Targeting high-grade B cell lymphoma with CD19-specific T cells.

Abstract:
Adoptive T cell therapy is an important additional treatment option for malignant diseases resistant to chemotherapy. Using a murine high-grade B cell lymphoma model, we have addressed the question whether the B cell differentiation antigen CD19 can act as rejection antigen. CD19(-/-) mice inoculated with CD19(+) B cell lymphoma cells showed higher survival rates than WT mice and were protected against additional tumor challenge. T cell depletion prior to tumor transfer completely abolished the protective response. By heterotypic vaccination of CD19(-/-) mice against murine CD19, survival after tumor challenge was significantly increased. To define protective epitopes within the CD19 molecule, T cells collected from mice that had survived the tumor transfer were analyzed for IFN? secretion in response to CD19-derived peptides. The majority of mice exhibited a CD4(+) T cell response to CD19 peptide 27, which was the most dominant epitope after CD19 vaccination. A peptide 27-specific CD4(+) T cell line protected CD19(-/-) mice against challenge with CD19(+) lymphoma and also cured a significant proportion of WT mice from recurrent disease in a model of minimal residual disease after chemotherapy. In conclusion, our data highlight CD19-specific CD4(+) T cells for...
adoptive T cell therapy of B cell lymphomas.