Talk

Patient-Derived Brain Organoids: A New Approach to Studying Brain Tumors

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ABSTRACT

Motivation: Brain tumors are the most common type of solid tumors in children and the leading cause of cancer-related deaths in this age group [1]. Although advances in diagnosis and treatment have significantly improved survival rates, patients are still dying due to this disease, so further research is still crucial. Current models used to study these tumors are cell cultures and animal models, which do not fully replicate the tumor biological complexity and the dynamic environment of the human brain. To address these limitations, we are developing patient-derived brain organoids—miniature brain models that closely mimic the human brain— which incorporate immune cells and tumor cells. These advanced organoids will provide an invaluable tool for studying current therapies and exploring potential future treatments.

Methods: Urine samples were collected from patients and processed until colonies of urine-derived epithelial cells appeared. These colonies were reprogrammed into iPSCs using the CytoTune™-iPS 2.0 Sendai Reprogramming Kit [2]. Once iPSC lines were established, patient-derived organoids (PDOs) were generated following Lancaster's protocol [3]. Some organoids were then co-cultured with microglia to promote its development, while others were injected with CFSE-labeled DAOY medulloblastoma cells on day 40 and allowed to grow. PDOs were subsequently analyzed using immunohistochemistry techniques to assess cell composition, as well as the presence of microglia and tumor cells.

Results: PDOs exhibited markers of neural progenitors (Nestin) which were actively proliferating (Ki67 positive), and immature neurons (Doublecortin), indicating that the organoids accurately mimic the structure of the brain. Additionally, microglia successfully populated the brain organoid, rendering the model immunocompetent. We also assessed engraftment of CFSE-labeled tumor cells within the PDOs, which survived and proliferated, further supporting the relevance of the model. The next step will be integrating these insights into a single organoid to create a comprehensive model and to test how the PDOs respond to cancer treatments, such as radiotherapy.

Conclusions: These findings demonstrate that our model will serve as a valuable and reliable tool for investigating therapeutic strategies for brain tumors. Moreover, since it is patient-derived, the model offers great potential for advancing personalized medicine by enabling more customized and precise treatment approaches.

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