fuhrmann

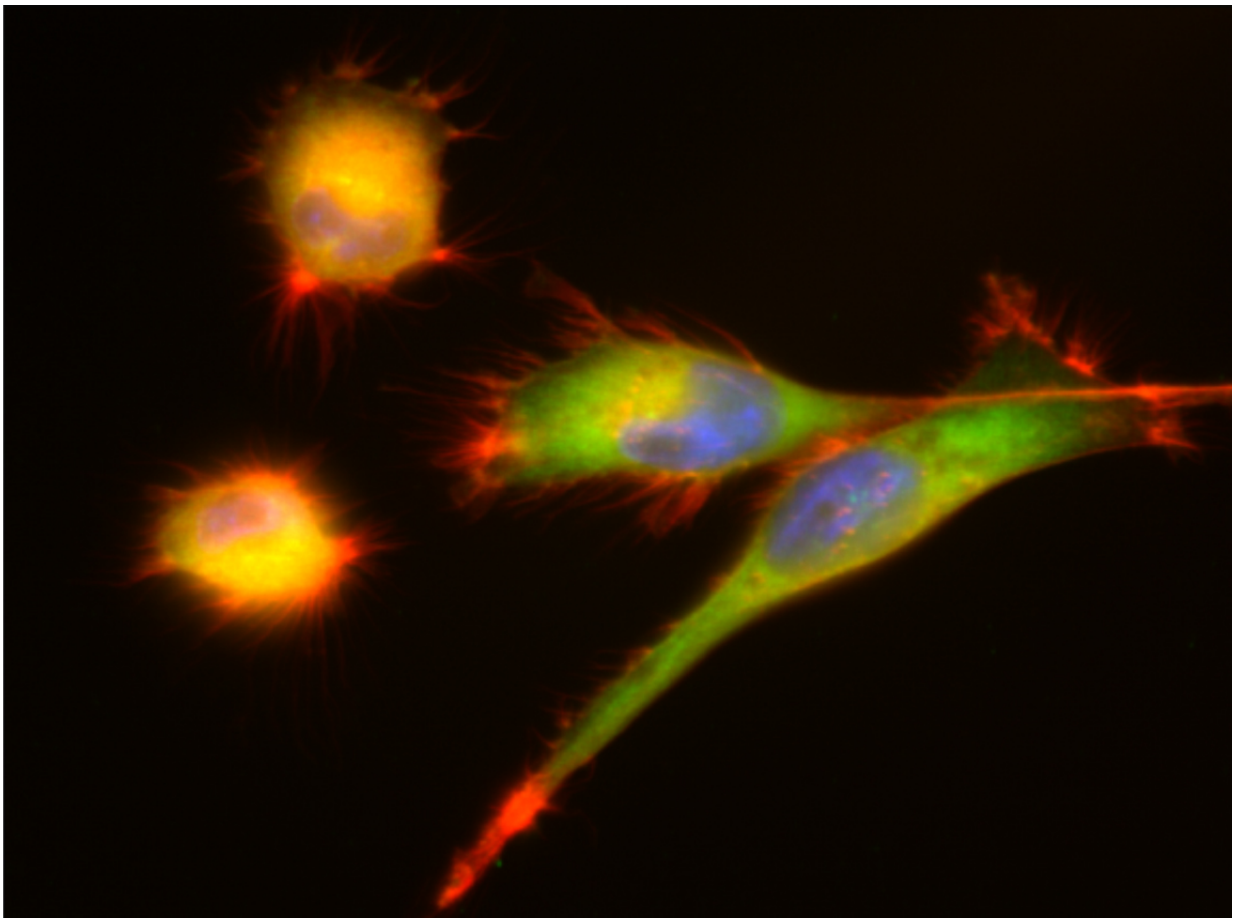
How strongly tumor cells adhere to the surrounding tissue could indicate

the likelihood that cancer will spread to other parts of the body, according to a study published February 28 in *Biophysical Journal*. Using a spinning disc device, the researchers found that tumor cells characterized by weak adhesion strength are more likely to migrate and invade other tissues compared with strongly adherent cells. The study may provide a much-needed marker to identify highly metastatic cells within a broader tumor cell population.

"There is no common biological marker that says that a tumor is more likely to spread," says senior study author Adam Engler of the University of California, San Diego. "However, our device shows that there may in fact be a physical marker that is predictive of the likelihood of spreading."

Cancer cells spread by detaching and migrating away from the primary tumor to form a secondary metastatic site. However, only a small subset of cancer cells from a tumor or even from a cancer cell line is capable of forming secondary tumors. Efforts to identify a universal molecular marker that identifies metastasizing cells across tumor types have been unsuccessful.

By contrast, some studies have suggested that a biophysical marker—the strength with which cells attach to the surrounding tumor tissue—could indicate the likelihood of secondary tumor development. But even within an individual tumor, cells exhibit substantial variability in their adhesive strength. "We reasoned that understanding adhesive heterogeneity within an invasive population may improve our ability to physically monitor cancer cells and predict invasive behavior," says study co-author Afsheen Banisadr, a Ph.D. student in the Engler lab at the University of California, San Diego.



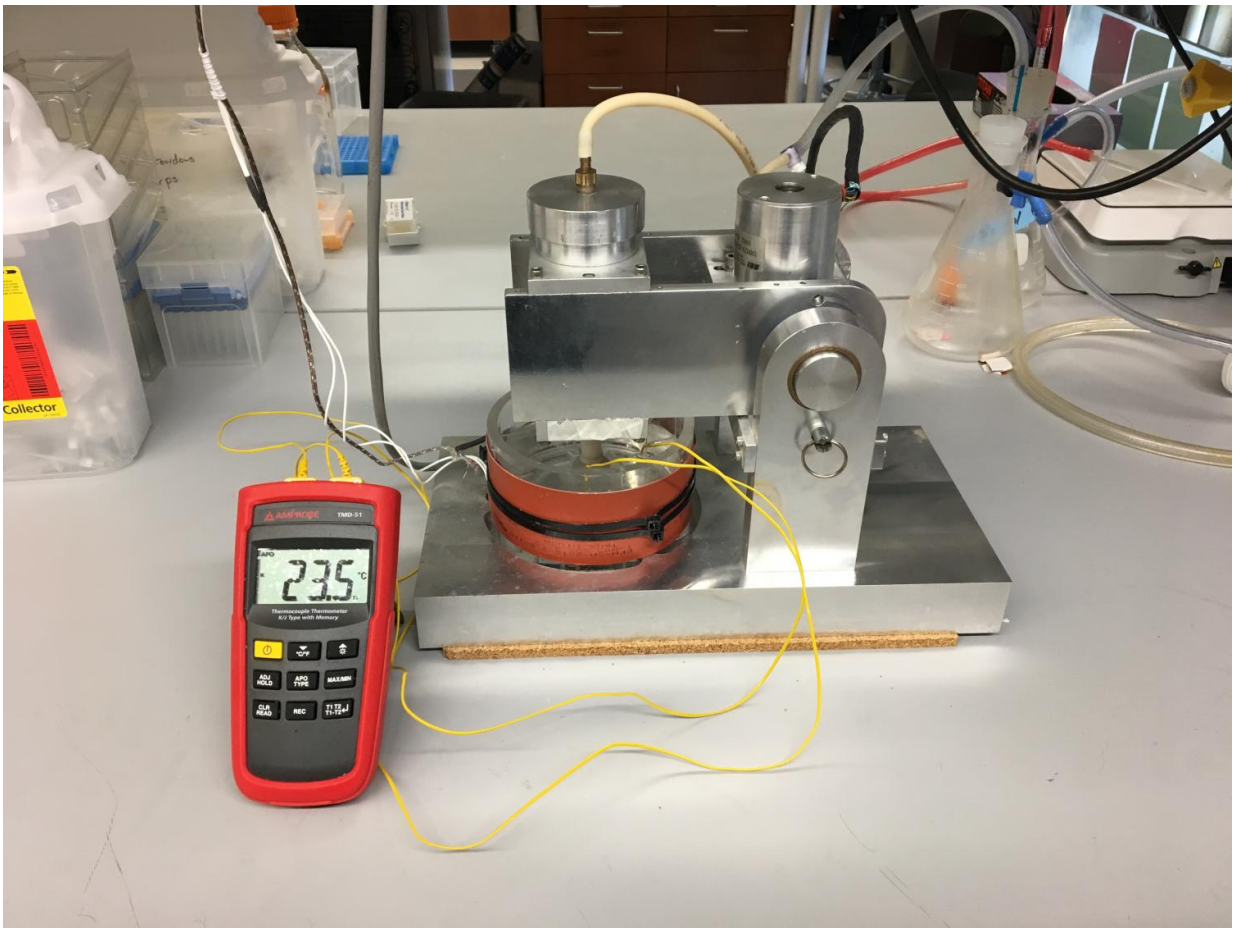
The adhesions (green) of less adherent and migrating metastatic cancer cells. Credit: Alexander Fuhrmann

To test this idea, Engler's lab teamed up with co-author Thea Tlsty of the University of California, San Francisco, to build a custom spinning disc device that could measure the adhesion strength of breast and prostate cancer cells of varying metastatic potential. The researchers attached cells to a coverslip coated with extracellular matrix proteins—molecules that provide structural and biochemical support to the surrounding cells. Then they mounted the coverslip on a spinning rod and applied force in a quantifiable and reproducible manner across the cell population, measuring the shear required to detach the cells from the extracellular

matrix protein-coated coverslip.

Using this spinning disc shear assay, they found that metastatic cells exhibit remarkable heterogeneity in their adhesion strength, unlike their non-metastatic counterparts. Strongly adherent metastatic cells exhibit less migratory behavior, similar to non-metastatic cell lines. Taken together, the findings suggest that adhesion strength may serve as a general, highly accurate marker of metastatic cells.

Building on these findings, Engler and his team have developed a second-generation device that isolates weakly adherent migratory cells. In future studies, they will test whether these cells, when injected into mice, will form tumors at a higher rate than a general population of tumor cells. If this hypothesis is correct, the researchers will then examine tissues adjacent to tumors in mice and humans to detect these weakly adherent cells and correlate their concentration to cancer-free survival times for patients.



The spinning disc device with the spinner submerged in buffer to test a sample. Credit: Afsheen Banisadr and Pranjali Beri

"If we find a correlation between low numbers of weakly adherent tumor cells in the tissue surrounding a tumor and long cancer-free survival times, we believe that this could serve as an indicator for metastatic potential of the patient's tumor," says study co-author Pranjali Beri, a Ph.D. student in the Engler lab at the University of California, San Diego.

In the future, clinicians could use this device to examine tumor biopsies and estimate the likelihood of metastasis, using this information to assess

whether patients might need more aggressive treatment at earlier disease stages. "However, patients should realize that that the timing for these results to hit even the initial clinical trials is several years away," Engler says.

More information: *Biophysical Journal*, Fuhrmann et al.; "Metastatic State of Cancer Cells May be Indicated by Adhesion Strength" www.cell.com/biophysj/fulltext … 0006-3495(17)30029-2 , DOI: 10.1016/j.bpj.2016.12.038

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