

ABSTRACT | APRIL 01 2007

Activity of Anti-PD-1 in Murine Tumor Models: Role of “Host” PD-L1 and Synergistic Effect of Anti-PD-1 and Anti-CTLA-4 (48.37) FREE

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Abstract

PD-1, like CTLA-4, is a negative regulator of T cell function. The PD-1 ligand, PD-L1, is expressed by dendritic cells/antigen presenting cells and by activated T cells. Many tumors express PD-L1 and its expression has been linked to poor prognosis. PD-L1 expression is also upregulated by γ IFN. We studied the activity of anti-PD-1 in two subcutaneous tumor models which differ with regard to PD-L1 expression: Sa1N fibrosarcoma, which is negative for PD-L1, and cannot be induced to express PD-L1 by γ IFN; and, MC38 colon adenocarcinoma, which expresses low levels of PD-L1 which is upregulated by γ IFN. Anti-PD-1 blockade resulted in partial tumor growth inhibition in both models demonstrating that the activity of anti-PD-1 is independent of PD-L1 expression on the tumor. This suggests that host PD-L1 (and/or PD-L2) expression limits anti-tumor activity. In the MC38 model, the concurrent use of anti-PD-1 and anti-CTLA-4 antibodies was significantly more potent than either of the individual antibodies or sequential administration of the antibodies regardless of order. These results are consistent with a role for PD-1 and CTLA-4 in T cell priming and suggest that they play non-redundant roles during T cell activation. Cell subsets implicated in the activity of PD-1 and CTLA-4 blockade in the MC38 model are under investigation.

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