Supplemental Figure Legends (captions)

Supplementary Figure 1. *Establishment of chimerism in the lamina propria of parabionts*. (**a**) Microscopic analysis of the small intestine of a CAG-tdTomato mouse (i) conjoined with a CAG-GFP mouse (ii). Original magnification 20x; scale bars 100 μm. (**b**) Quantification of the number of transferred cells per 40x field of view. Data are presented as means ± SEM.

Supplementary Figure 2. *Surgical separation of parabiosis pairs prior to TNBS challenge moderately reduces the rescue effects.* (**a**) Body weight change in an unpaired, sham surgery mouse (n=3) and parabiont separation surgery mouse (n=6) 24 hours prior to 2.5 mg TNBS instillation, and parabiont mouse (n=11 pairs) with 2.5 mg TNBS instillation. Mice whose weight loss of 20% or more were euthanized. Data are presented as means ± SEM. (**b**) (i) Macroscopic images of colons from day3 after 2.5 mg TNBS instillation. (ii) Colon length of 2.5 mg TNBS-treated parabiosis mouse (n=8 pairs), unpaired sham mouse (n=3), and parabiont separation mouse (n=6). Data are presented as means ± SEM. (**c**) Representative H&E-stained sections from an unpaired sham mouse (i), parabiont mouse (ii), and parabiosis separation mouse (iii). Colon 3 days after 2.5 mg TNBS instillation. Original magnification 20x; scale bars 100 μm. Data are presented as means ± SEM. (**p < 0.01, ***p < 0.001)

Supplementary Figure 3. *Depletion of bone marrow cells by 4 Gy radiation in an unpaired mouse*. (**a**) Flow cytometry analysis shows the number of total cells in bone marrow with and without 4 Gy whole-body radiation (i and ii) The percentage of $CD45^-$ cells in bone marrow is shown with and without 4 Gy whole-body radiation (iii and iv).

Supplementary Figure 4. *Recruitment of adaptive immune cells is dispensable for ameliorating intestinal inflammation in radiated parabionts.* (**a**) Body weight change in 8 Gy radiated parabiont mice of wild-type to wild-type pairings (n=7 pairs), $Rag1^{-/-}$ to wild-type pairings (n=3 pairs), and unpaired mice (n=14). Data are presented as means ± SEM. (**b**) Representative H&E-stained sections from 8 Gy radiated unpaired mice (i), wild-type to wild-type pairings (ii), and $Rag1^{-/-}$ to wild-type pairings (iii). Original magnification 20x; scale bars 100 μm.

Supplementary Figure 5. *The effect of recruitment of bone marrow cells on mucosal healing in TNBS-induced colitis.* (**a**) Body weight change in 2.5 mg TNBS-received parabiont mice (n=7 pairs), unpaired mice with bone marrow cell injection (n=3), and unpaired mice without bone marrow cell injection. (n=10). Data are presented as means ± SEM. (**b**)(i) Macroscopic images of colons from 2.5 mg TNBS-received parabiont mice, unpaired mice with or without bone marrow cell injection. (ii) Colon length of 2.5 mg TNBS-received parabiont mice (n=7 pairs), unpaired mice with bone marrow cell injection (n=3), and unpaired mice without bone marrow cell injection. (n=10). Data are presented as means ± SEM. (**c**) Representative H&E-stained sections from TNBS-received parabiont mice (i), unpaired mice without bone marrow cell injection (ii), and unpaired mice with bone marrow cell injection (iii). Original magnification 20x; scale bars 100 μm. (**d**) Body weight change in 8 Gy radiated unpaired mice with vehicle (n=2), $CD45^{+}$ bone marrow cell (n=2), and $CD45^{-}$ bone marrow cell injection (n=2). Data are presented as means ± SEM. (**e**) Representative H&E-stained sections from 8 Gy radiated unpaired mice with vehicle (i), $CD45^{+}$ bone marrow cell (ii), and $CD45^{-}$ bone marrow cell injection (iii). Original magnification 20x; scale bars 100 μm. (*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$)

Supplementary Figure 6. The effects of *MadCam-1 or CCR2 inhibitors on the protective effects of parabiosis on intestinal healing in TNBS-induced colitis.* (**a**) Body weight change in 2.5 mg TNBS-received parabiont mice in control group (n=1 pair), with CCR2 inhibitor (n=2 pairs), and with MAdCam-1 inhibitor (n=2 pairs). Data are presented as means ± SEM. (**b**)(i) Macroscopic images of colons from 2.5 mg TNBS-received parabiont mice in control group, with CCR2 inhibitor, and with MAdCam-1 inhibitor. (ii) Colon length of 2.5 mg TNBS-received parabiont mice in control group (n=1 pair), with CCR2 inhibitor (n=2 pairs), and with MAdCam-1 inhibitor (n=2 pairs). Data are presented as means ± SEM. (**c**) Representative H&E-stained sections from TNBS-received parabiont mice in control group (i), with CCR2 inhibitor (ii), and with MAdCam-1 inhibitor (iii); Representative Alcian blue-stained sections from TNBS-received parabiont mice TNBS-received parabiont mice in control group (iv), with CCR2 inhibitor (iv), and with MAdCam-1 inhibitor (vi). Original magnification 20x; scale bars 100 μm.

Supplemental Tables

Group	% tdTomato$^+$ Ecad$^+$ cells
Radiation, Bone marrow cell inj., Non-parabiosis	0.3
Uninjured, Parabiosis	2.2
Radiation, Parabiosis	1.5
TNBS, Parabiosis	0.2

Table 1. Quantification of tdTomato$^+$ cells that co-localize with the epithelial marker E-cadherin. The percentage of tdTomato/Ecad-double positive cells out of total tdTomato$^+$ cells shows the proportion of donor-derived intestinal epithelial cells in bone marrow cell transplant recipients with 12 Gy radiation (n=2), uninjured parabionts (n=2 pairs), 8 Gy radiated parabiosis mice (n= 3 pairs), and TNBS-treated parabiosis mice (n=2 pairs).

Histological parameters for radiation enteritis
Preservation of epithelial architecture -Epithelial injury/distorted villi -Thinner villi -Shortened length of villi -Denuded villi
Decreased number of crypts -Glandular dropout
Prominent Paneth cells
Infiltration of inflammatory cells in the lamina propria (lamina propria expansion)

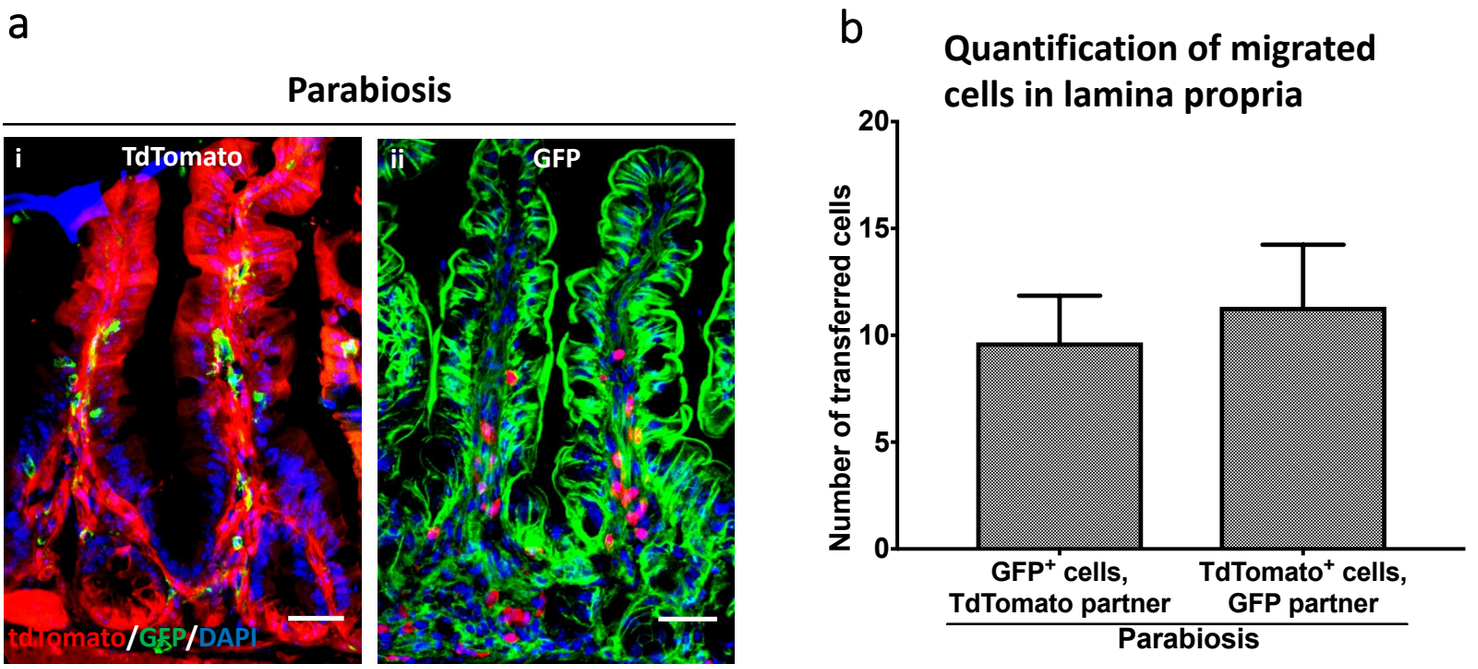
Supplementary Table 2. Histological scoring system for radiated induced enteritis; Evidence of intestinal mucosal injury was quantified in H&E stained sections of small intestine by a pathologist (LV) blinded to the treatment group (0=None, 1=Mild, 2=Moderate, 3=High).

Histological parameters for TNBS colitis
Epithelial injury -Increased number of apoptotic bodies in crypts -Crypt degeneration
Goblet cell phenotype -Mucin depletion or mucin extrusion
Decreased number of crypts -Glandular dropout
Inflammation -Inflammatory lamina propria expansion
Ulceration
Pseudomembrane
Ischemic changes
Mucosal erosion

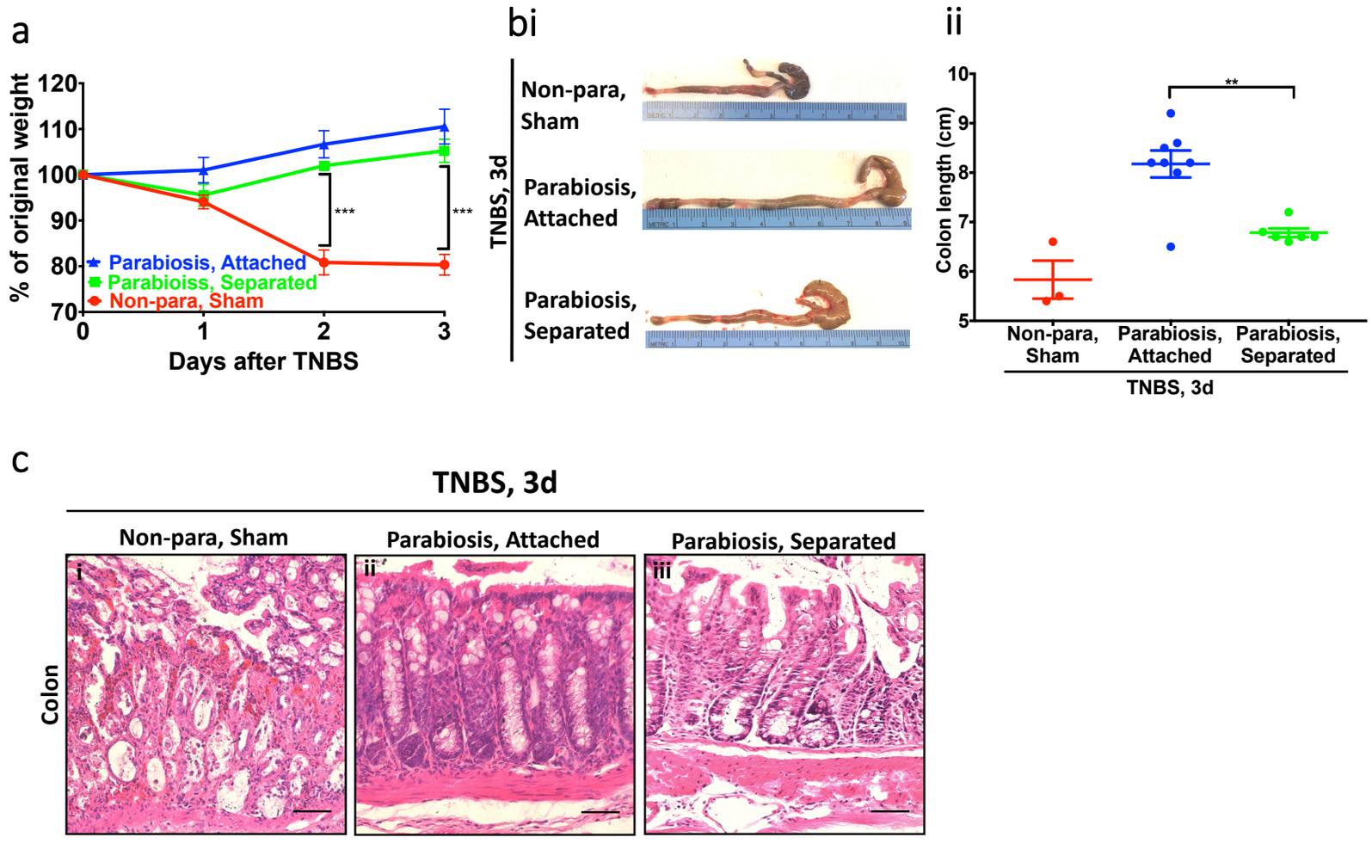
Supplementary Table 3. Histological scoring system TNBS induced colitis Evidence of intestinal mucosal injury was quantified in H&E stained sections of colon by a pathologist (LV) blinded to the treatment group (0=None, 1=Mild, 2=Moderate, 3=High).

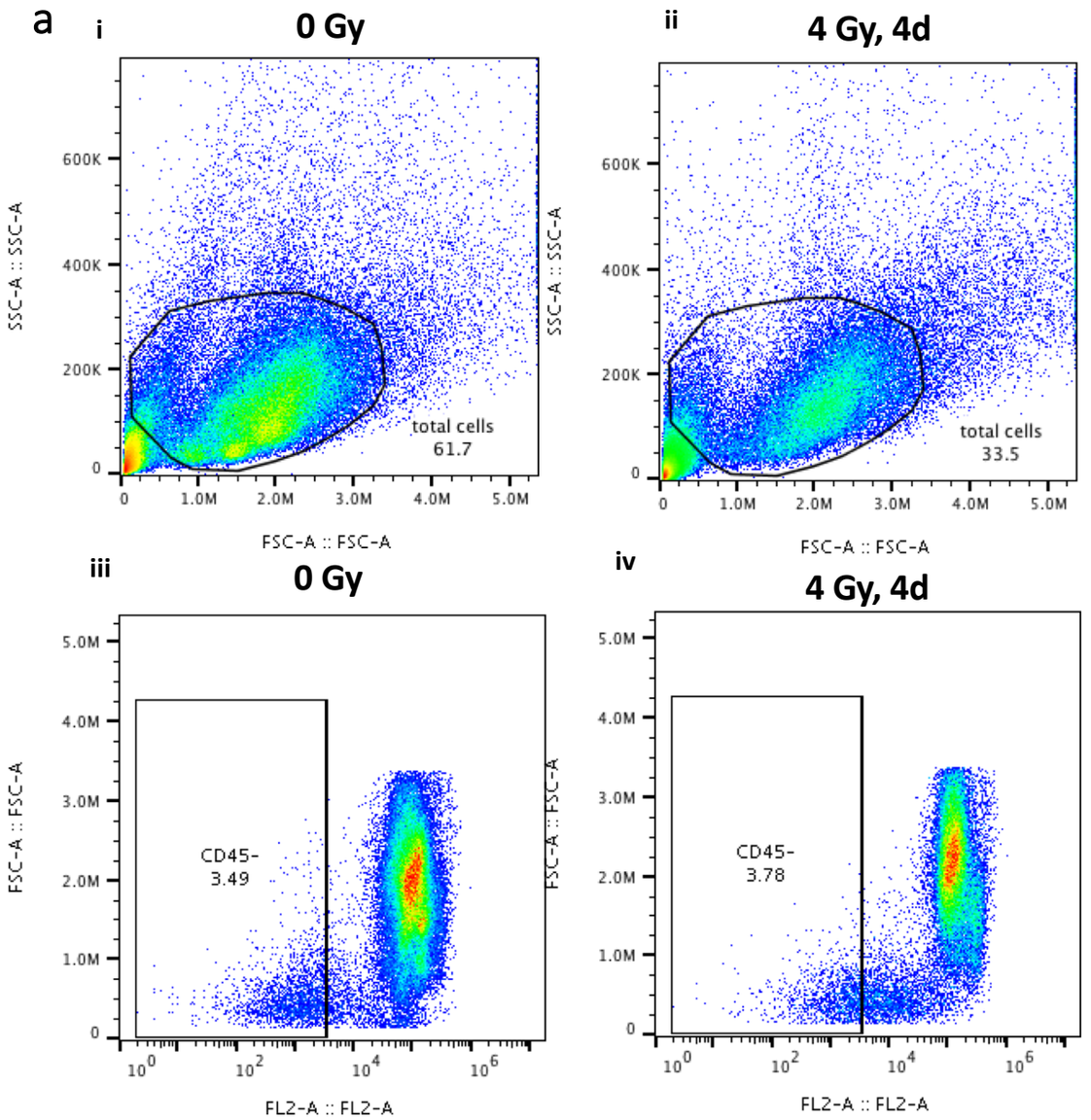
Gene	Forward primer	Reverse primer	Size
RPLO	GGCGACCTGGAAGTCCAACT	CCATCAGCACCACAGCCTTC	143 bp
TNF-α	TTCCGAATTCACTGGAGCCTCGAA	TGCACCTCAGGGAAGAATCTGGAA	144 bp
IL-1β	AGTGTGGATCCCAAGCAATACCCA	TGTCCTGACCACTGTTGTTTCCCA	175 bp
CCL2	ATGCAGTTAACGCCCCACTC	CCCATTCCTTCTTGGGGTCA	171 bp
SI	ATCCAGGTTCGAAGGAGAAGCACT	TTCGCTTGAATGCTGTGTGTTCCG	154 bp
CAR1	ACAGTAGCAACCAATCTGTTCTG	AGGCCATCAGCCTTGGAGA	207 bp
Lipocalin2	ACAACCAGTTCGCCATGGTAT	AAGCGGGTGAAACGTTCCTT	121 bp
MucII	TAGTGGAGATTGTGCCGCTGAAGT	AGAGCCCATCGAAGGTGACAAAGT	168 bp
iNOS	CTGCTGGTGGTGACAAGCACATTT	ATGTCATGAGCAAAGGCGCAGAAC	167 bp
Lgr5	TGAGCGGGACCTTGAAGATTTCCT	TACCAAATAGGTGCTCACAGGGCT	116 bp
Lysozyme	AAGCTGGCTGACTGGGTGTGTTTA	CACTGCAATTGATCCCACAGGCAT	178 bp
Dlck1	CAAATGCCGAGGCAAAGAGCACAT	ACAGTTCAGTCGGCACATCCATCT	113 bp
IL-6	CCAATTTCCAATGCTCTCCT	ACCACAGTGAGGAATGTCCA	182 bp
CXCL2	TCCAGAGCTTGAGTGTGACG	CTTCCGTTGAGGGACAGCAG	196 bp

Supplemental Table 4. List of primers for RT-PCR.

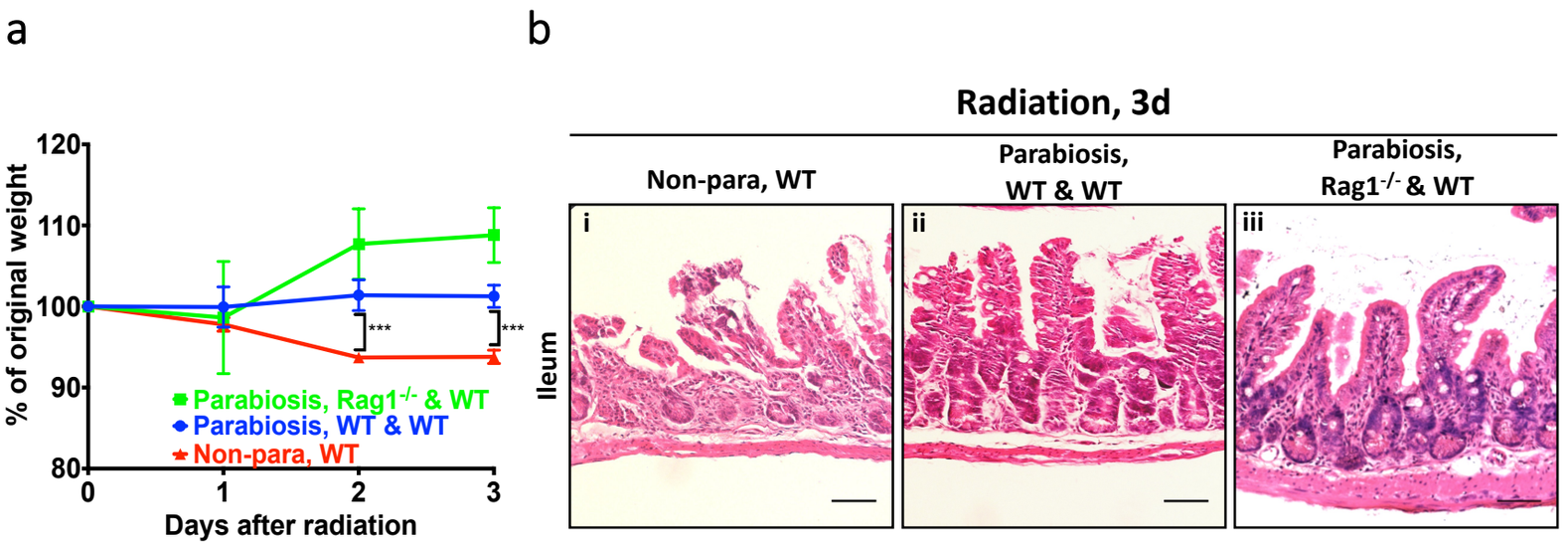

a
Parabiosis
i
TdTomato
tdTomato/GFP/DAPI
ii
GFP
b
Quantification of migrated cells in lamina propria
Number of transferred cells
20
15
10
5
0
GFP+ cells, TdTomato partner
TdTomato+ cells, GFP partner
Parabiosis

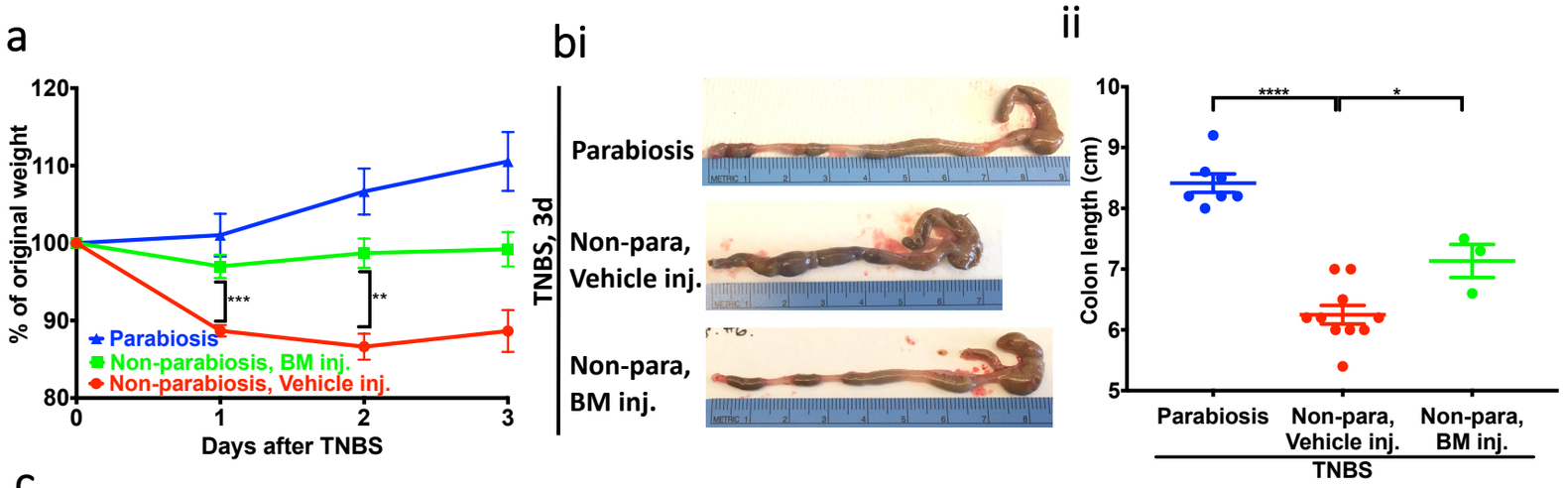
Sung, J. *et al*. Supplementary Figure 2.

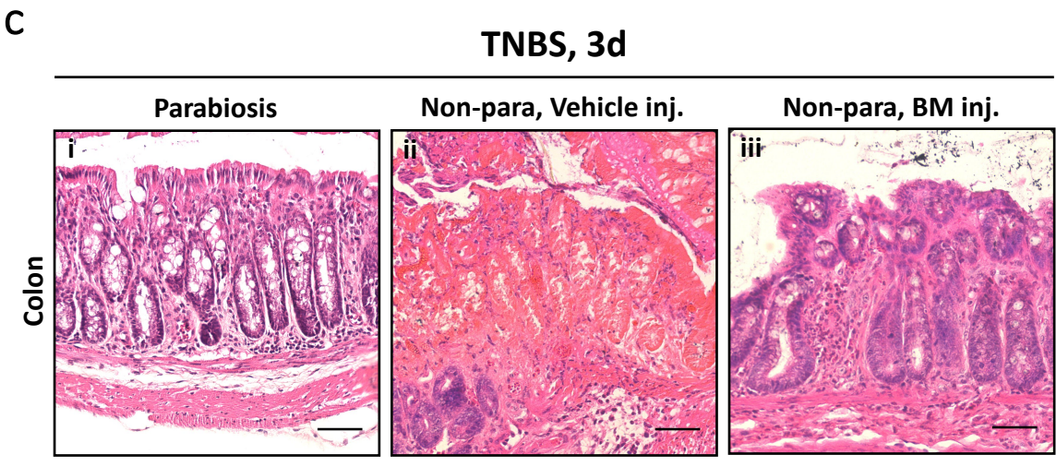


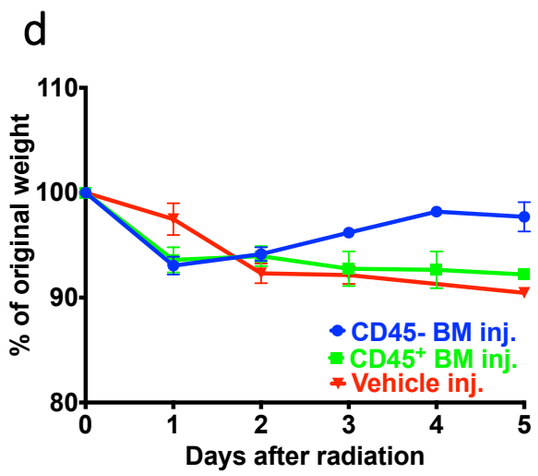

a
i
0 Gy
ii
4 Gy, 4d
SSC-A :: SSC-A
FSC-A :: FSC-A
total cells
61.7
total cells
33.5
iii
0 Gy
iv
4 Gy, 4d
FSC-A :: FSC-A
FL2-A :: FL2-A
CD45-
3.49
CD45-
3.78

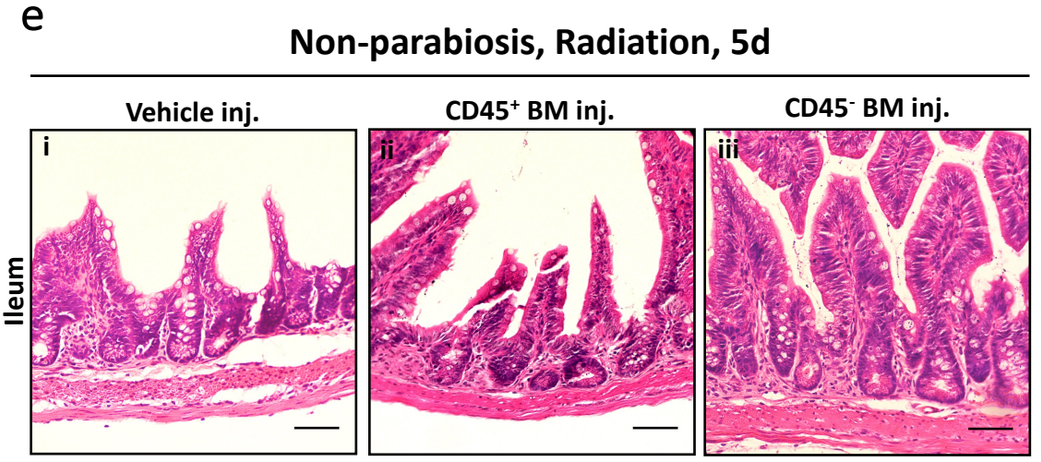
Sung, J. *et al*. Supplementary Figure 4.




a
% of original weight
Days after TNBS
Parabiosis
Non-parabiosis, BM inj.
Non-parabiosis, Vehicle inj.
***
**
bi
TNBS, 3d
Parabiosis
Non-para, Vehicle inj.
Non-para, BM inj.
ii
Colon length (cm)
****
*
Parabiosis
Non-para, Vehicle inj.
Non-para, BM inj.
TNBS


c
TNBS, 3d
Parabiosis
Non-para, Vehicle inj.
Non-para, BM inj.
Colon
i
ii
iii


d
% of original weight
Days after radiation
CD45- BM inj.
CD45+ BM inj.
Vehicle inj.


e
Non-parabiosis, Radiation, 5d
Vehicle inj.
CD45+ BM inj.
CD45- BM inj.
Ileum
i
ii
iii

Sung, J. *et al*. Supplementary Figure 6.