Bispecific T cell recruiting antibody enhances anti-tumor activity of adoptive T cell transfer

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Background: One bottleneck for adoptive T cell therapy (ACT) is the recruitment of T cells into the tumor. We hypothesized that adoptive transfer of tumor-specific T cells transduced with a marker antigen in combination with a bispecific antibody (BiAb) exclusively recognizing these T cells and tumor cells would result in improved T cell recruitment to tumors and enhance their therapeutic efficacy.
Methods: SV40 T antigen specific T cells were retrovirally transduced with truncated human EGFR as a marker protein. Targeting and killing by combined ACT and anti-EGFR x anti-EpCAM BiAb therapy of the murine gastric cancer cell line GC8 (SV40 T Ag^+ and $EpCAM^+$) was analyzed. Anti-EGFR x anti-c-Met BiAb was used for targeting of human T cells to the melanoma cell line mel624.38 and to the colon cancer cell line LS174T.
Results: The BiAb efficiently cross-linked EGFR-transduced T cells to tumor cells and enhanced tumor cell lysis. Combination therapy resulted in increased T cell infiltration of tumors, retarded growth of subcutaneous transplanted tumors and prolonged survival compared to treatment with T cells in combination with control antibody ($p< 0.0001$). In the human system this combination strategy translated into enhanced recruitment of T cells to c-Met expressing cancer cells and enhanced recognition of $tyrosinase^+$ melanoma cells as well as of CEA^+ colon cancer cells by TCR and by chimeric antigen receptor expressing T-cells, respectively.
Conclusions: BiAb recruiting tumor-specific T cells transduced with a marker antigen to tumor cells have the potential to enhance efficacy of adoptive T cell therapy. This strategy may overcome respective limitations of either approach alone.