Tumor organoids

- Optimizing GBM organoid construction with hydrogel-based models: GelMA-HAMA scaffold supports GBM organoids with clonal growth for drug screening
- Evaluation of TRPA1 as a Therapeutic Target in MYCN-Amplified Neuroblastoma
- Patient-derived organoids reveal marked heterogeneity in chemosensitivity profiles of colorectal cancer and a potential association with HER2 status
- Rational design matrix materials for organoid development and application in biomedicine
- Mitochondrial Translation Inhibition Uncovers a Critical Metabolic-Epigenetic Interface in Renal Cell Carcinoma
- Comparative Efficacy of Ribosome-Inactivating Protein-Containing Immunotoxins in 2D and 3D Models of Sarcoma
- Profiling Glioma Stem Cell Dynamics via 3D-Based Cell Cycle Reporter Assays
- BET inhibitors reduce tumor growth in preclinical models of gastrointestinal gene signature-positive castration-resistant prostate cancer

What Are Tumor Organoids

Tumor organoids are three-dimensional (3D) cell culture models derived from patient tumors that closely mimic the structure, genetic makeup, and behavior of the original cancer tissue. Unlike traditional 2D cell cultures or xenografts, tumor organoids retain key features of the tumor microenvironment, making them invaluable for studying cancer biology and testing therapeutic responses.

How Are Tumor Organoids Created

1. **Tumor Biopsy** – A small sample of tumor tissue is collected from a patient.

2. **Tissue Dissociation** – The sample is enzymatically or mechanically broken down into individual cells or small clusters.

3. **Embedding in Extracellular Matrix (ECM)** – The cells are embedded in a hydrogel-like matrix (e.g., Matrigel) to provide a 3D environment.

4. **Culture with Growth Factors** – Specific growth factors and culture media tailored to the tumor type support cell proliferation and differentiation.

5. **Expansion and Characterization** – The organoids grow into self-organized 3D structures that resemble the original tumor, maintaining its heterogeneity and genetic features.

Applications of Tumor Organoids

1. **Personalized Cancer Therapy**

    1. Tumor organoids can be used to test different drug treatments on a patient-specific model,

guiding oncologists in selecting the most effective therapy.
2. They help identify responders and non-responders to targeted treatments.

2. **Drug Discovery and Screening**

1. Pharmaceutical companies use tumor organoids to test new anticancer drugs in preclinical studies.
2. They enable high-throughput screening of compounds in a setting that closely resembles in vivo tumors.

3. **Cancer Biology Research**

1. Provide insights into tumor evolution, metastasis, and resistance mechanisms.
2. Help in studying the tumor microenvironment and cancer-stromal interactions.

4. **Immunotherapy Development**

1. Tumor organoids can be co-cultured with immune cells to evaluate immunotherapeutic strategies like checkpoint inhibitors and CAR-T cell therapies.

5. **Gene Editing and Functional Studies**

1. CRISPR/Cas9 technology can be used in tumor organoids to investigate genetic drivers of cancer and identify potential therapeutic targets.

Advantages Over Traditional Models

✔ **Genetic Fidelity** – Maintain the genetic heterogeneity of the original tumor.

✔ **Physiological Relevance** – Better replicate tumor architecture and drug response than 2D cell cultures.

✔ **Scalability** – Can be expanded for large-scale drug screening.

✔ **Patient-Derived** – Enable personalized medicine approaches.

Challenges and Future Directions

- **Standardization Issues** – Variability in culture conditions can impact reproducibility.

- **Lack of Immune Components** – Most tumor organoids lack a functional immune system unless co-cultured with immune cells.

- **Microenvironment Complexity** – While organoids mimic some aspects of the tumor microenvironment, they may still miss key stromal and vascular elements.

- **Cost and Labor-Intensive** – Generating and maintaining tumor organoids requires specialized expertise and resources.

Conclusion

Tumor organoids represent a groundbreaking advance in cancer research, bridging the gap between traditional in vitro models and in vivo studies. Their ability to recapitulate patient-specific tumor characteristics makes them a promising tool for personalized medicine, drug discovery, and understanding cancer biology. Further refinements in culturing techniques, integration with immune components, and standardization efforts will enhance their clinical and translational potential.

Preclinical translational research studies

Peng et al. developed a fast, efficient, and complex culture system (IPTO, individualized patient tumor organoids) that accurately recapitulates the cellular and molecular pathology of human brain tumors. Patient-derived tumor explants were cultured in induced pluripotent stem cell (iPSC)-derived cerebral organoids, thus enabling the culture of a wide range of human tumors in the central nervous system (CNS), including adult, pediatric, and metastatic brain cancers. Histopathological, genomic, epigenomic, and single-cell RNA sequencing (scRNA-seq) analyses demonstrated that the IPTO model recapitulates cellular heterogeneity and molecular features of original tumors. Crucially, they showed that the IPTO model predicts patient-specific drug responses, including resistance mechanisms, in a prospective patient cohort. Collectively, the IPTO model represents a breakthrough in the preclinical modeling of human cancers, which provides a path toward personalized cancer treatment [1)].

1)
Peng T, Ma X, Hua W, Wang C, Chu Y, Sun M, Fermi V, Hamelmann S, Lindner K, Shao C, Zaman J, Tian W, Zhuo Y, Harim Y, Stöffler N, Hammann L, Xiao Q, Jin X, Warta R, Lotsch C, Zhuang X, Feng Y, Fu M, Zhang X, Zhang J, Xu H, Qiu F, Xie L, Zhang Y, Zhu W, Du Z, Salgueiro L, Schneider M, Eichhorn F, Lefevre A, Pusch S, Grinevich V, Ratliff M, Loges S, Bunse L, Sahm F, Xiang Y, Unterberg A, von Deimling A, Platten M, Herold-Mende C, Wu Y, Liu HK, Mao Y. Individualized patient tumor organoids faithfully preserve human brain tumor ecosystems and predict patient response to therapy. Cell Stem Cell. 2025 Feb 5:S1934-5909(25)00002-5. doi: 10.1016/j.stem.2025.01.002. Epub ahead of print. PMID: 39938519.