Supplemental Methods:

Table S1. Flow cytometry antibodies used in the experiments

Antigen	Fluorochrome	Clone	Vendor
B220/CD45R	PE-Cy7	RA3-6B2	BD Biosciences
	BV 785	RA3-6B2	Biolegend
c-Kit (CD117)	BV 650	ACK2	Biolegend
CD11b	APC-Cy7	M1/70	Biolegend
	PE-Cy7	M1/70	Biolegend
CD127	BV 421	A7R34	Biolegend
CD19	AlexaFluor 700	6D5	Biolegend
	APC	6D5	Biolegend
CD25	BV421	PC61	Biolegend
CD3	APC-Cy7	17A2	Biolegend
	PE-Cy7	17A2	Biolegend
CD31	BV421	390	BD Biosciences
CD4	V500	RM4-5	BD Biosciences
	PE-Cy7	GK1.5	Biolegend
CD43	PE	1B11	Biolegend
CD45	APC-Cy7	30-F11	Biolegend
	APC	30-F11	Biolegend
CD51	PE	RMV-7	Biolegend
CD8	PE-Cy7	53-6.7	Biolegend
Flt3 (CD135)	PE	A2F10	Biolegend
Gr-1 (Ly-6G/Ly-6C)	PE-Cy7	RB6-8C5	Biolegend
	APC-Cy7	RB6-8C5	Biolegend
H-2Kb	PE-Cy7	AF6-88.5.5.3	ThermoFisher/eBioscience
IgM	BV 421	RMM-1	Biolegend
Ly-6D	FITC	49-H4	Biolegend
Sca-1	APC	D7	ThermoFisher/eBioscience
TER-119	APC-Cy7	TER-119	Biolegend

Supplemental Figures:

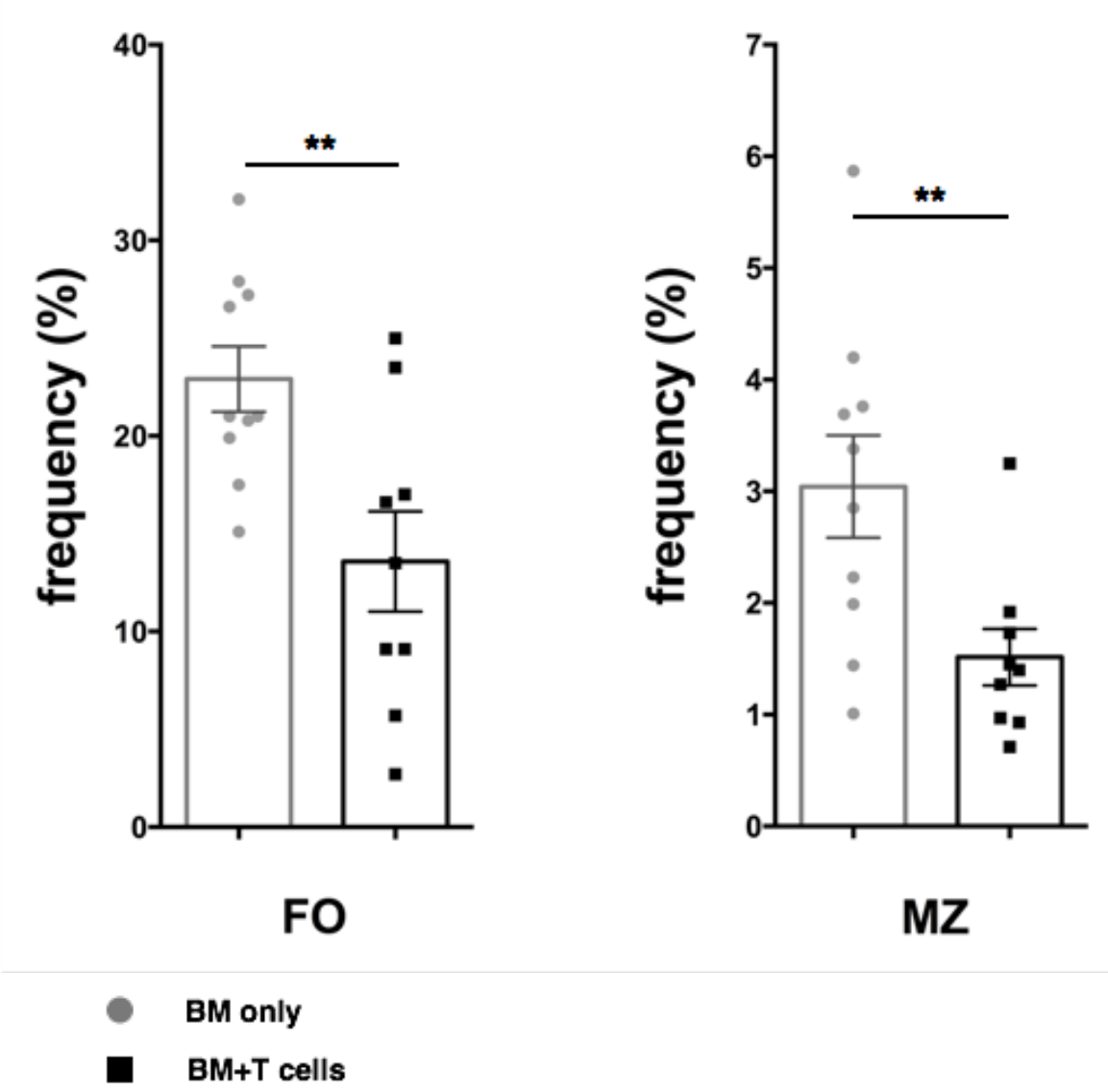

Figure S1. Reduced frequency of follicular and marginal zone B cells in the spleen of cGVHD animals. B10.BR mice were transplanted with BM only or BM and T cells from B6 donor mice and spleens were harvested on day 30.
Frequency of follicular (FO, $CD21^{int}IgM^{int}CD23^{+}$ $AA4.1^{-}$) and marginal zone (MZ, $CD21^{hi}IgM^{int}CD23^{-}AA4.1^{-}$) of donor origin in spleen of transplanted mice. Combined data from 3 independent experiments, ** $P<0.01$ (Mann-Whitney test), BM only N=10, BM+T cells N=9)

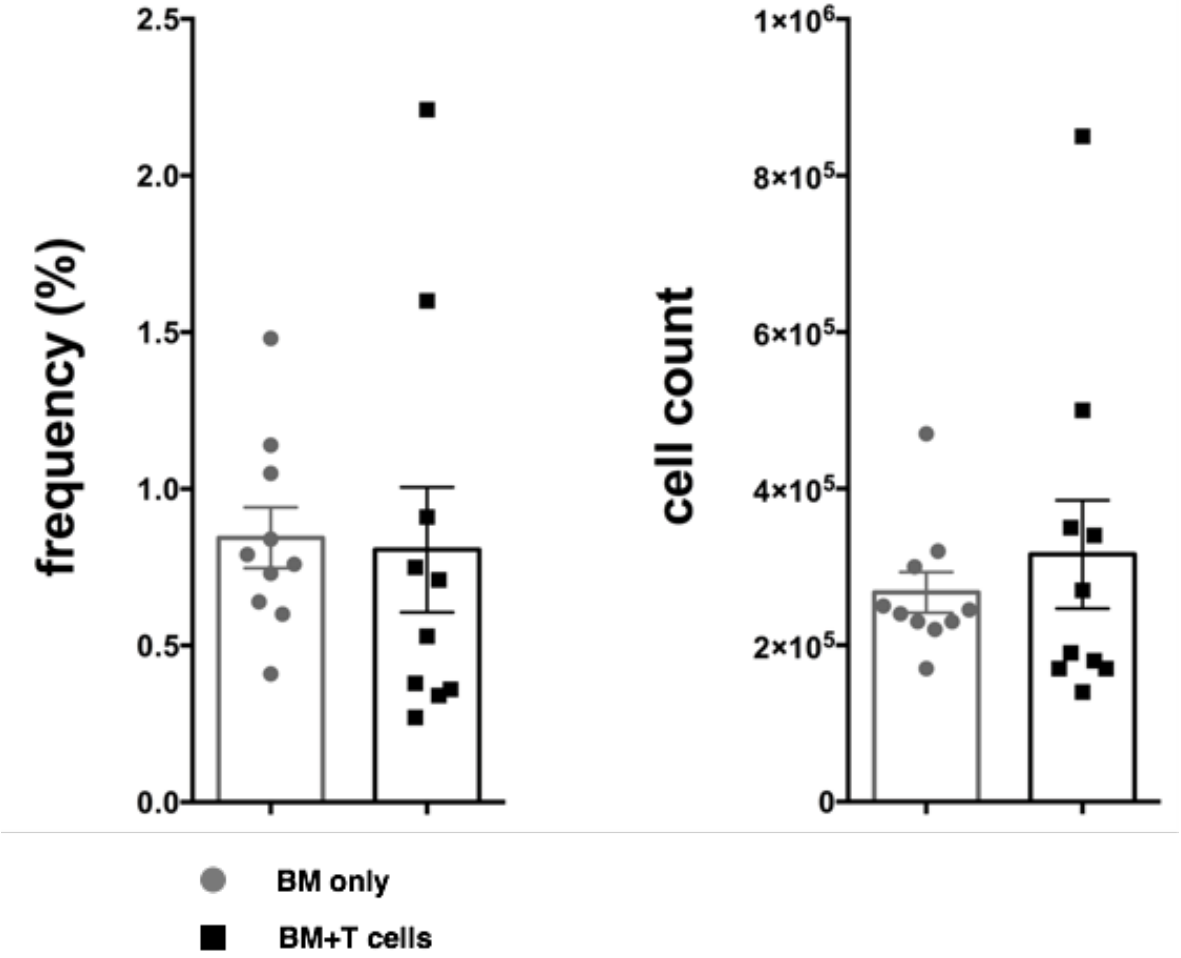

Figure S2. Hematopoietic stem and progenitor cells (HSPC) are not affected in cGvHD. B10.BR mice were transplanted with BM only or BM and T cells from B6 donor mice and BM cells from tibiae and femurs were harvested on day 30.
Frequency (left) and cell numbers (right) of HSPC ($Lin^-Kit^+Sca\text{-}1^+Flt3^-$) cells in the BM. Combined data from 3 independent experiments. Mann-Whitney test, N=10 in each group

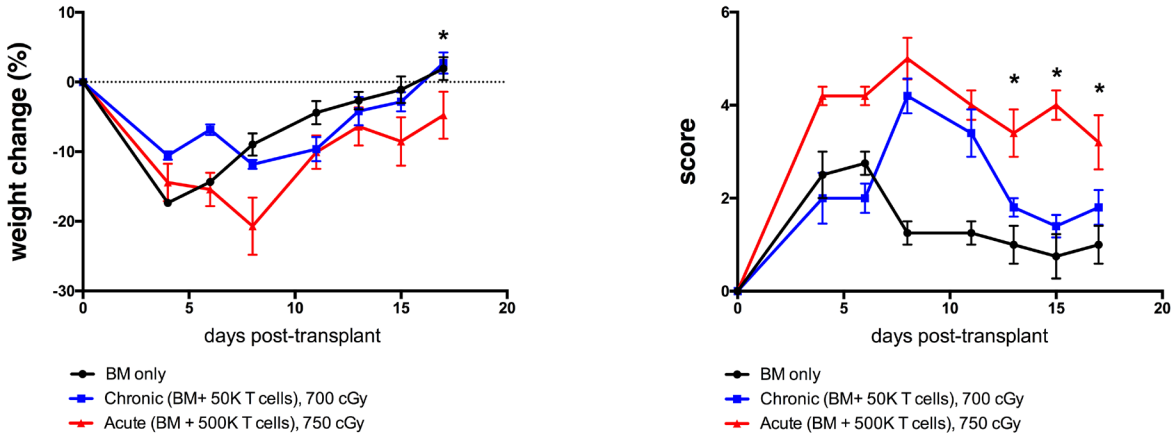

Figure S3. Comparison of weight change and clinical scores in acute and chronic GvHD mice. B10.BR mice were transplanted with BM only or BM and low dose ($5x10^4$) or high dose ($5x10^5$) of T cells from B6 donor mice. Mice in aGvHD group also received a higher dose of irradiation (750 cGy vs. 700 cGy)

Weight changes **(A)** and GvHD scores **(B)** of animals were tracked for 17 days after transplantation. Weight change and GvHD scores were compared using multiple t test method with Holm-Sidak correction for multiple comparisons (alpha = 0.05, * $P < 0.05$).

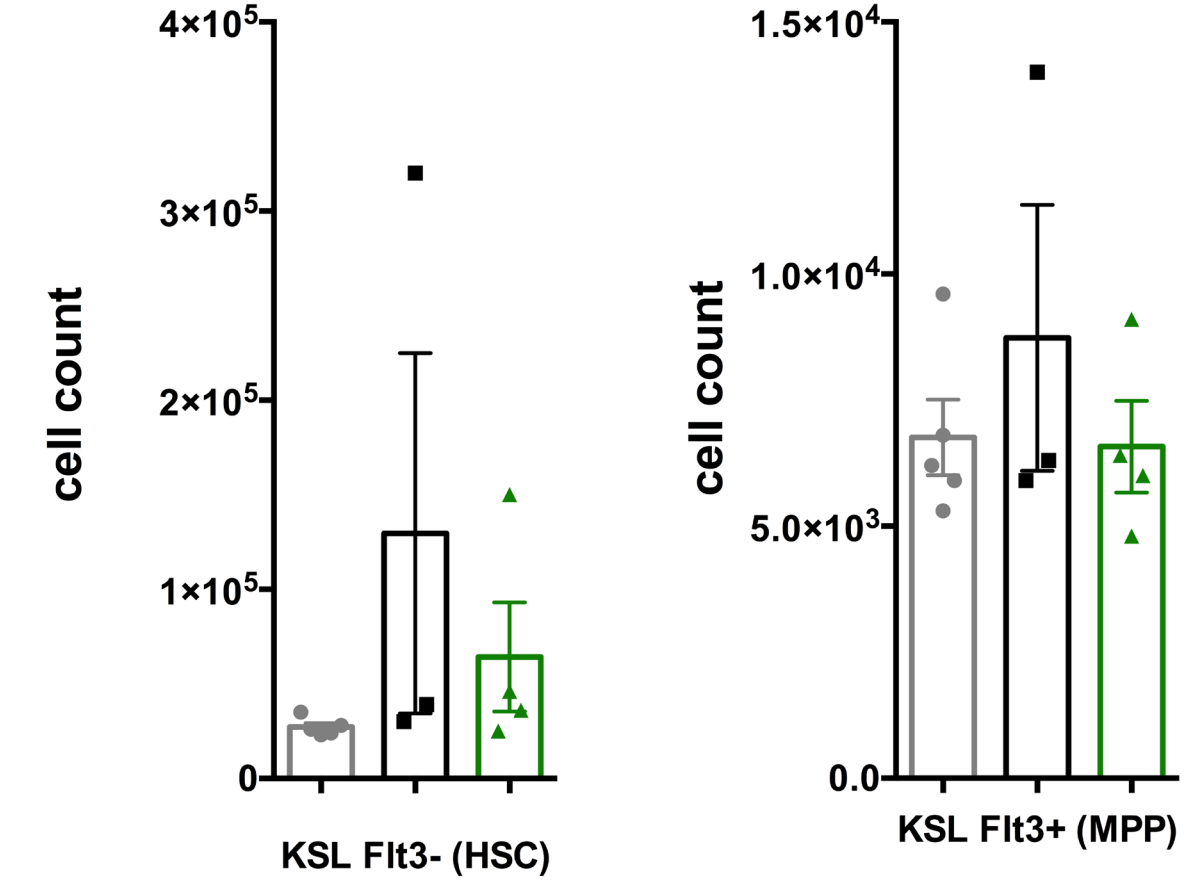

Figure S4. Injections of mIL-7 does not affect BM HSPC and MPP cells in cGvHD animals. Overall number of donor-derived HSPC ($Lin^-Kit^+Sca\text{-}1^+Flt3^-$) and MPP ($Lin^-Kit^+Sca\text{-}1^+Flt3^+$) isolated from BM of transplanted mice on day 30, BM+T group received either daily injections saline (black bars) or 1 ug/mouse of mIL-7 (green bars) during the first 2 weeks after transplantation, N = 5 for BM only, N=3 for BM+T cells (saline), N=4 for BM+T cells (mIL-7).

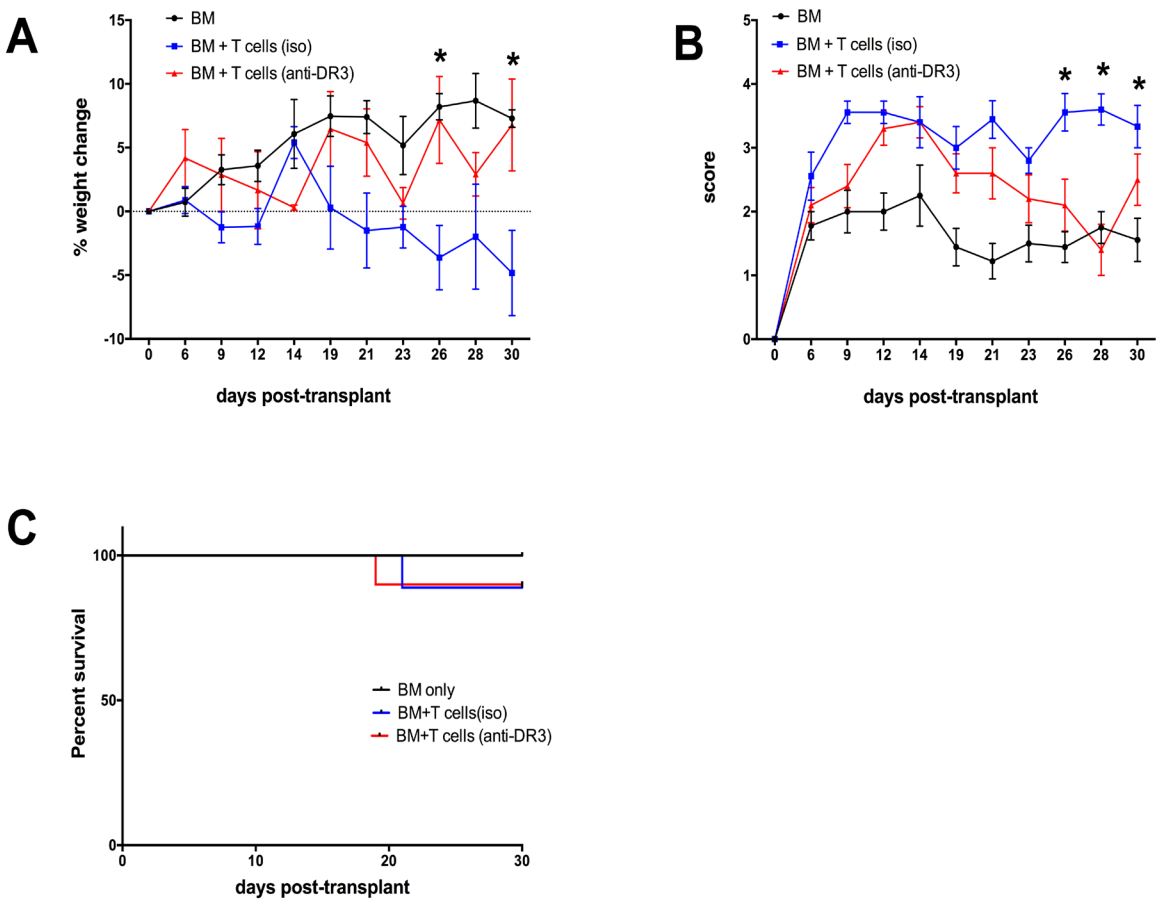

Figure S5. Infusion of splenic T cells from anti-DR3-treated donors reduces cGvHD severity. B10.BR mice were transplanted with BM only or BM and T cells from B6 donor mice injected with either anti-DR3 antibody (4C12, 0.5 mg/kg) or hamster isotype control IgG (NTK888) 3 days prior to procedure.

Weights (A), GVHD scores (B) and survival (C) of animals were tracked for 30 days after transplantation. Weight change and GvHD scores were compared using multiple t test method with Holm-Sidak correction for multiple comparisons (alpha = 0.05, * $P < 0.05$). Survival curves were compared using log-rank.

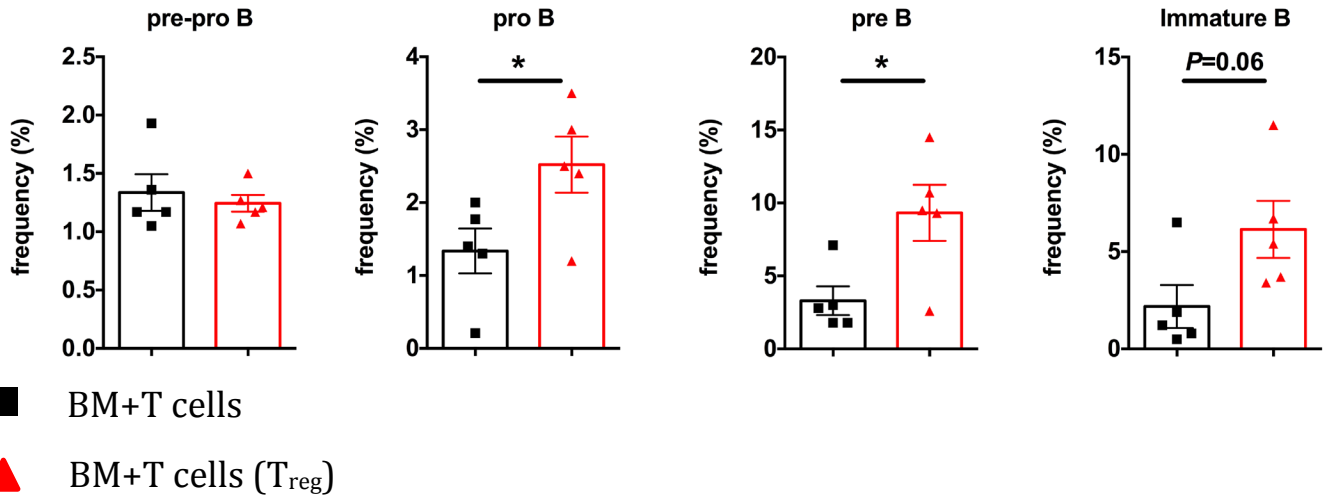

Figure S6. Prophylactically administered (Day 0) splenic Treg cells reduce cGvHD severity. B10.BR mice were transplanted with BM and T cells from B6 donor mice with (red triangles) or without (black squares) $2x10^4$ B6 T_{regs}/recipient. BM cells from tibiae and femurs were harvested on day 30. Unpaired *t*-test, * $P<0.05$, N=5 in each group