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Cell 'Stickiness' Could Indicate Metastatic Potential

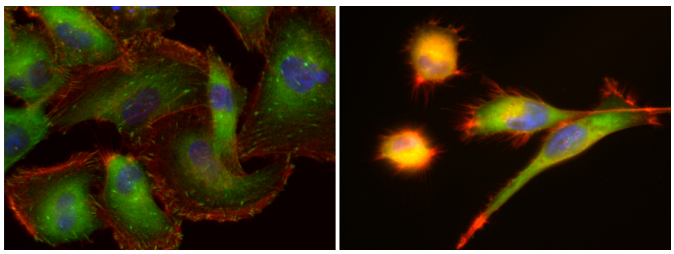

Image showing the adhesions (green) of: (left) strongly adherent, poorly migrating metastatic cancer cells and (right) weakly adherent, migrating metastatic cancer cells. Image credit: Engler Lab

How strongly tumor cells adhere to surrounding tissue could indicate how likely cancer will spread to other parts of the body, according to a new study led by bioengineers at the University of California San Diego. Using a spinning disc device, the researchers found that tumor cells that adhere weakly are more likely to migrate and invade other tissues compared with strongly adherent cells.

The study could provide a much-needed marker to identify highly metastatic cells within a broader tumor cell population. The study was published Feb. 28 in *Biophysical Journal*.

"There is no common biological marker that says that a tumor is more likely to spread," said Adam Engler, bioengineering professor at the UC San Diego Jacobs School of Engineering and senior author of the study. "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.

Some studies have suggested that 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 vary widely 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," said Afsheen Banisadr, a biomedical sciences Ph.D. student in Engler's lab and co-author of the study.

To test this idea, Engler's lab teamed up with Thea Tlsty, a professor in the Department of Pathology at 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 force required to detach the cells from the extracellular matrix protein-coated coverslip.

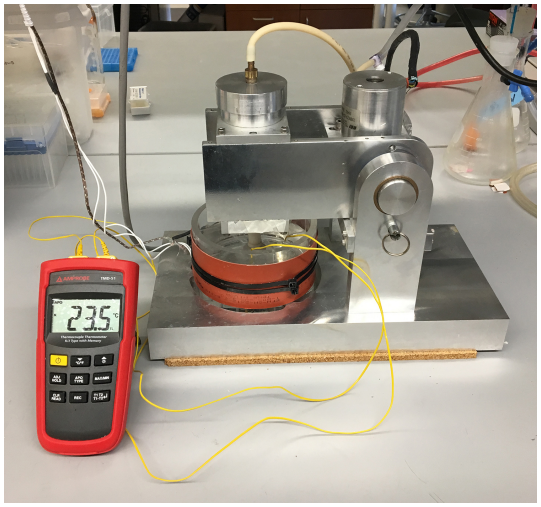

Image of the spinning disc device with the spinner submerged in buffer to test a sample. Image credit: Engler Lab

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. These findings suggest that adhesion strength could 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.

"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," said Pranjali Beri, a bioengineering Ph.D. student in Engler's lab and co-author of the study.

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 said.

Full paper: “Metastatic State of Cancer Cells May be Indicated by Adhesion Strength.” Authors of the study are Alexander Fuhrmann, Afsheen Banisadr, Pranjali Beri and Adam J. Engler of UC San Diego and Thea D. Tlsty of UC San Francisco.

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