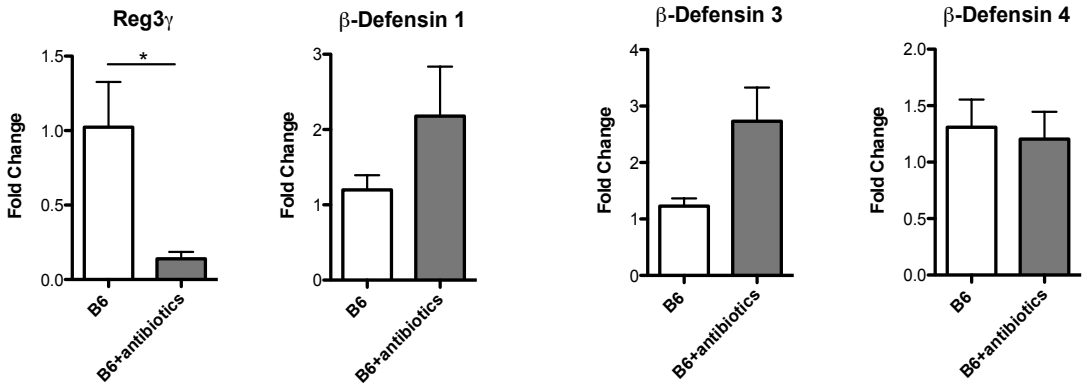
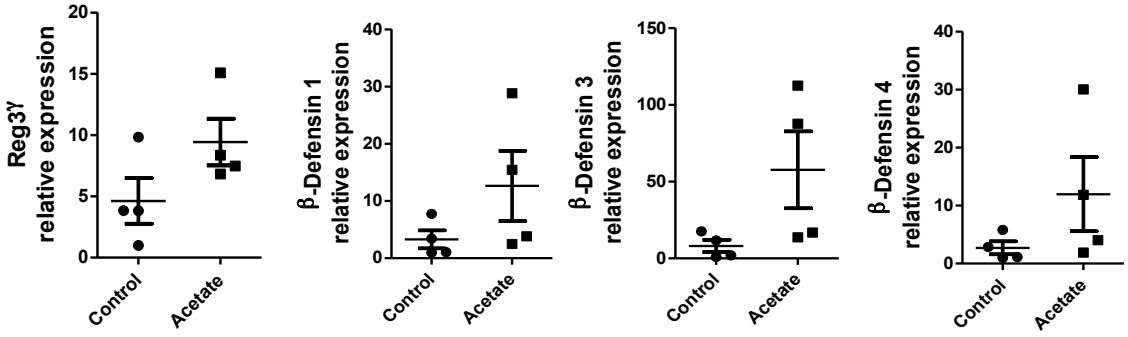
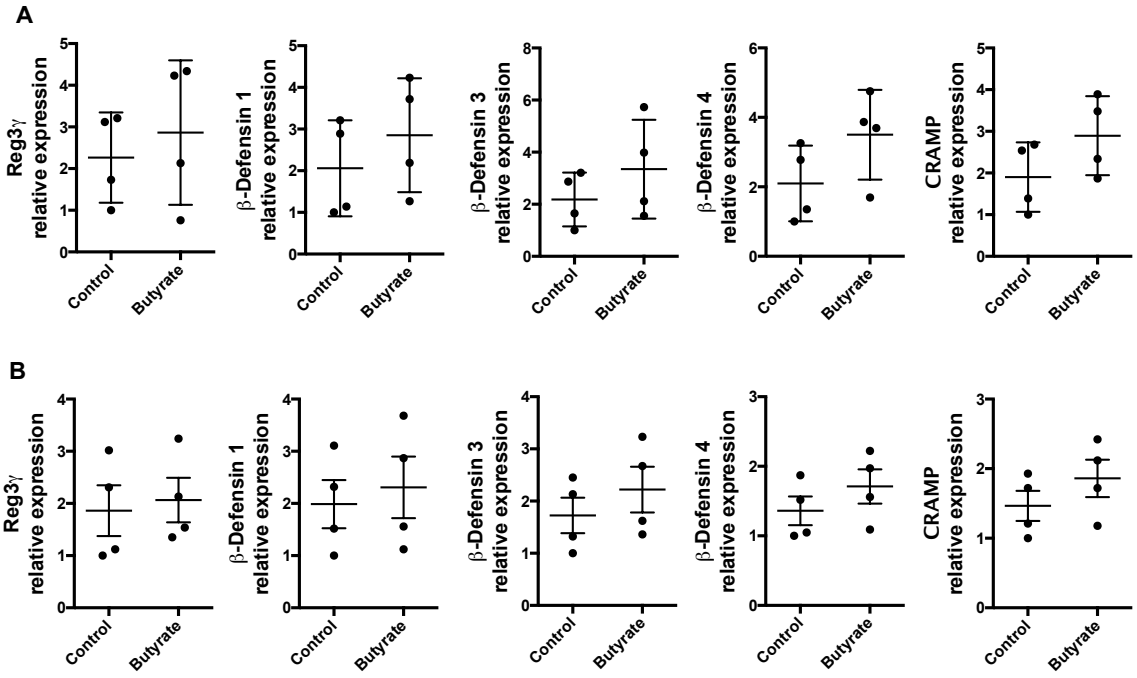
Supplementary Materials



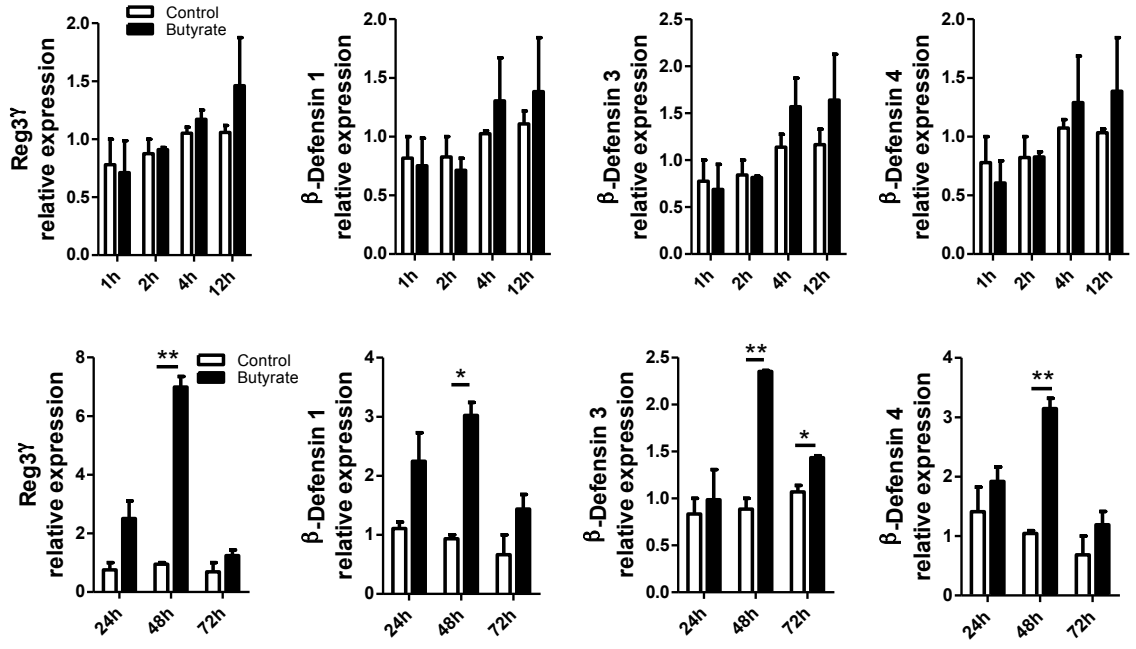
Supplementary Figure 1. **Antibiotics feeding decreases IEC expression of RegIIIγ but not β-defensins in vivo.** C57BL/6 mice were treated with broad-spectrum antibiotics for 10 days, IEC expression of RegIIIγ and β-defensins 1, 3, 4 was determined by qRT-PCR and normalized against gapdh. n=4 mice/group. *p<0.05. Data are reflective of 2 independent experiments.



Supplementary Figure 2. Acetate feeding slightly enhances IEC expression of RegIIIγ and β-defensins in vivo. C57BL/6 mice were treated with antibiotics for 10 days, followed by 300 mM acetate for 21 days. IEC expression of RegIIIγ and β-defensins 1, 3, 4 was determined by qRT-PCR and normalized against gapdh. Data are reflective of 2 independent experiments. n=4 mice/group.

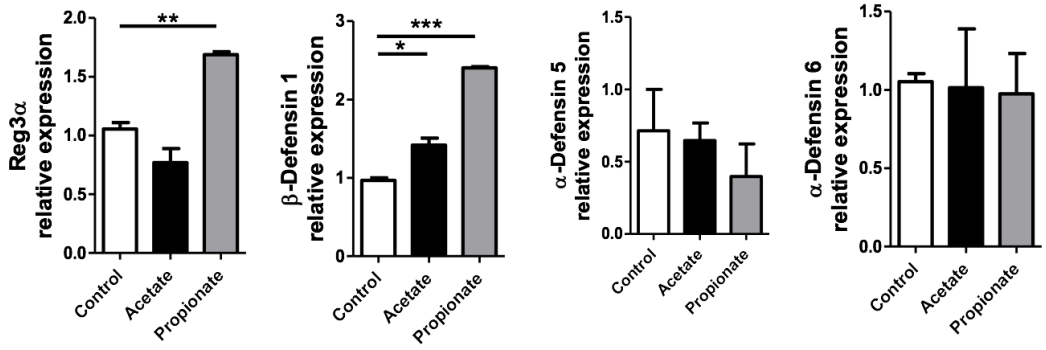


Supplementary Figure 3. Butyrate feeding does not induce expression of RegIIIγ and β-defensins in IEC of mouse without depletion of gut bacteria. WT and GPR43$^{-/-}$ C57BL/6 mice were fed with 300 mM butyrate for 21 days. IEC expression of RegIIIγ, β-defensins 1, 3, 4, and CRAMP in WT mice (A) and GPR43$^{-/-}$ mice (B) was determined by qRT-PCR and normalized against gapdh. Data are reflective of 2 independent experiments. n=4 mice/group.

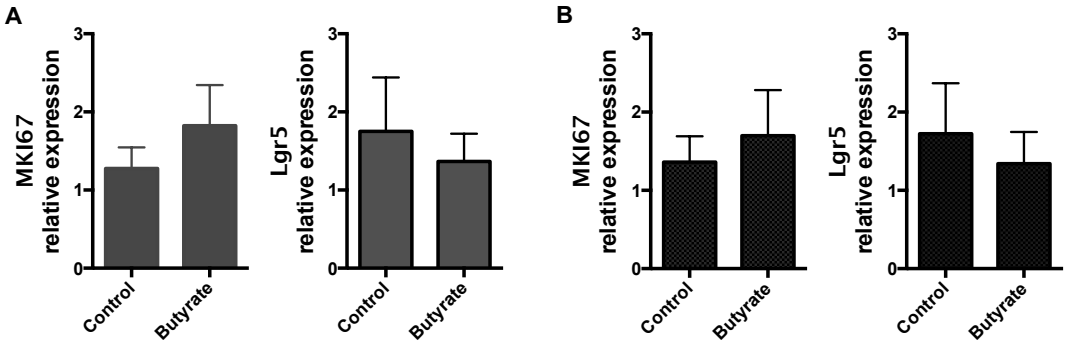


Supplementary Figure 4. Butyrate induces expression of RegIIIγ and β-defensins in

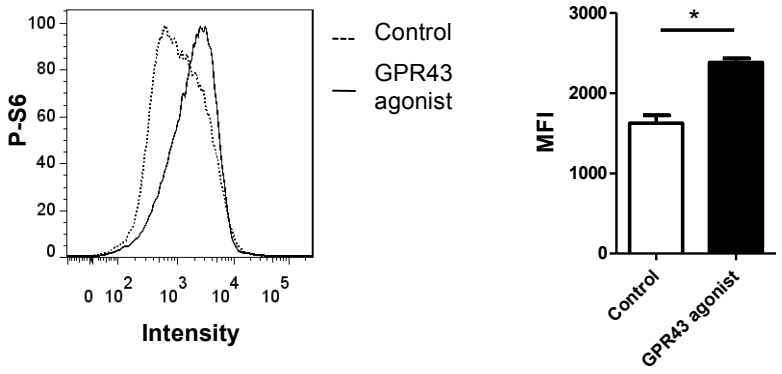
mouse IEC. MSIE cells were treated with 0.5 mM butyrate and the expression of RegIIIγ and β-defensins 1, 3 and 4 was determined by qRT-PCR at 1, 2, 4, 12, 24, 48, and 72 h. Data are normalized against gapdh. *p<0.05; **p<0.01. Data are reflective of 3 independent experiments.



Supplementary Figure 5. **Propionate induces expression of RegIIIα and β-defensin 1, but not α-defensins and acetate induces β-defensin 1 in human IECs.** HT-29 cells were treated with 0.5 mM acetate or propionate for 48 h. The expression of α-defensins 5 and 6, β-defensin 1 and RegIIIα was determined by qRT-PCR and normalized against gapdh. *p<0.05; **p<0.01; ***p<0.001. Data are reflective of 3 independent experiments.



Supplementary Figure 6. **Butyrate does not affect expression of MKI67 and Lgr5 in intestinal epithelial enteroids**. Intestinal epithelial enteroids were generated from either WT or GPR43$^{-/-}$ mice, and treated with 0.5 mM butyrate. The expression of MKI67 and Lgr5 in WT enteroids (A) and GPR43$^{-/-}$ enteroids (B) was determined by qRT-PCR at 48 h and normalized against *gapdh*. Data are reflective of 2 independent experiments.



Supplementary Figure 7. GPR43 agonist activates mTOR/S6K1 pathway in IECs. MSIE cells were treated with 5 μM GPR43 agonist for 48 h. The expression of phospho-S6K1 was determined by flow cytometry. Combined median fluorescence intensity (MFI) was presented. *$p<0.05$. Data are reflective of 3 independent experiments.

Supplementary Table 1. Lists of qRT-PCR primers

mRegIIIγ	Forward	5'-CGTGCCTATGGCTCCTATTGCT-3'
	Reverse	5'-TTCAGCGCCACTGAGCACAGAC-3'
mβ-defensin-1	Forward	5'-TAGTCTCTTCATCTGTGTTTTTGCATA-3'
	Reverse	5'-TTCAGCGCCACTGAGCACAGAC-3'
mβ-defensin-3	Forward	5'-CCAGGCTGATCCTATCCAGG-3'
	Reverse	5'-GTCCCATTCATGCGTTCTCT-3'
mβ-defensin-4	Forward	5'-TGGCCTCCAAAGGAGATAGACA-3'
	Reverse	5'-AGGCTGATCCTATCCAAAACACA-3
mCRAMP	Forward	5'-CAG CCC TTT CGG TTC AAG AA-3'
	Reverse	5'-CCC ACC TTT GCG GAG AAG T-5'
mGAPDH	Forward	5'-CCATGGAGAAGGCTGGGG-3'
	Reverse	5'-CAAAGTTGTCATGGATGACC-3
hRegIIIα	Forward	5'-TATGGCTCCCACTGCTATGCCT-3'
	Reverse	5'-TCTTCACCAGGGAGGACACGAA-3'
hβ-defensin-1	Forward	5'-ATACTTCAAAAGCAATTTTCCTTTAT-3'
	Reverse	5'-TTGTCTGAGATGGCCTCAGGTAAC-3'
hβ-defensin-6	Forward	5'-CCTCACCATCCTCACTGCTGTTC-3'
	Reverse	5'-CCATGACAGTGCAGGTCCCATA-3'
hLL-37	Forward	5'- TGC TAA CCT CTA CCG CCT CCT-3'
	Reverse	5'- CAC AAT CCT CTG GTG ACT GCT-3'
hGAPDH	Forward	5'-GAAGGTCGGAGTCAACGGATT-3'
	Reverse	5'-CGCTCCTGGAAGATGGTAAT-3'