Introduction: Glioblastoma is the most common cancer arising within the brain. Despite surgery, followed by DNA-damaging chemoradiotherapy, average survival remains between 12-15 months. Unacceptable survival rates underline the need to develop preclinical research models which recapitulate features underpinning therapeutic resistance in patients, such as intratumoural heterogeneity and treatment resistant glioblastoma stem cell (GSC) subpopulations which demonstrate elevated DNA damage response (DDR) activity.

Method: Tumour specimens from patients were used to generate 2D and 3D scaffold-based GSC models, with a range of preclinical survival and molecular assays used to interrogate cancer biology and assess therapeutic responses.

Result: We have developed a 'living biobank' of 20+ *ex-vivo* GSC models which reflect key clinicopathological diversity. These models include residual disease models based on careful macrodissection of rare *en-bloc*partial lobectomy specimens to liberate parallel GSC lines from the tumour core and adjacent infiltrated brain, to represent cells typically left behind after surgery. Therapeutic strategies targeting fundamental DDR processes demonstrate preclinical efficacy, for example dual inhibition of ATR and the FA DNA damage repair pathways elicits profound radiosensitisation (sensitiser enhancement ratio of 3.23 (3.03-3.49, 95%-CI)) with evidence of delayed DNA damage repair on single-cell gel electrophoresis. Finally, characterisation of our surgically-relevant resected and residual models reveals numerous divergent properties including elevated stem cell marker expression in residual models (p=0.0021), which may partially explain treatment resistance in disease left behind after surgery.

Conclusion: Our living biobank represents a useful resource for preclinical glioblastoma research and demonstrates the value of partnership between surgeons and laboratory-based scientists.

Take-home message: Our living biobank represents a useful resource for preclinical glioblastoma research and demonstrates the value of partnership between surgeons and laboratory-based scientists.

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TOWARDS A LIVING BIOBANK OF SURGICALLY-RELEVANT 3-DIMENSIONAL GLIOBLASTOMA STEM CELL MODELS TO EVALUATE NOVEL THERAPEUTICS AND INTERROGATE INTRATUMOURAL HETEROGENEITY

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