Immunologic Context of Pediatric Brain Tumors

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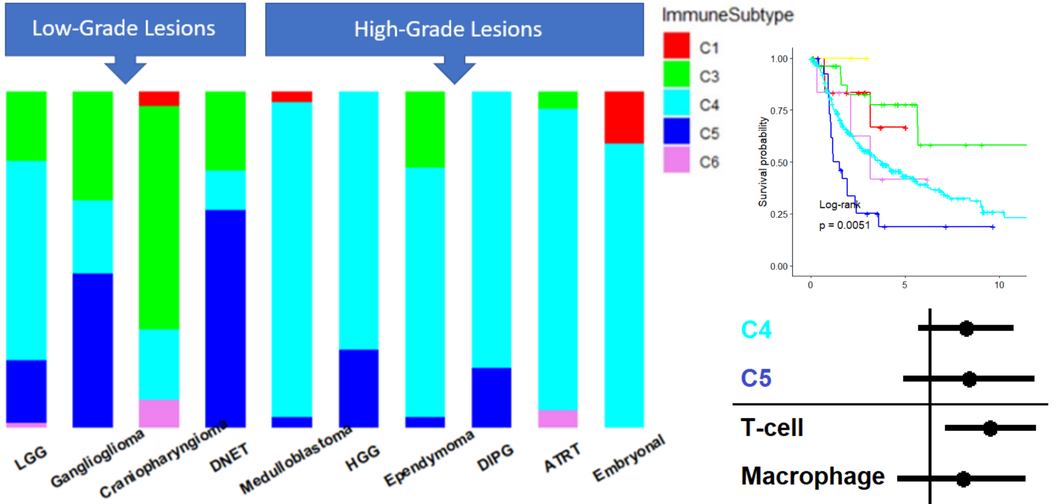
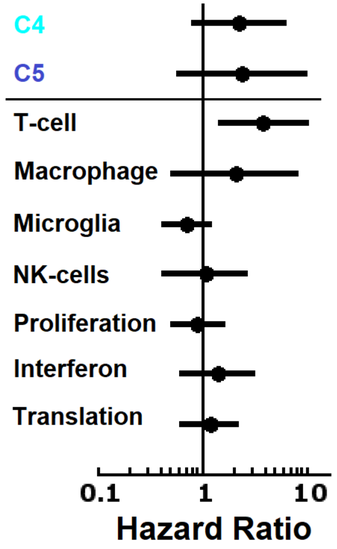
Lymphocyte deplete (C4) with rare inflammatory (C3) immune microenvironments characterize high-grade malignancies

Current therapy for pediatric CNS malignancies Is toxic and outcomes are suboptimal

- **Immunotherapy** is a promising modality, but pediatric neuro-oncology application is limited by poorly understood microenvironment and mechanisms of immune escape
  - The Children's Brain Tumor Network released the transcriptomic profile of ~700 primary brain tumors
  - The TCGA project identified 6 immune subtypes that span cancer types and convey information on immune infiltrate, immune-cancer signaling interactions, and transcription factors that modulate immune response

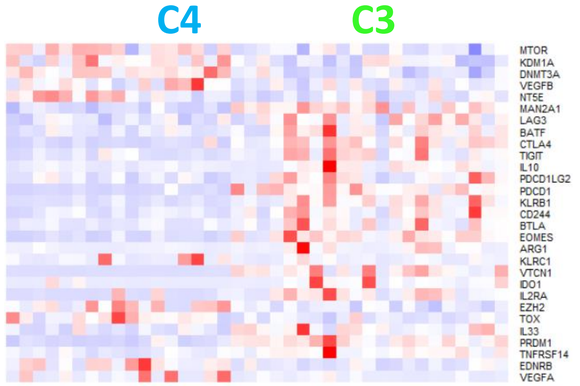
The TCGA immune microenvironment classification is applied to the pediatric CNS database. Immune signature deconvolution, survival analyses, and differential gene expression experiments between disease states help *identify potential inhibitory immunomodulator targets with translational potential*





- **C4** and **C5** (immunologically quiet) trend towards worse survival, adjusted for grade and resection extent, with no events in low-grade samples
- Low T-cell (OR 0.26, 0.1 – 0.5), and high macrophage (OR 3.7, 2 – 8) and proliferation (OR 3.3, 2 – 5) signatures, adjusted for grade, characterize **C4** relative to C3
- Microglia are sparse in high-grade, **C4**, and **C5** ($p < 0.001$)
- Adjusting for resection extent, increasing T-cell signature is associated with decreased survival time among high-grade tumors ($p = 0.008$)

Context-specific immunomodulators may contribute to immune escape



- Candidate immunosuppressive genes with active drug development are identified.
  - *eg, EZH2, KDM1A, and CD200, and CD276* are potent immune inhibitors upregulated in C4 / high-grade tumors
- Translational experimentation testing immune modulation of genes of interest represent next steps

Thorsson, V. et al. The Immune Landscape of Cancer. Immunity 48, 812-830.e14 (2018).

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