C-C chemokine receptor type-4 transduction of T cells enhances interaction with dendritic cells, tumor infiltration and therapeutic efficacy of adoptive T cell transfer.

Abstract:
T cell infiltration at the tumor site has been identified as a major predictor for the efficacy of adoptive T cell therapy. The chemokine C-C motif ligand 22 (CCL22) is highly expressed by immune cells in murine and human pancreatic cancer. Expression of its corresponding receptor, C-C chemokine receptor type 4 (CCR4), is restricted to regulatory T cells (Treg). We show that transduction of cytotoxic T cells (CTL) with CCR4 enhances their immigration into a pancreatic cancer model. Further, we show that binding of CCR4 with CCL22 strengthens the binding of T cell LFA-1 to dendritic cell (DC) ICAM-1 and increases CTL activation. In vivo, in a model of subcutaneous pancreatic cancer, treatment of tumor-bearing mice with CCR4-transduced CTL led to the eradication of established tumors in 40% of the mice. In conclusion, CCR4 overexpression in CTL is a promising therapeutic strategy to enhance the efficacy of adoptive T cell transfer (ACT).