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Researchers develop novel 3-D culture system for inflammatory breast cancer

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Inflammatory breast cancer (IBC) is a very rare and aggressive disease that progresses rapidly and is associated with a very low survival rate. To understand how this type of cancer spreads, it's crucial to characterize the interactions between cancer cells and their 3D environment. Researchers at Fox Chase Cancer Center have developed a novel, 3D culture system that mimics the environment surrounding these cancer cells. This model could be used to test new anticancer drugs capable of inhibiting the spread of IBC tumors.

"The tumor microenvironment plays a pivotal role in tumor development and progression, and it also plays a big role in restricting tumorigenesis," says senior study co-investigator Edna Cukierman, PhD, Associate Professor of Cancer Biology at Fox Chase. "So understanding the interactions between the tumor and the environment will help us to come up with new ways to target the tumor."

For the study, Cukierman, a tumor microenvironment expert, and her colleagues in the lab of Massimo Cristofanilli, MD, Professor at Fox Chase and a leading expert in inflammatory breast cancer, used tumor-associated stromal cells from patients with advanced IBC to build a 3D structure consisting of cell-derived extracellular matrix—scaffold that provides structural and biochemical support to cells.

After culturing a plethora of established and patient-derived cancer cells in the stromal 3D system, the researchers categorized them into two groups. While some cells showed a significant increase in proliferation

and resembled those seen in aggressive tumors, others were more similar to cells in less-aggressive tumors. These two types of cells modified the extracellular matrix in distinct ways, indicating that there is a dynamic interplay between cancer cells and the microenvironment.

Moreover, exposure to the matrix caused all of the cancer cells to increase their expression of the protein epithelial cadherin (i.e., E-Cadherin), whose levels are often elevated in IBC tumors. These findings suggest that the microenvironment may promote the proliferation, growth and invasion of IBC tumors.

"Our system could be used to predict the in vivo behavior of cells and to study the signaling mechanisms that are responsible for tumor-microenvironment interactions in IBC cancer," Cukierman says. "We have some gene candidates that we believe are responsible for the degree of aggressiveness we observe in the 3D model, so we would like to manipulate these genetically using mutants or pharmacologically using inhibitors to block the proteins that we believe are responsible. If that reverses the aggressiveness, it could give us a good hint of what types of targets we could perhaps try to develop and bring to the clinic in the future."

Provided by Fox Chase Cancer Center