Tissue Extraction and Preservation for Glioblastoma Specimens Used for Molecular Oncology and Personalized Therapy Studies

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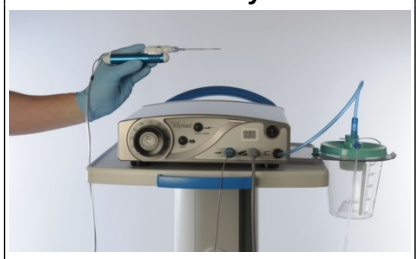
Introduction

The ability to establish cell cultures that preserve the genome and phenotype of the parental tumor for in-vitro and in-vivo studies has the potential to revolutionize development of animal models of disease for new, individualized treatments for glio-blastoma. In this study, we assessed how the collection methodology and tissue preservation techniques intra-op can be used to enhance the viability of tumor tissue for establishing primary cultures and patient derived xenografts (PDX) in immunocompromised mice.

Methods

Fresh brain tumor tissue samples were obtained by conventional en-bloc resect-ion technique and through use of a non-ablated piecemeal aspiration extraction system, with and without, an automated tissue preservation module that flushes and chills the specimen as it is collected in a filter. Both specimens were then bathed in hypothermosol solution and kept cool during transport to laboratory for pro-cessing within 2 hours from surgical removal. Percentage of viable cells for primary cultures was determined using an automated cell counter. Matched spec-imens from the same patient were also interrogated using time course viability, and in-vivo tumorigenicity assays.

Non-Ablated Aspiration Resection System

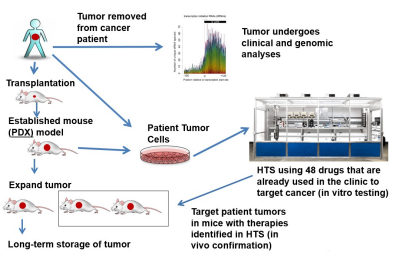


Myriad extraction system used for collecting the fresh glioma specimens.

Results

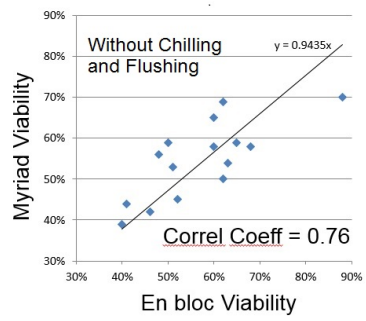
Comparison of en-bloc and aspiration ex-tracted specimens indicated that aspirat-ion resected samples can be effectively used for establishing cell cultures and PDX in vivo. Immediate flushing and chilling of the fresh tissues can increase viable cell count by at least 10%, but does not change long term cell viability or in-vivo tumorigenicty. Both en bloc and the aspiration resected samples were able to induce tumor growth in vivo, in an intracranial PDX model.

Personalized Medicine Work Flow



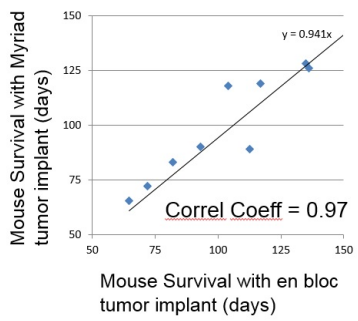
PDX studies: (1) genomic analyses, (2) in-vitro and (3) in-vivo drug screens.

Tissue Viability Scatter Plot



Strong Correlation in tissue viability is shown between en-bloc and aspiration extracted specimens.

Comparison of Mouse Survival after intracranial implantation



Very strong correlation shown in mouse survival (days) following intracranial implantation of the en-bloc versus aspiration extracted specimens.

Learning Objectives

By the conclusion of this session, participants should be able to:
(1) Describe how aspiration resected tissue specimens can be used effectively to produce cell cultures compared to en-bloc samples. Both specimens can be used for genomic analyses, in-vitro and in-vivo testing.
(2) Describe how individual patient-derived cell cultures and mouse avatars can be used to identify personalized glioblastoma treatment.
(3) Describe how automated tissue collection with immediate chilling and flushing of the fresh tumor tissue improves tissue preservation and increases cell viability.

Conclusions

Aspiration resection is currently the safest, most precise and least disruptive method for resecting glioblastoma. We have demonstrated that specimens collected using such tools, as compared to en-bloc excision, consistently yield robust cell cultures that can be used in generating PDX models for research, testing of individualized therapy, and possibly vaccine development.

References

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