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Breast cancer cells outsmart the immune system and thrive

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Scientists discovered a new way breast cancer cells dodge the immune system and promote tumor growth, providing a fresh treatment target in the fight against the disease. While comparable mechanisms to avoid the immune system have been identified in mice with breast and other cancers, the study tested human breast tumor cells, putting researchers closer to understanding how the disease progresses in real patients.

The study, published in the journal *Cancer Research*, found high levels of the protein Hsp27 (heat shock protein 27) are released from human breast cancer cells and may not only render immune cells unresponsive to the tumor, but increase blood flow to the tumor as well, both of which fuel tumor growth.

"Our study is very unique because we used human breast cancer cells, which are extremely difficult to get," said Asit De, Ph.D., lead author and research associate professor in the Department of Surgery at the University of Rochester Medical Center, who worked closely with physicians at the Wilmot Cancer Center. "The way tumor cells operate in mice is not identical to humans, so we need to do more of these types of human studies to confirm or reject cancer-related discoveries in mice."

Past research reports Hsp27 is present in high levels inside breast tumor cells and is associated with resistance to chemo and radiation therapy. De and his team discovered Hsp27 is also released, or pushed out of breast tumor cells, into the area surrounding the tumor, known as the breast tumor microenvironment.

Once outside the cells, Hsp27 may transform circulating white blood cells called monocytes that enter the tumor into cells known as macrophages, which do the opposite of what they are meant to do. Usually, macrophages work to wipe out tumor cells, but in this case they help, rather than hurt, tumor cells. These particular macrophages may make human T cells – the main immune cells that attack and kill foreign invaders, like tumors – totally indifferent to the tumor and the body's call to destroy it.

In addition to suppressing the immune response to the tumor, these macrophages encourage rapid formation of extra blood vessels that can help in supplying blood to the tumor – a process known as angiogenesis – essentially feeding the tumor so it can continue to grow.

Elevated levels of Hsp27 have been found in the blood of cancer patients with other solid tumors, such as liver and pancreatic cancer tumors, leading study authors to believe the protein may play a role in tumor progression beyond breast cancer.

"Our finding that Hsp27 aids tumor progression is just the start – we know there are several other molecules that help breast tumor cells suppress the immune system and we hope to identify more of them in future research," noted De.

Hsp27 is a ubiquitous protein that is important in all the body's cells. When it remains inside cells at normal levels it acts as a chaperone, protecting cells from stress, such as exposure to high heat or chemicals. Only when the protein is let loose outside cells does it appear to have a detrimental effect on the immune system.

To carry out the study, De worked closely with clinicians in surgical oncology and plastic surgery at the Medical Center to obtain and analyze tumor-containing breast tissue samples from breast cancer patients

undergoing surgery and normal breast tissue samples from healthy volunteers undergoing breast reduction. He also collected and tested blood samples from untreated breast cancer patients and age-matched healthy women.

Besides skin cancer, breast cancer is the most commonly diagnosed cancer among women in the United States. It is also the second leading cause of cancer-related death in American women, behind lung cancer. The development of treatment strategies that stop a tumor's ability to silence or circumvent the immune system require a better understanding of tumors' various avoidance mechanisms, such as the one identified by De.

De plans to continue research on Hsp27 in breast cancer, studying whether blocking Hsp27 slows tumor growth.

Provided by University of Rochester Medical Center