Transcriptional signatures in histologic structures within glioblastoma tumors may predict personalized drug sensitivity and survival


Neuro-Oncology & Blood-Brain Barrier Program, Oregon Health & Sciences University. Portland, OR, USA; Veterans Administration Medical Center, Portland, OR, USA

PURPOSE / OBJECTIVE(s)

- To assess whether differing tissue composition of GBM samples influences the results of known prognostic and diagnostic gene signatures.
- To determine if assessing a consistent intra-tumoral structure could provide more valid metrics for inter-tumoral comparisons.
- To create an improved prognostic gene signature.

RESULTS

Figure 1. Intra- and inter-tumoral heterogeneity in GBM. Intra-tumoral heterogeneity refers to variation between different patients' tumors. Intra-tumoral heterogeneity describes variation within a single GBM, where one region of the tumor appears dissimilar (histologically and/or on NMR) from other regions of the same tumor. Image adapted from (1).

Figure 3. Gene set enrichment analysis (GSEA) revealed distinct biological processes enriched in each tumor structure.

Figure 4. Molecular subtype classification depends on structure, with CT able to distinguish biologically distinct subtypes.

Figure 6. Novel prognostic gene signature created utilizing solely cellular tumor (CT) sample gene expression data. Kaplan-Meier survival analysis of (A) NRGAP CT samples, (B) CT-predicted** TCGA GBM samples, (C) all NRGAP samples, and (D) all TCGA samples dichotomized into high and low-risk groups based on MGMT promoter methylation status (left) and using our novel model (right).

SUMMARY / CONCLUSION

- Histologic structures within a GBM are molecularly distinct, with unique biological processes enriched in each structure.
- Molecular subtype classification established by The Cancer Genome Atlas depends on structure.
- CT sampling allows the ability to distinguish between biologically distinct subtypes.
- Expression patterns of established prognostic gene signatures are driven by tumor structure.
- Variations in histology may confound results of gene signatures created from mixed-tissue samples.

REFERENCES / ACKNOWLEDGEMENTS


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