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IMMU-20: INNATE IMMUNE EVASION IN MYC-AMPLIFIED MEDULLOBLASTOMA
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BACKGROUND: While major advances have been made in improving the quality of life and survival of children with most forms of medulloblastoma
Abstracts

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**PEDIATRIC GLIOBLASTOMA**

**IMMU-21. B7-H3 NANOBODY CAR-T CELL THERAPY IN**

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...with MYC-driven tumors (Grp3-MB) still suffer significant morbidity and mortality. Here, we report a cell surface proteome analysis of Group3-MB cell lines after direct MYC inhibition to identify changes in surface proteins and sensitivity to macrophage-mediated phagocytosis. **METHODS:** We had previously demonstrated the preferential activity of HDACi (CD94) in MYC-driven medulloblastoma. CD94 showed significant cell viability reduction mediated by reduction in the MYC (mRNA and protein), induction of apoptosis in MYC-driven medulloblastoma. In this study, we directly inhibited MYC using MYC975 and OMO-MYC and carried out a cell surface proteomic analysis on Group3-MB cell lines to reveal CD24 and CD59 as potential immune evasion markers. While CD24 is a potential don’t eat me signal, CD59 is a ubiquitously expressed cell-surface glycosylphosphatidylinositol-anchored protein that acts as an inhibitor to the membrane attack complex and protects cells from CDC. In certain tumors, CD59 expression is enhanced, posing a significant obstacle to treatment by hindering effective monoclonal antibody-induced CDC. We use inhibitors to CD24 and CD59 to confirm their role as innate immune evasion proteins in Group3MB. **RESULTS:** Meta-analysis of published datasets reveals CD24 and CD59 as strong prognostic indicators in Group3-MB as well as within the Group3g-subtype. Inhibition of MYC reduces surface levels of CD24, increasing macrophage-mediated phagocytosis. The use of a blocking anti-CD24 mAb significantly enhanced macrophage-mediated phagocytosis. Furthermore, a significant reduction in surface expression was observed in CD59. Blocking CD59 mAb significantly enhanced anti-CD47 mAb mediated phagocytosis. Combined treatment of anti-CD24 and anti-CD47 significantly enhanced the survival of Grp3-MB tumor-bearing mice.