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[◀ Previous Article](#) | [Table of Contents](#) | [Next Article ▶](#)

TRANSPLANTATION

Brief Report

Absence of donor T-cell–derived soluble TNF decreases graft-versus-host disease without impairing graft-versus-tumor activity

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Tumor necrosis factor (TNF) plays an important role in graft-versus-host disease (GVHD) and graft-versus-tumor (GVT) activity after allogeneic bone marrow transplantation (allo-BMT). TNF can be expressed in a membrane-bound form (memTNF) and as a soluble (solTNF) molecule

after being cleaved by the TNF- α converting enzyme (TACE). To study the contribution of donor T-cell–derived memTNF versus solTNF in GVHD and GVT, we used mice containing a noncleavable allele in place of endogenous TNF (memTNF Δ/Δ) as donors in murine BMT models. Recipients of memTNF T cells developed significantly less GVHD than recipients of wild-type (wt) T cells. In contrast, GVT activity mediated by

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memTNF T cells remained intact, and alloreactive memTNF T cells showed no defects in proliferation, activation, and cytotoxicity. These data suggest that suppressing the secretion of solTNF by donor T cells significantly decreases GVHD without impairing GVT activity.

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