PD-L1 expression in medulloblastoma: An evaluation by subgroup

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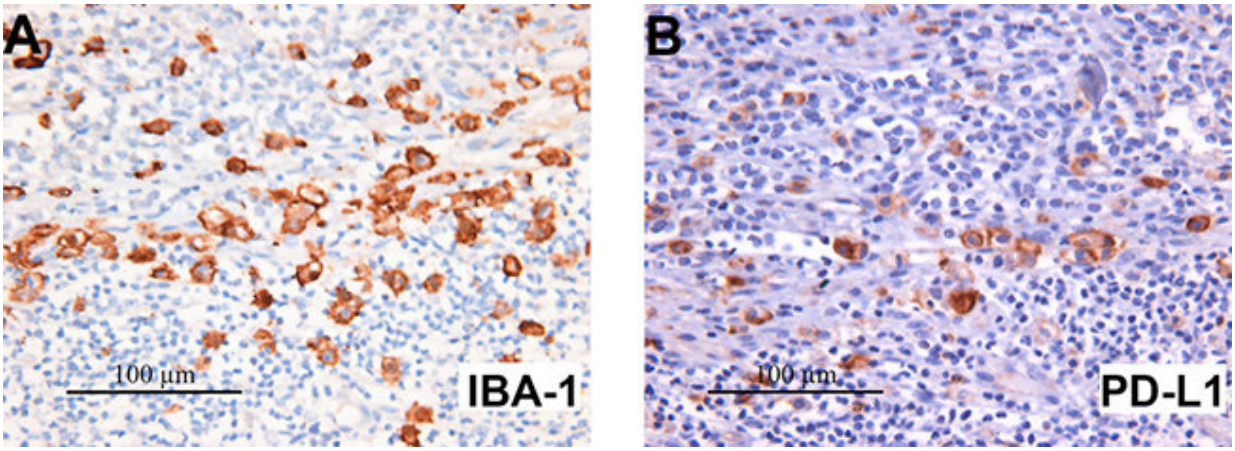

IBA-1 staining reveals heavy microglial infiltration in SHH MB with many microglia co-expressing PD-L1. Immunohistochemistry of one representative SHH MB, 18872, stained for IBA-1 (A) and PD-L1 (B). Many of the IBA-1 expressing microglial cells are also PD-L1+. All images 400× original magnification. Credit: Allison M. Martin

This study evaluated the expression of PD-L1 and markers of immune mediated resistance in human medulloblastoma, the most common malignant pediatric brain tumor.

In cell lines, SHH MB, which are low-MYC expressing, demonstrated both constitutive and inducible expression of PD-L1 while those in Group 3/4 that expressed high levels of MYC had only inducible

expression.

MB expresses low levels of PD-L1 facilitating immune escape.

"Tumors in the SHH subgroup are characterized by genetic alterations activating this key developmental pathway. WNT subgroup tumors have alterations in the wingless/ -catenin developmental pathway."

Most patients are assessed for PD-L1 expression prior to starting therapy, but the expression of PD-L1 during the entire course of treatment remains unclear, as does the relationship between changing PD-L1 expression and therapeutic responses.

In support of PD-L1 pathway activity in human MB, the researchers demonstrated that MB cell lines robustly up-regulated PD-L1 when they simulated an anti-tumor immune response in vitro by exposing the cell lines to recombinant human IFN-.

In further support of the notion that MB adaptively up-regulates PD-L1 as a specific response to immune mediated stimulation is the finding that radiation induced PD-L1 expression but not to the extent generated by IFN-.

The finding that both IFN- and radiation induced PD-L1 expression in vitro and the paucity of PD-L1 expression in vivo in the absence of TIL further emphasizes the concept that immune adjuvants will likely be needed to fully realize the benefit of PD-1 blockade in cold tumors such as MB.

Expression of MHC II by MB is unusual as this molecule is usually a feature of dendritic cells and other APCs indicating that this tumor may be directly inhibiting anti-tumor immune responses by masquerading as an inhibitory APC MHC II expression may also indicate a role for the

immune checkpoint molecule, lymphocyte activating gene-3 in MB whose primary ligand is MHC II.

More information: Allison M. Martin et al. PD-L1 expression in medulloblastoma: an evaluation by subgroup, *Oncotarget* (2018). DOI: 10.18632/oncotarget.24951