

## Scientific Abstract

Interleukin-2 (IL-2) is an important cytokine for the induction of anti-tumor immunity that has been used clinically, with some success, for a number of years. Unfortunately, the efficacy of IL-2 is limited by severe toxicity. In an attempt to overcome this toxicity, a number of investigators are testing gene therapy approaches in which tumor vaccines are genetically modified to secrete IL-2 at the site of injection. Such studies have demonstrated that IL-2 gene therapy is safe and can generate humoral and cellular anti-tumor immune responses. We previously demonstrated that vaccination with genetically modified tumor cells mixed with fibroblasts modified to secrete IL-2 can induce anti-tumor immune responses in colon cancer and glioma patients without the toxicity associated with IL-2 infusion. Other clinical studies evaluated genetically modified allogeneic fibroblast cells as components of immunotherapeutic vaccine therapies for brain, skin, colon and breast cancers. These studies demonstrated that the approach is safe and can generate humoral and cellular anti-tumor immune responses. Our group recently performed a preliminary clinical trial that evaluated intra-tumoral injection of IL-2 gene modified fibroblasts in two colorectal carcinoma patients with hepatic metastases. Therapy was well tolerated with no significant adverse events. These data support the evaluation of a phase I/II study of intra-tumor injections of IL-2 secreting fibroblasts. In this study, IL-2 secreting fibroblasts will be injected intra-tumorally in patients with various histologies. Patients will be followed for toxicity, tumor regression/progression, and for the development anti-tumor immune responses.