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Scientists link protein with breast cancer's spread to the brain

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A cancer-research team at the University of Wisconsin-Madison has identified a protein that may be a major culprit when breast cancer metastasizes to the brain.

Brain metastasis is a terrifying complication of advanced breast cancer, with a grim prognosis and few treatment options. The cancer's spread to the brain is often undetected until patients start to develop symptoms such as seizures, headaches, and trouble thinking. Scientists hope a better understanding of the molecular events that regulate brain metastasis will lead to earlier diagnosis and improved therapies.

Using cell models, the researchers found that breast cancer cells harness a protein called alphaB-crystallin to help them stick to endothelial cells that line the small blood vessels in the brain. In addition, this protein enhances the penetration of breast cancer cells through the blood-brain barrier, which normally prevents cells and many molecules from entering the brain. Once in the brain, the breast cancer cells are able to form metastases.

The study, published in *Clinical Cancer Research*, and featured on the journal cover, was led by Dr. Vincent Cryns, professor of medicine at the University of Wisconsin School of Medicine and Public Health and a member of the University of Wisconsin Carbone Cancer Center.

Cryns and his colleagues also developed new mouse models of breast-cancer brain metastasis that mimic many features of the human disease.

They found that reducing the expression of alphaB-crystallin in breast cancer cells hindered the cells' ability to form brain metastases in mice.

"These observations in our mouse models suggest that alphaB-crystallin may be a promising drug target that should be explored further," said Cryns. "Although there are no drug inhibitors of this protein currently, we are actively pursuing studies to identify drugs that might reduce the expression of the protein or block its effects," he added.

In addition, by examining tissue from breast-cancer patients who developed brain metastasis, the investigators discovered that women with breast tumors that expressed alphaB-crystallin had a shorter survival than women with breast tumors that did not express this protein. These studies were conducted in collaboration with researchers at the University of North Carolina at Chapel Hill, Duke University and other institutions.

Furthermore, the team found breast tumors that expressed alphaB-crystallin were more likely to be triple-negative breast cancers—an aggressive type of cancer, which lacks three receptors (estrogen receptor, progesterone receptor and HER-2) expressed in other types of breast cancer. Triple-negative breast cancers are known to have a high incidence of brain metastasis.

"Our findings suggest that alphaB-crystallin may contribute to the tendency of triple-negative breast cancers to metastasize to the brain and to their poor prognosis," said Cryns. Yet, he cautioned these findings need to be validated in additional studies.

Provided by University of Wisconsin-Madison

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