STEMNESS SIGNATURE STRATIFIES GLIOMAS BASED ON AGGRESSIVENESS, HISTOPATHOLOGIC AND MOLECULAR FEATURES

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QUESTION

How does a prediction model based on fetal astrocyte gene expression signature separate gliomas based on their classification?

BACKGROUND

→ Classification and treatment of gliomas are still suboptimal
→ The transcriptomic profile of fetal astrocytes may be related to aggressiveness
→ New technologies and algorithms have the potential to elucidate biological questions

METHODS

1. Public scRNAseq data containing fetal astrocyte samples (n=730)
2. Access / Quality Control / Normalization / Clustering
3. Identification of Fetal Astrocytes (AST) by marker genes (n=89)
4. Application of the machine learning algorithm (OCLR)
5. Application of the prediction model in TCGA (n=11070) and GLASS (n=384)
6. Generation of the AST Stemness Index (ASTsi 0-1)
7. Correlation of ASTsi with clinical and molecular data

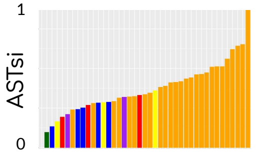
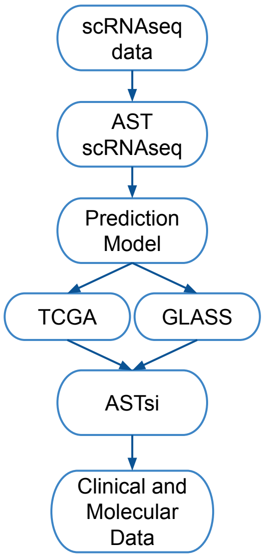


fig1. Prediction model validation (astrocytes in orange and whole brain in color)



scRNAseq data
AST scRNAseq
Prediction Model
TCGA
GLASS
ASTsi
Clinical and Molecular Data

fig2. Methodology pipeline

RESULTS

TCGA glioma samples

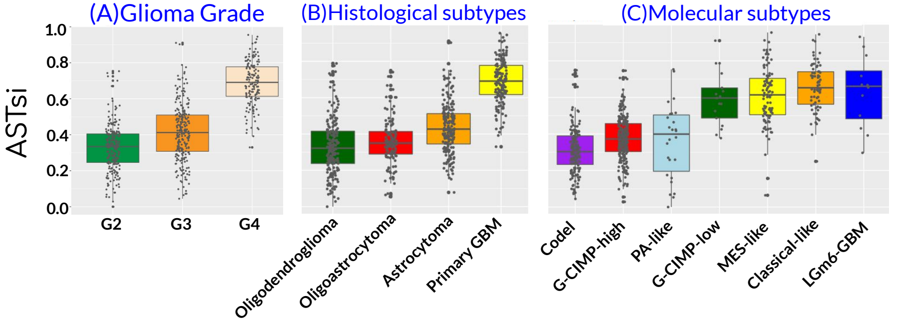


fig3. Boxplots of ASTsi of TCGA data and characteristics. (A)Glioma grade; (B) Histological subtypes and (C)Molecular subtypes

GLASS glioma samples

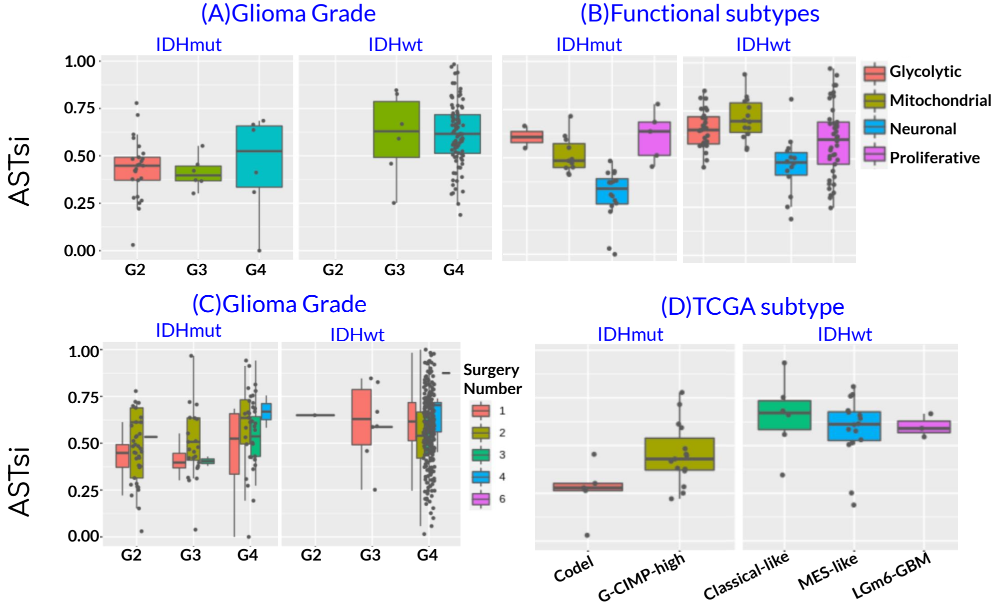


fig4. Boxplots of ASTsi of GLASS data and characteristics, separating by IDHmut and IDHwt (A)Glioma grade; (B) Functional subtypes; (C)Glioma grade and surgery number and (D)TCGA subtype

DISCUSSION

As we can see in the boxplots, the ASTsi was able to divide the gliomas by their degree of malignancy (grade), molecular and histological subtypes. It was also observed in the GLASS samples that ASTsi increased in the second recurrence of IDHmut gliomas and decreased in the IDHwt gliomas. There were other interesting results such as the indices observed in the functional subtypes and in the TCGA subtypes

CONCLUSION

The prediction model built using fetal astrocyte signatures was able to generate stemness indices that, when applied to glioma samples, stratified glioma samples by histopathology and molecular subtypes and showed correlation with cancer aggressiveness, being potentially a good metric to be aggregated in the identification and diagnosis of patients.

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