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USC Norris Comprehensive Cancer Center
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Comprehensive Molecular Characterization of Spinal Cord Gliomas

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Introduction

- Spinal gliomas have an incidence of 1700 new cases per year (USA) and account for 1-3% of all primary spinal cord tumors.[1]
- Treatment guidelines for spinal gliomas do not exist, and there is no clear survival advantage with surgical resection, radiation, or chemotherapy.[1]
- Clinical management of spinal gliomas is based on clinical data and experience from intracranial gliomas.[2]
- However, there is increasing evidence spinal gliomas may be molecularly distinct from intracranial gliomas.[2,3]
- Identifying unique molecular signatures may shed light on more effective therapeutic targets.
- **We hypothesize that spinal gliomas are molecularly distinct from brain gliomas**, which may guide prognosis and the use of different therapeutic targets.

Methods

- Tissue was centrally reviewed by a Neuro-Pathologist to confirm histological diagnosis.
- Next-generation sequencing was performed on genomic DNA extracted from formalin-fixed paraffin-embedded (FFPE) tumor samples through 592 gene NextSeq or WES Novaseq.
- Whole Transcriptome Sequencing was performed by extracting tumor-specific RNA from FFPE specimens.
- De-identified DNA and RNA sequencing data was analyzed using the Caris Life Sciences CodeAI Platform.
- X2/Fisher's-exact/Mann-Whitney U tests was utilized for comparison with a significance of $p<0.05$ ($q<0.05$).

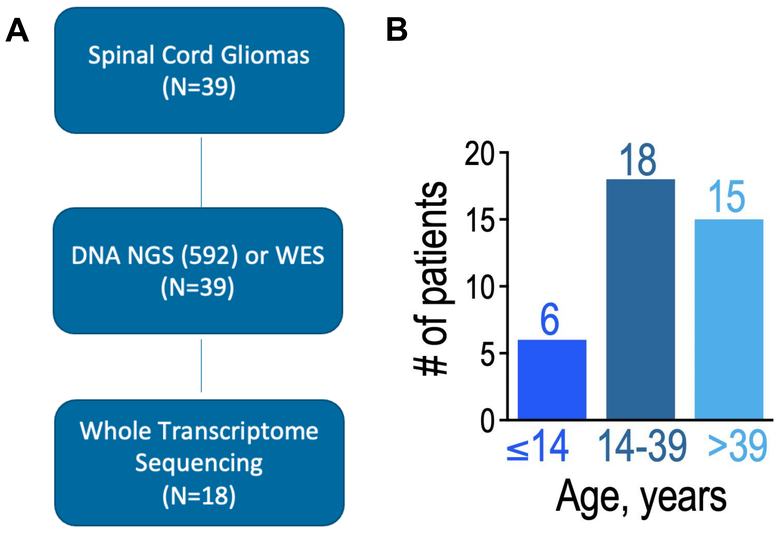


Figure 1 Consort Diagram & Cohort Characteristics: A. Centralized pathology review categorized 36/39 tumors into high grade versus low grade tumors (3 tumors were unable to be classified). Ependymomas were excluded due to their existing distinct molecular characterization. **B.** Age ranges are based on National Cancer Institute age guidelines for Pediatrics (<15y), Adolescent & Young Adult (15-39y), and Adults (>39y).[4]

Results

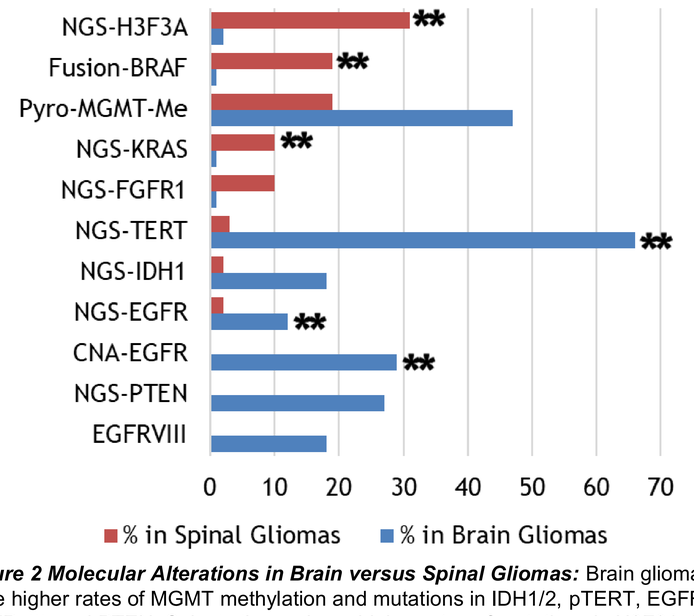


Figure 2 Molecular Alterations in Brain versus Spinal Gliomas: Brain gliomas have higher rates of MGMT methylation and mutations in IDH1/2, pTERT, EGFR, EGFRvIII, and PTEN. Spinal gliomas have higher rates of mutations in H3F3A, KRAS, FGFR, and BRAF fusions.

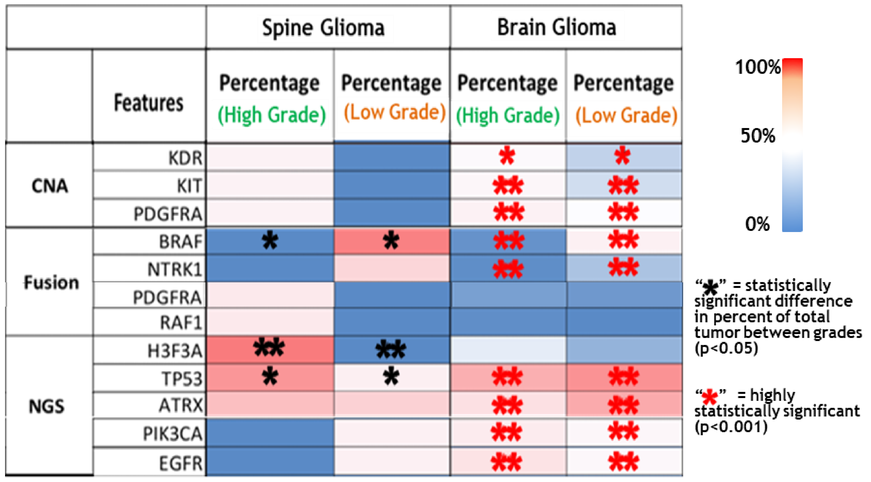
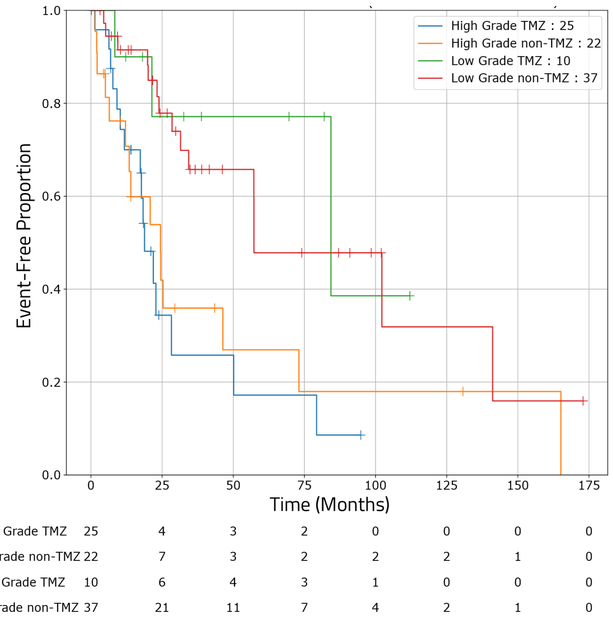


Figure 3 Comparing Brain versus Spinal Gliomas by Grade: Both spinal and brain gliomas have more frequent BRAF fusions in low grade tumors and more frequent 4q12 amplification (PDFGRA, CKDR) in high grade tumors.

- **TP53 mutation** is more frequent in high grade spinal and low grade brain tumors.
- **ATRX mutation** is frequent in low grade brain but shows no difference in the spine.
- **PI3KCA** and **EGFR mutations** are more frequent in high grade brain and low grade spinal gliomas.



High Grade TMZ	25	4	3	2	0	0	0	0
High Grade non-TMZ	22	7	3	2	2	2	1	0
Low Grade TMZ	10	6	4	3	1	0	0	0
Low Grade non-TMZ	37	21	11	7	4	2	1	0

Figure 4 Event-Free Survival in High versus Low Grade Spine Treated with or without TMZ: TMZ may lead to better event-free disease outcomes in low grade versus high grade spinal gliomas ($p<0.0014$). Data is based on ongoing analysis with additional patients. High Grade TMZ Median is 18.8 m (95% CI: 11.7 m-28.3 m). High Grade non-TMZ Median is 24.4 m (95% CI: 12.1 m-73.1 m). Low Grade TMZ Median = 84.3 m (95% CI: 8.4 m-Inf months). Low Grade non-TMZ Median = 57.3 m (95% CI: 31.5 m – 141.1 m)

Conclusion

Our results show unique molecular signatures of spinal gliomas, underscoring their genetically distinct framework from brain gliomas. We provide a biological explanation for the limited effectiveness of current therapies in spinal gliomas, with potential implications for further investigations in chemotherapy and targeted therapy.

References

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