Kinetic phases of distribution and tumor targeting by T cell receptor engineered lymphocytes inducing robust antitumor responses.

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Public Summary:
A key issue in advancing the use of adoptive cell transfer (ACT) of T cell receptor (TCR) engineered lymphocytes for cancer therapy is demonstrating how TCR transgenic cells repopulate lymphopenic hosts and target tumors in an antigen-specific fashion. ACT of splenocytes from fully immunocompetent mice transduced with a chimeric murine/human TCR specific for tyrosinase, together with lymphodepletion conditioning, dendritic cell (DC)-based vaccination, and high-dose interleukin-2 (IL-2), had profound antitumor activity against large established MHC- and antigen-matched tumors. Genetic labeling with bioluminescence imaging (BLI) and positron emitting tomography (PET) reporter genes allowed visualization of the distribution and antigen-specific tumor homing of TCR transgenic T cells, with trafficking correlated with antitumor efficacy. After an initial brief stage of systemic distribution, TCR-redirected and genetically labeled T cells demonstrated an early pattern of specific distribution to antigen-matched tumors and locoregional lymph nodes, followed by a more promiscuous distribution 1 wk later with additional accumulation in antigen-mismatched tumors. This approach of TCR engineering and molecular imaging reporter gene labeling is directly translatable to humans and provides useful information on how to clinically develop this mode of therapy.

Scientific Abstract:
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