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TMIC-86. SPATIAL ORGANIZATION OF THE PEDIATRIC HIGH-GRADe Glioma TuMOR-immune lANdSCAPE
Thijs van den Broek1, Raoull Hoogendijk1, Mariette Kranendonk2, Cristian Ruíz2, Wout I. Megchelenbrink3, Julie Lammers4, Mario G Ries5, Eelco Hoving1, Jasper van der Lugt1, Anne C Rios2, Hendrik Stunnenberg1, Dannis van Vuurden1, and Anoek Zomer3; 1Princess Máxima Center for Pediatric Oncology, Utrecht, Utrecht, Netherlands, 2Princess Máxima Center for Pediatric Oncology, Utrecht, Utrecht, Netherlands, 3Princess Maxima Center for Pediatric Oncology, Utrecht, Netherlands, 4University Medical Center Utrecht, Utrecht, Netherlands

BACKGROUND: Advances in cellular immunotherapies have shown promising results for brain tumors, including pediatric-type diffuse high-grade gliomas (pHGG). A comprehensive understanding of the tumor-immune microenvironment (TME) is essential for efficient target identification and novel therapeutic strategies. The interplay between cells and their spatial localization within the TME may affect immune cell phenotype and function. We characterized these interactions and phenotypes by single-cell (SC) spatial proteomic analysis. METHODS: Thirty-two tissue biopsies of pHGGs were collected from the Princess Máxima Center biobank consisting of 14 diffuse midline gliomas, H3K27-altered (DMG) and 18 other pHGGs. Three cores per biopsy were assembled in a tissue micro-array (TMA). A cyclical multiplex immunofluorescence antibody staining technique by means of chemical antibody-removal was applied to the TMA sections. This resulted in hyperplexed images enabling detailed mapping of the spatial organization. Survival data of patients was collected retrospectively. Clusters of interacting cells were detected using cellular neighborhood (CN) analysis and SC distance analysis. RESULTS: SC analysis revealed a large fraction of myeloid cells in the TME, up to 21% of total cells within a tumor, characterized by expression of IBA1 and CD68. We also identified some significant differences in the composition and spatial organization of DMGs compared to other pHGGs. More specifically, DMG biopsies showed lower abundance of CD163+/CD206+ immunosuppressive myeloid cells compared to other pHGGs (p<0.001). Additionally, the presence of T cells was significantly lower in DMGs compared to other pHGGs (p<0.001). CN analysis revealed a higher occurrence of myeloid/astrocyte-like neighborhoods in pHGGs other than DMG. The presence of this cluster in these tumors is associated with higher risk of dying (p<0.05). Thus, the combination of our spatial proteomic SC technology framework and unique patient sample collection will offer essential insights into the cellular interplay in the TME, and its influence on patient outcomes.