Supplementary Figures for

Corticosteroids impair epithelial regeneration in immune-mediated intestinal damage.

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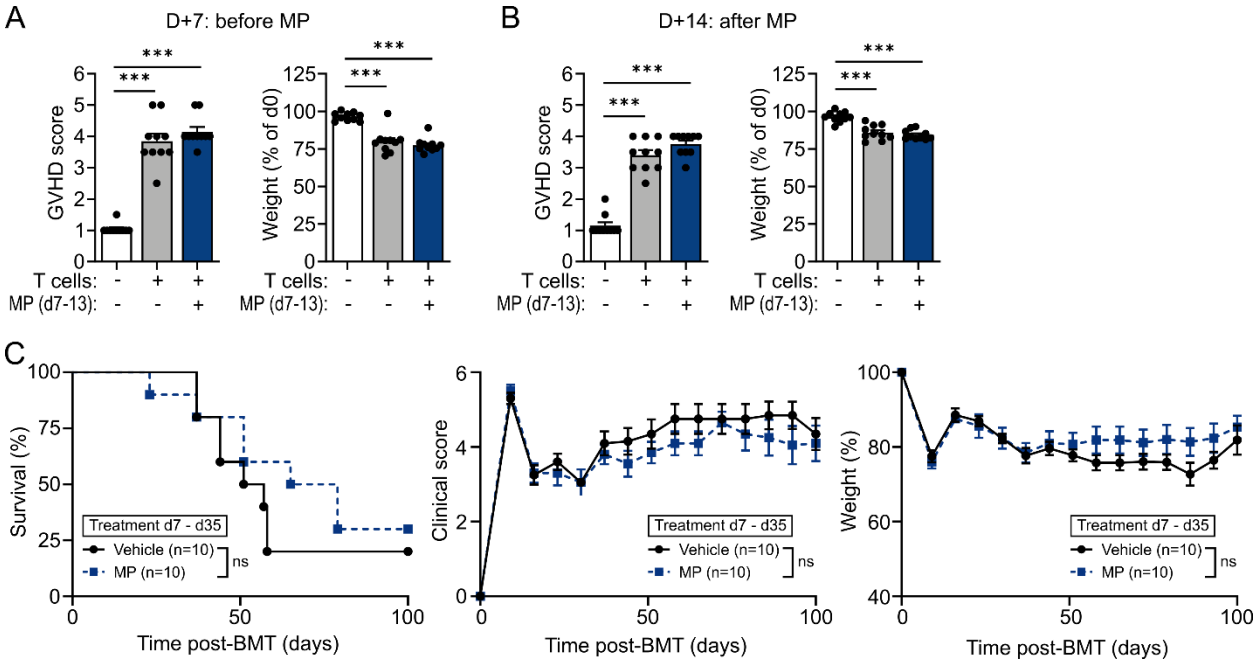
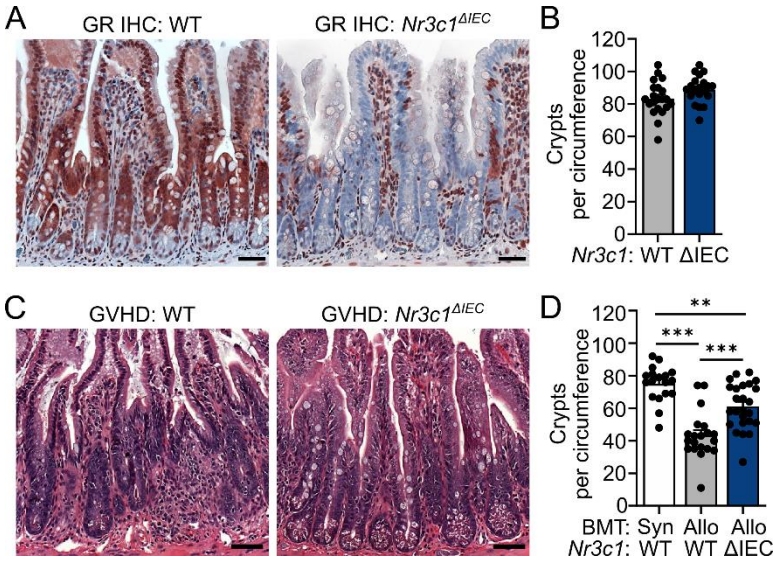
Supplemental Figure 1



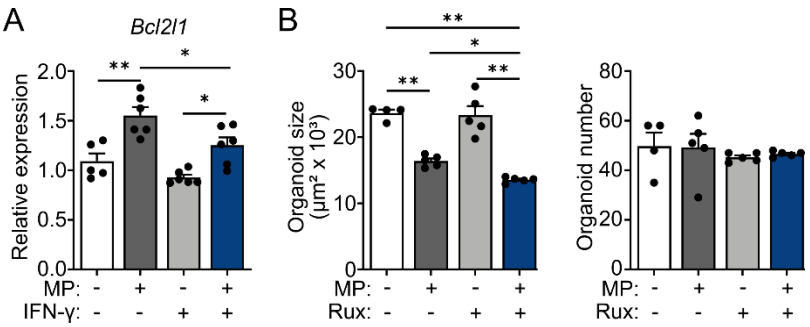
Supplemental Figure 1. Systemic signs of GVHD after allo-BMT with or without corticosteroid treatment starting day 7 post-BMT. (**A**-**B**) B6-into-BALB/c transplant of BM with or without T cells. Recipients were treated with methylprednisolone (MP; 2 mg/kg) or vehicle i.p. daily starting on day 7 after BMT. GVHD score and body weight, 7 and 14 days after BMT (*n* = 10 mice per group). (**C**) Percentage survival, clinical score of GVHD, and relative weight of recipients in a B6-into-BALB/c transplant of BM and T cells with or without MP treatment (2 mg/kg, i.p. daily) from day 7 to 35 post-BMT (*n* = 10 mice per group). Statistics performed with 1-way ANOVA (A and B) or log–rank analysis (C); NS, not significant; ***$P < 0.001$. Data are combined from 2 experiments (A and B) or representative of at least 2 independent experiments (C).

Supplemental Figure 2



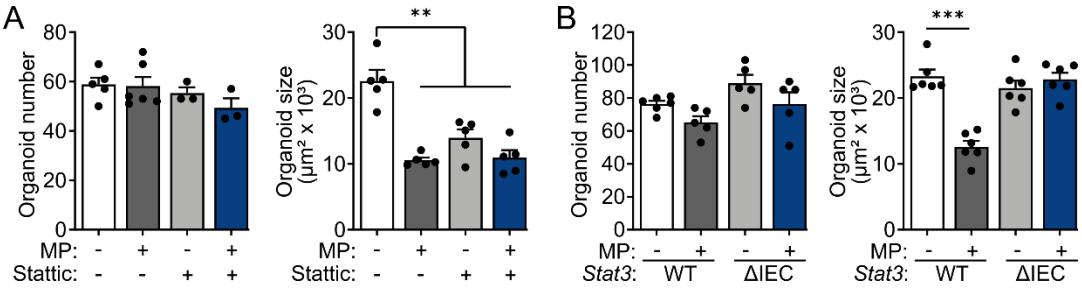
Supplemental Figure 2. Intestinal epithelium-specific GR deletion reduces GVHD-associated intestinal injury. (**A**-**B**) Representative glucocorticoid receptor (GR) IHC images and ileal crypt frequency of *Nr3c1*$^{fl/fl}$ *Olfm4-CreERT2* (*Nr3c1*$^{\Delta IEC}$) mice and WT littermates after tamoxifen treatment (*n* = 20-21 sections per group). Scale bars: 50 μm. (**C**-**D**) B10.BR-into-B6 transplant of syngeneic or allogeneic BM and T cells with WT and *Nr3c1*$^{\Delta IEC}$ recipients. Representative images and ileal crypt frequency on day 14 post-BMT (*n* = 18-25 sections per group). Scale bars: 50 μm. Statistics performed with 2-sided *t* test or 1-way ANOVA; ***P*<0.01, ****P* < 0.001. Data are combined from 2 experiments.

Supplemental Figure 3



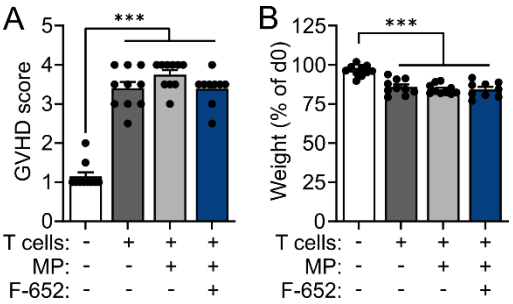
Supplemental Figure 3. Ruxolitinib treatment does not prevent corticosteroid-mediated suppression of organoid growth. (**A**) RT-qPCR of *Bcl2l1* in SI organoids cultured with or without MP (10 μM) and rmIFN-γ (1 ng/ml) for 3 days (*n* = 5-6 wells per group). (**B**) Size of SI organoids cultured with or without MP (10 μM) and ruxolitinib (10 nM) for 3 days (*n* = 4-5 wells per group). Statistics performed with 1-way ANOVA; **P* < 0.05, ***P* < 0.01. Data are representative of at least 2 independent experiments.

Supplemental Figure 4



Supplemental Figure 4. STAT3 inhibition during corticosteroid-mediated suppression of ex vivo organoid growth. (**A**) Frequency and size of SI organoids cultured with or without MP (10 μM) and Stattic (50 μM) for 5 days (*n* = 3-6 wells per group). (**B**) Frequency and size of *Stat3*$^{fl/fl}$ *Villin-Cre* (*Stat3*$^{\Delta IEC}$) and WT SI organoids cultured with or without MP (10 μM) for 5 days (*n* = 5-6 wells per group). Statistics performed with 1-way ANOVA; ***P* < 0.01, ****P* < 0.001. Data are representative of 2 independent experiments.

Supplemental Figure 5



Supplemental Figure 5. Systemic signs of GVHD after treatment with corticosteroids and F-652 starting day 7 post-BMT. (**A**-**B**) B6-into-BALB/c transplant of BM with or without T cells. Recipients were treated with or without MP (2 mg/kg i.p. daily) and with or without F-652 (100 µg/kg s.c. every other day). Shown are the clinical GVHD score and body weight loss 14 days post-BMT (*n* = 9-10 mice per group). Statistics performed with 1-way ANOVA; ***P < 0.001. Data are combined from 2 independent experiments.