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GLICO Platform: Patient-Specific Brain Tumor Organoids for Precision Drug Development

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Patient-Specific Brain Tumor Organoids for Precision Drug Development

Background & Unmet Need

- Glioblastoma (GBM) remains an incurable cancer with a poor prognosis (median survival ~15 months)
- Despite many efforts, there has been little progress in developing effective treatments for GBM, and its biology remains incompletely understood
- One barrier to developing new therapies is that current preclinical models of GBM do not reflect the biology or genetics of primary tumors
- Modeling GBM's interaction with the tumor microenvironment has also been a challenge and has yet to be successfully replicated
- **Unmet Need:** Preclinical models of GBM which reflect the biology, genetics, and environment of in-situ tumors and can be used for the development of effective therapies

Technology Overview

- **The Technology:** A patient-specific platform for modeling GBM and its TME in an organoid culture
- Tumor-bearing organoids are generated by co-culturing patient-derived glioma stem cells (GSCs) with hESC-derived cerebral organoids
- The resulting organoids have tumors grown from from patient-derived GSCs embedded within them
- **PoC Data:** GLICO models demonstrate tumor proliferation and infiltration, with 20% of tumor cells staining positive for Ki67
- GLICO organoids display similar pathology to GBM patients, like spontaneous microtubule formation
- Response rates to GBM drugs in GLICOs are closer to in vivo rates compared to 2D cultures (24-43% GLICO vs 80-90% cell line), and vary by patient
- RNA-seq data shows that GLICO transcriptomes are significantly more correlated to those of patient tumors than current GBM models

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Publications:

Pine et al. *Cancer Discov*. 2020.
Linkous et al. *Cell Rep*. 2019.

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Technology Applications

- High-throughput screening for glioblastoma drug development and neurotoxicity studies
- Patient-specific screening for personalized medicine
- Identification of new therapeutic targets for GBM
- Understanding of basic GBM biology and interaction with tumor-microenvironment

Technology Advantages

- GLICOs can be maintained in culture for 4 months or longer
- GLICO models reflect the basic biology of GBM better than 2D cultures and traditional organoids
- Organoids and their environments are easy to manipulate and control for experimentation
- GLICO models are easily scalable, making them an ideal candidate for high-throughput screening

Supporting Data / Figures

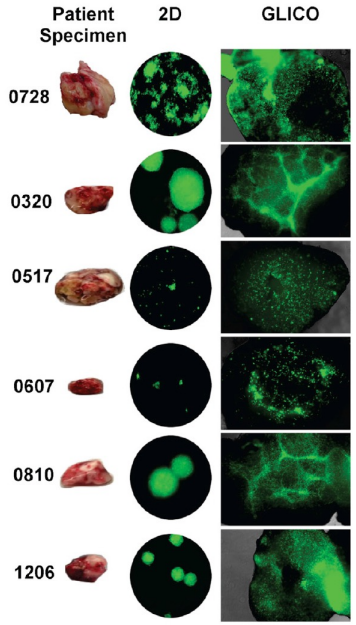

Figure 1: GLICO models recapitulate patient-derived cell line behavior via differentiated patterns of invasion. More aggressive cell lines (0728, 1206) demonstrate more diffuse patterns of invasion compared to slower-growing cell lines (0517, 0607). GSCs are labeled with GFP.

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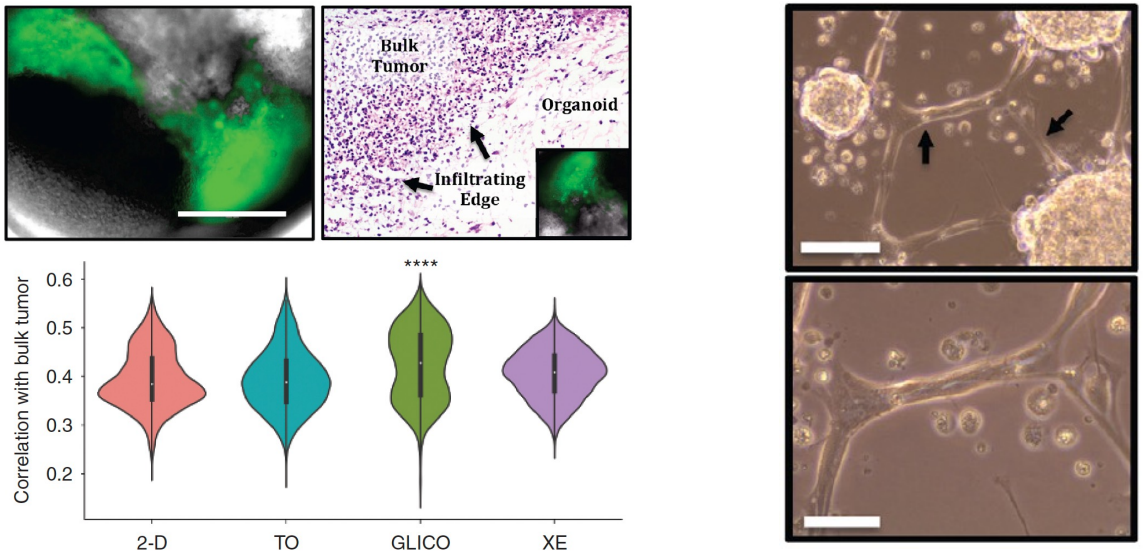

Figure 2: Top Left: Leading edge of infiltrating GSCs into a cerebral organoid. GSCs are labeled with GFP **Bottom Left:** GLICO transcriptomes have a significantly higher correlation with those of primary tumors than existing GBM models **Right:** GLICO models demonstrate spontaneous microtubule formation similarly to patient tumors.

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