Expanded View Figures

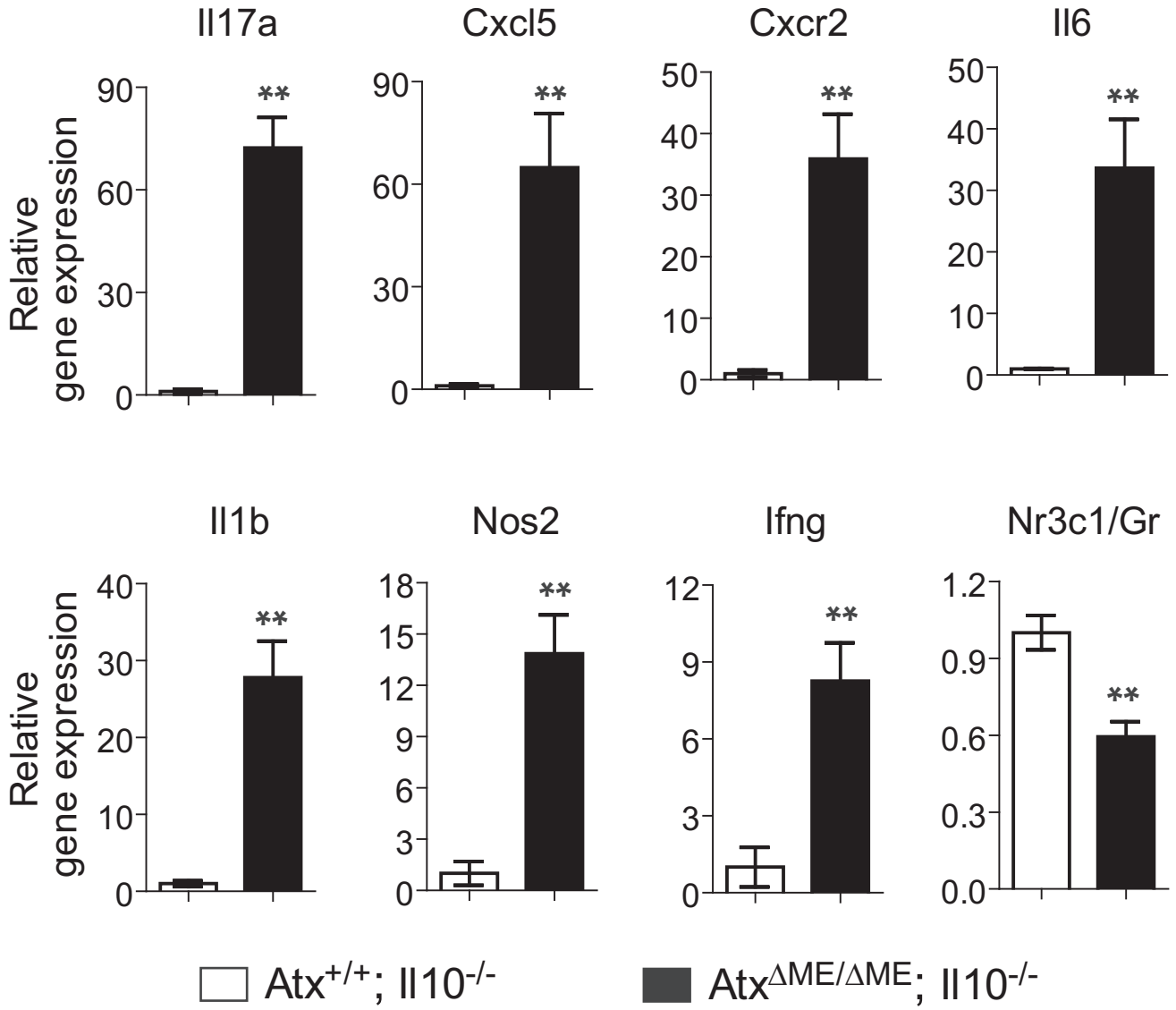


Figure EV1. Pro-inflammatory cytokine gene expression is up-regulated in the colon of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice compared to $Atx^{+/+}$;$Il10^{-/-}$ mice.

The mRNA level of pro-inflammatory cytokine genes was evaluated through qPCR with the full-thickness colon of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ and $Atx^{+/+}$;$Il10^{-/-}$ mice. $n = 6$/group. The data are shown as mean ± SEM. $^{**}P < 0.01$ (Mann–Whitney *U*-test).

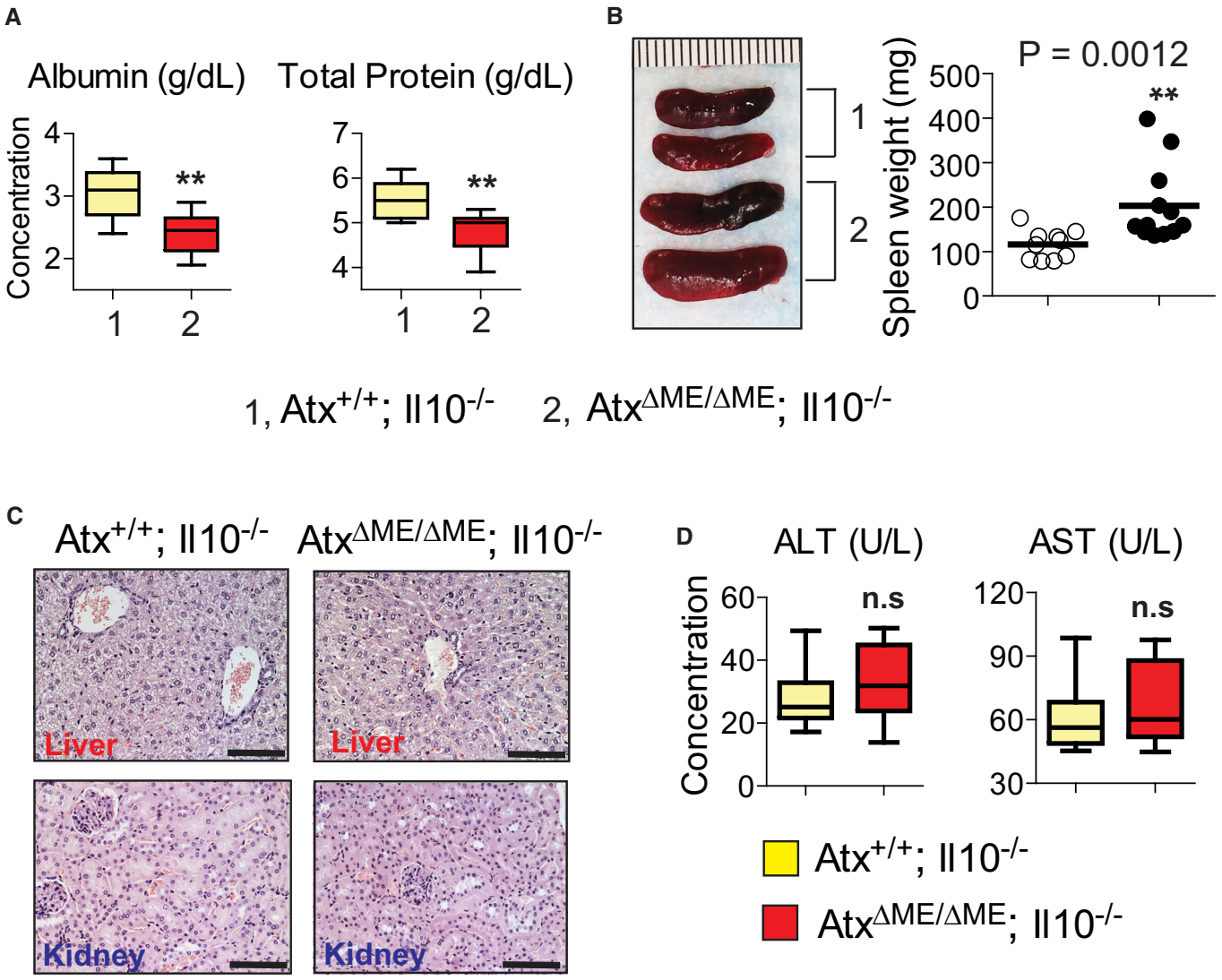


Figure EV2. $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice exhibit no pathologic phenotype in the liver and kidney.

Age (8 weeks old)- and sex-matched $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice and $Atx^{+/+}$;$Il10^{-/-}$ littermates were examined.

A Albumin and total protein were measured in the blood serum of the mice (n = 12/group).

B Gross images of the spleen (left) and spleen weight (right) were presented. Each line on a ruler represents a millimeter (mm).

C Presented are representative photographs of H&E-stained sections of the liver and kidney. Scale bar indicates 100 μm.

D The level of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) protein was measured from the mouse blood serum. $^{**}P < 0.01$ (Mann–Whitney U-test). not significant (n.s.).

Figure EV3. Altered fecal microbiome of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice signifies the microbial manifestation of mouse colitis.
Fecal microbiome of age (8 weeks old)-matched, co-housed $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice and $Atx^{+/+}$;$Il10^{-/-}$ littermates (n = 6/group) was analyzed by 16S rRNA gene sequencing.

A A dual hierarchal dendrogram was generated based on the predominant genera using Ward's minimum variance clustering and Manhattan distances. More similar microbial populations between $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ and $Atx^{+/+}$;$Il10^{-/-}$ mice were mathematically clustered closer together. The samples with a more similar consortium of genera cluster closer together with the length of connecting lines (top of heatmap) related to the similarity; shorter lines between two samples indicate closely matched microbial consortia. The heatmap represents the relative percentages of each genus. The legend for the heatmap is provided in the upper left corner. The predominant genera are represented along the right *Y*-axis. $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mouse is indicated by "k", while "c" stands for $Atx^{+/+}$;$Il10^{-/-}$ mice.

B Principal coordinates analysis (PCoA) plot of weighted UniFrac metrics was generated. PCoA plots represent the three (PC1, PC2, and PC3) highest discriminating axes, explaining 87.3 percent of the variation between the groups (P = 0.003).

C The major species identified in the fecal samples of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice (k) and $Atx^{+/+}$;$Il10^{-/-}$ littermates (c) were analyzed to compare the abundance at the species level. The abundance of *Bacteroides* was dramatically increased in the fecal samples of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice compared to $Atx^{+/+}$;$Il10^{-/-}$ mice. Results are means ± SD, *P < 0.05, **P < 0.01 (Mann–Whitney U-test).

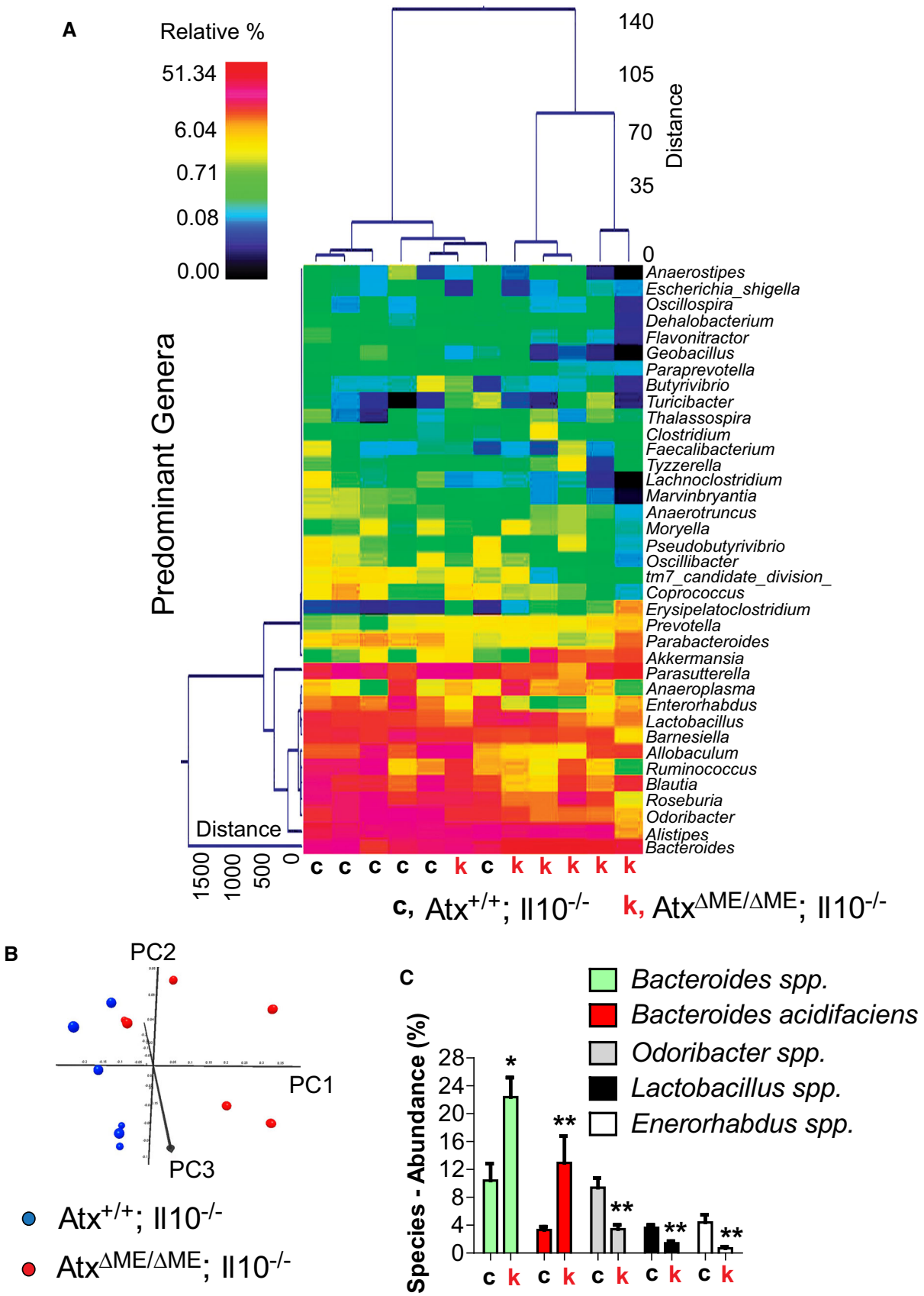

A
Relative %
51.34
6.04
0.71
0.08
0.00
140
105
70
35
0
Distance
Predominant Genera
Anaerostipes
Escherichia_shigella
Oscillospira
Dehalobacterium
Flavonitractor
Geobacillus
Paraprevotella
Butyrivibrio
Turicibacter
Thalassospira
Clostridium
Faecalibacterium
Tyzzerella
Lachnoclostridium
Marvinbryantia
Anaerotruncus
Moryella
Pseudobutyrivibrio
Oscillibacter
tm7_candidate_division_
Coprococcus
Erysipelatoclostridium
Prevotella
Parabacteroides
Akkermansia
Parasutterella
Anaeroplasma
Enterorhabdus
Lactobacillus
Barnesiella
Allobaculum
Ruminococcus
Blautia
Roseburia
Odoribacter
Alistipes
Bacteroides
Distance
1500
1000
500
0
c c c c c k c k k k k k
c, Atx+/+; Il10-/- k, AtxΔME/ΔME; Il10-/-
B
PC2
PC1
PC3
Atx+/+; Il10-/-
AtxΔME/ΔME; Il10-/-
C
Bacteroides spp.
Bacteroides acidifaciens
Odoribacter spp.
Lactobacillus spp.
Enerorhabdus spp.
Species - Abundance (%)
28
24
20
16
12
8
4
0
*
**
**
**
**
c k c k c k c k c k

Figure EV3.

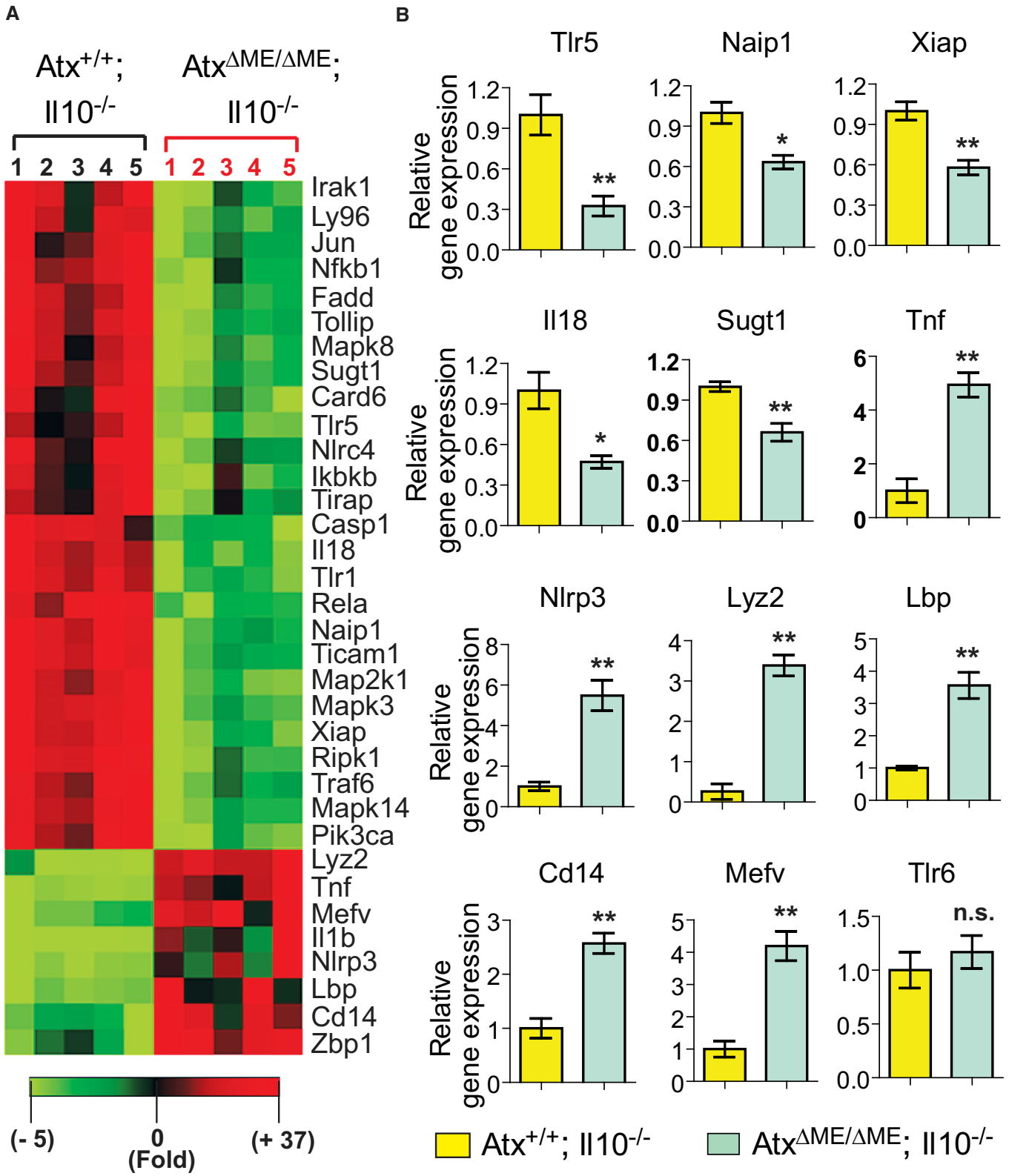


Figure EV4.

Figure EV4. Altered anti-bacterial responses in the colon of $Atx^{\Delta ME/\Delta ME}$;$Il10^{-/-}$ mice compared to $Atx^{+/+}$;$Il10^{-/-}$ littermates.

A The expression of anti-bacterial response-focused genes was evaluated using the full-thickness colon tissues of $Atx^{\Delta ME/\Delta ME}$; $Il10^{-/-}$ mice and $Atx^{+/+}$;$Il10^{-/-}$ littermates. An array of gene expression revealing a significant difference was visualized in the heatmap.

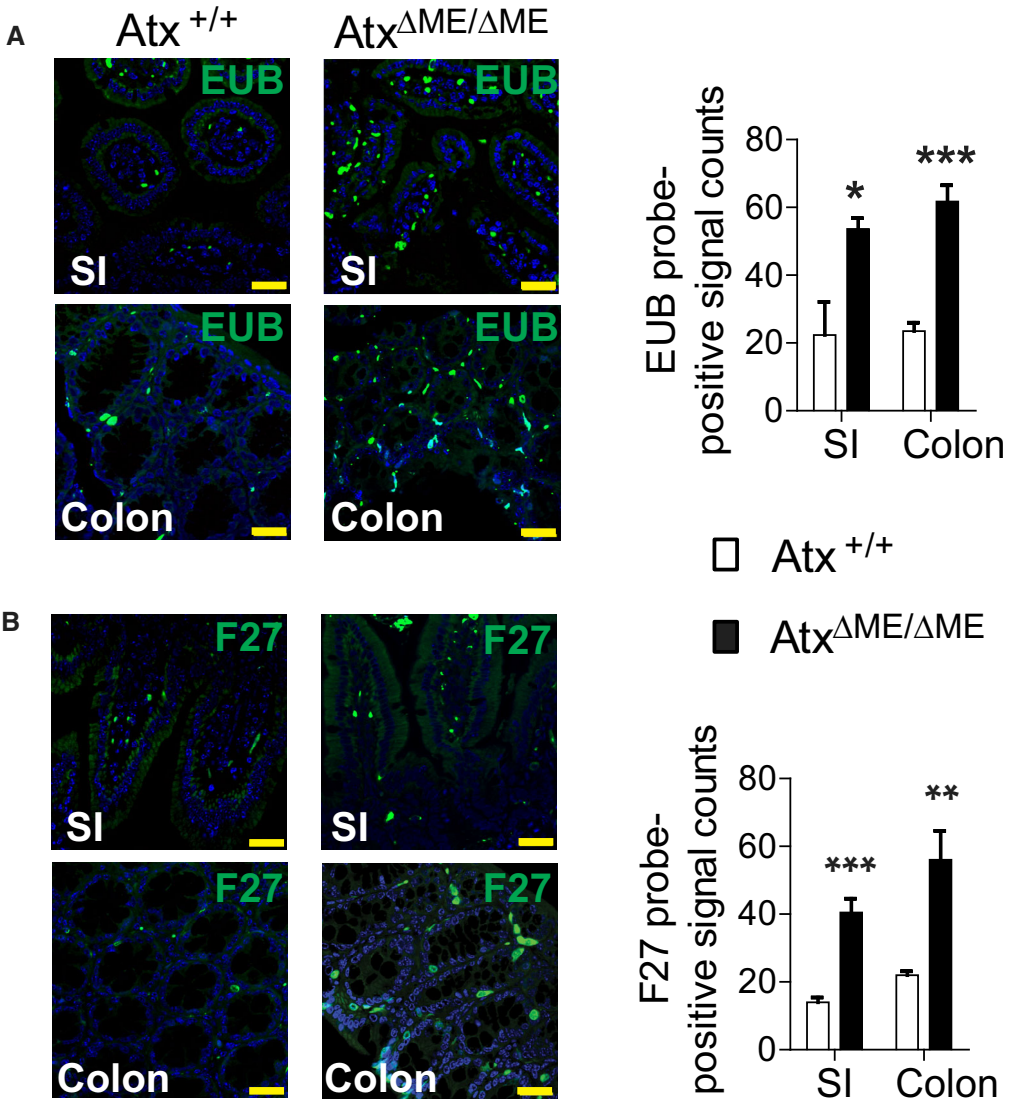
B Representative gene expression exhibiting a significant difference was independently confirmed by qPCR. n = 5/group. Error bars indicate ± SEM. *$P < 0.05$, **$P < 0.01$ (Mann–Whitney U-test). not significant (n.s.).

Figure EV5. $Atx^{\Delta ME/\Delta ME}$ mice have elevated levels of bacteria in the intestinal mucosa.

A, B The bacterial load in the intestinal mucosa of $Atx^{\Delta ME/\Delta ME}$ and $Atx^{+/+}$ mice was evaluated by Fluorescent *In Situ* Hybridization (FISH) using FITC-labeled pan-bacterial EUB probe (A) and FITC-labeled pan-bacterial F27 probe (B). Scale bar is 30 μm. Graph indicates the count of FITC-positive signals quantified from three or more independent experiments (n = 3–4 per group). The data are shown as mean ± SEM. Small Intestine (SI).

C Electron micrographs of intact cell-to-cell adhesion in the colonic epithelium from age (8 weeks)-matched $Atx^{\Delta ME/\Delta ME}$ mice and $Atx^{+/+}$ littermate. Tight junction (TJ), Adherens junction (AJ), Desmosome (DSM). Scale bar indicates 500 nm.

Data information: All images presented are the representative from at least three independent experiments. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ (one-tailed unpaired t-test).



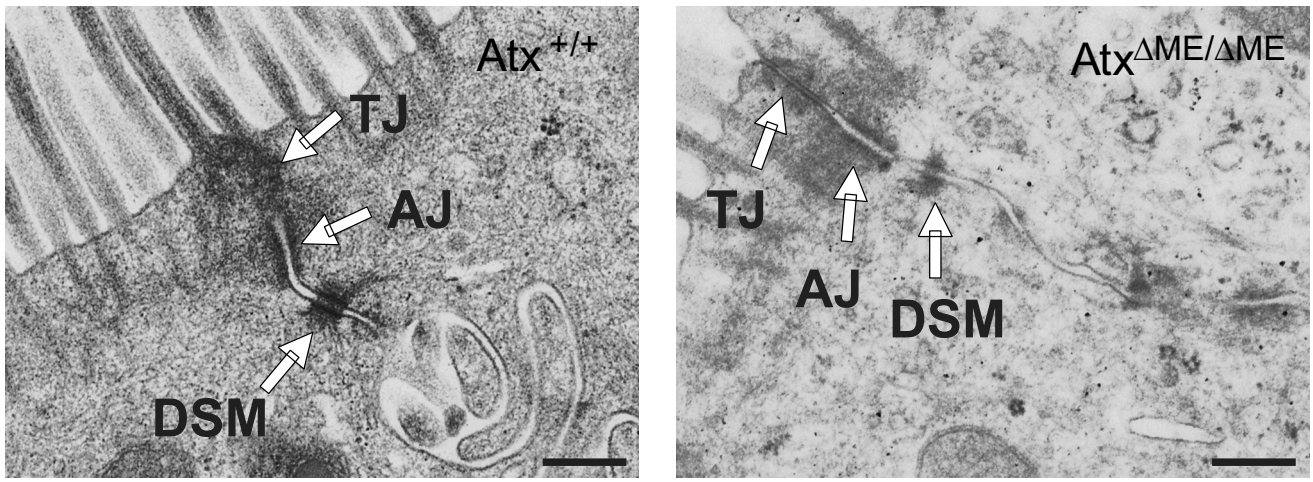


Figure EV5.