FOXC1 expression in Meningiomas

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Background

- Meningiomas account for nearly 1/3 of brain tumors and are characterized by a low mutational burden and dysregulation of DNA methylation.
- The promoter of FOXC1 is hypomethylated relative to dura mater, suggesting a role as a meningele identity gene.
- Here we perform a multi-omic analysis of FOXC1 expression in a large cohort of meningiomas

Methods

- Next-generation DNA sequencing (NGS) provides a comprehensive view of the genetic landscape of meningiomas.
- RNA sequencing (RNA-Seq) provides a comprehensive view of the transcriptome of meningiomas.
- Meningiomas were classified into different grades based on the World Health Organization (WHO) classification system.
- The craniofacial patterning transcription factor FOXC1 was found to be significantly dysregulated in meningiomas.

Results

1: FOXC1 is widely expressed in meningiomas. (Q1: bottom quartile; Q4: top quartile)

2: There were no significant differences in patient characteristics between FOXC1 expression quartiles.

3: FOXC1 expression inversely correlated with WHO histologic grade.

4: NF2 mutations were significantly more common in FOXC1 high-expressing tumors (45% vs. 68%, p < 0.05).

5: In WHO grade I & II meningiomas, NF2 expression is inversely correlated with WHO tumor grade.

6: Low transcript levels of FOXC1 are correlated with low expression of both PD-L1/CD274 and MHC-1 markers HLA-A/B/C as well as a high interferon gamma signature (IFN-γ).

Conclusions

- The craniofacial patterning transcription factor FOXC1 was found to be widely expressed in a large cohort of meningiomas.
- FOXC1 expression is inversely correlated with WHO tumor grade.
- FOXC1 expression is significantly more common in NF2 meningiomas than FOXC1 meningiomas.
- FOXC1 expression is inversely correlated with WHO tumor grade.
- FOXC1 expression levels are correlated with high expression of other meningiinal genes, suggesting low levels of FOXC1 may represent de-differentiation to a more immature state.

References

- Wedemeyer et al. 2022, Neurosurg. Adv "Epigenetic dysregulation in meningiomas"
- Zerball et al. 2008, PNAS "Cortical dysplasia and skull defects in mice with a Foxc1 allele reveal the role of meningeal differentiation in regulating cortical development."

Tables and Figures

- Table 1: Summary of patient characteristics.
- Figure 1: Heatmap of FOXC1 expression levels.
- Figure 2: Distribution of FOXC1 expression levels.
- Figure 3: Association between FOXC1 expression and NF2 mutation status.
- Figure 4: Association between FOXC1 expression and IFN-γ signature.

Graphs and T-tests

- Graph 1: Comparison of NF2 mutation status in meningiomas.
- Graph 2: Comparison of IFN-γ signature in meningiomas.

Significant results are indicated by asterisks (*) in the tables and figures.