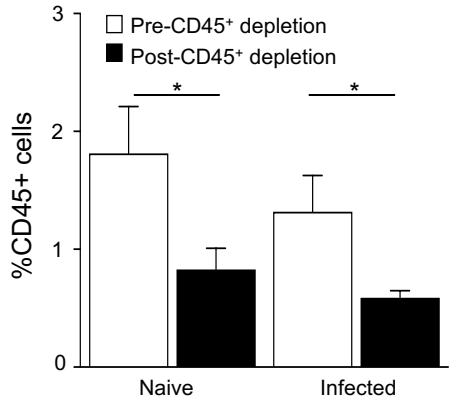

Figure S1, related to Figure 1. Examination of leukocyte depletion. %CD45$^+$ cells in IECs isolated from colon of wildtype mice prior to and following CD45$^+$ depletion. Infected mice were assessed at day 12 post gavage with C. *rodentium*. Results are shown as mean s.e.m. *p<0.05.

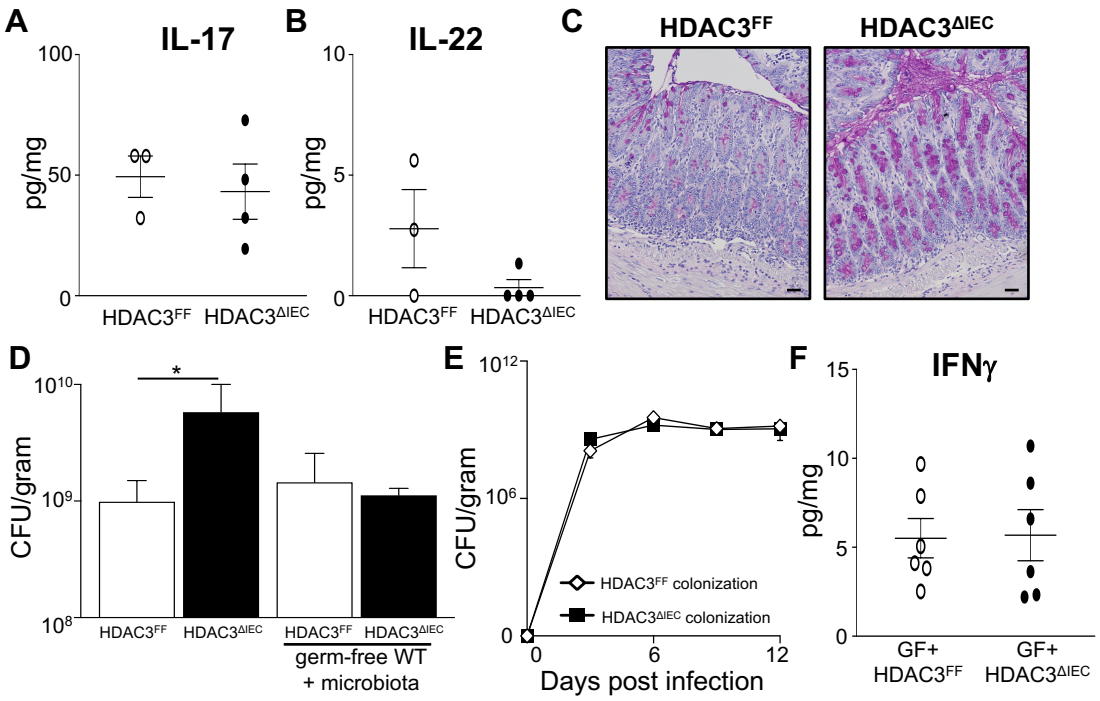

Figure S2, related to Figure 2. Microbiota composition of HDAC3$^{\Delta IEC}$ mice is not sufficient to impair defense against *C. rodentium*. **(A)** IL-17 and **(B)** IL-22 in colonic tissue of HDAC3^{FF} and HDAC3$^{\Delta IEC}$ mice measured by ELISA. **(C)** PAS/Alcian blue stained sections from distal colon of *C. rodentium* infected HDAC3^{FF} and HDAC3$^{\Delta IEC}$ mice, scale bar 50µm. **(D)** Enumeration of *C. rodentium* CFU in stool of HDAC3^{FF}, HDAC3$^{\Delta IEC}$, and germ-free (GF) wildtype mice reconstituted with microbiota from HDAC3^{FF} or HDAC3$^{\Delta IEC}$ mice at day 12 post *C. rodentium* infection. **(E)** Timecourse of *C. rodentium* infection in reconstituted mice. **(F)** IFNγ in colonic tissue of GF wildtype mice reconstituted with microbiota from HDAC3^{FF} or HDAC3$^{\Delta IEC}$ mice measured by ELISA. Data are at day 12 post infection and representative of at least 2 independent experiments containing 3-6 mice per group. Results are shown as mean ± s.e.m.

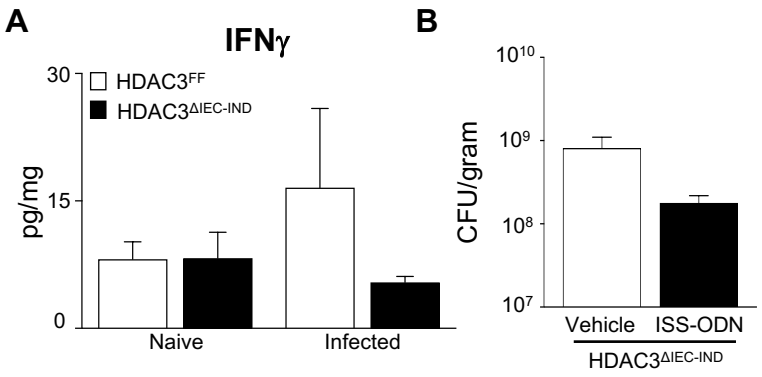

Figure S3, related to Figure 3. IEC-intrinsic HDAC3 actively regulates susceptibility and IFNγ-dependent defense against *C. rodentium*. (A) IFNγ in colonic tissue of $HDAC3^{FF}$ and $HDAC3^{\Delta IEC\text{-}IND}$ mice measured by ELISA. **(B)** Enumeration of C. *rodentium* CFU in stool of $HDAC3^{IND\text{-}\Delta IEC}$ mice treated with PBS or ISS-ODN. Data are 5 days after tamoxifen administration was completed (12 d post infection) and representative of at least 2 independent experiments containing 3-6 mice per group. Results are shown as mean ± s.e.m.

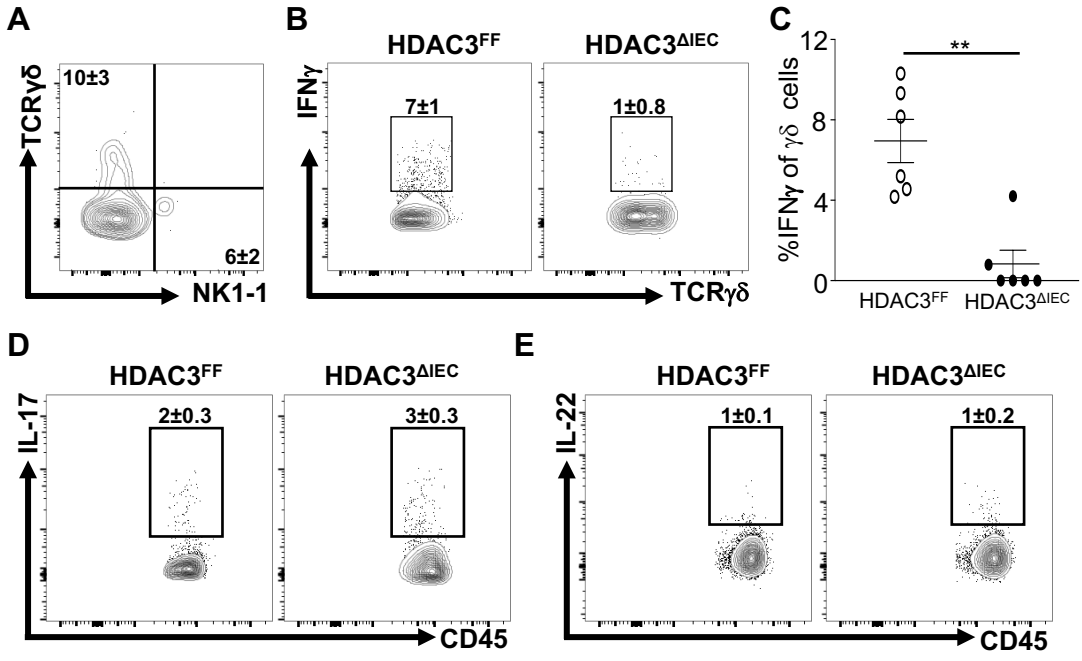

Figure S4, related to Figures 4 and 5. Infection-induced IFNγ-producing γδ intraepithelial lymphocytes are decreased in HDAC3$^{\Delta IEC}$ mice. (A) Characterization of IFNγ-producing IELs from infected mice in (Fig. 4a) based on T cell receptor (TCR) γδ and NK1-1 staining. **(B, C)** %IFNγ-producing γδ IELs. **(D)** %IL-17 and **(E)** %IL-22 producing CD45^{+} IELs. Data are at day 6 post C. *rodentium* infection and representative of at least 2 independent experiments containing 3-4 mice per group. Results are shown as mean ± s.e.m. ***p*<0.01.

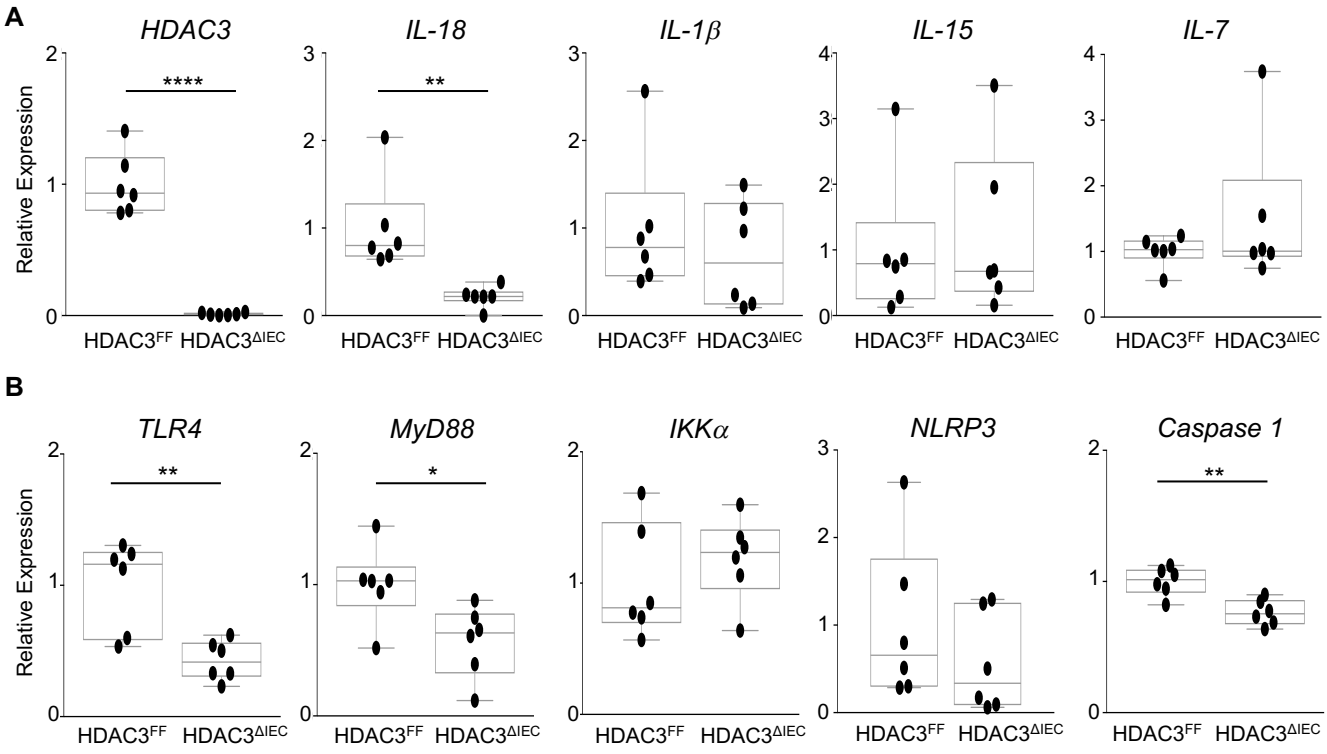

Figure S5, related to Figure 7. mRNA expression in infected mice lacking IEC-intrinsic HDAC3 expression. (A, B) mRNA expression in IECs from HDAC3^{FF} and HDAC3$^{\Delta IEC}$ mice at day 6 post *C. rodentium* infection. Data are representative of at least 4 independent experiments containing 3-6 mice per group. Results are shown as mean ± s.e.m. *p<0.05,**p<0.01.

Supplemental Figure 6

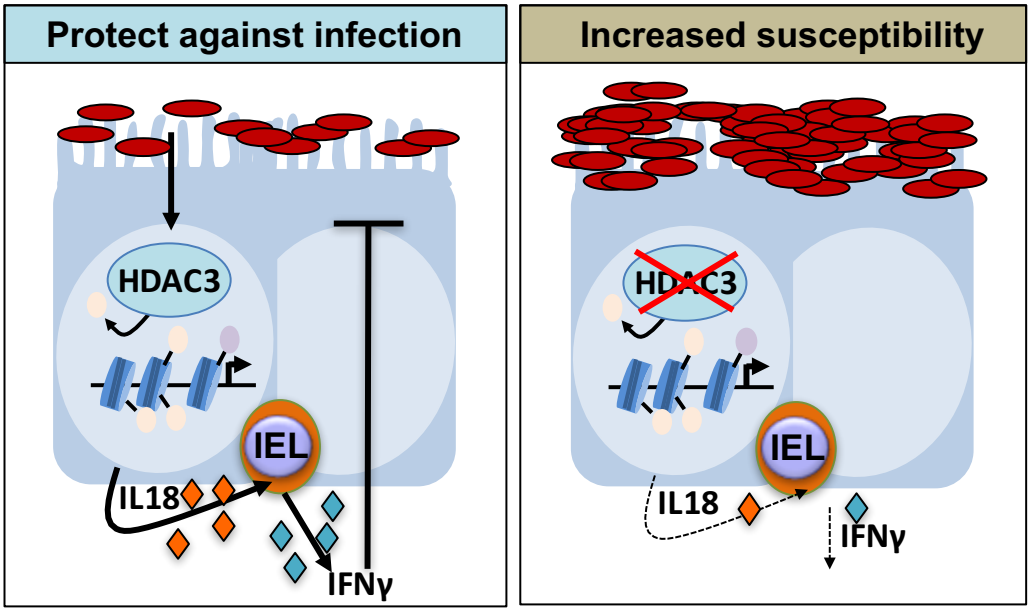

Figure S6, related to Figures 1-7. An essential role for epithelial HDAC3 in instructing host defense against enteric infection. IEC-intrinsic HDAC3 calibrates host susceptibility to mucosal infection by coordinating a protective IEL response against bacterial pathogens. Loss of epithelial HDAC3 regulation results in impairment of IFNγ production by local IELs and increased infection.

	Forward	Reverse
HDAC3	TTGGTATCCTGGAGCTGCTT	GACCCGGTCAGTGAGGTAGA
IL-18	CAGGCCTGACATCTTCTGCAA	TCTGACATGGCAGCCATTGT
IL-1b	ACCTTCCAGGATGAGGACATGA	CTAATGGGAACGTCACACACCA
IL-15	GTCAGTGTAGGTCTCCCTAAA	TTCTCCTCCAGCTCCTCACAT
IL-7	AATCGTGCTGCTCGCAAGTT	CACCAGTGTTTGTGTGCCTTGT
TLR-4	TGTTCTTCTCCTGCCTGACA	TGTCATCAGGGACTTTGCTG
MyD88	CACCTGTGTCTGGTCCATTG	CTGTTGGACACCTGGAGACA
IKKa	GACCGTGAACATCCTCTGACATGTG	GCTCTGGTCCTCATTTGCTTCACG
NLRP3	CGAGACCTCTGGGAAAAAGCT	GCATACCATAGAGGAATGTGATGTACA
Caspase1	ATCTTTCTCCGAGGGTTGG	AAGTCTTGTGCTCTGGGCAG

Table S1, related to Experimental Procedures. Primer sequences for quantitative PCR.