MicroRNA Molecule May Serve as Biomarker, Target for Brain Metastases in Breast Cancer Patients

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- MicroRNA molecule called miR-7 decreased in highly metastatic cancer stem-like cells.
- miR-7 attenuated cancer stem-like cells' capacity for brain metastasis in mice.
- MicroRNA molecule suppressed KLF4 expression.

PHILADELPHIA — Researchers have identified two molecules that could potentially serve as biomarkers in predicting brain metastases in patients with breast cancer, according to data published in *Cancer Research*, a publication of the American Association for Cancer Research.

Currently, most deaths from breast cancer are a result of metastatic disease. New research shows that cancer stem-like cells — commonly defined as cells within a tumor with the capacity to initiate a new tumor, proliferate rapidly, differentiate and cause chemotherapy resistance — may play a role in breast cancer metastasis.

"Recent research has shown that microRNAs are involved in tumor initiation and progression, and we hypothesized that they also may play a role in metastasis, particularly in relation to cancer stem-like cells," said Kounosuke Watabe, Ph.D., associate director for basic science at the University of Mississippi Medical Center in Jackson, Miss.

Watabe and colleagues performed microRNA profile analysis on RNA extracted from cancer stem-like cells isolated from a human breast cancer cell line and two highly metastatic variants of this cell line.

"We found that miR-7 is a metastasis suppressor in cancer stem-like cells," Watabe said. "When we increased expression of miR-7 in cancer stem-like cells from metastatic human breast cancer cell lines, it suppressed their metastatic properties."

Next, the researchers examined the molecular pathway downstream of miR-7 to find its targets and discovered that miR-7 suppressed expression of KLF4.

"High expression of KLF4 was inversely associated with brain metastasis-free survival but was not associated with bone metastasis," Watabe said. "This was confirmed in an animal model when we found that expression of miR-7 significantly

suppressed the ability of cancer stem-like cells to metastasize to the brain but not the bone."

Finally, the researchers tested tumor samples from patients with breast cancer whose disease metastasized to the brain. Results showed that miR-7 was downregulated and KLF4 was upregulated. The miR-7/KLF4 axis played a critical role in cancer stem-like cell brain metastasis, according to Watabe.

Few treatments currently exist for brain metastasis because few drugs can penetrate the blood–brain barrier, which prevents chemotherapy from reaching the brain.

"Cancer cells find the brain to be a kind of sanctuary where they can survive longer," Watabe said. "It is possible that miR-7 and KLF4 may serve as diagnostic or prognostic markers, or therapeutic targets for the prediction of, or treatment of, brain metastasis."

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