



A Novel Immune Checkpoint Inhibitor Anti-NKG2A Antibody Promotes Anti-Tumor Immunity by Unleashing Both T and NK Cells

Immune checkpoint inhibitors, in particular anti-PD-1/L1, have revolutionized cancer treatment over the past decade, providing long-lasting benefits. However, only a subset of patients respond favorably to PD-1/L1 blockade. One of the biggest challenges of immunotherapy is overcoming anti-PD-1/L1 resistance by targeting new immune checkpoints and mastering therapeutic combinations.

Eric Vivier's group from Innate Pharma have published new research showing that blocking NKG2A with an anti-NKG2A antibody simultaneously stimulates the anti-tumor activity of NK cells and T cells. NKG2A is an inhibitory checkpoint receptor for HLA-E which is frequently overexpressed in human tumors. By expressing HLA-E, cancer cells can protect themselves from killing by NKG2A⁺ immune cells.

The authors demonstrate that combination of an NKG2A blocking antibody with a PD-L1 blocking antibody provides an additive effect towards the activation of anti-tumor immunity both *in vitro* and in tumor-bearing mice.

The authors then developed a humanized anti-NKG2A antibody called monalizumab. Initial tests confirmed that monalizumab promotes the anti-tumor cell activities of human NK cells and CD8 T cells. Interim results of a phase II clinical trial of monalizumab in combination with anti-EGFR (cetuximab) in squamous cell carcinoma of the head and neck showed that 31% of patient tumors shrunk or stabilized.

Overall, this research suggests that NKG2A targeting is a novel checkpoint inhibitory mechanism promoting anti-tumor immunity by enhancing the activity of both T and NK cells, which may complement first-generation immunotherapies against cancer.

The authors used Bio X Cell's anti-mouse PD-1 antibody (clone RMP1-14) in combination with anti-NKG2A in preclinical mouse models. The authors also used Bio X Cell's anti-mouse CD8 α (clone YTS 169.4) and anti-mouse NK1.1 (clone PK136) antibodies to deplete CD8 T cells and NK cells respectively.

See the complete article in Cell: [https://www.cell.com/cell/fulltext/S0092-8674\(18\)31322-9](https://www.cell.com/cell/fulltext/S0092-8674(18)31322-9)