

Glioblastoma Research

- Optimizing GBM organoid construction with hydrogel-based models: GelMA-HAMA scaffold supports GBM organoids with clonal growth for drug screening
- Comprehensive multi-omics approach reveals critical genes and immunometabolic networks in glioblastoma
- Ultrasound-Mediated Drug Diffusion, Uptake, and Cytotoxicity in a Glioblastoma 3D Tumour Sphere Model
- Role of Amide Proton Transfer Weighted MRI in Predicting MGMTp Methylation Status, p53-Status, Ki-67 Index, IDH-Status, and ATRX Expression in WHO Grade 4 High Grade Glioma
- Molecular and clinical determinants of response to checkpoint inhibitor immunotherapy in glioblastoma
- Barcoded viral tracing identifies immunosuppressive astrocyte-glioma interactions
- O(6)-Methylguanine-DNA Methyltransferase (MGMT) Promoter Methylation Analysis in Glioblastoma Patients
- Profiling Glioma Stem Cell Dynamics via 3D-Based Cell Cycle Reporter Assays

Key areas of ongoing glioblastoma research

1. Molecular and Genetic Insights

- **IDH Mutation Status**
- **MGMT Promoter Methylation**: Predicts response to temozolomide (TMZ) chemotherapy.
- **TERT Promoter Mutations**: Associated with poor prognosis.
- **Glioblastoma Subtypes** (Proneural, Classical, Mesenchymal): Identified through transcriptomic analysis, influencing treatment strategies.
- **Single-Cell RNA Sequencing**: Reveals tumor heterogeneity and therapy resistance mechanisms.

Innovative Therapeutic Approaches

a. Immunotherapy - Checkpoint Inhibitors: Limited success due to GBM's immunosuppressive microenvironment. - **Chimeric Antigen Receptor (CAR) T-Cells**: Targeting EGFRvIII, IL13R α 2, and HER2. - **Cancer Vaccines**: DCVax-L (dendritic cell vaccine) shows promising results in clinical trials. - **Oncolytic Viruses**: Engineered viruses like DNX-2401 selectively replicate in tumor cells.

b. Targeted Therapy - EGFR Inhibitors: Mixed results due to tumor heterogeneity. - **PI3K/AKT/mTOR Pathway Inhibitors**: Targeting GBM's frequent PI3K mutations. - **BRAF/MEK Inhibitors**: Potentially effective in rare GBMs with BRAF V600E mutations.

c. Tumor Microenvironment and Blood-Brain Barrier (BBB) Modulation - Repurposing Drugs (e.g., Metformin, Chloroquine): Target metabolic vulnerabilities. - **BBB Disruptors (e.g., Focused Ultrasound, Mannitol)**: Enhance drug delivery. - **Anti-VEGF Therapy (Bevacizumab)**:

Used for recurrent GBM but does not improve overall survival.

d. Personalized and AI-Driven Approaches - Organoids and 3D Cultures: Patient-derived GBM models for precision medicine. - **Artificial Intelligence (AI):** Predicts drug response and disease progression. - **Liquid Biopsies (cfDNA, miRNAs):** Non-invasive monitoring of GBM evolution.

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3. Current and Emerging Clinical Trials - Combination Therapies: Investigating TMZ with immune checkpoint inhibitors. - **Gene Therapy Approaches:** CRISPR and RNA-based therapies targeting GBM mutations. - **Tumor-Treating Fields (TTFields, Optune):** FDA-approved for GBM, disrupting mitosis using electric fields.

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4. Challenges in GBM Research - High Tumor Heterogeneity: Limits effectiveness of single-agent therapies. - **Immune Evasion:** GBM's suppressive microenvironment resists immunotherapy. - **Drug Delivery Limitations:** The BBB restricts many systemic treatments. - **Recurrence Mechanisms:** Resistance often develops after initial treatment.

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5. Future Directions - Neoantigen-Based Personalized Vaccines: Custom therapies based on patient-specific tumor mutations. - **Multi-Omics Approaches:** Integrating genomics, proteomics, and metabolomics for better therapeutic targeting. - **Nanotechnology:** Developing nanoparticles for improved drug delivery across the BBB.

Artificial Intelligence for glioblastoma research

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Last update: **2025/02/26 21:21**

