Antibodies Targeting Resokine, a Soluble Immune Modulator, Inhibit Tumor Growth in Syngeneic Mouse Models

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Abstract

A number of autoimmune syndromes have been linked to autoantibodies generated from the B(2)M/Resokine gene family. One of these is a novel autoimmune syndrome characterized by hyperglycemia, β-cell loss, insulinopenia, and diabetes in mice. Antibodies against Resokine, a soluble immune modulator, have been generated and tested for their anti-tumor activity in mouse models of breast and melanoma. Antibodies that block the PD-L1 receptor were compared to antibodies that block the IFN-γ receptor. Synergistic activity in these models was observed in a variety of immunodeficient and syngeneic mouse models. Similar for: IFN γ•, IFN γ••, IFN γ•••, IFN γ••••

Resokine Proteins: Extracellular Histidyl-tRNA Synthetase Gene Products With Immune Modulation Activity

Resokine Reduces Cytokine and Granulocyte Release During T Cell Activation

Efficacy in B16 Melanoma Model

Anti-Resokine (1:1) + Microisorb

Anti-Resokine (1:1) + iNKT

Efficacy in Colon Tumor CT26 Model (Prophylactic Dosing)

Anti-Resokine (1:10) + Microisorb

Anti-Resokine (1:10) + iNKT

Efficacy in CT26 Colon Tumor Model (Therapeutic Dosing)

Anti-Resokine (1:10) + iNKT

Anti-Resokine (1:10) + Microisorb

Efficacy in 4T1 Breast Cancer Model

Anti-Resokine (1:10) + iNKT

Anti-Resokine (1:10) + Microisorb

Tumor Rechallenge With No Therapeutic Agent Administered

Anti-Resokine (1:10) + iNKT

Anti-Resokine (1:10) + Microisorb

Anti-Resokine Antibodies Harness an Immune-Based Mechanism

Anti-Resokine Antibodies Do Not Provok Autoimmune Diabetes

The Resokine Pathway Modulates Disease Induction in a Model of Autimmune Diabetes

1. Resokine Antibodies block the PD-L1 receptor in breast, colon, and melanoma xenograft models in mice. Blockade of PD-L1 signaling in these models leads to tumor regression and is dependent on both CD8+ T-cells and NK cells.

2. In a syngeneic mouse model of autoimmune diabetes, Resokine antibodies do not provoke autoimmune diabetes, even in mice receiving high doses of anti-PD-L1 antibody alone.

3. These data support the development of Resokine antibodies as a novel immunomodulatory approach against a variety of malignancies and autoimmune disease.

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