

CANCER MATTERS

Latest Findings Open Way to Treat Breast Cancer that Spreads to the Brain



Date: June 9, 2024 | 0 Comments

Berandasehat.id – Experts continue to seek solutions to treat breast cancer, even those that have metastasized (spread) to other organs, including the brain. A study led by researchers from the University of Arizona Cancer Center at UArizona Health Sciences identified a biological mechanism that could lead to more effective treatment for breast cancer that has spread to the brain.

By studying metabolic differences between primary breast cancer cells and cells that metastasize to the brain, they determined that autophagy was significantly upregulated in brain metastases.

Autophagy is a cell recycling process that cancer cells can use to stay alive when faced with stressful conditions such as those triggered by anticancer drugs.

“The prognosis for individuals with brain metastases from breast cancer is extremely unfavorable, and treating breast cancer metastases in the brain remains a formidable challenge,” said senior author Jennifer Carew, Ph.D. “We were able to disrupt the ability of breast cancer cells to form brain metastases by disrupting the autophagy pathway.”

In research published in *Clinical and Translational Medicine*, researchers first showed that targeting the key autophagy regulator gene ATG7 significantly reduced the ability of breast cancer cells to form brain metastases in a mouse model.

With the goal of developing a strategy to convey these findings to patients, the research team investigated whether hydroxychloroquine, a drug approved by the US Food and Drug Administration (FDA), could potentially be used to treat breast cancer brain metastases.

Hydroxychloroquine inhibits autophagy at later stages in the pathway and importantly, readily crosses the blood-brain barrier.

“Most drugs don't efficiently cross the blood-brain barrier, and that's one of the main reasons why brain metastases are so difficult to treat,” said Carew, a professor of medicine at UArizona College of Medicine Tucson and a member of the UArizona Cancer Center's Clinical and Translational Oncology Program.

The research team combined hydroxychloroquine with lapatinib, which is FDA-approved to treat breast cancer. They showed that this drug combination successfully reduced the number and size of breast cancer brain metastases in a mouse model.

Hydroxychloroquine has been combined with a number of other anticancer agents in early phase clinical trials, but this is the first time researchers have studied its effectiveness when combined with lapatinib for breast cancer therapy.

Carew said the team was amazed by how significantly they were able to reduce the ability of breast cancer cells to form brain metastases by targeting just one pathway.

Unfortunately, cancer cells have evolved in many ways that make it difficult for us to stop their growth or kill them, Carew acknowledged. “It's always surprising to see how impactful changing just one thing can be,” he said.

“Our group and other groups have shown that activation of autophagy makes it difficult for many types of cancer therapies to kill cancer cells and this drives drug resistance,” said first author Steffan Nawrocki, Ph.D., a professor at the UArizona School of Medicine.

“Because hydroxychloroquine and lapatinib are already FDA approved, we can advance this drug combination quickly into clinical trials for patients with breast cancer brain metastases,” added Nawrocki.

Brain metastases are the most common adult central nervous system tumors, with 20% to 30% of cases caused by breast cancer patients, especially those with triple negative and HER2-amplified disease.

Managing breast cancer metastases in the brain is a challenge, considering that only 20% of patients with breast cancer brain metastases survive more than five years, *MedicalXpress* reports. (BS)

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