CD4 T cells transduced with CD80 and 4-1BBL mRNA induce long-term CD8 T cell responses resulting in potent antitumor effects

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Therapeutic cancer vaccines are an attractive alternative to conventional therapies to treat malignant tumors, and more importantly, to prevent recurrence after primary therapy. However, the availability of professional antigen-presenting cells (APCs) has been restricted by difficulties encountered in obtaining sufficient professional APCs for clinical use. We have prepared an alternative cellular vaccine with CD4 T cells that can be expanded easily to yield a pure and homogeneous population in vitro. To enhance their potency as a therapeutic vaccine, in vitro expanded CD4 T cells were transfected with RNAs encoding the costimulatory ligands CD80, 4-1BBL, or both (CD80-T, 4-1BBL-T, and CD80/4-1BBL-T cells, respectively). We observed augmented cell vitality in CD80/4-1BBL-T cells in vitro and in vivo. Significant CD8 T cell responses eliciting in vivo proliferation and cytotoxicity were obtained with CD80/4-1BBL-T cell vaccination compared to CD80-T and 4-1BBL-T cell vaccinations. Furthermore, CD80/4-1BBL-T cell immunization resulted in curing established EG7 tumors, resulting in the generation of memory CD8 T cell responses, and elicited therapeutic antitumor responses against B16 melanoma. These results suggest that CD4 T cells endowed with costimulatory ligands allow the design of effective vaccination strategies against cancer.

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