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New perspectives for personalized therapy of brain tumors

Scientists from the German Cancer Research Center (DKFZ) and ShanghaiTech University have developed an innovative method for growing brain tumors of individual patients in the laboratory that mimic the original structure and the molecular property of the parental tumor as closely as possible. Drug tests in this model were found to correlate very well with actual patient responses, making it a valuable method for investigating therapies.

Tumor organoids, i.e. mini-tumors grown from surgical material in the culture dish, are now widely used in cancer research. Numerous research groups have already developed approaches to cultivate brain tumors in the laboratory, especially for the very aggressive glioblastomas. However, the complexity of the tumors is a major challenge for this research. In many of the existing methods, the mini-tumors quickly lose important properties or the interactions between tumor cells and their environment cannot be adequately represented.

The new model from Haikun Liu, DKFZ, relies on cerebral organoids – a type of "mini-brain" generated from induced human pluripotent stem cells. In these organoids, which exhibit brain-like properties, the researchers grow freshly collected tumor samples. This creates a model of the tumor that accurately mimics the diversity of cell types, the complex tumor environment, and the molecular characteristics of the original tumor. The researchers named the new method IPTO (Individualized Patient Tumor Organoid). This method was tested in patient samples from hospitals in Heidelberg, Mannheim and further validated in a large number brain tumor patients in Shanghai in collaboration with ShanghaiTech Univeristy.

"With IPTOs, we can not only maintain the structure and heterogeneity of the tumors, but also predict their response to different therapies," explains study leader Haikun Liu. What makes this method so special is that it can be applied to a wide range of tumors of the central nervous system, from aggressive brain tumors such as glioblastomas to brain metastases, which occur in about 20 percent of all cancer patients. In the current study, the team cultured IPTOs from up to 48 tumor entities including pediatric brain tumors, different forms of glioblastoma, and breast, lung or colon cancer brain metastases.

"We hypothesize that the communication between neurons and cancer cells in the IPTO model favors the growth of central nervous system tumors, reflecting recent developments in cancer neuroscience," Liu explains.

The researchers found the IPTO model to be particularly useful for testing the efficacy of chemotherapy or other anti-cancer drugs on individual tumors. In a prospective study of 35 glioblastoma patients, the IPTOs were able to accurately predict the response to the important drug temozolomide. This marks IPTO the first brain tumor preclinical model that predicts patient response in prospective clinic setting. In experiments with IPTOs grown from brain metastases, the mini-tumors in the culture dish also accurately reflected the therapy results with targeted drugs – a decisive step towards personalized medicine. Since the amount of immune cells also matches between IPTOs and their parent tumors, the mini-tumors are already being tested for their suitability to predict the effectiveness of immunotherapies.

"We are very excited that doctors from many different countries already approached us to explore how to use the IPTO model to find the best treatment options for their patients more quickly and reliably," says stem cell expert Liu, who has just founded a DKFZ spin-off with his colleagues to further explore the potential of IPTOs for drug testing, the team will collect the high quality molecular data from the drug treatment and use this data for training advanced artificial intelligence models which may help find the best treatment for brain cancer patients. However, the method still needs to be evaluated further before it can be used in patient care.

Info:

With more than 3,000 employees, the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) is Germany's largest biomedical research institute. DKFZ scientists identify cancer risk factors, investigate how cancer progresses and develop new cancer prevention strategies. They are also developing new methods to diagnose tumors more precisely and treat cancer patients more successfully. The DKFZ's Cancer Information Service (KID) provides patients, interested citizens and experts with individual answers to questions relating to cancer.

To transfer promising approaches from cancer research to the clinic and thus improve the prognosis of cancer patients, the DKFZ cooperates with excellent research institutions and university hospitals throughout Germany:

- National Center for Tumor Diseases (NCT, 6 sites)
- German Cancer Consortium (DKTK, 8 sites)
- Hopp Children's Cancer Center (KiTZ) Heidelberg
- Helmholtz Institute for Translational Oncology (HI-TRON Mainz) - A Helmholtz Institute of the DKFZ
- DKFZ-Hector Cancer Institute at the University Medical Center Mannheim
- National Cancer Prevention Center (jointly with German Cancer Aid)

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Publication:

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