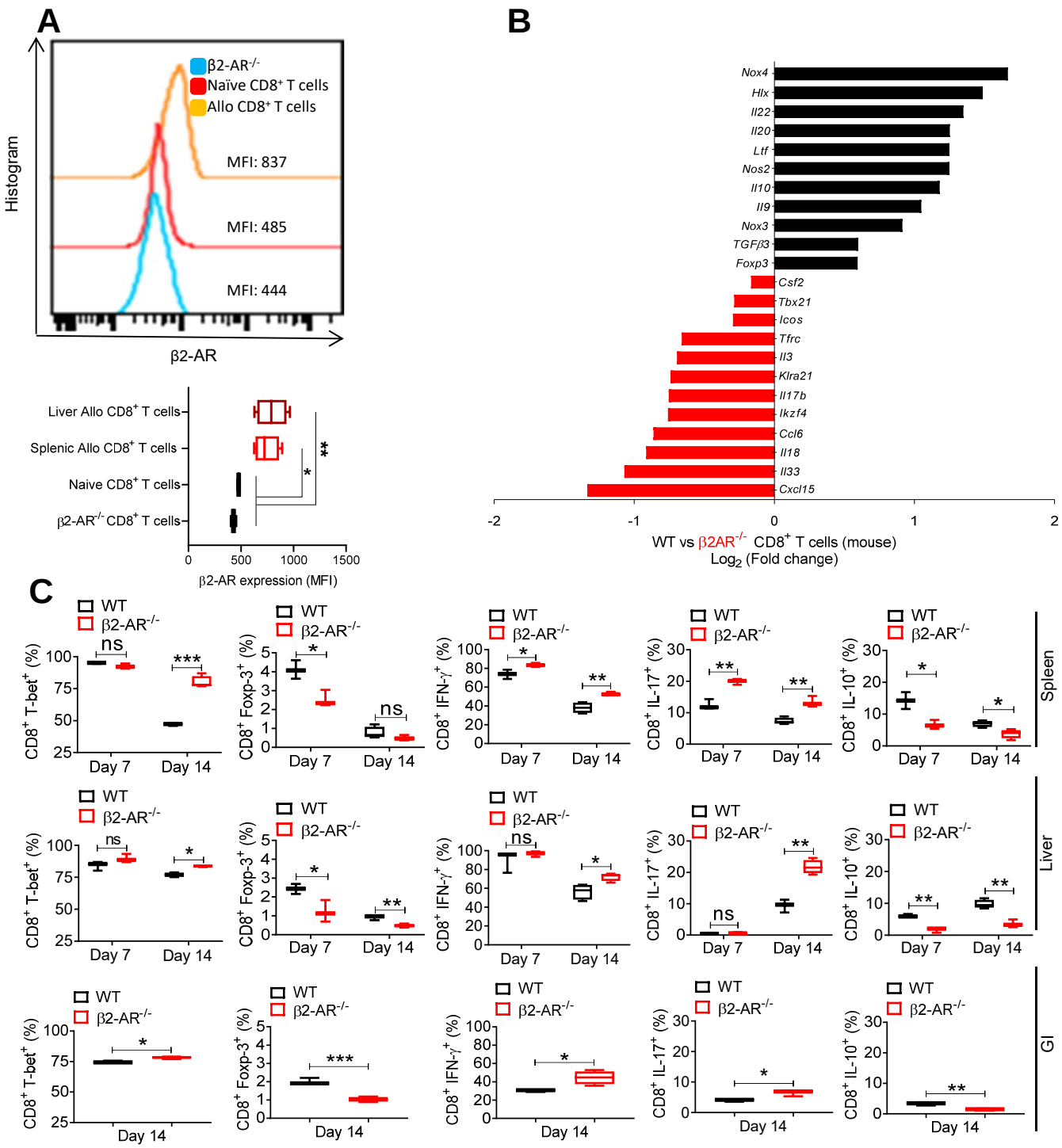
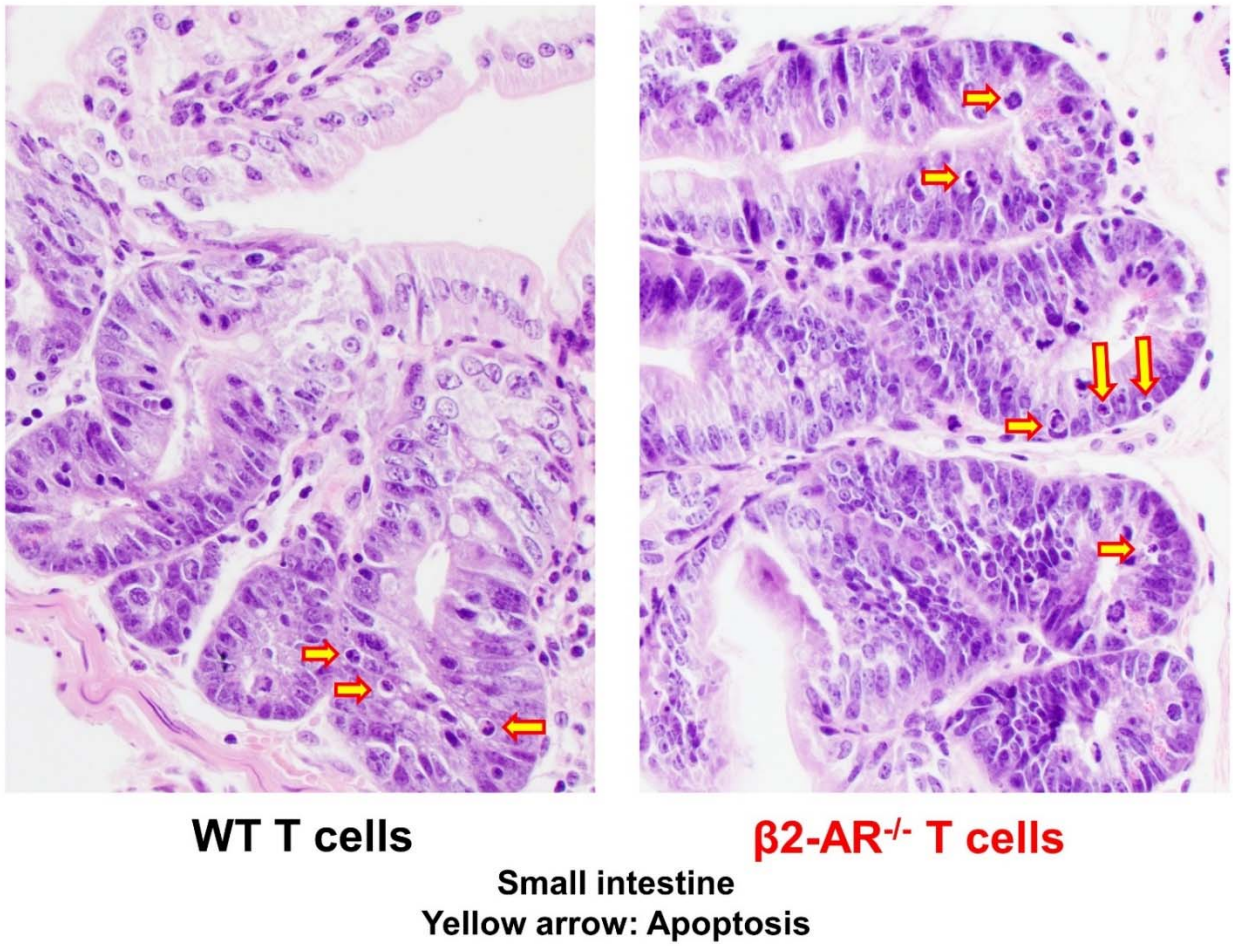


Fig. S1. Expression of the β2-AR in T cells regulates T cell phenotypes during allo-HCT responses. (A) β2-AR expression in WT or β2-AR$^{-/-}$ CD8$^+$ T cells harvested from the spleen day 14 after allo-HCT. CD8$^+$ T cells were gated from single live H-2^{b+} H-2^{d-} CD45$^+$ CD3$^+$ cells (n=5 per group from two independent replicates). **(B)** Immune related gene expression in WT or β2-AR CD8$^+$ T cells sorted from the spleen day 14 after allo-HCT in B6→BALB/c model transplanted with 3.5×10^6 WT C57BL/6 TCD-BM alone or combined with 0.7×10^6 WT C57BL/6 or β2-AR$^{-/-}$ T cells using Nanostring mRNA micro array (Splenocytes pooled from 5-6 mice before CD8$^+$ T cell sorting). **(C)** T-bet, Foxp-3, IFN-γ, IL-17, and IL-10 positive frequencies in CD8$^+$ T cells within single live H-2^{b+} H-2^{d-}CD45$^+$ CD3$^+$ populations from spleen and liver, 7 and 14 days and GI tract, 14 days after allo-HCT. (Pooled data from two individual experiments, n=5-6 per group). For comparison of the means, an unpaired two-tailed t test was used in (C). *$P < 0.05$, **$P < 0.01$. Data are shown as median ± min to max.



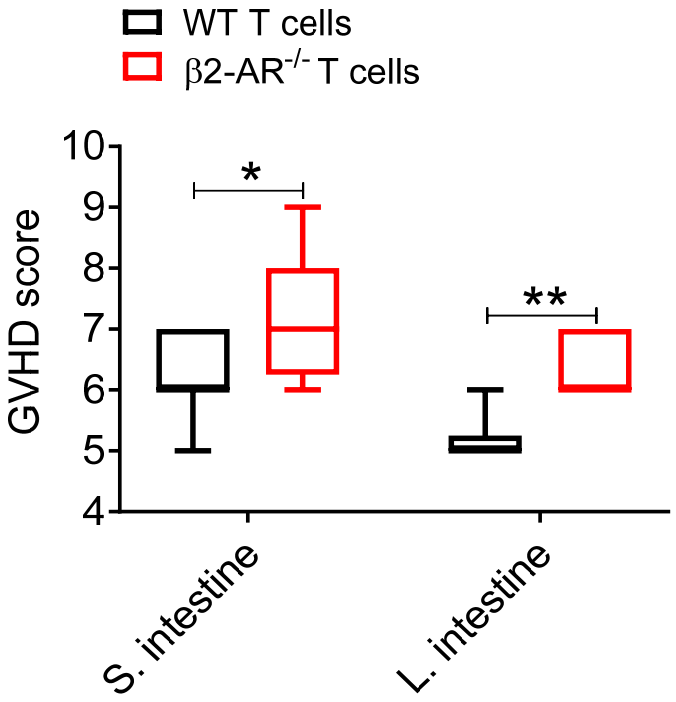


Fig S2. Clinical GvHD score and representative pathology figures (100x) in small and large intestine day 14 after allo-HCT (B6 →BALB/C) using 3.5×10^6 WT C57BL/6 TCD-BM alone or combined with 0.7×10^6 WT C57BL/6 or β2-AR$^{-/-}$ pan T cells. (Pooled data from at least three individual experiments, each with n=4-5 per group). For comparison of the means, an unpaired two-tailed t test was used. *$P < 0.05$, **$P < 0.01$. Data are presented as median ± min to max

Fig. S3

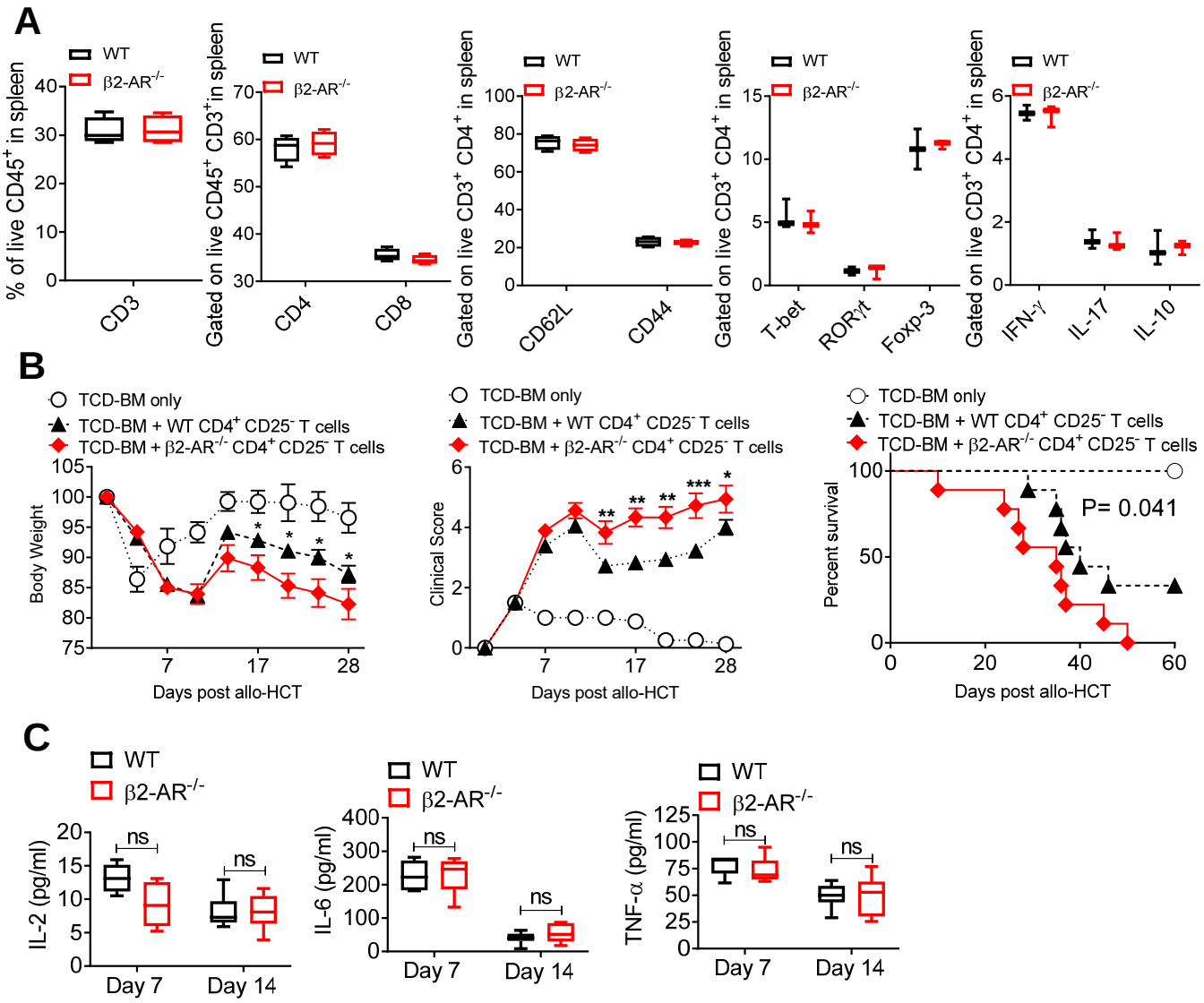


Fig. S3. Comparative analysis of T cell phenotypes and plasma cytokine levels in WT and β2-AR$^{-/-}$ mice. (A) Flow cytometric analysis of splenic T cell population frequencies, and cytokine expression in naïve C57BL/6 WT and β2-AR$^{-/-}$ mice. (Data from n=4 per group). **(B)** Body weight and survival of lethally irradiated BALB/c mice after allo-HCT with 3.5×10^6 WT C57BL/6 TCD-BM alone or combined with 5 × 10^4 WT C57BL/6 or β2-AR$^{-/-}$ CD4$^+$ CD25$^-$ T cells. (Pooled date from two individual experiments, n=4-5 per group, total of n=8-10 per group). For comparison of survival curves, a log-rank (Mantel-Cox) test was used in **(B)**. **(C)** Plasma inflammatory cytokine levels in irradiated BALB/c mice transplanted with TCD-BM plus WT or β2-AR$^{-/-}$ T cells 7 and 14 days after allo-HCT. For comparison of the means, an unpaired two-tailed *t* test was used in (A). Two-way analysis of variance (ANOVA) with Tukey's multiple comparisons test was used for body weight and clinical score difference in (B). *$P < 0.05$, ***$P < 0.001$. Body weight, clinical score and survival data are shown as means ± SEM. Other data are presented as median ± min to max.

Fig. S4

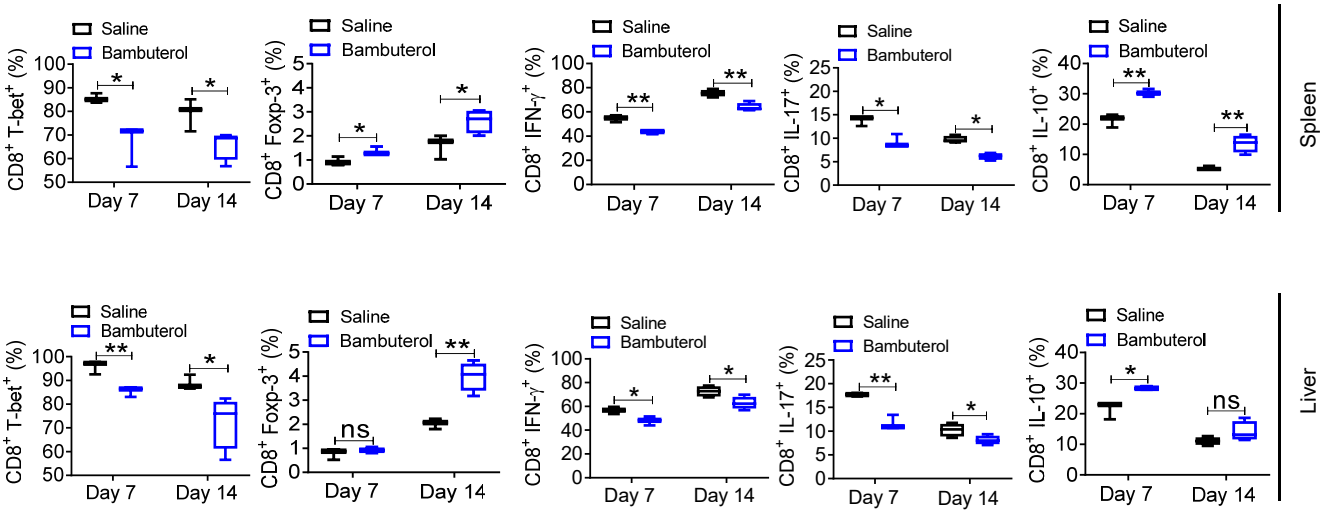


Fig. S4. The activation of β2-AR by the selective β2-AR agonist bambuterol regulates the T cell phenotypes during allogeneic responses. Frequencies of T-bet, Foxp-3, IFN-γ, IL-17, and IL-10 positive frequencies in $CD8^+$ T cells within single live H-2^{b+} H-$2^{d-}CD45^+$ $CD3^+$ populations from spleen and liver of mice 7 and 14 days after allo-HCT. B6 → BALB/c mice were transplanted with 3.5×10^6 WT C57BL/6 TCD-BM combined with 0.7×10^6 WT C57BL/6 pan T cells and treated with daily injection of saline and bambuterol. (Data pooled from two individual experiments, total n=5-6 per group). For comparison of the means, an unpaired two-tailed t test was used. *$P < 0.05$, **$P < 0.01$. Data are presented as median ± min to max.

Fig. S5

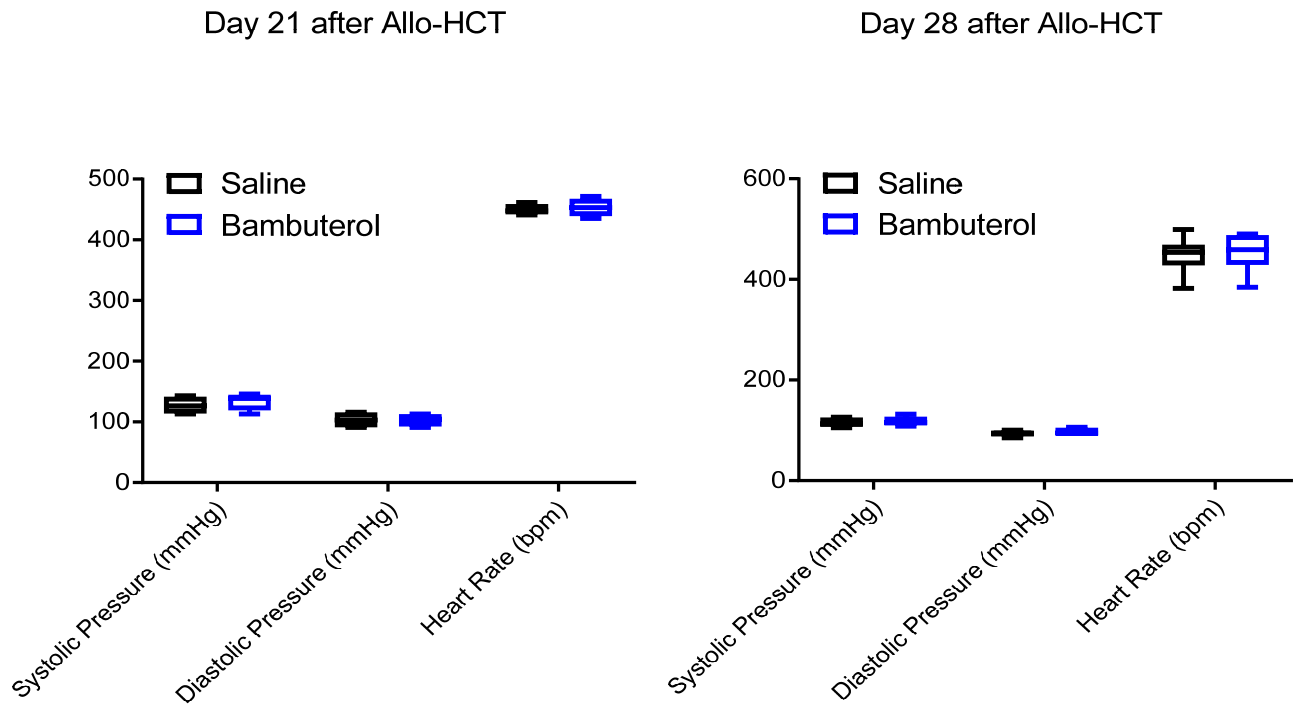


Fig. S5. Daily injection of bambuterol does not change the blood pressure and heart rate in mice after Allo-HCT. Blood pressure and heart rate in mice treated with saline or Bambuterol day 21 and 28 after allo-HCT (B6 →BABL/c). Lethally irradiated mice were transplanted with 3.5×10^6 WT C57BL/6 TCD-BM combined with 0.7×10^6 WT C57BL/6 pan T cells. Mice were injected daily with saline or Bambuterol after allo-HCT. Data are presented as median ± min to max.

Fig. S6

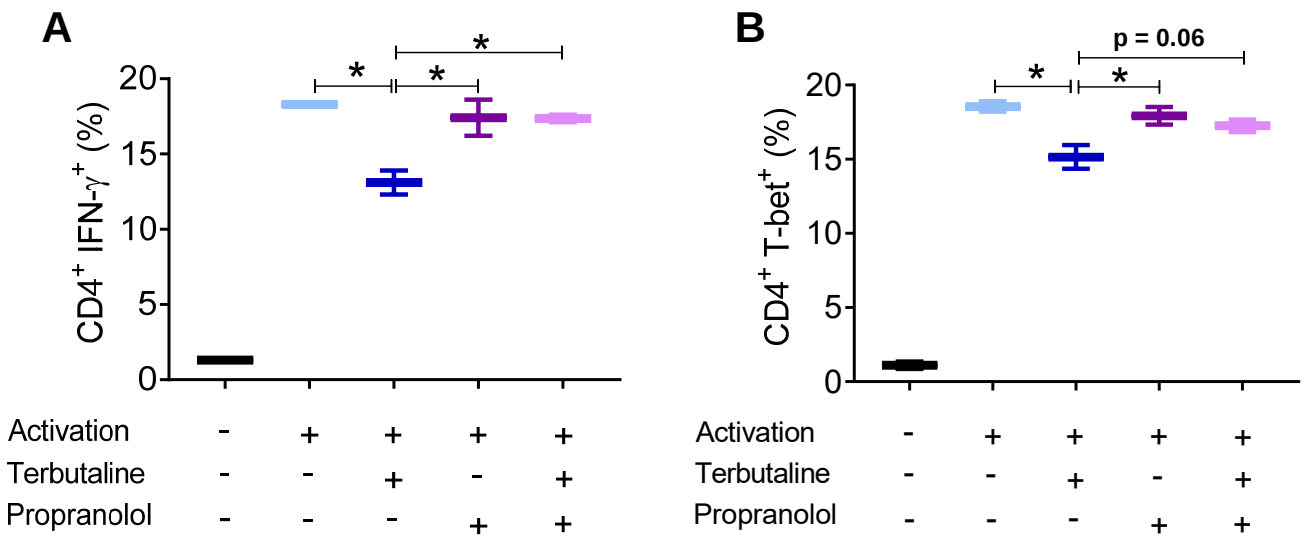


Fig. S6. The activation of β2-AR in T cells suppresses the development of Th1 cells. CD4+ T cells sorted from the spleens of healthy C57BL/6 mice were cultured in Th1 media plus CD3/C28 in different groups. Frequencies of (A) IFN-γ and (B) T-bet positive T cells within singlet live CD4+ T cell population were analyzed using flow cytometry. Data were pooled from three individual experiments, each with n = 2-3 replicates per group. *P < 0.05. Data are presented as median ± min to max.

Fig. S7

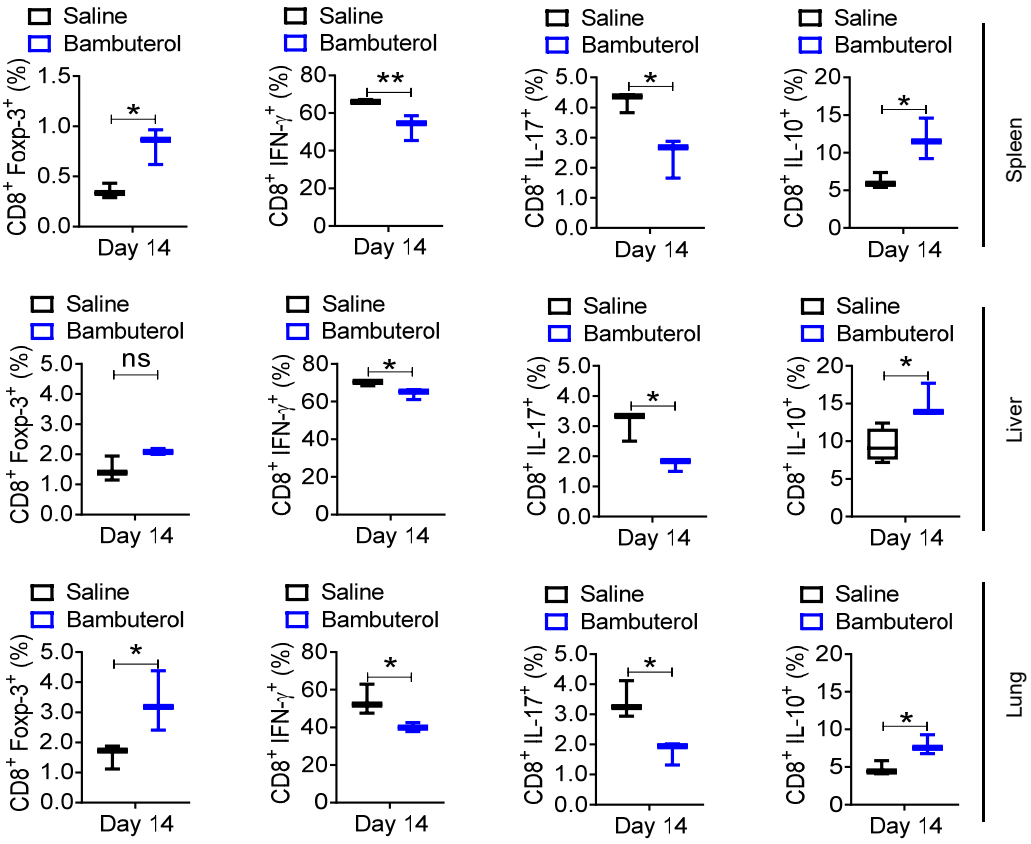


Fig S7. The activation of β2-AR by the selective β2-AR agonist bambuterol regulates human T cell phenotypes in the NSG model of GvHD. Frequencies of Foxp-3, IFN-γ, IL-17, and IL-10 positive in $CD8^+$ T cells within single live $CD45^+$ $CD3^+$ populations from spleen, liver and lung of mice 14 days after allo-HCT. MDSCs were gated from single live $CD45^+$ $CD3^-$ populations. (Data pooled from two individual experiments, n=2-3 per group, total of n=4-6 per group). For comparison of the means, an unpaired two-tailed t test was used. *$P < 0.05$, **$P < 0.01$. Data are presented as median ± min to max.

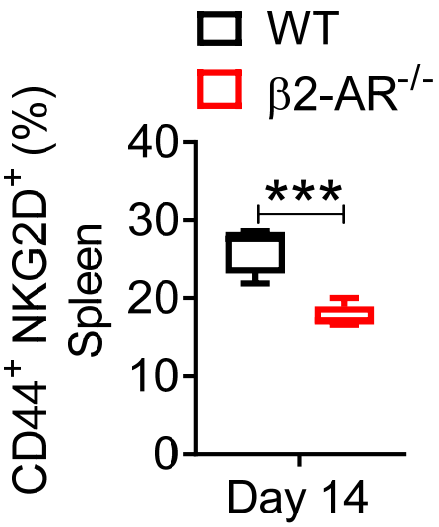


Fig. S8. The activation of β2-AR in T cells increases the expression of NKG2D on effector cells. Lethally irradiated BALB/c mice were transplanted with WT C57BL/6 TCD-BM alone or combined with 0.5×10^6 T cells purified from spleens of C57BL/6 WT or β2-AR$^{-/-}$ mice. Frequencies of CD44$^+$ NKG2D$^+$ in CD4$^+$ T cells within single live H-2^{b+} H-2^{d-} CD45$^+$ CD3$^+$ populations from spleen day 14 after allo-HCT. (Data pooled from two individual experiments, n= 2-3 per group, total of n=4-6 per group). ***$P < 0.001$. data are presented as median ± min to max.

Table S1: Scoring system (modified from ref [35]) was used for acute GvHD scoring

GvHD criteria	Grade 1	Grade 2	Grade 3	Grade 4
Weight loss	5-10%	10 – 15%	15 – 20%	> 20%
Posture	Hunching noted only at rest	Mild hunching also at movement	Moderate hunching and slightly impairs movement	Severe hunching impairs movement
Activity	Mildly decreased	Moderately decreased	Noticeably decreased	Isolated in the corner and severely decreased
Fur texture	Mild ruffling	Moderate ruffling	Severe ruffling / poor grooming	Fur loss
Skin integrity	Mild patchy scaling of skin	Moderate scaling	Several patchy scaling and inflammation of skin	Diffuse ulcerative skin lesions and severe inflammation

Abbreviations: GvHD – graft-versus-host disease.

Table S2: List of antibodies

Mouse antibodies		
Antigens	Clones	Manufacturers
CD8	53-6.7	BD Horizon™
CD4	GK1.5	BD Horizon™
CD3	17A2	BD Pharmingen™
CD45	30-F11	BioLegend™
$H2^b$	AF6-88.5	BioLegend™
$H2^d$	SF1-1.1	BioLegend™
RORγt	Q31-378	BD Horizon™
T-bet	4B10	BD Pharmingen™
Foxp-3	150D	BioLegend
CD45.1	A20	Invitrogen™
CD45.2	104	Invitrogen™
Live/dead	Aqua	Invitrogen™
IFN-γ	XMG1.2	BD Horizon™
IL-17	TC11-18H10.1	BioLegend™
IL-10	JES5-16E3	BioLegend™
CD11b	M1/70	BD Horizon™
Gr-1	RB6-8C5	BD Optibuild™
β2-AR	Orb15065	Biorbyt
CD16/32 Block	2.4G2	BD Pharmingen™
CD44	IM7	BioLegend™
CD62L	MEL-14	BioLegend™
NKG2D	CX5	BioLegend™
Human antibodies		
β2-AR	R11E1	Santa Cruz Bio
CD8	RPA-T8	BD Horizon™
CD4	A161A1	BioLegend™
CD3	SK7	BD Pharmingen™
CD33	P67.6	BioLegend™
CD14	63D3	BioLegend™
IFN-γ	4S.B3	BioLegend™
IL-17	N49-653	BD Pharmingen™
IL-10	JES-9D7	BD Horizon™
Foxp-3	150D	BioLegend™