Reversal of CD8 T-Cell-mediated mucocutaneous graft-versus-host-like disease by the JAK inhibitor tofacitinib.

The utility of allogeneic hematopoietic stem cell transplantation is limited by graft-versus-host disease (GVHD), a significant cause of morbidity and mortality. Patients with GVHD exhibit cutaneous manifestations with histological features of interface dermatitis followed by scleroderma-like changes. JAK inhibitors represent a class of immunomodulatory drugs that inhibit signaling by multiple cytokines. Herein we report the effects of tofacitinib in a murine model of GVHD. Oral administration of tofacitinib prevented GVHD-like disease manifested by weight loss and mucocutaneous lesions. More importantly, tofacitinib was also effective in reversing established disease. Tofacitinib diminished the expansion and activation of murine CD8 T cells in this model, and had similar effects on IL-2-stimulated human CD8 T cells. Tofacitinib also inhibited the expression of IFN-? inducible chemoattractants by keratinocytes, and IFN-? inducible cell death of keratinocytes. Tofacitinib may be an effective drug for treatment against CD8 T-cell-mediated mucocutaneous diseases in patients with GVHD.