In vivo Anti-Cancer Efficacy of Recombinant Mouse IL-17E in Syngeneic Mouse Colon and Melanoma Models in Balb/c and C57BL/6 Mice

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Abstract

Flexible infiltration (p< 0.06) of recombinant mouse IL-17E (rmIL-17E) can induce a significant tumor growth inhibition in a mouse model of CT26 tumor xenografts. rmIL-17E is a novel proinflammatory cytokine that induces a Th2-type immune response, which includes the induction of eosinophils through the production of IL-5, and elevated gene expression of IL-4 and IL-13 in multiple tissues. In a mouse model with implanted CT26 tumors, low-dose rmIL-17E (0.25 μg every 2 days) was found to induce antitumor activity. The mechanism of action of rmIL-17E is thought to involve the induction of T helper type 2 cells, which secrete cytokines that inhibit tumor growth.

Introduction

IL-17E is a novel proinflammatory cytokine that induces a Th2-type immune response, which includes the induction of eosinophils through the production of IL-5, and elevated gene expression of IL-4 and IL-13 in multiple tissues. In a mouse model with implanted CT26 tumors, low-dose rmIL-17E (0.25 μg every 2 days) was found to induce antitumor activity. The mechanism of action of rmIL-17E is thought to involve the induction of T helper type 2 cells, which secrete cytokines that inhibit tumor growth.

Summary of Results

- rmIL-17E was efficacious in vivo in both the mouse CT26 and B16-F10 syngeneic tumor models and mediated significant anti-tumor activity in a dose-dependent manner.
- rmIL-17E was capable of inducing significant cell growth inhibition and apoptosis in mice and in vitro studies with tumor xenografts.
- rmIL-17E showed significant anti-metastatic activity in our B16-F10 lung metastasis model resulting in a reduced burden of tumor nodules and nodules in the lungs of tumor-bearing mice compared to controls.
- No apparent rmIL-17E treatment related clinical signs of toxicity such as decreased body weight, morbidity, and abnormal changes in blood cell counts were observed at the end of the study.

Apoptosis Assay

In vitro and in vivo studies with tumor xenografts showed that rmIL-17E possessed the ability to induce apoptosis and cell death in tumor cell lines. The mechanism of action of rmIL-17E is thought to involve the induction of T helper type 2 cells, which secrete cytokines that inhibit tumor growth.

Haematology Results

- Platelet count: Normal reference range for blood cell counts was 150-400x10^9/L.
- Leucocytes: Normal reference range for blood cell counts was 4.0-11.0x10^9/L.