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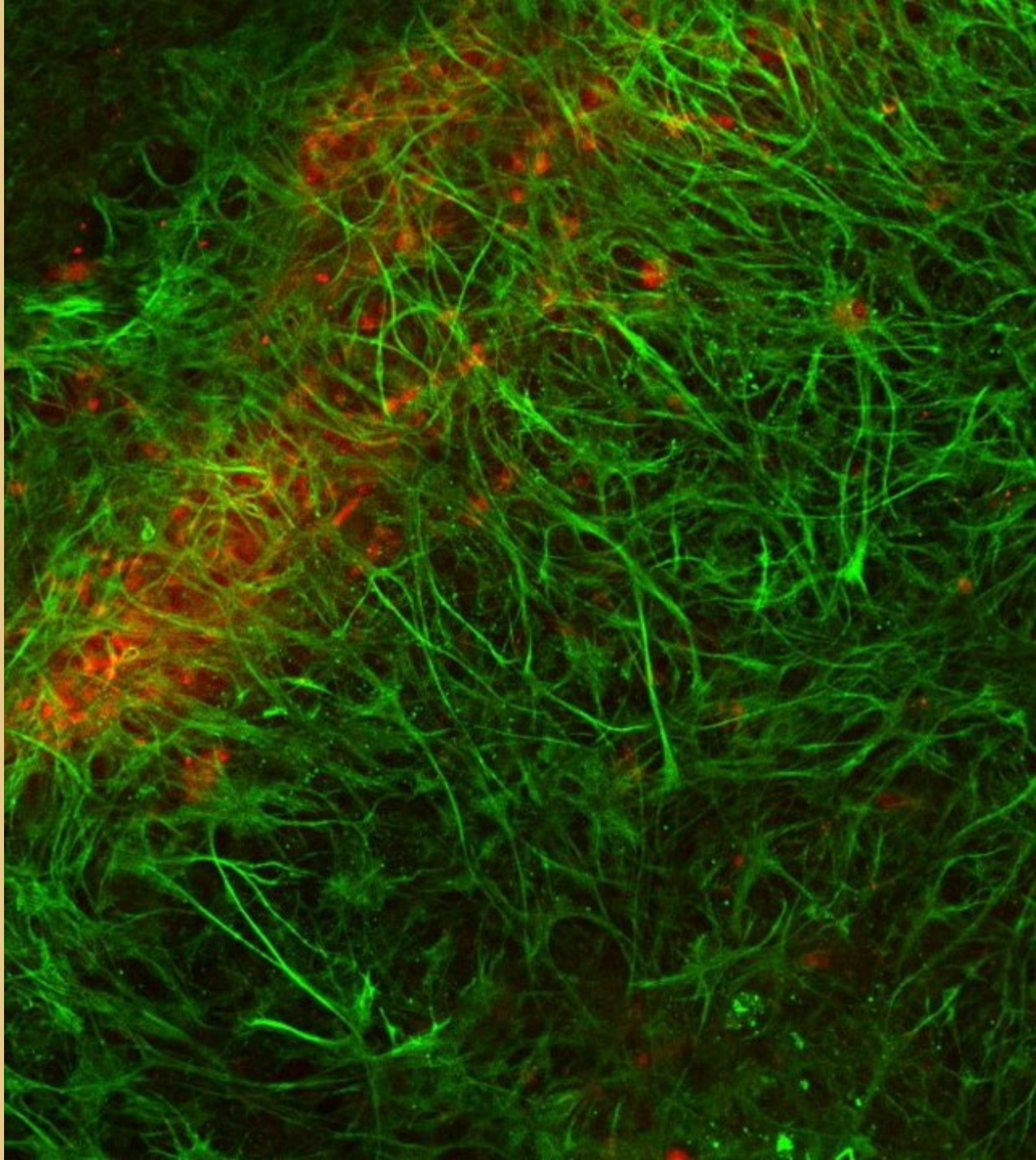
The Screening Live Explants (SLiCE) Program:

Accelerating the Drug Development Pipeline

Andrew Satterlee, Assistant Professor
The University of North Carolina at Chapel Hill
September 27th, 2024

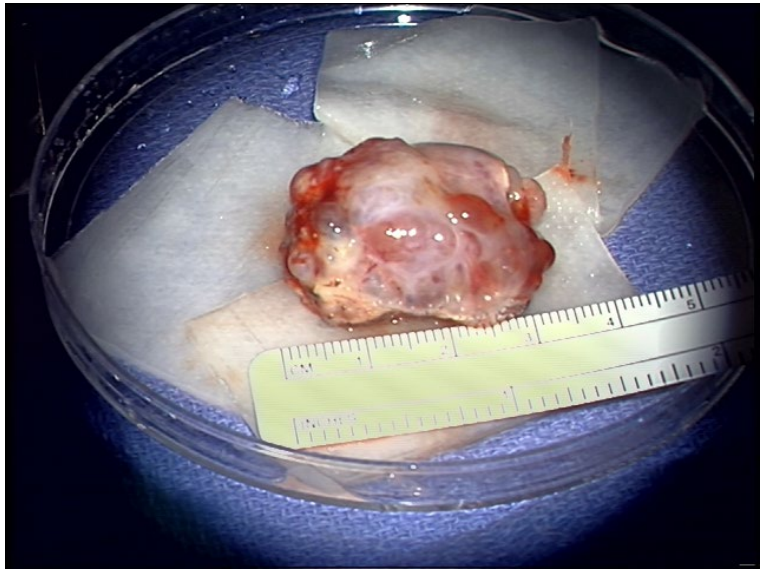


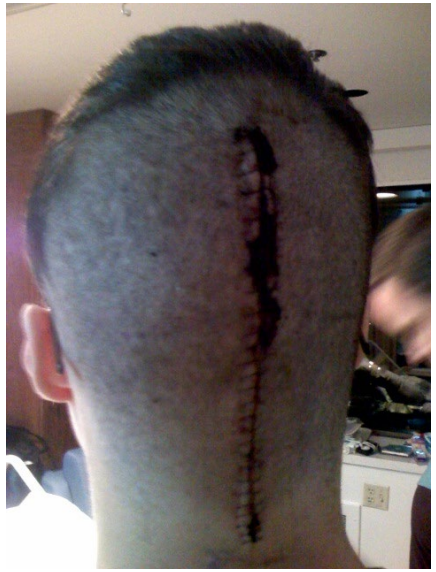
Affiliations and Disclosures

Dr. Andrew Satterlee is an Assistant Professor in a translational institute called **Eshelman Innovation** at the University of North Carolina at Chapel Hill and in the **Division of Pharmacoengineering and Molecular Pharmaceutics** in the Eshelman School of Pharmacy at UNC. He is also the **Director of the Screening Live Cancer Explants Core Facility** at UNC.

Andrew Satterlee is listed as an inventor on Intellectual Property related to this work.

The Problem: The Drug Development Pipeline Lacks the Proper Tools to Design and Prescribe Optimal Treatments



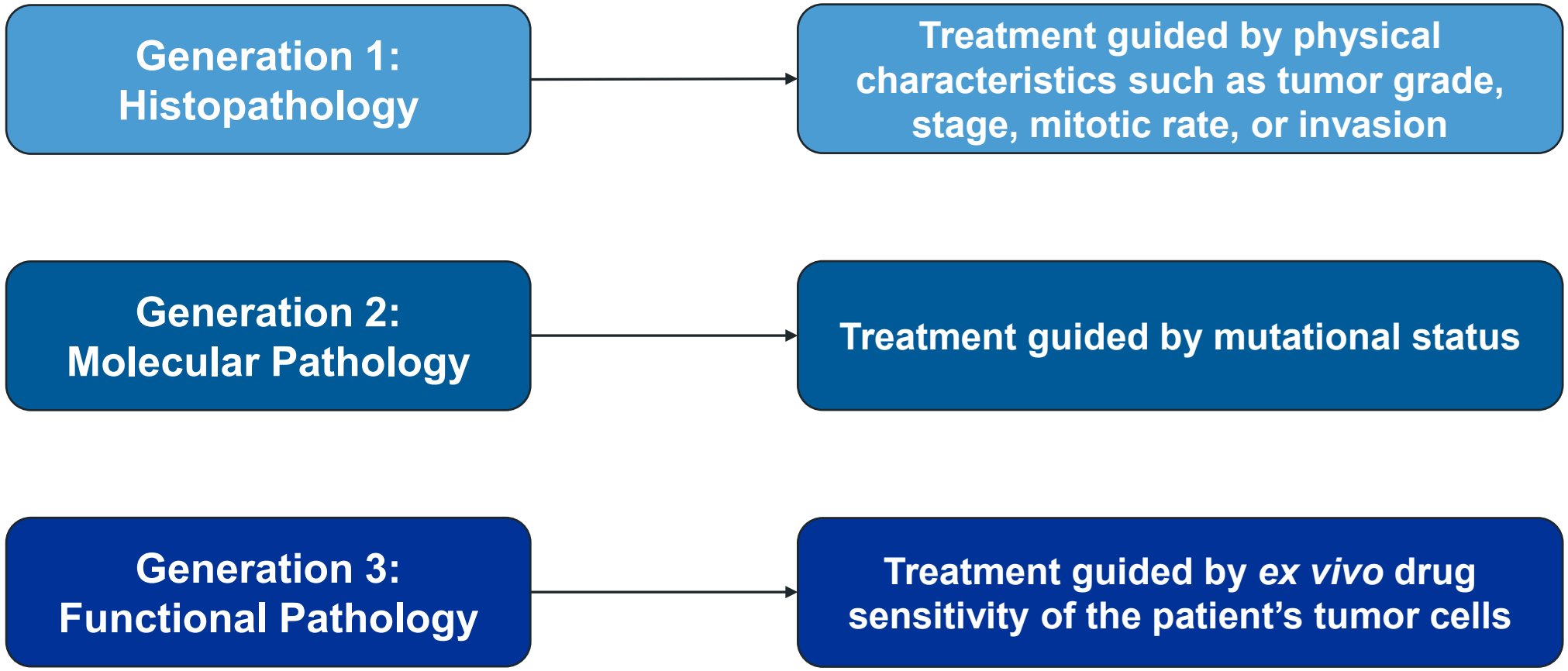


- This was a ***rare***, ***heterogeneous*** tumor
- The pathology report suggested chemo- and radiotherapy, but experts in the field ***disagreed*** on treatment details
- Physicians ***lacked the proper tools*** to determine the most effective treatment plan

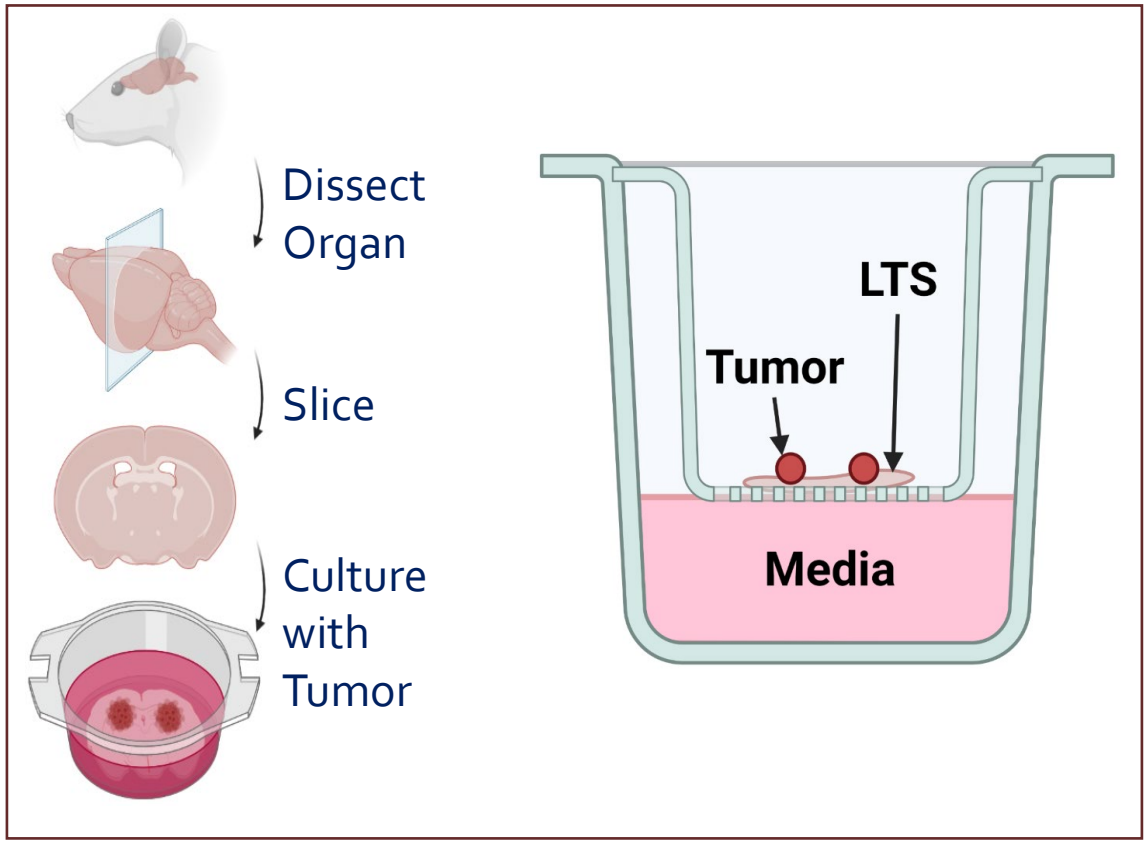
- These two girls have the ***same*** brain tumor type with the ***same*** molecular mutation
- Both girls received the ***same*** drug
- One tumor has ***completely disappeared***, but the other ***hasn't shrunk*** at all

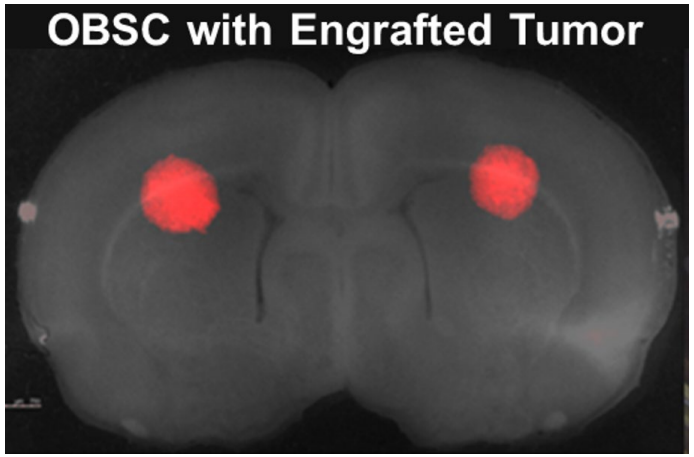
We need a ***better way*** to determine optimal treatments for ***each*** person

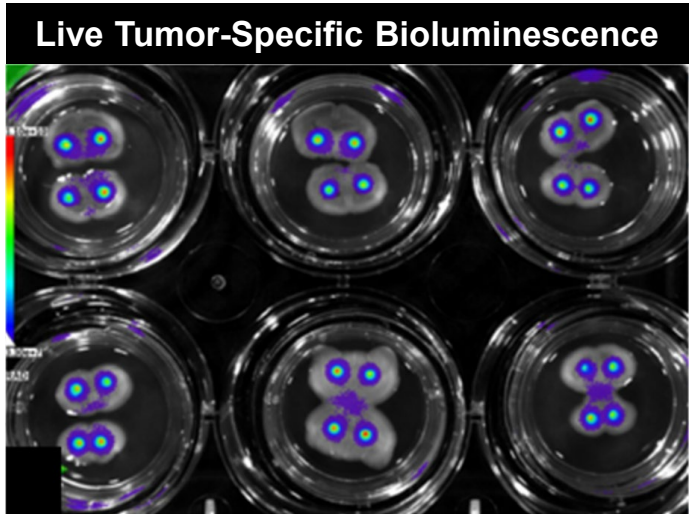
Cancer Treatment is Progressing Toward Personalized Solutions



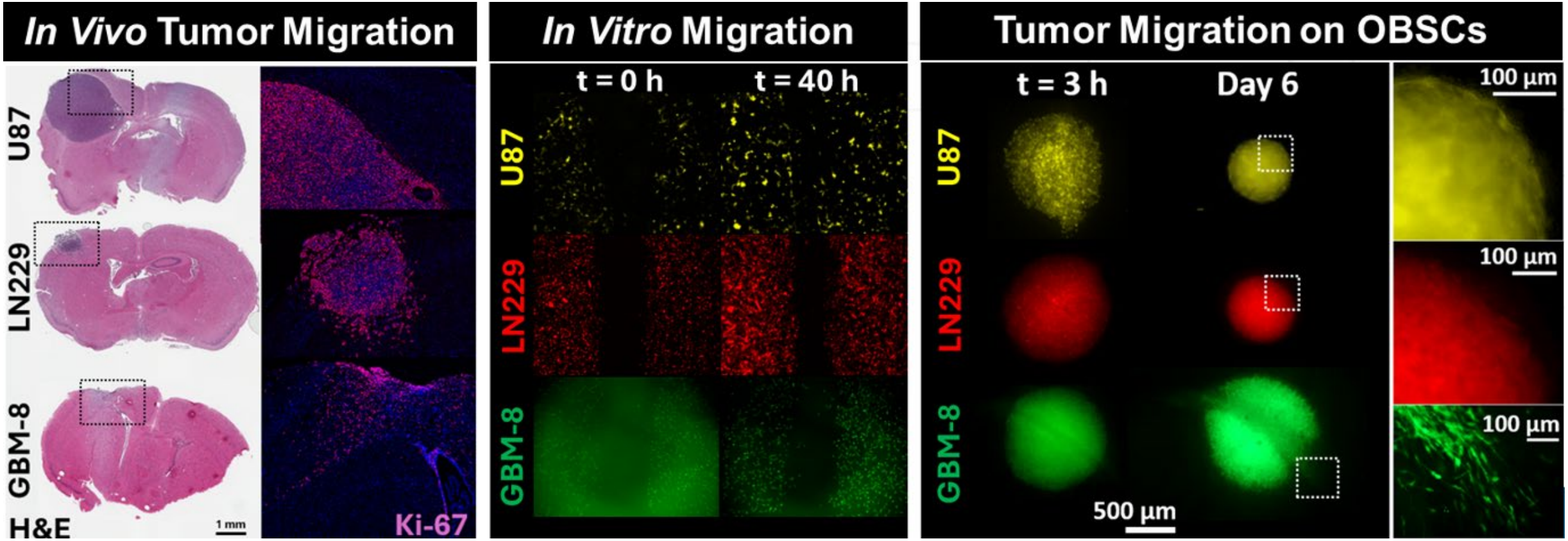
The SLiCE Platform Maintains Tumors atop Living Tissue Substrates





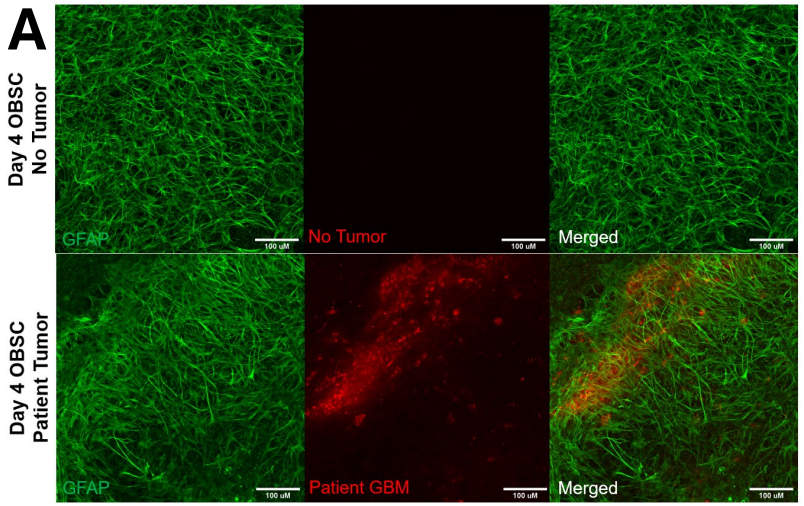


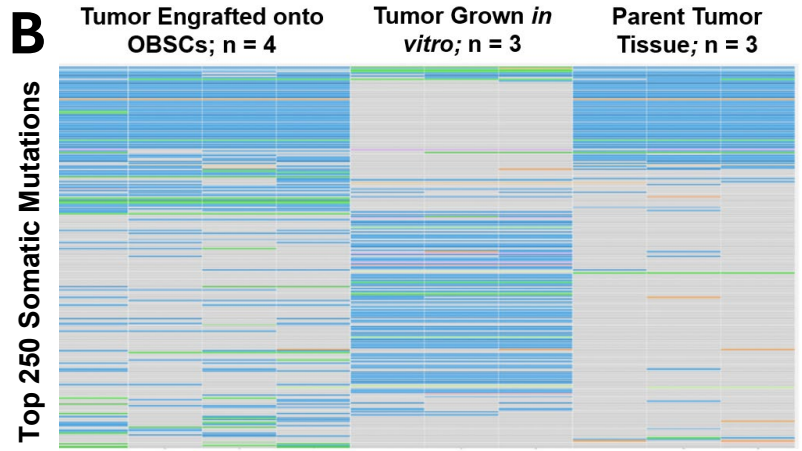
Tumors Engrafted atop Organotypic Brain Slice Cultures (OBSCs) Recapitulate In Vivo Characteristics



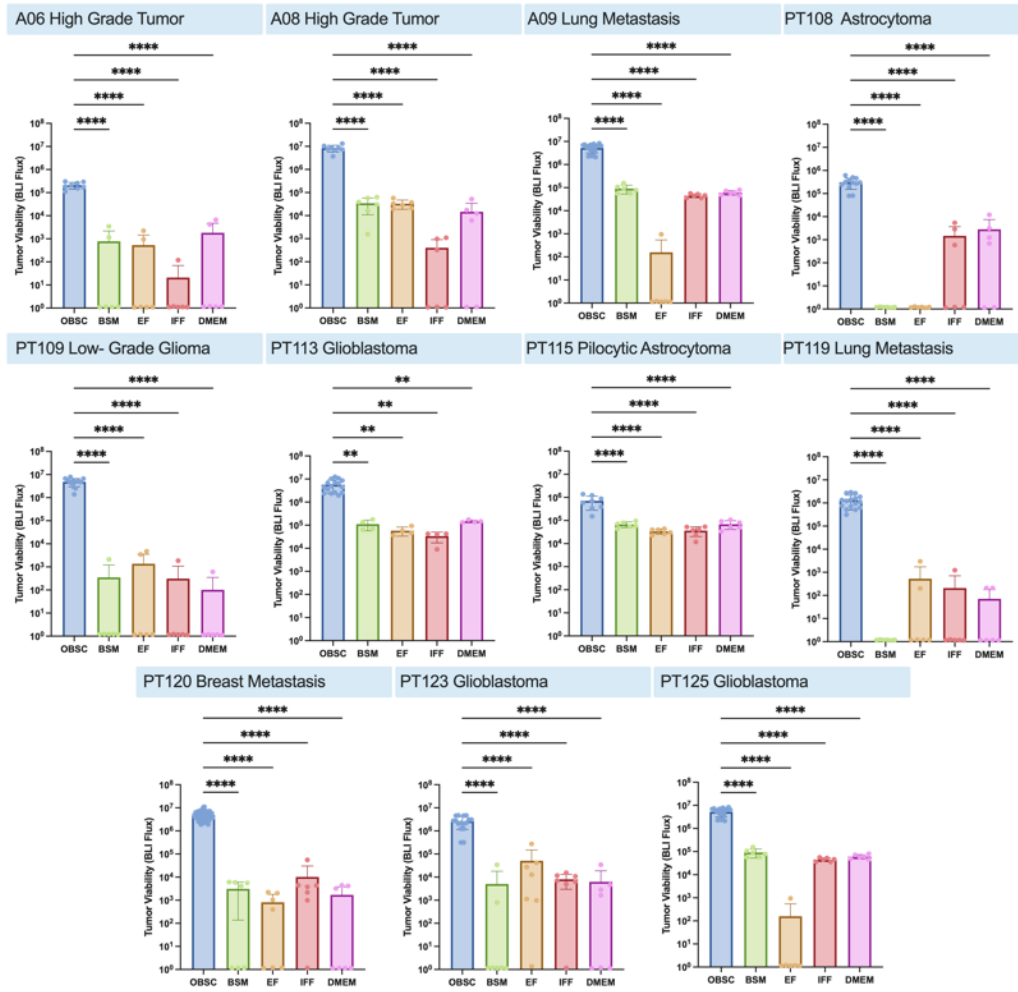
Satterlee et al, Neuro-Oncology, 2019

The SLiCE Platform Uniquely Maintains Uncultured Patient **Brain** Tumor Tissues on **OBSCs**





Mann et al, Cell Reports Medicine, 2023

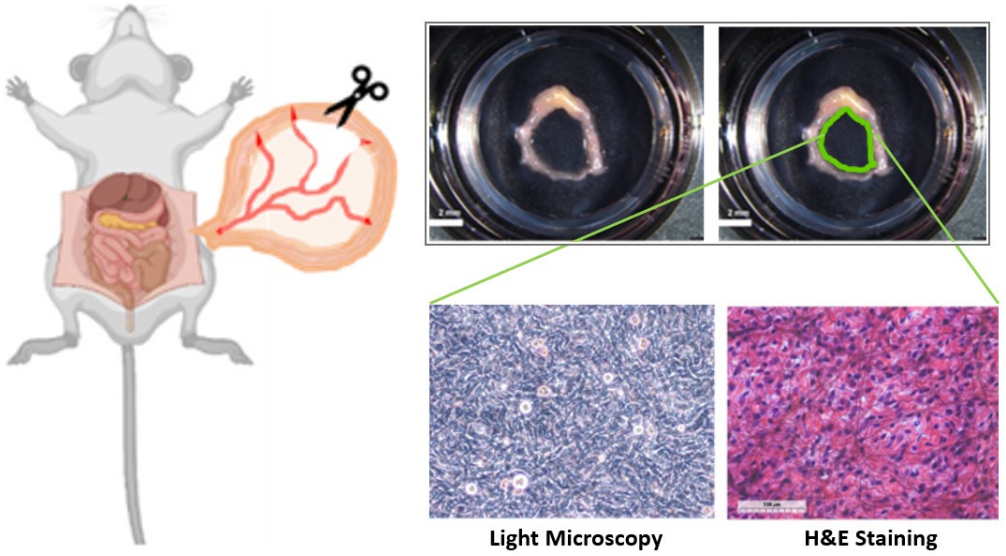


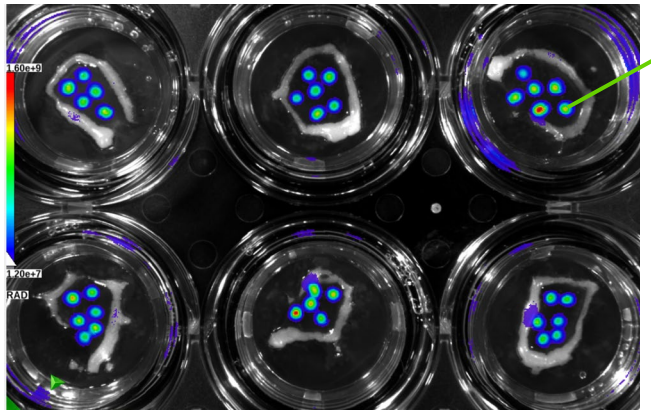
Unpublished data

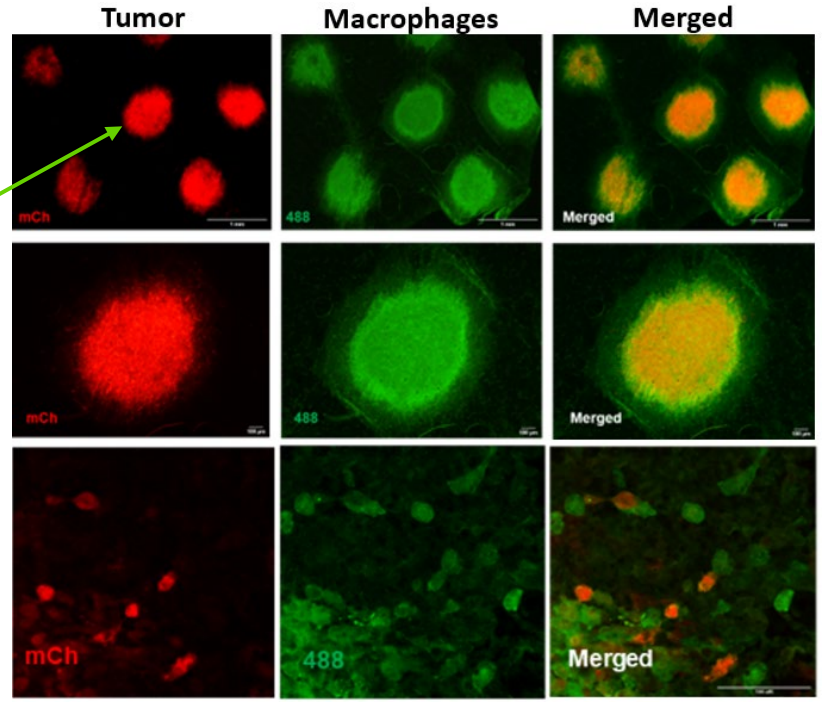
Breanna Mann, PhD

eha Sf(PM)

The SLiCE Platform Uniquely Maintains Uncultured Patient **Ovarian** Tumor Tissues on Organotypic Mesenteric Membrane Cultures (**OMMCs**)

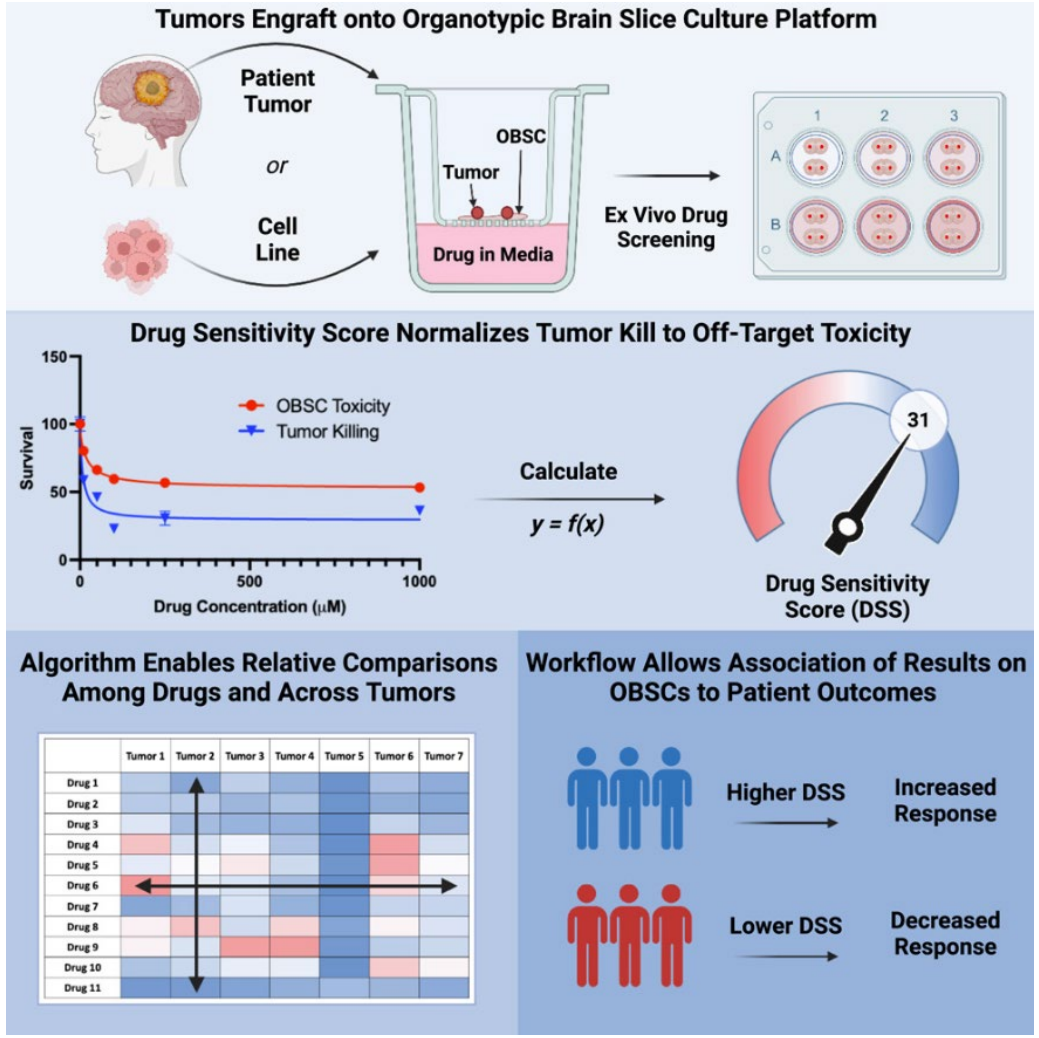






Valdivia et al, BioRxiv, 2024

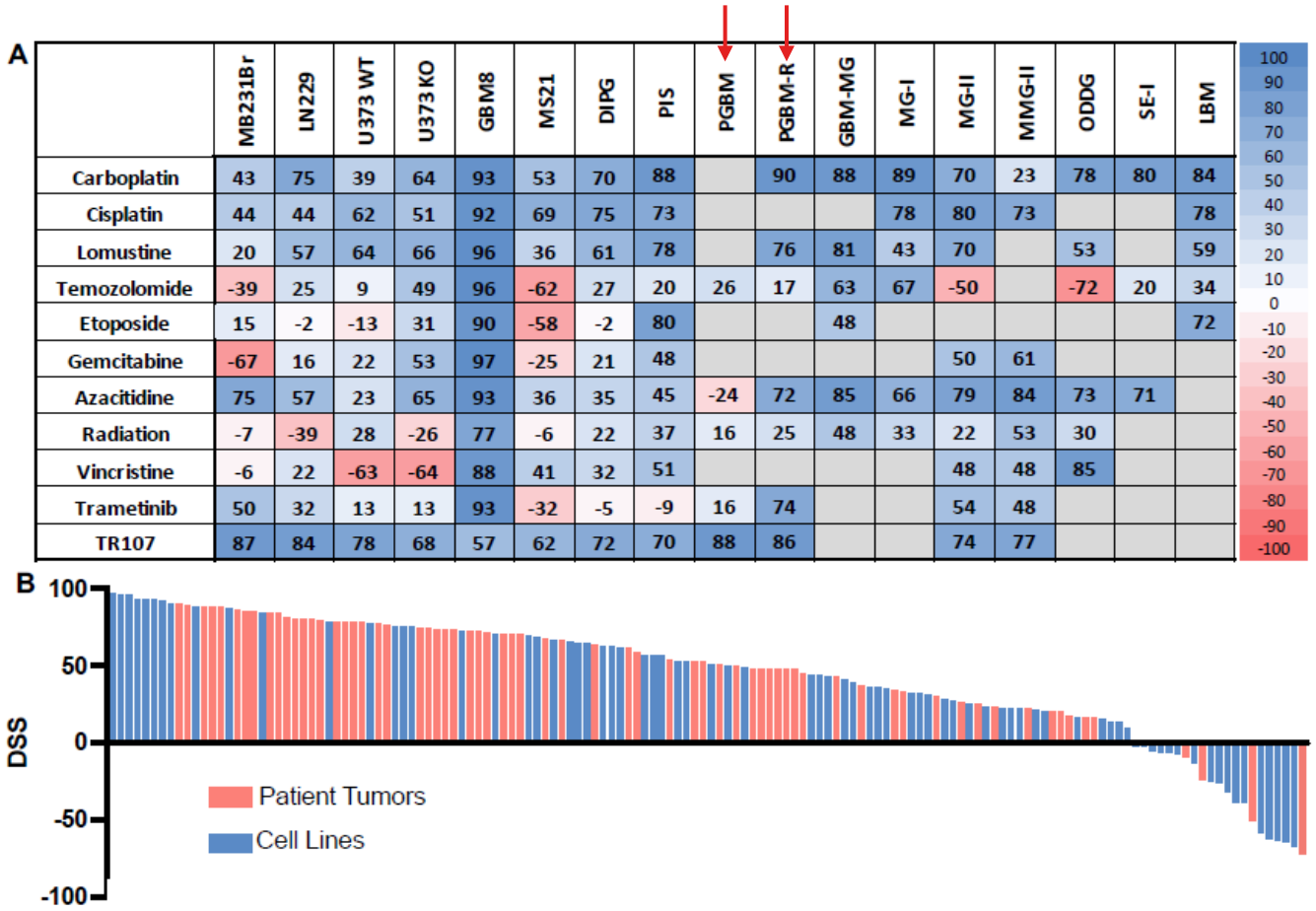
Our Standardized, Normalized Process to *Functionally* Measure Tumor Response to Treatment



- LTSs allow drug screening of cell lines and uncultured patient tumor tissue in just **four days**
- Tumor **cryopreservation** protocol allows long-term storage of several representative aliquots, as well as shipment across sites
- The SLiCE Assay contains robust **standardization** and **quality control** measures
- Our drug sensitivity score normalizes tumor kill to **off-target toxicity** for each drug
- Our A.I.-driven **automated** image analysis and dose-response model fitting program saves time
- This workflow allows association of results on OBSCs to **patient outcomes**

Mann et al, Cell Reports Medicine, 2023

Our Standardized, Normalized Process to *Functionally* Measure a Patient Tumor's Response to Treatment



Mann et al, Cell Reports Medicine, 2023

Types of Analysis:

- **"Across the panel of preclinical therapeutics you provided, Isoform #3 performed better than all others"**
- **"Your therapeutic was more effective than Standard of Care in 90% of Adult High-Grade Gliomas"**
- **"Patient X was a responder to Drug Y and thus should be enrolled on the trial"**
- **"Your metastatic tumor was less sensitive to Drug Z than any other tumor we profiled"**

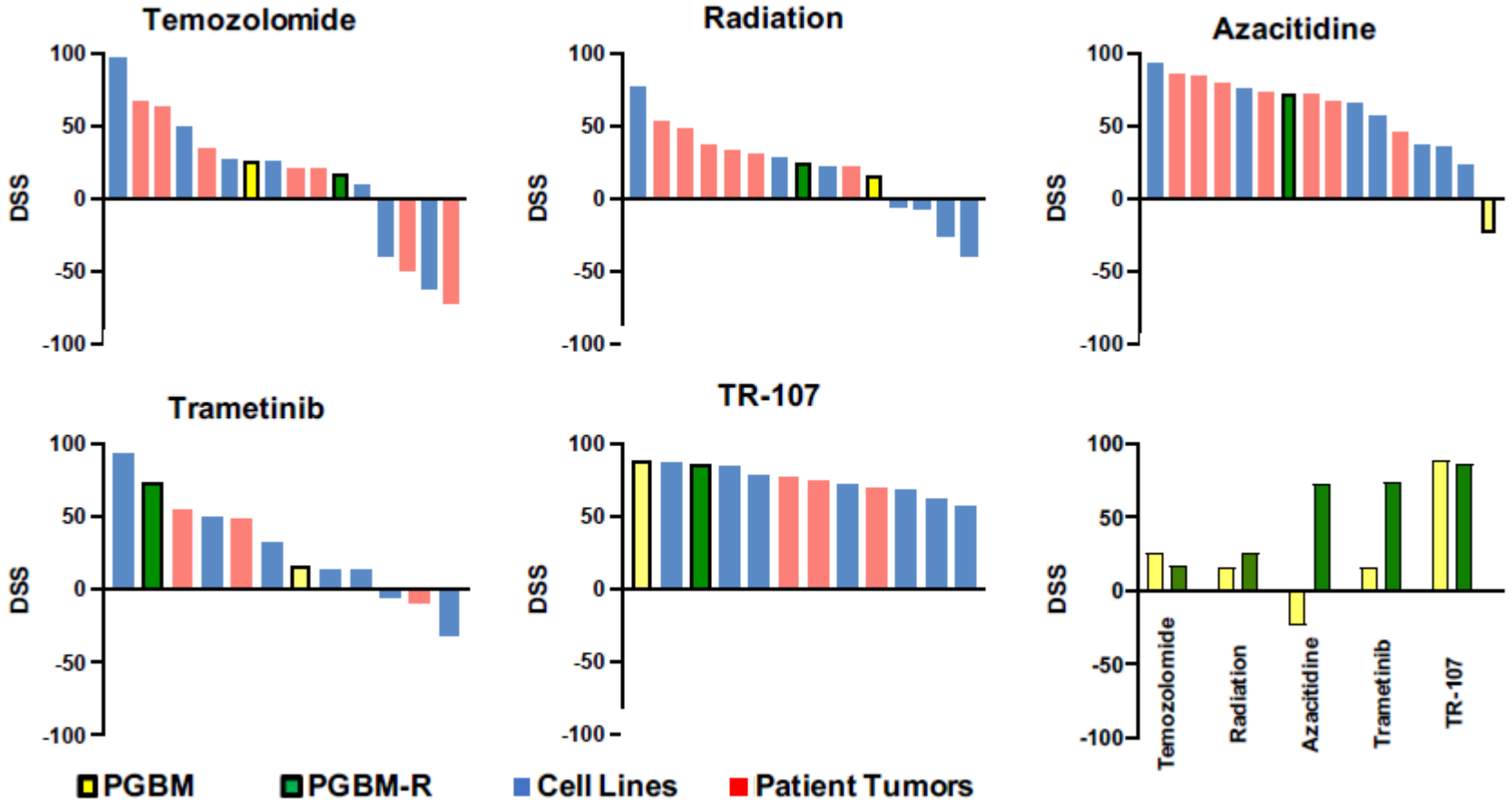
Case Study of a Pediatric Glioblastoma

Patient's mutational profile is complex but suggests sensitivity to TMZ + XRad

Tumor Name	Primary pathology diagnosis	Age	Mutations	Treatment
PGBM	GBM	Pediatric	IDH1/2 IDH1 c.395G>A mutation detected, TERT-, methylated MGMT, GFAP+, OLIG2+, IDH1132H+, H3K27M-, patchy expression of BRAF V600E, MS-Stable, IDH1 = R132H, PIK3CA = H1047R, CDK4 amplification, PAX5 = V129M, TP53 = R273C	Xrad, Veliparib, TMZ
PGBM-R	GBM (Recurrent tumor from same patient as PGBM)	Pediatric	MS-stable, CDK4 amplification, IDH1 R132H, PAX5 V129M, PIK3CA H1047R, TP53 R273C	TMZ; then moved onto a trial

Patient had rapid tumor recurrence and a second surgery six months after the first surgery

PGBM and PGBM-R DSS for each tested therapy relative to other tumors: TMZ and Xrad Scored Poorly



Mann et al, Cell Reports Medicine, 2023

Collaborate with us!

- We’re building the SLiCE Platform as a tool to help:
  - Academic labs and companies with therapeutic compounds in **preclinical development**
  - Pharma and biotech companies with therapeutics in **clinical trials**
  - Patients and physicians who need personalized **treatment guidance**
- We’ve opened a **Core Facility within UNC** to make collaborating as easy as possible, helping other groups test their own therapeutics on uncultured, living tumor tissue resected from patients at UNC Hospitals

Visit Our Website!

Check out our Core Facility!