Abstract

Pro-inflammatory cytokines have been approved by the FDA for the treatment of metastatic melanoma and renal carcinoma. However, effective cytokine therapy is limited by its short half-life in circulation and the severe adverse effects associated with high systemic exposure. To overcome these limitations, we developed a clinically translatable localized cytokine delivery platform composed of polymer encapsulated epithelial cells that produce localized natural cytokines (IL2, IL7, IL10, or IL12) with temporal regulation. Tumor-adjacent local administration of these cytokine factories demonstrated predictable dose modulation with spatial and temporal control and provided ovarian cancer immunotherapy without systemic toxicities. Treatment of peritoneal tumors using IL2 producing cytokine factories provided sustained eradication of peritoneal tumors in an ovarian cancer mouse model. Our data confirmed local increases in the activation (CD25+CD8+) and proliferation (Ki67+CD8+) of cytotoxic T cells within the IP space of cytokine factory treated mice. Significantly, this platform produced local and systemic T cell biomarker profiles that predict efficacy without toxicity in non-human primates.

hEC-mIL2 Increases Local Cytotoxic T cell Proliferation

Above: a) CD8+ counts, percentage of Ki67+, CD25+, or CD44+CD62L- T cells as frequency of CD8+ T cells, b) CD4+ counts, percentage of Ki67+, CD25+, or CD44+CD62L- T cells as frequency of CD4+ T cells analyzed via flow cytometry.

hEC-hIL2 is Well Tolerated in Primates

Above: a) IP fluid hIL2 concentration as a function of dose 5 days post administration. b) Serum IL2 concentration over time. c) Body weight and d) temperature over time (n=3). e) Percentage of K67+ cells as a frequency of CD8+ T cells. f) Percentage of regulatory T cells as a frequency of total cells.