Tumor-causing cells are squishier, study finds

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(Medical Xpress)—A new tool developed by scientists at The Methodist Hospital separates tumor-causing cancer cells from more benign cells by subjecting the cells to a microscopic game of Plinko—except only the squishiest cells make it through.

As reported in this week's Proceedings of the National Academy of Sciences (early edition online), the more flexible, tumor-causing cells navigated a gamut of tiny barriers, whereas the more rigid, more benign cells had trouble squeezing through 7 micrometer holes. Methodist scientists worked with University of Texas MD Anderson Cancer Center researchers to test the device with different kinds of cancer cells.

The work supports the hypothesis that cell squishiness indicates tumor potential. Most normal cells contain a developed cytoskeleton—a network of tiny but strong rod-shaped proteins that give cells their shape and structure. In their feverish drive to divide, cancer cells may be diverting resources away from developing a cytoskeleton in favor of division, hence the squishiness.

"We have created many pathways for cells to cross barriers," said Methodist nanomedical faculty Lidong Qin, Ph.D., the project's principal investigator. "The throughput of a MS-Chip is at the level of one million cells. When a stiff cell blocks one particular barrier, many other bypasses will allow flexible cells to flow through."

Cancer stem cells are known to be squishier than other cancer cells. The

team of scientists showed that flexible cells separated by the MS-Chip exhibited gene expression patterns consistent with cancer stem cells.

"Many papers indicate the presence of cancer stem cells means a worse prognosis for patients," said cancer scientist Jenny Chang, M.D., co-principal investigator and director of Methodist's Cancer Center. "Yet they are not typically quantified by doctors."

Subsequent analysis of separated cells by the Methodist and MD Anderson team showed the flexible cells were less likely to express cell cytoskeleton genes and more likely to express the motility genes that could contribute to metastasis.

By testing for the presence of metastatic cells, doctors may be able to tell whether cancer treatment was successful, or an as-yet untreated cancer's likelihood of metastasizing to another part of the body.

A growing awareness of cancer stem cells' role in cancer metastasis and recurrence and has been frustrated by the absence of technology that makes this knowledge useful to doctors and their patients. Up to now, there has been no way of quickly and reliably separating and identifying the more dangerous tumor-causing cells from a biopsy.

The new device, which was developed at Methodist, successfully enriched tumor-causing cells from a mixture of cancer cells. It is called the Mechanical Separation Chip, or MS-Chip. Cells separated by the device can be easily collected and studied. The current standard for cell separation, flow cytometry, is relatively slow and relies on cell surface biomarkers.

"Our microfluidics cell separation via MS-Chip provides a high throughput method that can particularly sort cells to different levels of stiffness, which opens a new avenue to study stiffness related cellular

and molecular biology," Qin said. "Downstream molecular analysis, including genomic and proteomic profiling of the cell subtypes, provides an approach to identifying new biomarkers relevant to cancer stem cells and cancer metastasis."

Right now, each MS-Chip costs about $10 to produce.

"If massively produced, MS-Chip cost could be at the level of one dollar per chip," Qin said. "Running a mechanical cell separation will be even less expensive than flow cytometry cell sorting."

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