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Abstract: Mature donor-derived T cells in allogeneic bone marrow (BM) transplants mediate the graft-versus-tumor (GVT) effect by recognizing alloantigens on leukemic cells. However, alloantigen reactivity towards non-malignant tissues also induces graft-versus-host disease (GVHD). Defining T-cell subpopulations that mediate the GVT effect in the absence of GVHD induction remains a major challenge in allogeneic BM transplantation. In this study, we show that in vitro-generated alloantigen-specific CD8(+) cytotoxic T cells (CTLs) established by weekly stimulation with alloantigen-expressing antigen-presenting cells did not induce GVHD in two major histocompatibility complex-mismatched BM transplantation models, where induction of lethal GVHD is dependent on the presence of either CD4(+) or CD8(+) T cells. Despite their strong alloantigen specificity, transplantation of CTLs did not induce the expression of GVHD-associated cytokines IFN-? and TNF-? or clinical or histological signs of GVHD, and lead to a survival rate of above 90%. However, transplantation of unstimulated CD8(+) T cells, which were not primed by the alloantigen in vitro, induced GVHD in both the transplantation models. Although CTLs were impaired in GVHD induction, they efficiently eradicated Bcr-Abl-transformed B-cell leukemias or mastocytomas. Thus, in
vitro-derived CTLs might be useful for optimizing anti-tumor therapy in the absence of GVHD induction.