## Supplemental data



Figure S1. The anti-Ly6g antibody efficiently depleted neutrophils in different tissues. In DSS-induced colitis model, WT mice received Ly6G-depleting antibody (4 mg/kg) every 3 days. Neutrophil depletion in the spleen, Mesenteric lymph nodes (MLN), small bowel (SB), and large bowel (LB) was measured by flow cytometry. n = 4 per group per experiment. FACS plots are representative of 2 independent experiments.



Figure S2. TGF $\beta$  induces AREG production in primary IECs. (A and B) mRNA expression level of AREG in isolated primary IECs treated with (A) different reagents, and (B) AREG. The data were normalized to one sample of 3 in nontreatment control group. n.s., no significant difference; Data are presented as mean  $\pm$  SEM of three independent experiments; \*\*\*P < 0.001 one-way ANOVA.



**Figure S3. MEK1/2 regulates TGFβ-induced AREG production in IECs.** (A) Transfection efficiency of siRNA targeted either MEK1 or MEK2 in MSIE cells. (**B and C**) MEK1 was knocked out in MSIE cells by CRISPR, and then treated with TGFβ for 6 h. (**B**) mRNA expression level of AREG in WT and MEK1 KO MSIE cells. (**C**) CRISPR knock out efficiency. n.s., no significant difference; Data are presented as mean  $\pm$  SEM of three independent experiments. \*P < 0.05, \*\*P < 0.01 Student's t test, one-way ANOVA.

PCR primers		
mGAPDH	Forward	5'-CCATGGAGAAGGCTGGGG-3'
	Reverse	5'-CAAAGTTGTCATGGATGACC-3'
mAREG	Forward	5'-CCTCCTTCTTTCTTCTGTTTCTCC-3'
	Reverse	5'-GTCACTATCTTTGTCTCTGCCA-3'
TGFβ	Forward	5'-TGACGTCACTGGAGTTGTACGG -3'
	Reverse	5'-GGTTCATGTCATGGATGGTGC-3'
HNF4a	Forward	5'-TGTTCTTGCATCAGGTGAGG-3'
	Reverse	5'-TCCAGTTCATCAAGCTCTTCG-3'
hGAPDH	Forward	5'-GAAGGTCGGAGTCAACGGATT-3'
	Reverse	5'-CGCTCCTGGAAGATGGTAAT-3'
hAREG	Forward	5'-CGAACCACAAATACCTGGCTA-3'
	Reverse	5'-TCCATTTTTGCCTCCCTTTT-3'
CRISPR-guide RNA oligo sequences		
MEK1	Forward	5'-CACCGCTTGTGCTTCTCCCGAAGAT-3'
	Reverse	5'-AAACATCTTCGGGAGAAGCACAAGC-3'

## Table S1. PCR primers and CRISPR-guide RNA oligo sequences