Physics research suggests new pathways for cancer progression

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Observing that certain cancer cells may exhibit greater flexibility than normal cells, some scientists believe that this capability promotes rapid tumor growth. Now computer simulations developed by Boston University Biomedical Engineering Assistant Professor Muhammad Zaman and collaborators at the University of Texas at Austin appear to support this view. A 3D model of healthy and cancer cells that they've created indicates that the softening of cancer cells not only accelerates their proliferation but also extends their lifetime—a one-two punch that may trigger the rapid growth of malignant tumors.

The team's simulations and findings herald a new, quantitative approach to understanding tumor development centered on a small number of mechanical properties rather than multiple biochemical factors.

"Our study is unique in that it takes into account in vivo data on the mechanical properties of cancer cells," said Zaman. "Our novel computer simulation provides a platform to examine how stiffness of cancer cells influences their growth, and could lead to the development of early interventions."

Combining Zaman's expertise in cancer and cell migration with UT-Austin Chemical Engineering Professor Roger Bonnecaze's knowledge of fluid mechanics and postdoctoral fellow Parag Katira's computer simulation skills, the researchers produced a 3D computer model that systematically traces the impact of cell softness and other mechanical factors on cell behavior within a tissue. The model represents each cell

as a liquid core encased by a spherical, viscous, elastic shell that can bind or stick to other cells to form a tissue-like mass. In simulations, individual cells are programmed to live, die or divide based on a set of rules drawn from real-time, in vivo experiments with tumor cells.

To emulate tumor growth, the researchers established a baseline simulation of tissue composed exclusively of hard-shelled, healthy cells, and then introduced a small number of soft-shelled, mutant cancer cells. When that number reached eight, the mutants began to multiply at a much higher rate than normal cells, and the more mutants introduced, the higher the rate. Interpreting this phenomenon as the emergence of a tumor, the researchers speculated that a cluster of at least eight soft mutant cells is needed to overcome the resistance of neighboring stiff, normal cells so that the mutants can stretch and divide rapidly.

The team also modeled the strength at which cancer cells stick to one another, and varied both cell softness and stickiness in several simulations. They found that increasing softness, rather than varying stickiness, led to the most substantial increase in tumor growth.

"This study focused only on the first step in tumor growth," said Zaman. "Our next step is to set up computational experiments to determine what leads tumors to metastasize. Our computer simulations will also allow us to model breast, prostate and other cancers—even different stages within those diseases—much more efficiently than in laboratory experiments."

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