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The kinetics of accumulation of adoptively transferred ovalbumin-specific T cells in a transgenic, ovalbumin-expressing murine tumor

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We have studied the recruitment of adoptively transferred tumor-specific CD8-positive T cells in a mouse model system. Subcutaneous tumors of the transgenic, ovalbumin-expressing murine melanoma cell line B16-OVA were established in mice, which subsequently received intravenous transfer of ovalbumin-specific T cells, derived from the mouse strain OT-I, transgenic for a T cell receptor recognizing an ovalbumin-derived peptide, SIINFEKL.

Specific T cells from OT-I spleen were expanded in culture in the presence of SIINFEKL peptide prior to transfer. The homing of adoptively transferred cells to B16-OVA tumors was demonstrated using several methods, and the kinetics of the accumulation of the cells in the tumor tissue was delineated by flow cytometry. Quantitative measurements of the content of SIINFEKL/H-2 Kb tetramer and CD8 double positive cells in single cell suspensions from extirpated, collagenase treated tumors were performed each day for 8 consecutive days following adoptive transfer. The presence of double positive cells increased gradually until day 5, when an average number of 3.3×10^6 (n = 9) double positive cells per gram tumor tissue was found. The number of double positive cells per gram tumor remained fairly constant until day 8, which was the latest day examined.

Our results establish a baseline for the tumor accumulation of transferred T cells in this model, and form a foundation for studies of different experimental protocols for adoptive transfer of T cells. Monitoring the effect on the specific accumulation of transferred T cells in this model we are presently studying various strategies for injecting and supporting the transferred cells. Results from these investigations could hopefully contribute towards optimizing adoptive immunotherapy of cancer in human subjects.