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Battery of tests on cancer cells shows them as 'squishy,' yet tactically strong

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A team of student researchers and their professors from 20 laboratories around the country have gotten a new view of cancer cells. The work could shed light on the transforming physical properties of these cells as they metastasize, said Jack R. Staunton, a Ph.D. candidate at Arizona State University in the lab of Prof. Robert Ros, and the lead author of a paper reporting on the topic.

Metastasis is a critical step in the progression of cancer. It is when the cancer spreads from one organ or part to another. While much is known about metastasis, it remains an incomplete understanding of the physical biology of the transition.

To get a better understanding of metastasis, more than 95 graduate students, post docs and professors in a variety of laboratories across the U.S. subjected two cell lines to a battery of high-tech tests and measurements. Their results, outlined in the paper "A physical sciences network characterization of non-tumorigenic and metastatic cells," were published today (April 26, 2013) in *Scientific Reports*.

The researchers performed coordinated molecular and biophysical studies of non-malignant and metastatic breast cell lines to learn more about what happens to a cell when it transitions to a metastatic state.

Each laboratory is part of the National Cancer Institute's Physical Sciences Oncology Center (PSOC), a network of 12 centers devoted to understanding the physical sciences of cancer. ASU's center, the Center

for the Convergence of Physical Science and Cancer Biology, is led by Prof. Paul Davies.

Each PS-OC was supplied with identical cell lines and common reagents, and considerable effort was made to ensure that all the conditions were standardized and documented at regular intervals. Staunton said the ASU group made three contributions to the study.

Other ASU researchers involved in the project and co-authors on the paper are: Alexander Fuhrmann, Vivek Nandakumar, Laimonas Kelbauskas, Patti Senechal, Courtney Hemphill, Roger H. Johnson and Deirdre Meldrum.

"We compared the stiffness of normal breast cells and highly metastatic breast cancer cells, and found the cancer cells to be significantly more 'squishy' or deformable," Staunton said. "This makes sense because in order for a cell to metastasize, it has to squeeze through tight passages in the lymphatics and microvasculature, so being squishy helps cancer cells spread through the body."

"We also looked at the morphology of their nuclei," he added. "The cancer cell nuclei were found to have a characteristic 'crushed beach-ball' shape that might correspond to the abnormal chromosomal rearrangements associated with cancer."

"Finally, we took individual cells, put each one in an airtight chamber, and measured how much oxygen they consumed," Staunton said. "This tells us about their metabolism. We found the cancer cells use less oxygen, relying more on glycolysis, kind of like what bacteria and yeast do."

Taken together, researchers at the 12 PSOC's used some 20 distinct techniques, including atomic force microscopy, ballistic intracellular

nano-rheology, cell surface receptor expression levels, differential interference contrast microscopy, micro-patterning and extracellular matrix secretion, and traction force microscopy.

The work has enabled a comprehensive cataloging and comparison of the physical characteristics of non-malignant and metastatic cells, and the molecular signatures associated with those characteristics. This made it possible to identify unique relationships between observations, Staunton said.

"We were surprised that even though the cancer cells are softer, they are able to exert more contractile forces on the fibers surrounding them – which was determined at the Cornell University PSOC by a method called traction force microscopy. This pair of characteristics is somewhat contradictory from a purely physical perspective, but it makes sense for a cancer cell, since both traits improve their chances of metastasizing. Understanding why is still an active area of research," explained Staunton, who is working towards his doctorate in physics.

"Another interesting finding was that a protein called CD44, which doubles as a cancer stem cell marker and as a molecule that helps the cell stick to certain fibers in the extracellular matrix, is equally abundant in the normal and cancer cells. But in the cancer cells the proteins don't make it to the cell surface," he added.

"For some reason they stay inside the cytoplasm, so the cancer cells are not as sticky," added Staunton whose hometown is Buffalo, N.Y. "This is another trait that contributes to their ability to spread through the body."

The PSOC network went to great lengths to have all of the studies performed under comparable conditions. While the cell lines studied are well understood, part of the effort for the network was to prove they could consistently coordinate the research.

Staunton, who has been involved in ASU's center since its inception, says the experience has helped his growth as a researcher.

"It is the perfect habitat for budding scientists and for transdisciplinary collaborations," he said.

Provided by Arizona State University

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