EPIGENOMICS STEMNESS PREDICTION MODEL STRATIFIES IDHWT GLIOMAS BASED ON OVERALL SURVIVAL

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Background

Stem cell phenotypes may underline glioma IDHwt, a poor prognosis cancer subtype, therapeutic resistance due to the stemness properties as self-renewal and proliferative potential. Although glioma molecular alterations have been described, there are no prognosis distinctions noticed regarding IDHwt

Objectives

We propose to define a novel metric to measure stemness in tumors using a non-tumor induced Neural Stem Cell (iNSC) DNA methylation signature.

Methods

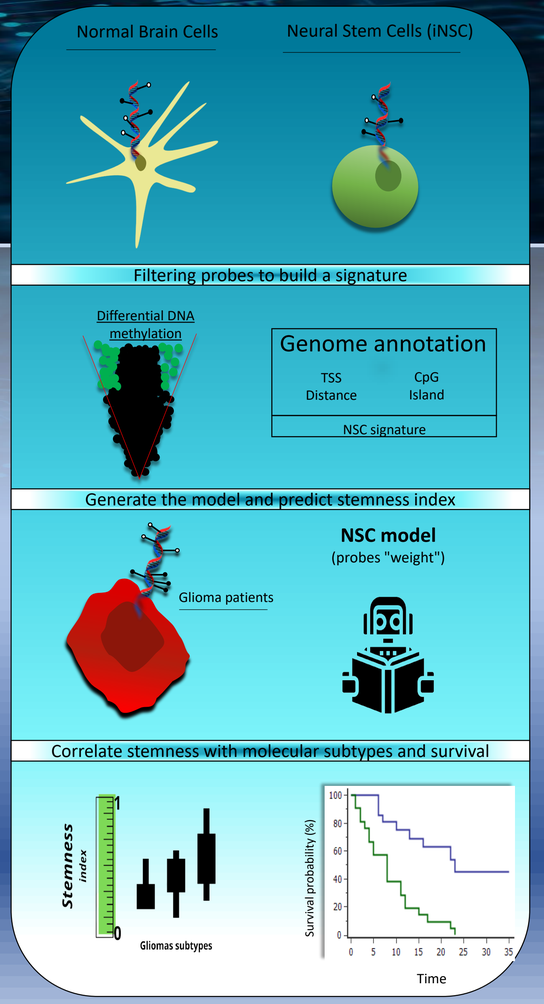

Figure 1. Scheme to build NSC DNA methylation signature and its model to predict stemness index.

Results

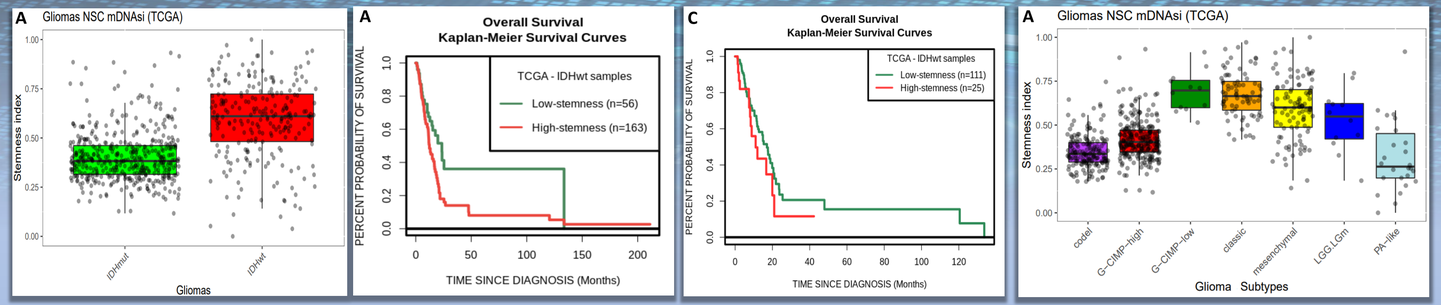

Figure 2. Gliomas IDH mutant or wildtype stemness index generated by NSC model. A) TCGA gliomas. B) GLASS gliomas. mDNAsi = DNA methylation stemness index;

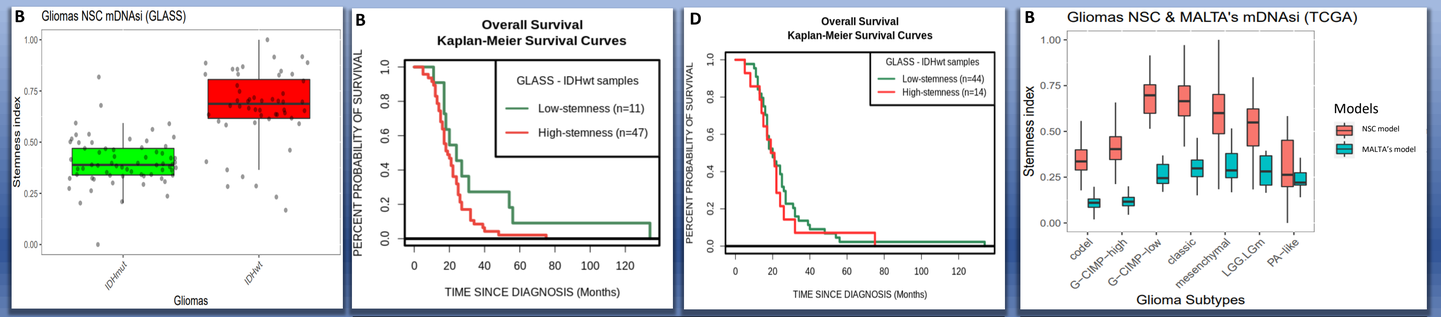

Figure 3. Survival analysis stratified by stemness among gliomas IDH wt. A) TCGA gliomas and NSC stemness index; B) GLASS gliomas and NSC stemness index; C) TCGA gliomas and MALTA's stemness index; D) GLASS gliomas and MALTA's stemness index. MALTA's model is based on iPSC and ES non-cancer cells (Malta, T.M et. al. 2018).

Figure 4. Gliomas subtypes stemness index from (TCGA). A) NSC stemness index; B) Stemness index comparison between NSC and MALTA's model.

Conclusions

Our model stratified gliomas IDHwt by the stemness indices with significant differences in survival in both cohorts. The higher the stemness index the poorer the overall survival after adjusting for age and molecular subtype. Our prediction results indicated an enrichment of stemness features in glioma, which is associated with prognosis.

Next steps

- Stemness prediction on others CNS tumors;
- Adjustment in NSC model trough similiarities within GSC signatures
- Enrichment pathway analysis from final glioma stemness signature
- Improve undertanding in stemness and agressiveness correlation in gliomas

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