responses and can play an important role in cell-mediated immunity against intracellular pathogens.

[0008] IL-12 has been the subject of intense investigation because it modulates important components of the immune system and has been demonstrated to have dramatic anti-tumor effects in the laboratory and in animal studies. IL-12 has been implicated, for example, in inhibiting growth of human lung adenocarcinoma and acute myeloid leukemia. However, the use of exogenous IL-12 in a therapeutic regimen has been limited by high toxicity in humans.

SUMMARY

[0008a] In one aspect, the present disclosure refers to a composition comprising between one and six intradermal doses, between one and two intratumoral doses and between five and ten intravenous doses of activated allogeneic Th1 cells with cross-linking agents that cross-link CD3 and CD28 cell surface moieties, wherein the intradermal doses comprise between 1×10^6 to 1×10^7 cells/ml, the intratumoral doses comprise between 1×10^7 to 1×10^8 cells/ml and the intravenous doses comprise between 1×10^7 to 1×10^9 cells/ml, respectively, wherein the cross-linking agents are immobilized on surface of biodegradable beads and wherein the Th1 cells, the cross-linking agents and the biodegradable beads are suspended in a non-nutrient media.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] Fig. 1 is a graph illustrating the IL-12 level in a patient's plasma over more than a year. Allogeneic, activated Th-1 cells were administered to the patient at various times using various modes of administration.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0010] The present invention relates to compositions and methods that lead to detectable levels of IL-12 in the plasma of a patient. The present invention includes a composition that, when administered to a patient, can lead to the production of detectable levels of endogenous IL-12 in the patient's plasma, without any significant toxicity. The endogenous IL-12 can surprisingly be detected in patients with cancer. The composition preferably includes allogeneic activated T-cells. T-cells are not capable of producing IL-12, therefore the T-cell composition administered to the patient elicits the production of IL-12 by the patient's own APC.

[0011] The present invention also includes methods of inducing production of endogenous IL-12 in a patient by the patient's own immune system. The method includes administering a composition of allogeneic material, preferably allogeneic activated T-cells. The composition may be administered as a single dose or multiple doses. Preferably, the allogeneic activated T-cells are administered in frequent, low doses. The allogeneic cells can be administered by intradermal, intravenous or intralesional routes. Preferably, the frequency is not less than every 3 days. When these compositions are administered, the patient's own immune system can be induced to produce detectable levels of endogenous IL-12 in the plasma, even in a patient with a cancer. Generally, IL-12 is not found in patients with cancer because tumors can inhibit expression of IL-12. Surprisingly, the methods described herein can overcome this inhibition