Models for exploring the development of brain metastasis

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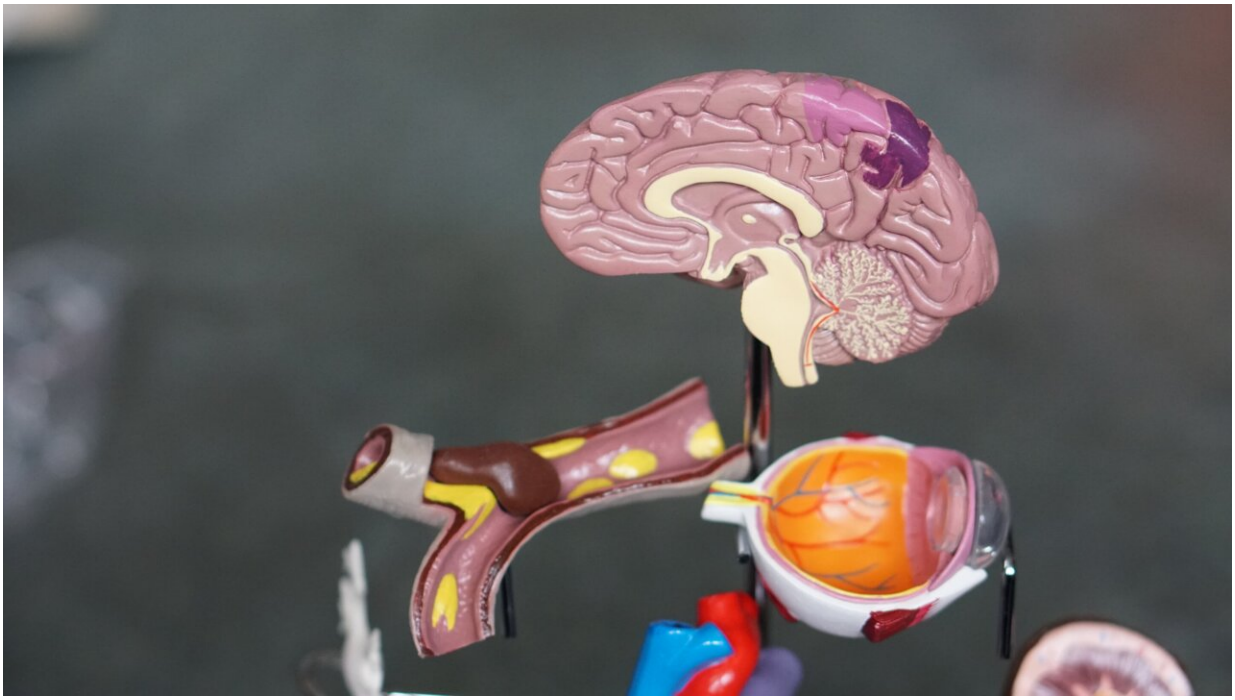

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The spreading of different types of cancer cells to the brain, forming brain metastases, is the main cause of morbidity and mortality associated with cancer. Now, a new study led by Cláudia C. Faria, principal investigator in the group of João Taborda Barata at the Instituto de Medicina Molecular João Lobo Antunes (iMM; Portugal) and neurosurgeon at the Hospital Santa Maria (HSM, CHULN, Portugal),

published today in the scientific journal *Cell Reports Medicine* created a library of models to study brain metastases that recapitulate the disease in humans. These models can be a relevant tool to understand the disease and discover new therapeutical approaches tailormade to each patient.

"We collected brain metastases from cancer patients, that originated from tumors located in different organs, and used those metastatic cells to generate disease models that mimic the disease of each patient, including the dissemination of the cancer cells to form metastases. These unique and tailored models can now be used to study brain metastases and test new anticancer compounds," explains Cláudia C. Faria, first author and leader of the study. The mice models were obtained using cells from metastases samples from patients undergoing surgery at the Hospital Santa Maria. "We created mice models using brain tumor tissue derived directly from patients. These models work like a library that mimics the characteristics of each patient observed in the clinic. We can now go back to this library to study cancer brain metastases," adds Rita Cascão, also first author of the study.

The tumor models reflect the clinical manifestations of the cancer in the patient. Cancer cells in these models disseminate to the same organs as in the patients, and the tumor formation is more efficient when using cells from patients with more aggressive disease. Besides the similarities in the clinical development of the tumors, the models also repeat the biological characteristics of the originating tumor since the genes that are active in the cancer cells in mice are similar to the ones that are active in the patients. These tools can be valuable for personalized medicine, to decipher the best clinical approach to treat each individual patient. "The models that we created in this study are like mirrors that recapitulate the disease in humans," says Cláudia C. Faria, and adds "like mirrors, the models can be used to study attentively the disease."

In this study, the researchers tested the ability of these models to serve as

tools to evaluate the therapeutic value of different therapies. The team tested two known drugs that are already used as cancer treatments in the clinic and act upon processes implicated in the formation of metastases. Similar to the clinic, these treatments are efficient and reduce the growth and size of the tumors in the models. By testing these accepted treatments and showing their efficiency, the researchers demonstrated the potential of the models to explore new therapeutic approaches for brain metastases in the future.

More information: Claudia C. Faria, Patient-derived models of brain metastases recapitulate human disseminated disease, *Cell Reports Medicine* (2022). DOI: 10.1016/j.xcrm.2022.100623

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