Researchers find a potential therapeutic target to prevent dissemination of cancer cells in the central nervous system

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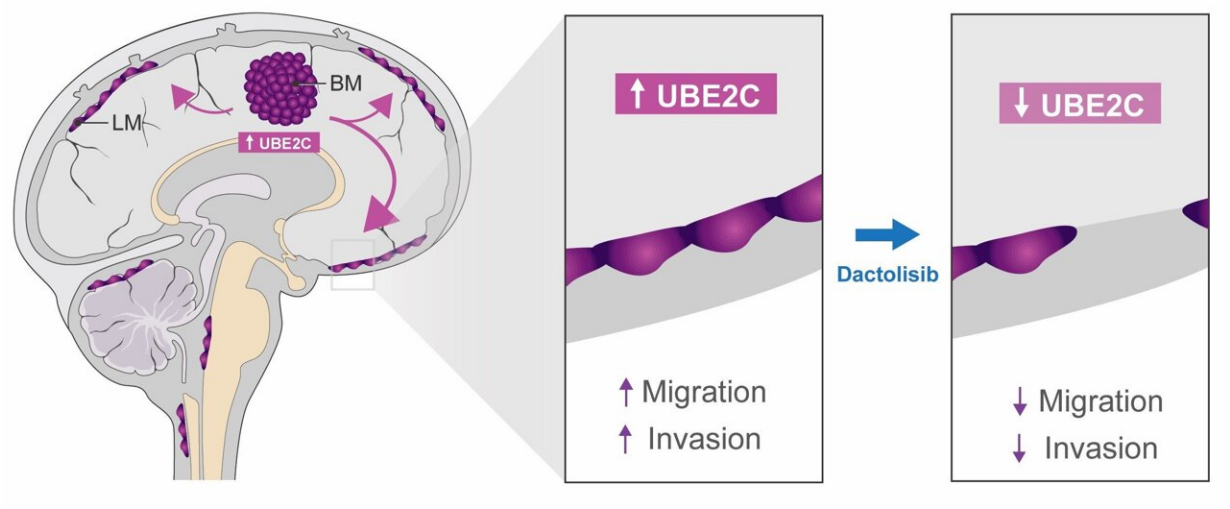

Graphical abstract. Credit: *Neuro-Oncology Advances* (2023). DOI: 10.1093/noajnl/vdad048

A new study led by Cláudia C. Faria, researcher in the lab of João Taborda Barata at the Instituto de Medicina Molecular João Lobo Antunes (iMM, Lisbon) and neurosurgeon at the Centro Hospitalar Universitário Lisboa Norte (CHULN-Hospital de Santa Maria, Lisbon), identified a protein present in brain metastases that could be a potential therapeutic target to limit disease progression.

The work, published April 28 in the journal *Neuro-Oncology Advances*, showed that the presence of high levels of the protein UBE2C in samples of brain metastases from patients with various types of cancer is associated with worse disease prognosis.

The researchers began by analyzing the general gene expression in brain metastasis samples from 30 patients with cancer originating in different organs. "We analyzed which genes are present at higher levels in brain metastases. Among the five most promising genes, we identified the gene that originates the protein UBE2C, a protein involved in cell cycle. To confirm the clinical relevance of this finding, we analyzed a larger group of patients with brain metastases (89 patients with various types of cancer), and found that the presence of high levels of UBE2C is associated with a worse prognosis," explains Faria, leader of the study.

Using mice as a model, the researchers found that high levels of UBE2C increase the spread of tumor cells in the central nervous system, which can also happen in cancer patients, making the disease more aggressive and difficult to treat.

Cláudia Faria and her team at iMM. Credit: Carlos Custódia, iMM

With the goal of finding therapeutic targets that could be used in the clinic, the research team sought to identify compounds capable of modulating UBE2C levels. "We tested 650 drugs already approved for patient use by the FDA (Food and Drug Administration, U.S.) or used in phase 3 or 4 clinical trials, and identified a small molecule inhibitor that decreases UBE2C levels and prevents the dissemination of tumor cells in the central nervous system, when administered at an early stage of the disease," adds Eunice Paisana, Ph.D. student at iMM, and first author of the study.

"Our focus throughout this research has always been to contribute to the discovery of new therapeutic targets. In our team, we study biological

samples from patients to generate knowledge that could contribute to clinical practice in the future," adds Paisana.

"In fact, brain metastases are the main cause of morbidity and mortality associated with cancer. The prognosis is particularly negative when tumor cells spread along the central nervous system, making the disease more aggressive and difficult to respond to current treatments. This is why it is so urgent to develop new therapies," adds Faria on the clinical relevance of the study.

In this work, the researchers found that UBE2C protein is associated with the dissemination of cancer cells in the central nervous system, which is indicative of disease prognosis, and a potential therapeutic target to prevent brain metastization.

More information: Eunice Paisana et al, UBE2C promotes leptomeningeal dissemination and is a therapeutic target in brain metastatic disease, *Neuro-Oncology Advances* (2023). DOI: 10.1093/noajnl/vdad048

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