Microenvironment composition of meningiomas associates with chromosome 22 loss and distinct tumor biology

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Disclosures

• None
Introduction

• Tumor microenvironment (TME) is a promising area of study in neuro-oncology
• Can explain tumor heterogeneity and treatment resistance
• Avenue through which several novel therapeutics have been proposed
• Meningioma TME remains poorly understood
• Chromosome 22 loss is a common karyotype aberration in meningioma

**Hypothesis:** Chromosome 22 loss drives key changes in meningioma microenvironment
Methods

1) Transcriptomic data from 158 human meningiomas obtained from GEO omnibus

2) Tumors clustered by grade (WHO I vs WHO II/III) and chromosome 22 loss, inferred from expression of chromosome 22 genes

3) Compute relative purity (tumor cells), immune, and stromal fractions of each subgroup with ESTIMATE gene enrichment analysis

4) Further annotate subgroups with expression of marker genes

5) Assess for potential underlying receptor-ligand interactions using the publicly available FANTOM repository
Results 1: TME subgroups

Group 1
Non-Cr22, high-grade

Group 2
Non-Cr22, low-grade

Group 3
Cr22 loss, high-grade

Group 4
Cr22 loss, low-grade

ESTIMATE-based TME characterization:

* Kruskal Wallis p<0.05 for all plots
Results 2: Subgroup characterization and validation

CD4 T-cells

Monocytes

CD8 T-cells

Neutrophils

Pericytes

\[ \rho = -0.83^* \]

\[ \rho = +0.83^* \]

\[ \rho = +0.42^* \]

\[ \rho = -0.34^* \]

*p<0.05
Results 3: Thrombospondin as a group 4 marker

*Kruskal Wallis p<0.05
Discussion

• Group 4 (chromosome 22 loss, WHO grade 1) is the largest subgroup and has a distinct TME:
  • High immune/stromal fractions, low purity
  • Enriched in CD4+ T-cells and monocytes
  • Enriched in thrombospondin, which associates strongly with monocytes, CD4+ cells. This may therefore serve as a therapeutic target for this subpopulation of meningioma

• Group 2 (WHO grade I, no chromosome 22 loss) is pericyte-enriched
• As expected, immune score correlates with CD45 expression and purity correlates with SSTR-2 expression, a meningioma-specific marker
• This work helps clarify the effect of chromosome 22 loss on meningioma microenvironment, and may lead to subgroup-specific treatments based on TME modulation
Summary points

• We characterize the tumor microenvironment of 158 human meningiomas grouped by WHO grade and chromosome 22 loss

• We find a distinct TME in WHO grade I tumors with chromosome 22 loss, which is associated with high immune fraction and thromboplastin signaling

• This may lead to better characterization of meningioma biology and subgroup-specific therapeutics