Background
Adoptive T cell therapies have shown promising results in clinical trials for solid tumor indications, but efficacy and safety are still suboptimal. We constructed non-replicating and replicating adenoviruses encoding the immunostimulatory cytokines Tumor Necrosis Factor alpha (TNFa) and Interleukin-2 (IL-2), and studied their ability to enhance adoptive T cell therapy. TCR transgenic OT-I T cells were used in mouse studies, while tumor-infiltrating lymphocytes (TIL) grown from syngeneic Syrian hamster tumors were used in studies with oncolytic adenoviruses, since this rodent species supports human adenovirus replication in its tissues. In addition, delivery of IL-2 into solid tumors from an adenoviral vector was compared directly with systemic IL-2 administration in the context of T cell transfer.

Results
Cytokine-armed adenovirus vectors control B16.OVA melanoma growth in combination with OT-I T cell transfer

Adenovirus-mediated local IL-2 delivery is superior to systemic administration in the context of adoptive T cell therapy

Conclusions
• Adenovirus-mediated TNFa and IL-2 delivery enhances adoptive TCR transgenic T cell therapy of murine melanoma by inducing T cell trafficking into tumors.
• Oncolytic adenoviruses coding human TNFa and IL-2 synergize with adoptive TIL transfer against pancreatic cancer tumors in adenovirus-permissive Syrian hamsters.
• Local IL-2 delivery is more effective than traditional systemic IL-2 administration.