Common cholesterol drugs could slow spread of breast cancer to brain

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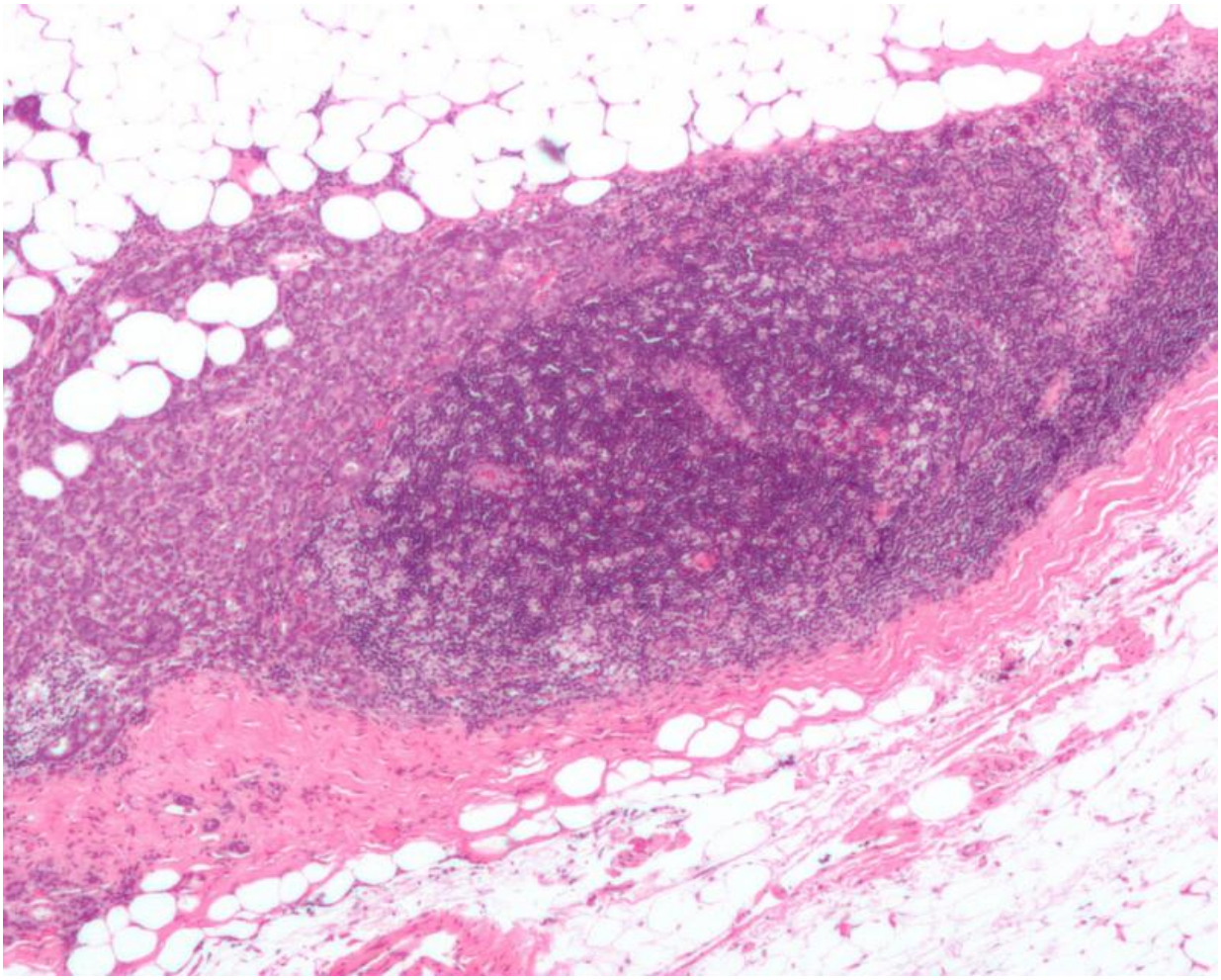

Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

A new study from the University of Notre Dame shows drugs used to treat high cholesterol could interfere with the way breast cancer cells adapt to the microenvironment in the brain, preventing the cancer from taking hold. Patients with breast cancer who experience this type of metastasis typically survive for only months after diagnosis.

Statins, a group of drugs commonly prescribed for those with high cholesterol, were shown to interfere with a pathway that allows a cancer cell to recycle cell surface proteins and therefore make it easier for cancer cells to live within the brain.

"It normally takes a decade to develop new medications. Instead of waiting, we can repurpose medications people are already taking," said Siyuan Zhang, the Dee Associate Professor in the Department of Biological Sciences, and principal investigator of the study published in *Nature Communications*. "Statins are relatively safe drugs, and they can even be given, if doctors choose, to try to prevent metastasis."

The protein Rab11b brings "recycled" proteins back to the surface like a fast-moving Ferris wheel, Zhang said. Statins suppress breast cancer survival in the brain by inhibiting the ability of Rab11b to recycle surface proteins. As a result of less recycling, the surface of metastatic tumor cells is less sticky. This limits the survival of cancer cells, and ultimately slows the rate of tumor colonization in the brain microenvironment.

To complete the research, Zhang's lab completed gene profiling to screen for genes that were functionally important in inhibiting the way tumor cells adapted to the brain, Zhang said. Then, they used a fruit fly tumor model to perform a genetic tumor growth screen, allowing the team to quickly narrow down a subset of genes that might be important for tumor formation in the brain.

"We knew Rab11b sits downstream of an enzyme that is important for cholesterol synthesis, so once we recognized its role, we thought that statins could knock Rab11b back from its role in pushing the other proteins up to the surface in metastatic breast cancer in the brain," said Zhang, who is affiliated with the Harper Cancer Research Institute.

Zhang's lab seeks uses of already-FDA-approved drugs to target cancer metastasis because they are already known to be safe, which allows for quicker testing without waiting several years for new therapeutics to be developed and tested.

More information: Erin N. Howe et al. Rab11b-mediated integrin recycling promotes brain metastatic adaptation and outgrowth, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16832-2

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