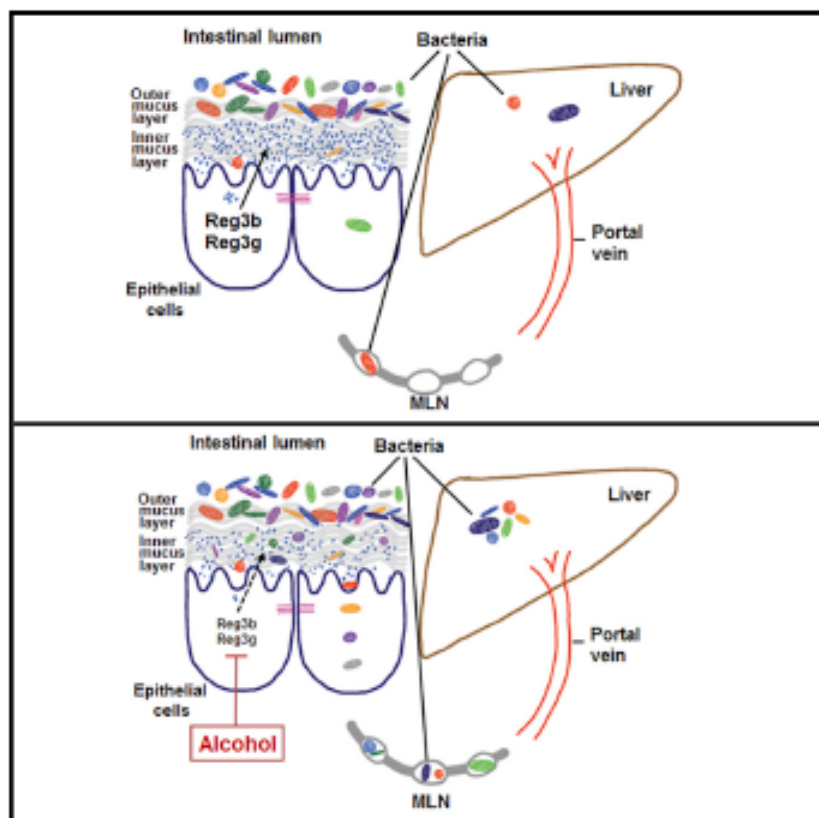


Cell Host & Microbe

Intestinal REG3 Lectins Protect against Alcoholic Steatohepatitis by Reducing Mucosa-Associated Microbiota and Preventing Bacterial Translocation

Graphical Abstract



Authors

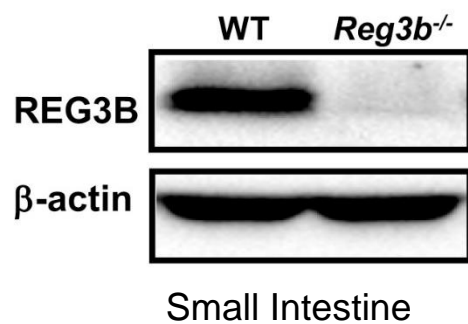
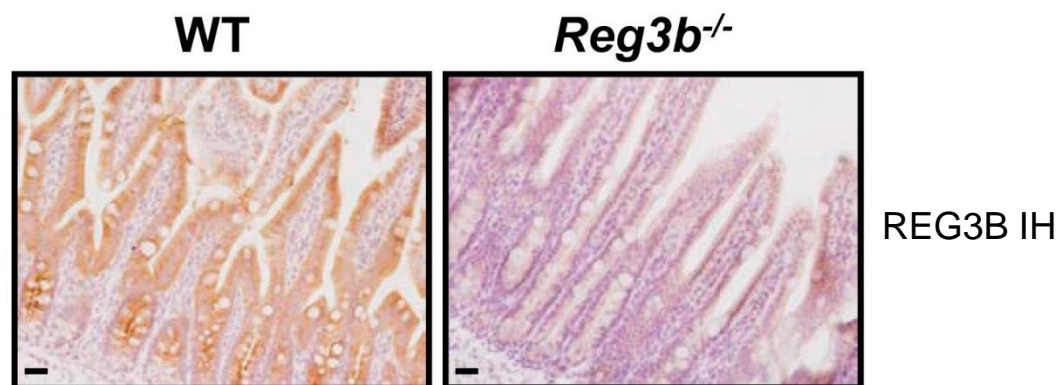
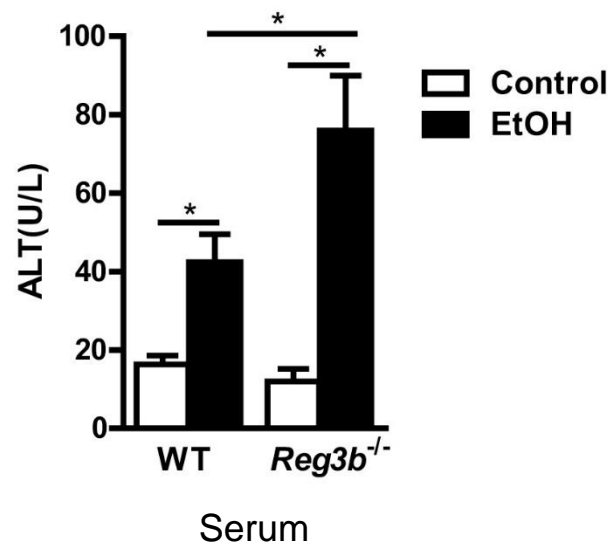
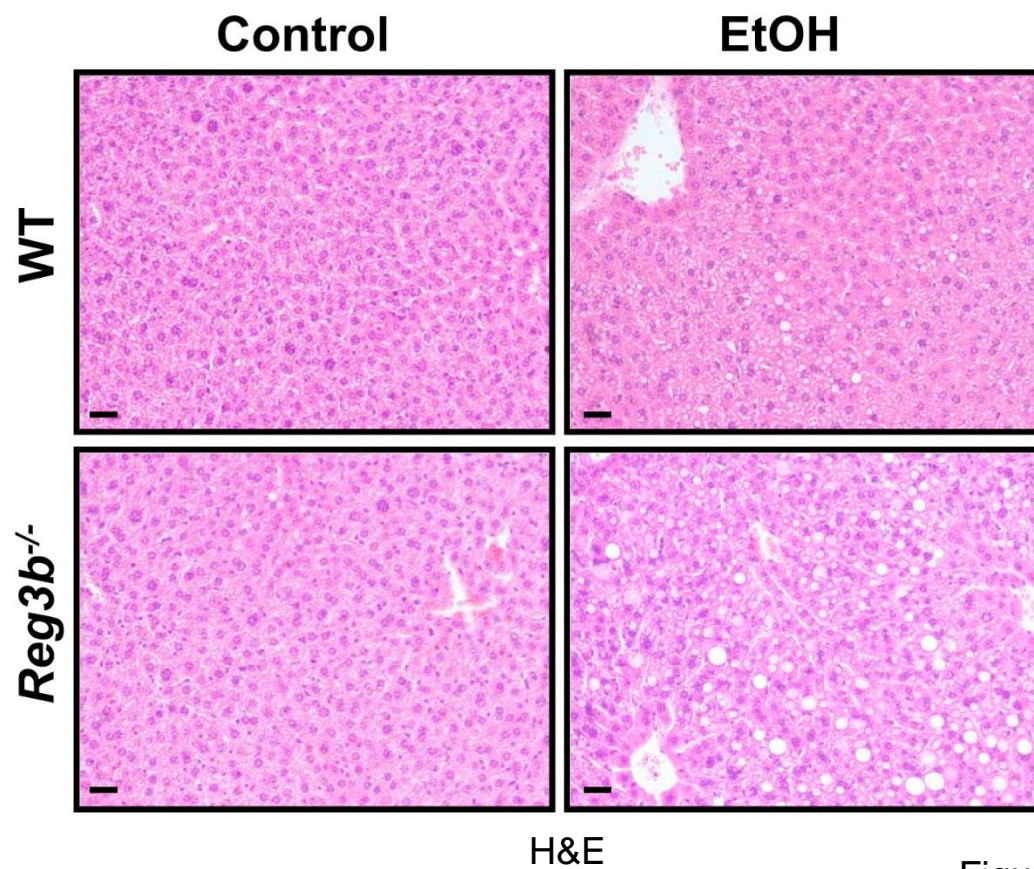
Lirui Wang, Derrick E. Fouts, Peter Stärkel, ..., David A. Brenner, Lora V. Hooper, Bernd Schnabl

Correspondence

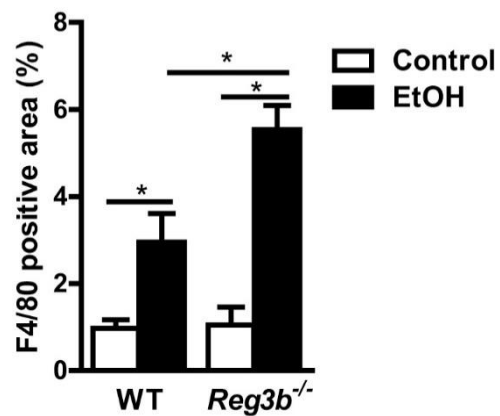
beschnabl@ucsd.edu

In Brief

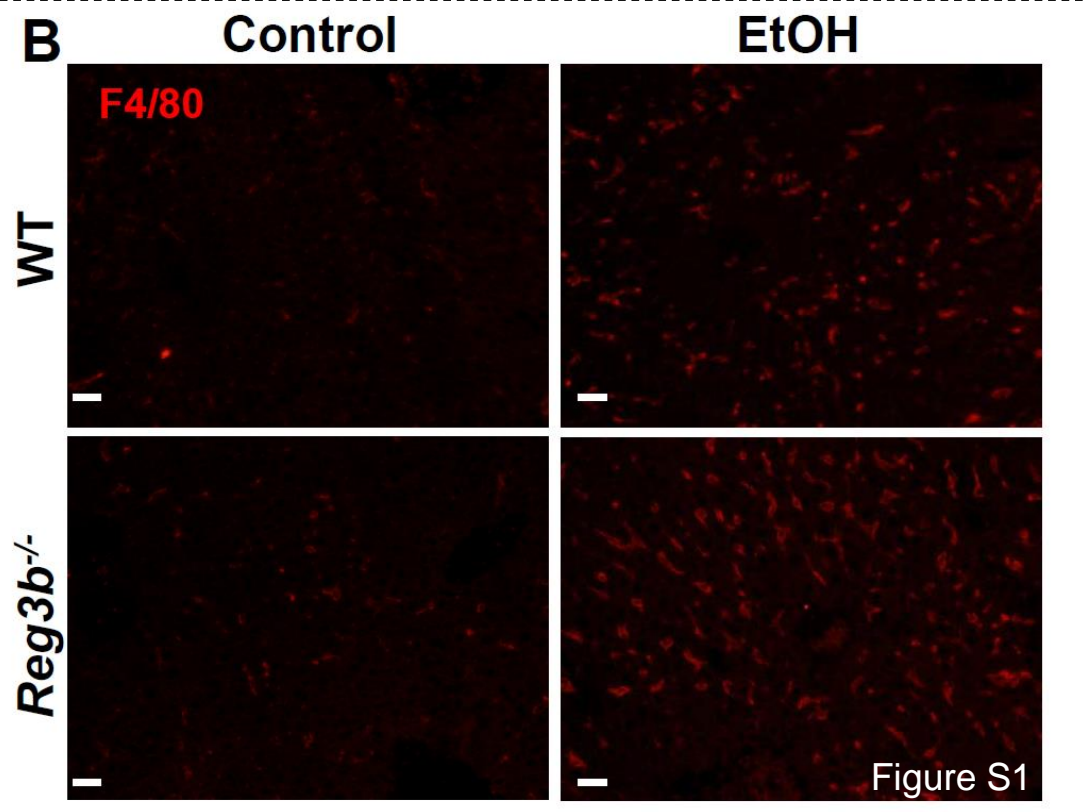
The mechanism by which chronic alcohol consumption alters the microbial composition in the intestine is unknown. Wang et al. demonstrate that alcohol reduces intestinal expression of REG3 lectins, increasing the number of mucosa-associated bacteria. The subsequent translocation of bacteria to mesenteric lymph nodes and liver exacerbates alcoholic liver disease.

A**B****C****D****Figure 1**

G



B



H

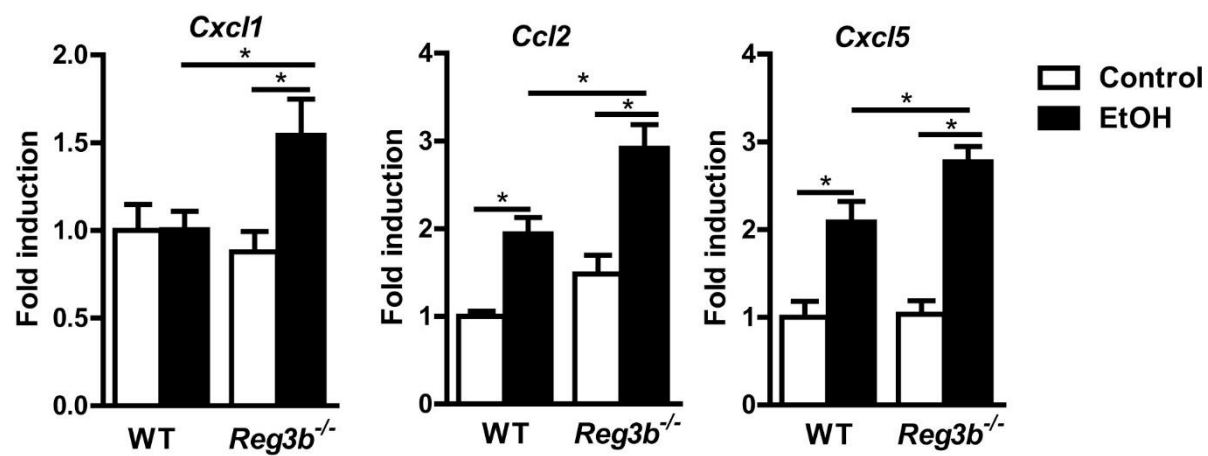
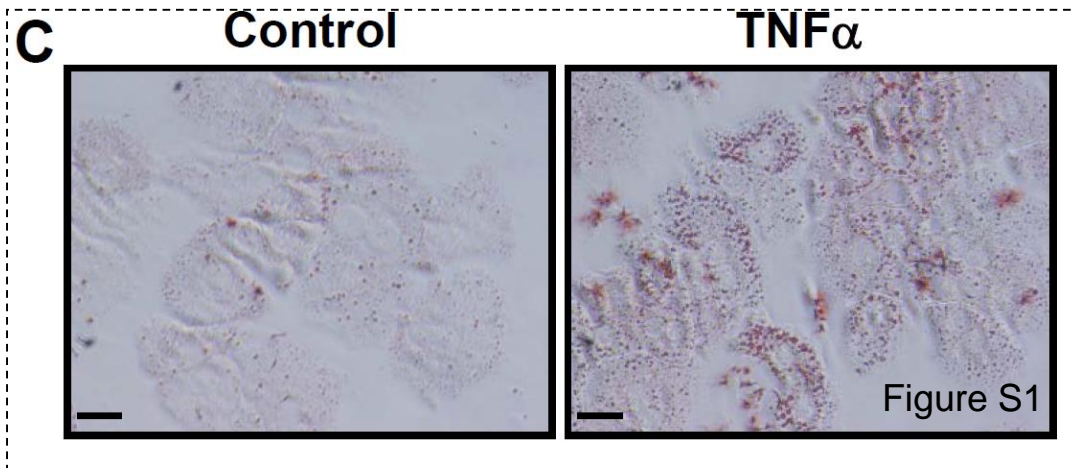
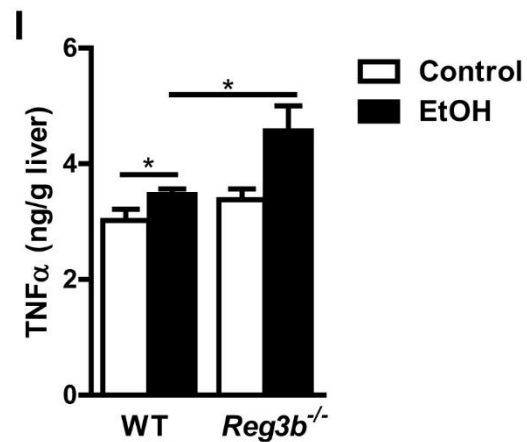


Figure 1



Oil red O-stained – Hepatocytes primary culture +/-TNF α

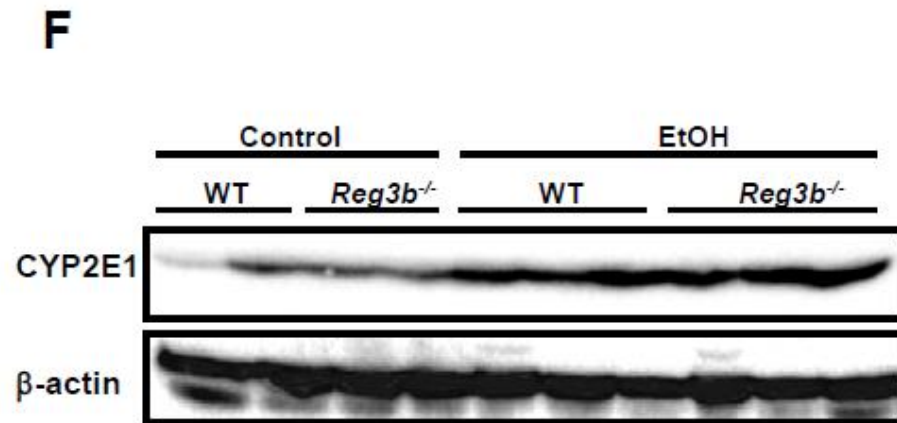
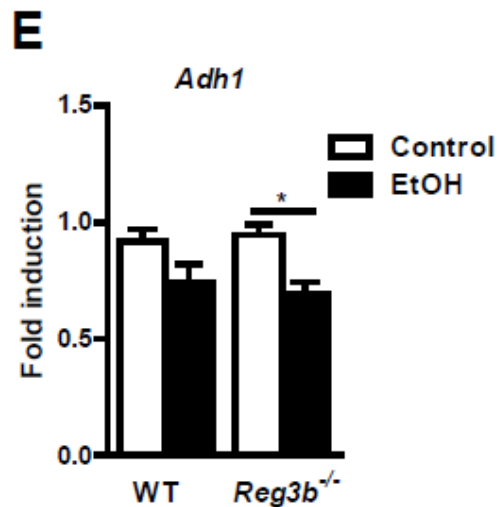
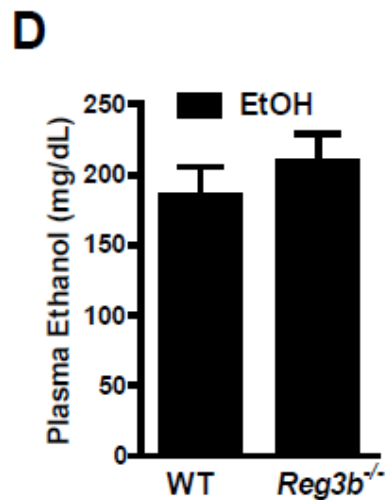


Figure S1

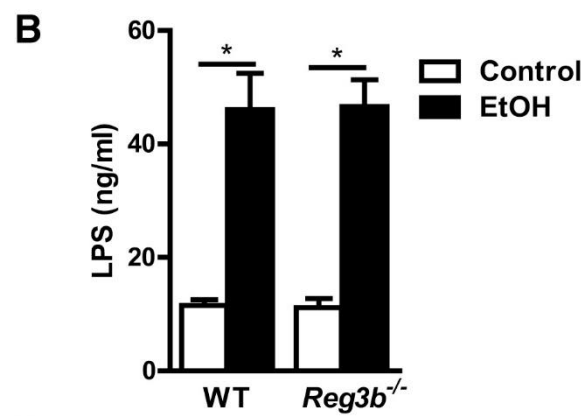
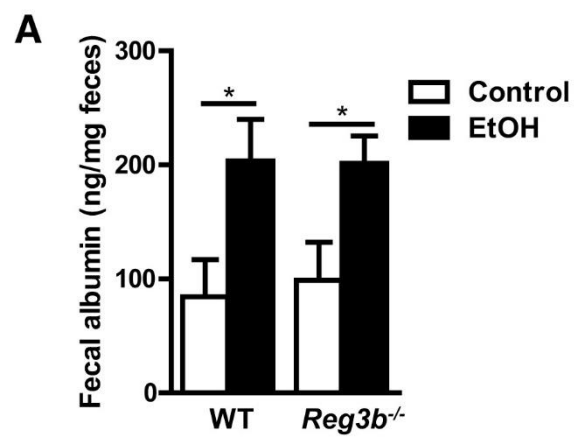


Figure 2

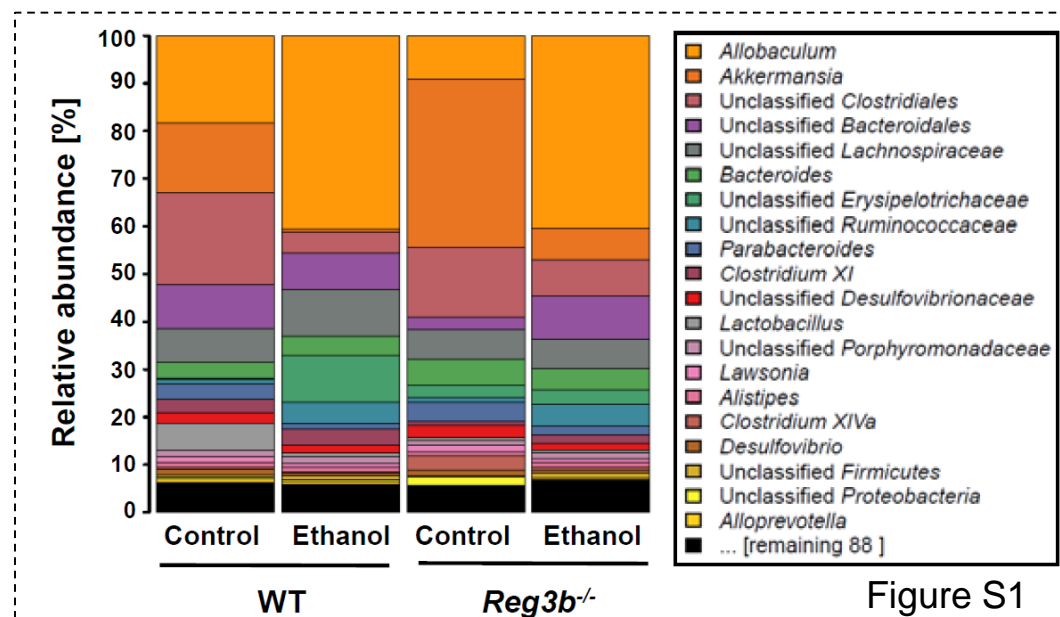
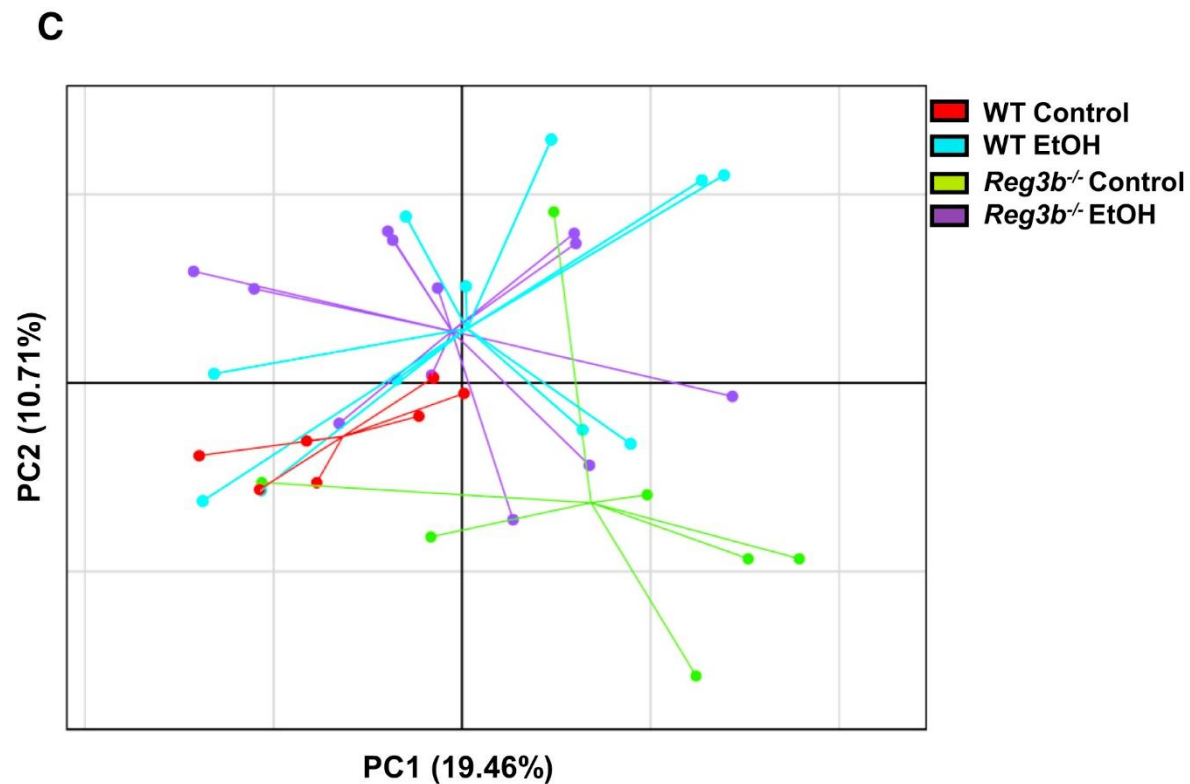
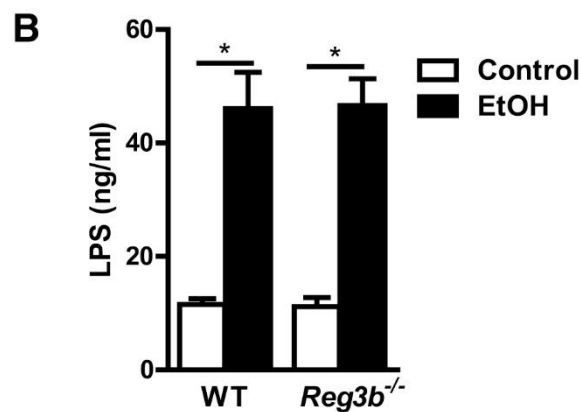
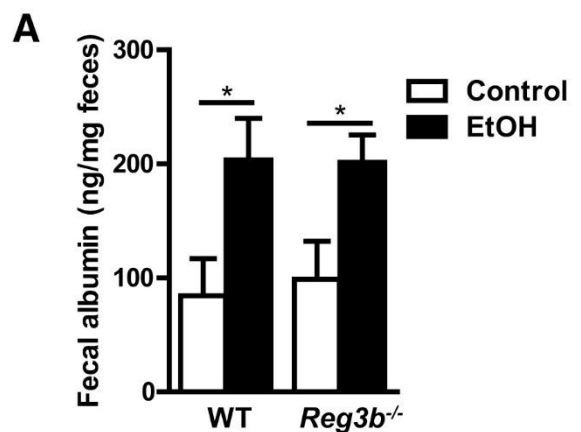
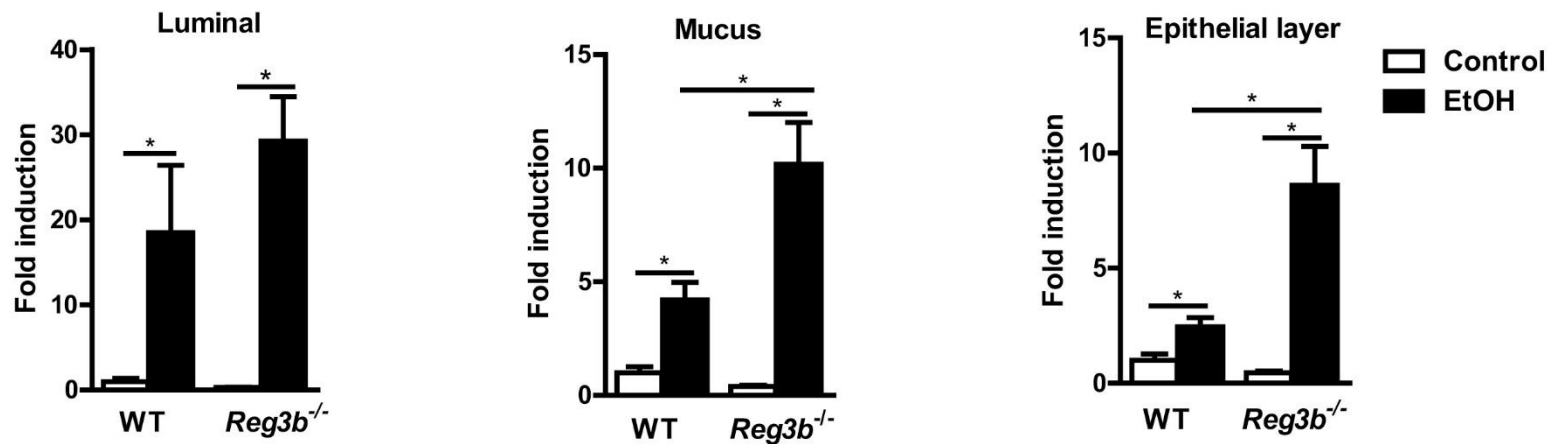


Figure S1

Figure 2

D



E

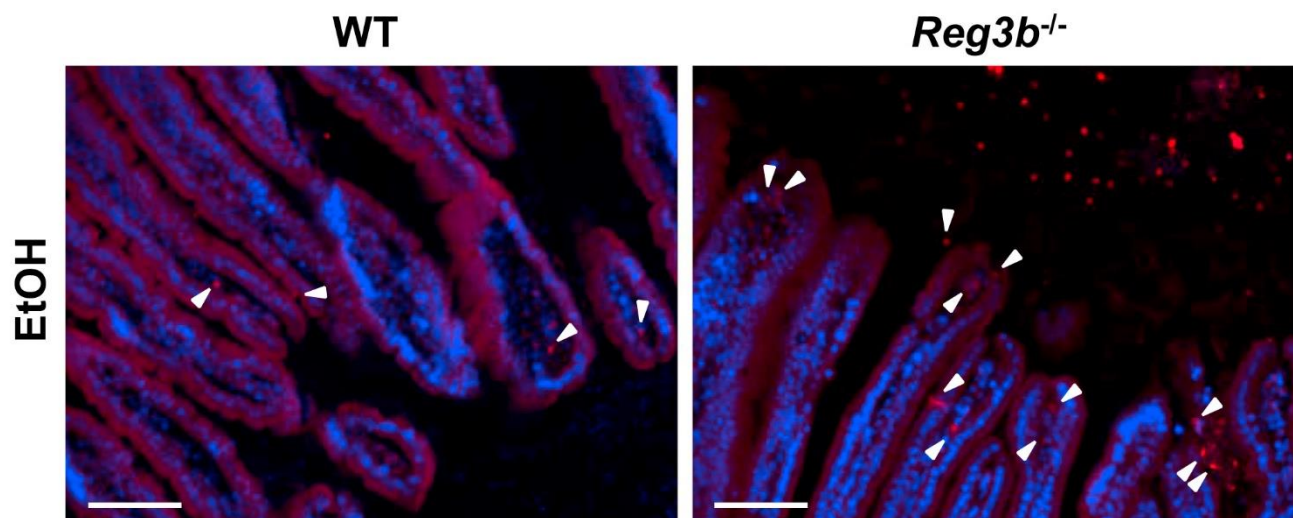
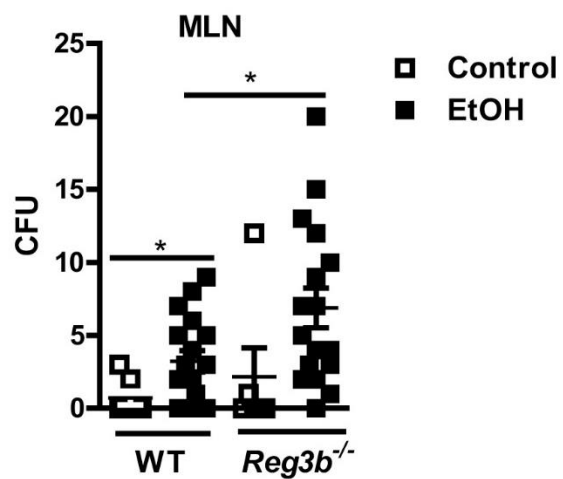


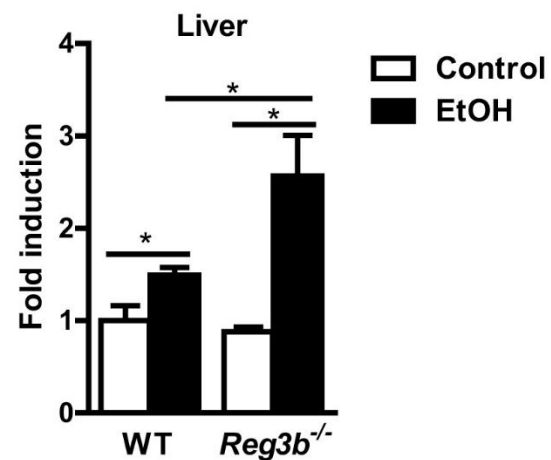
Figure 2

F



Total CFUs counting
anaerobic plates

G



Total liver bacterial
quantification by 16S qPCR
normalized by host 18S

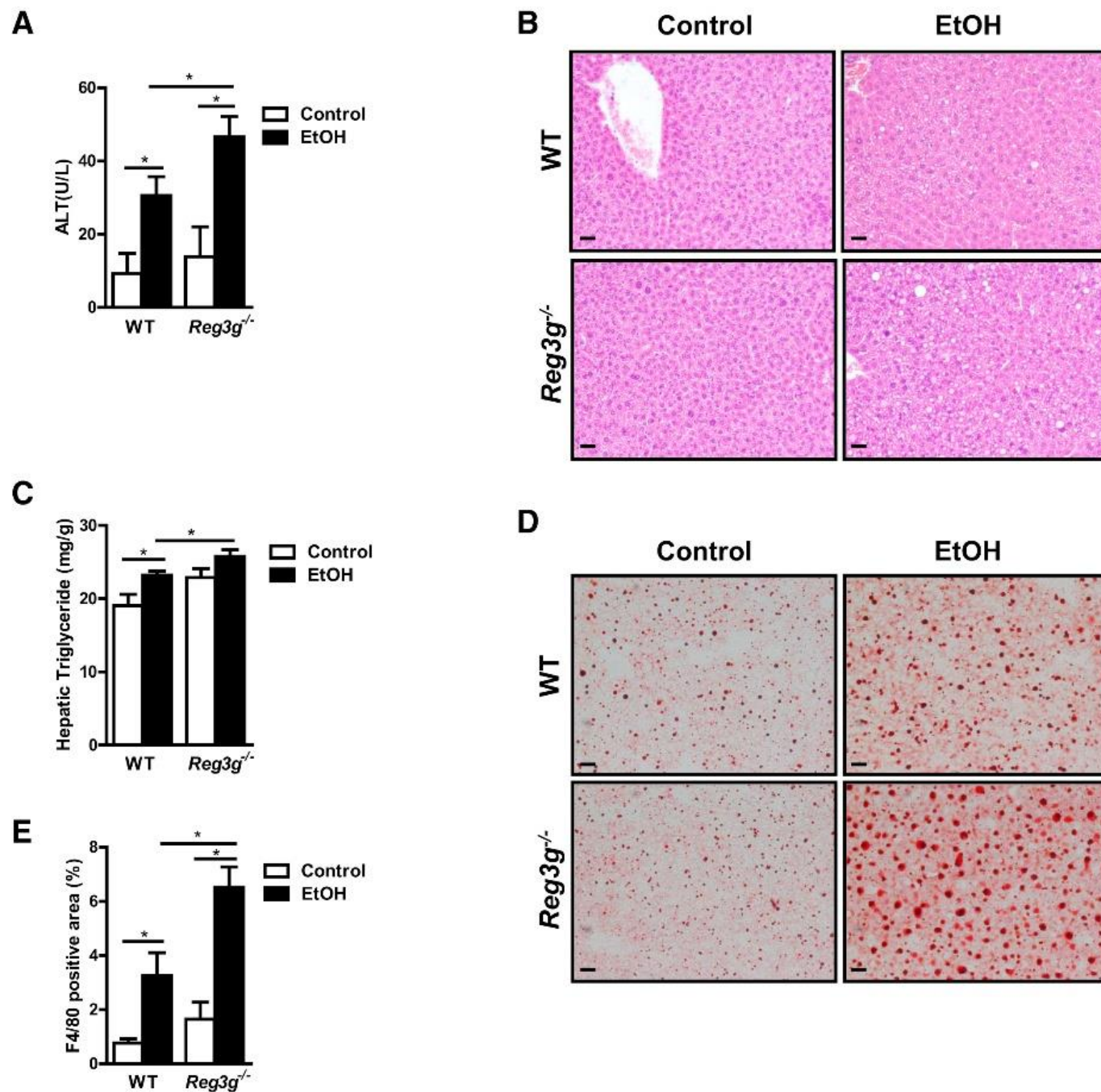


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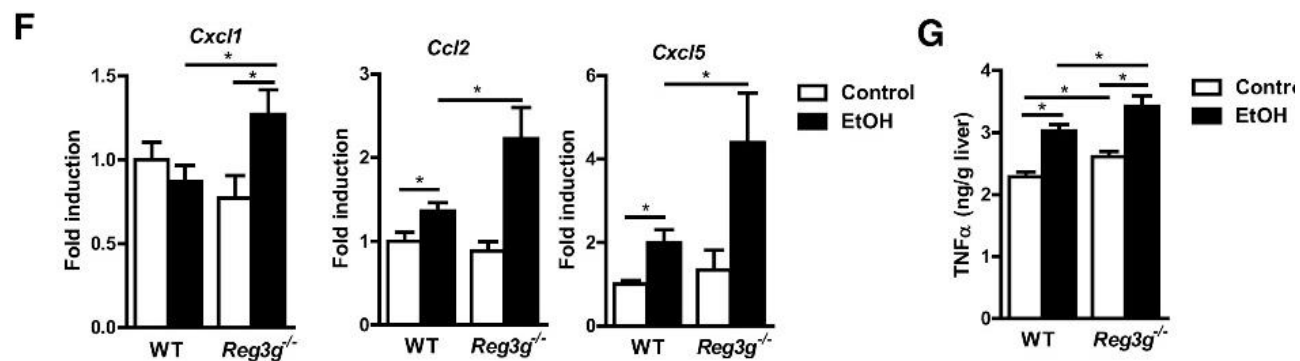
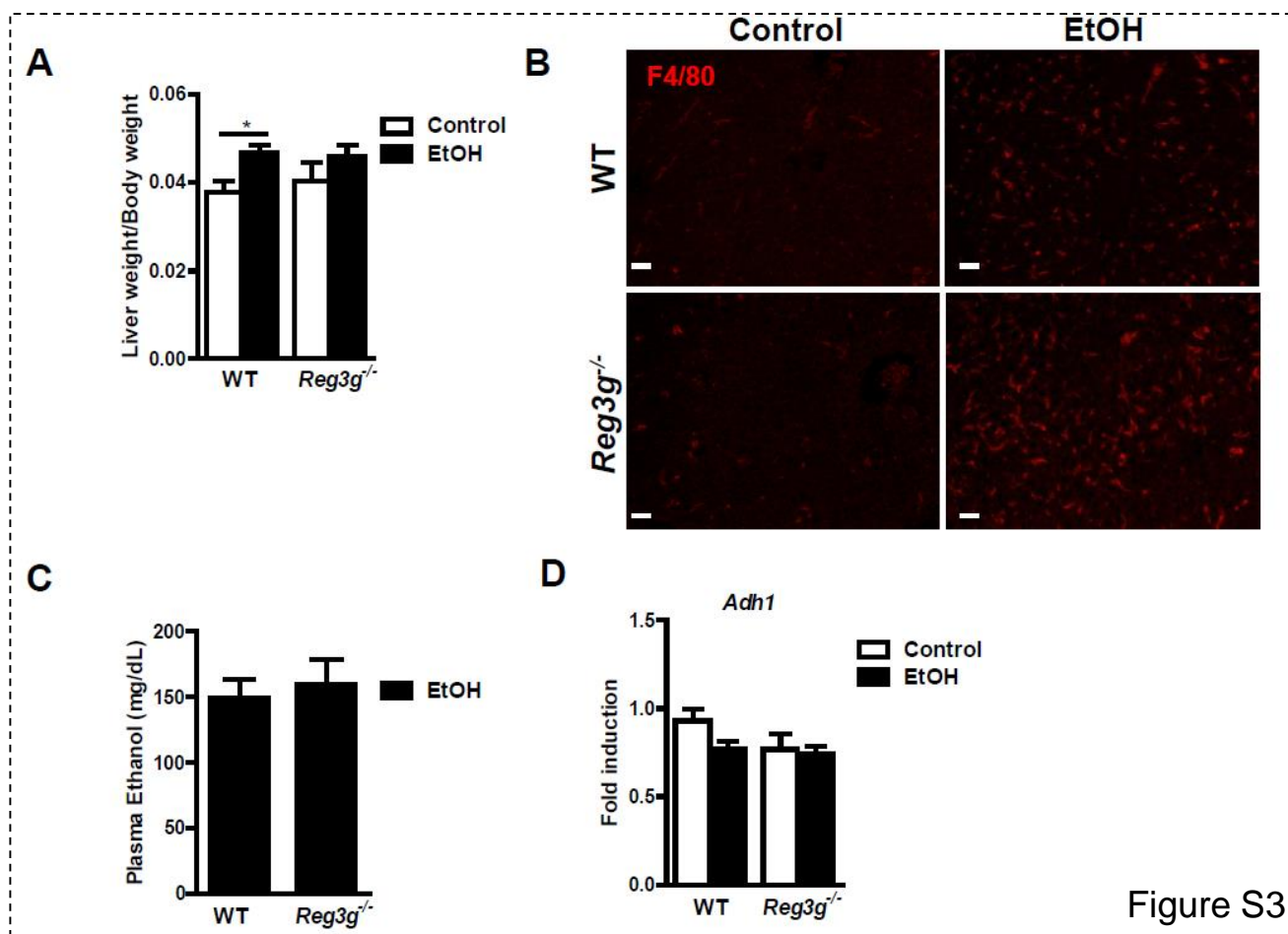


Figure 3

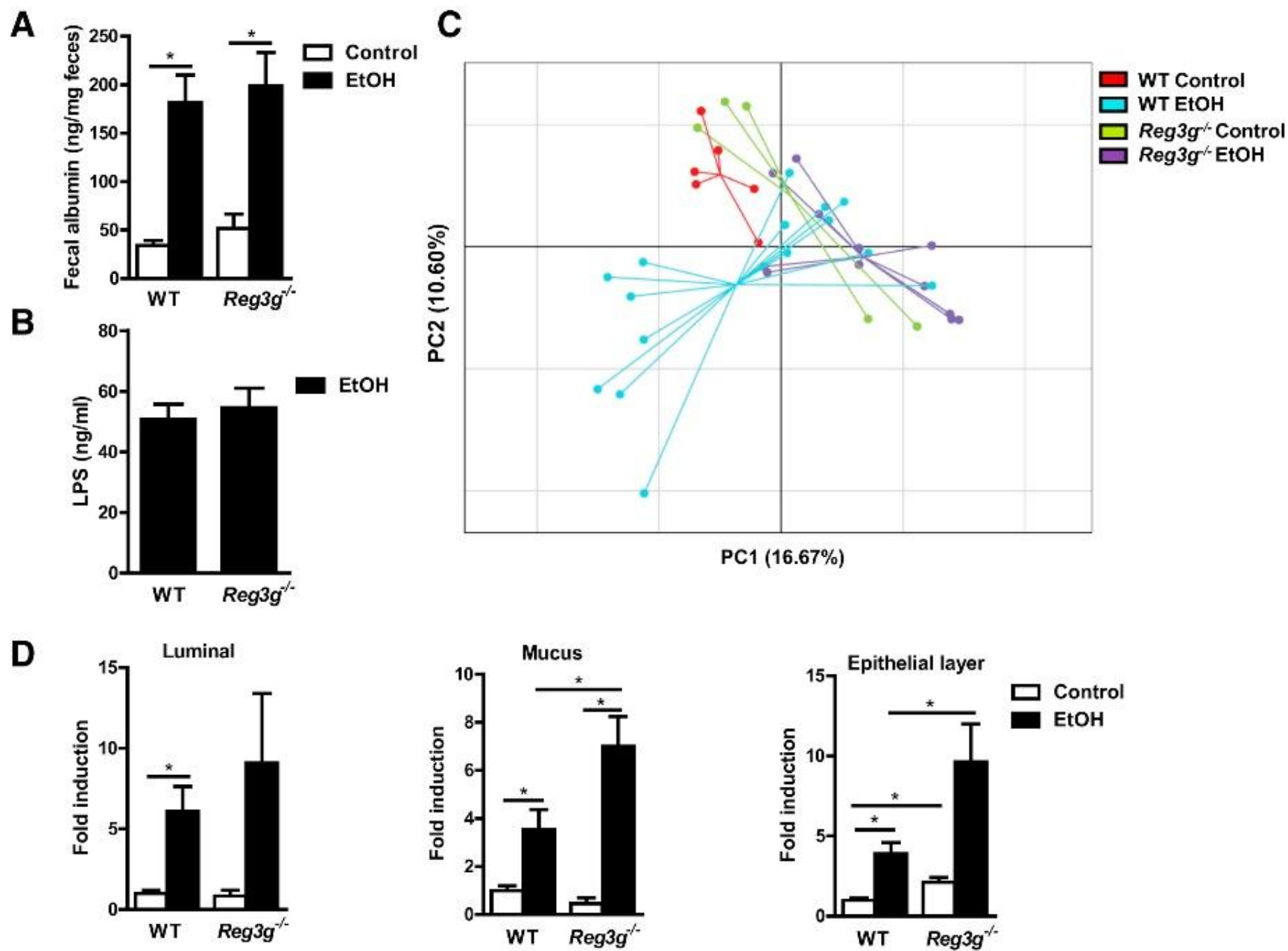


Figure 4

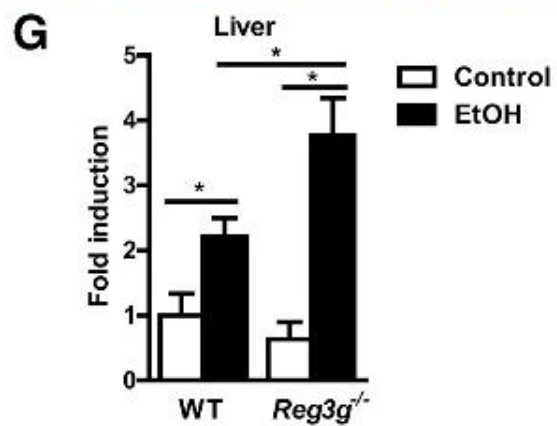
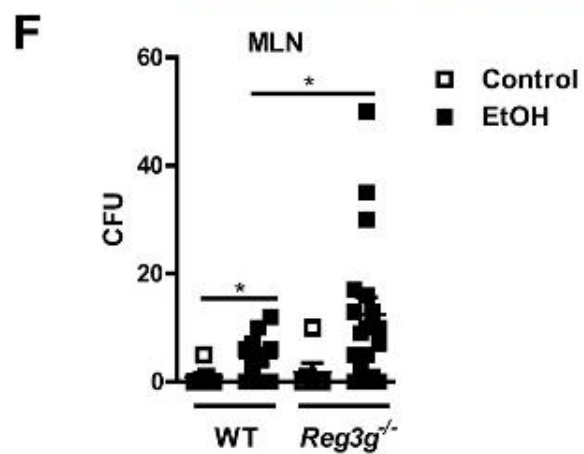
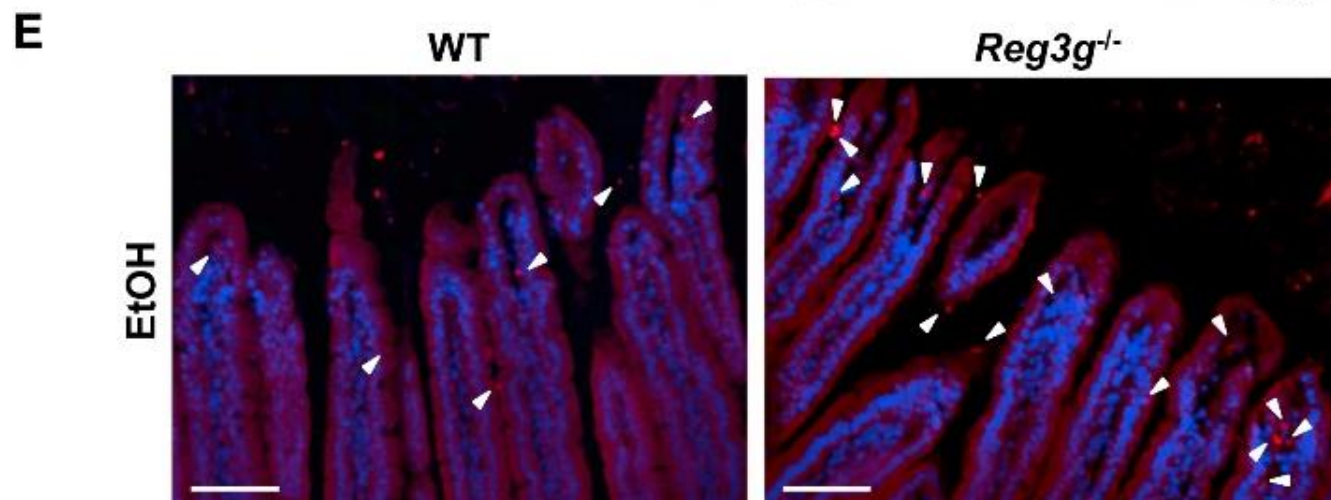


Figure 4

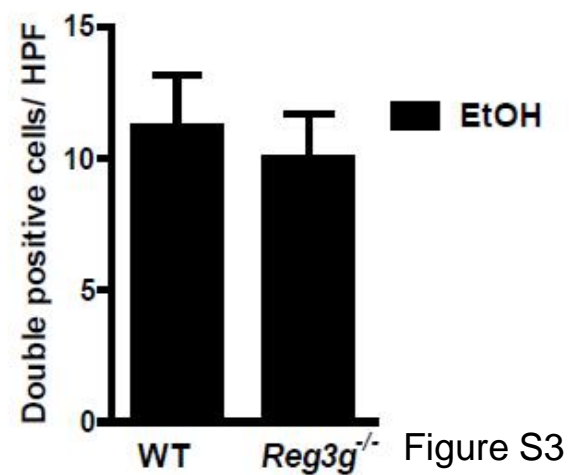
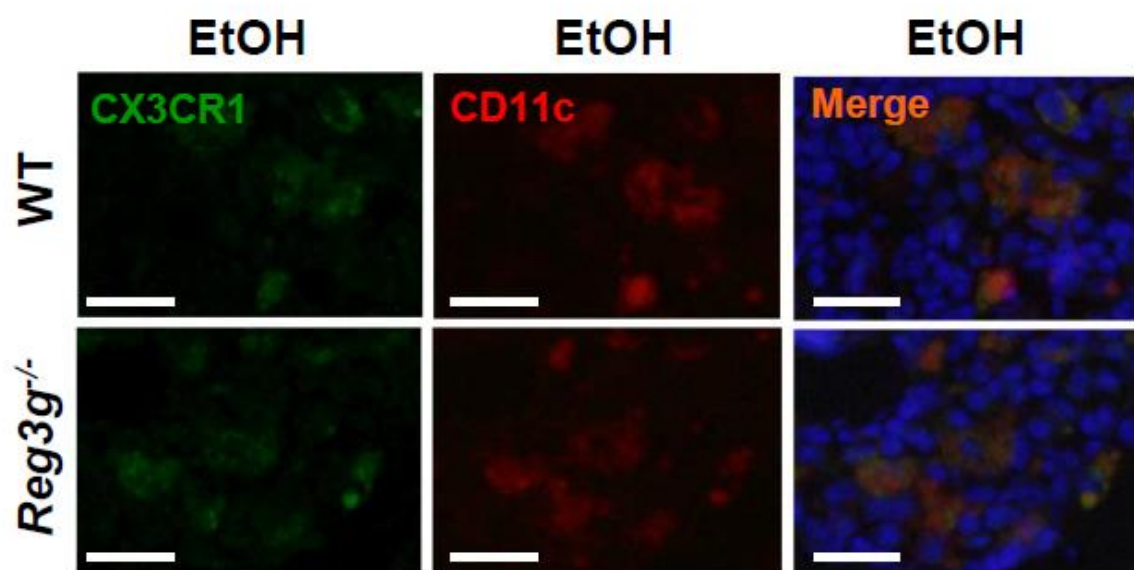
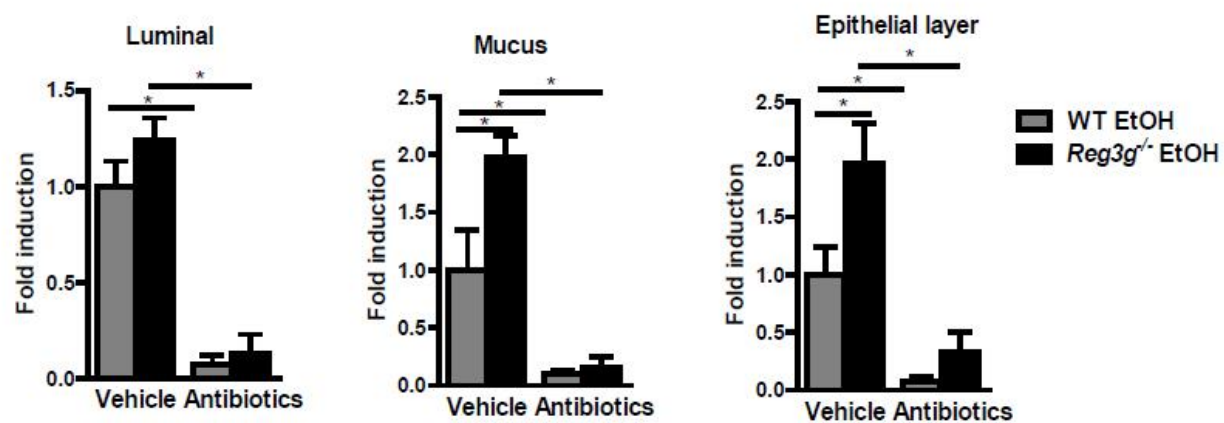
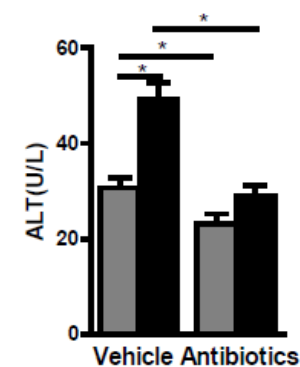
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Figure S3

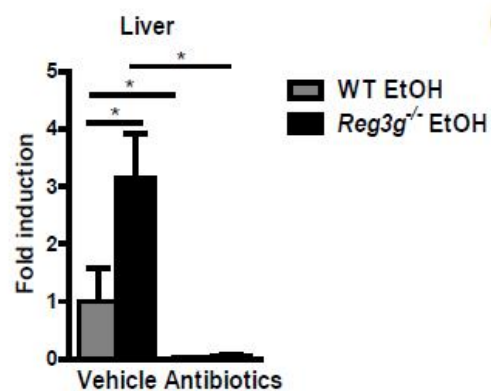
A



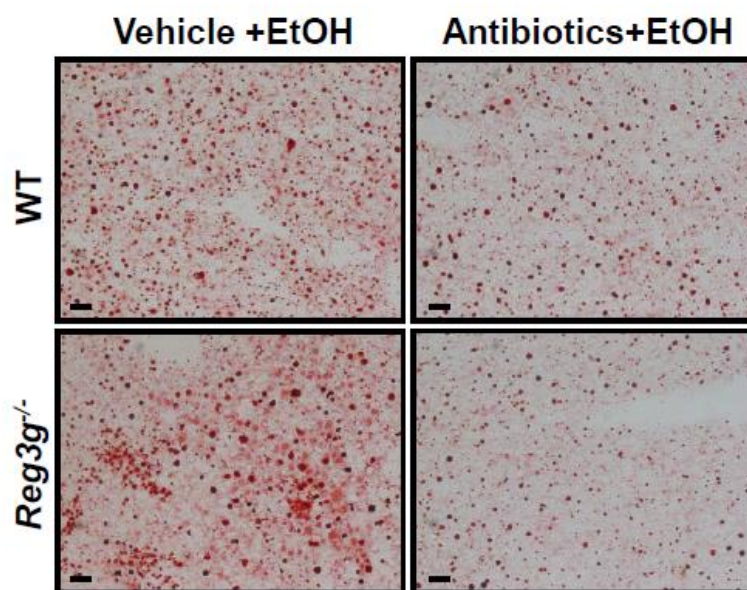
D



B



C



E

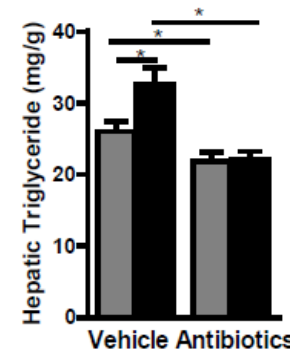


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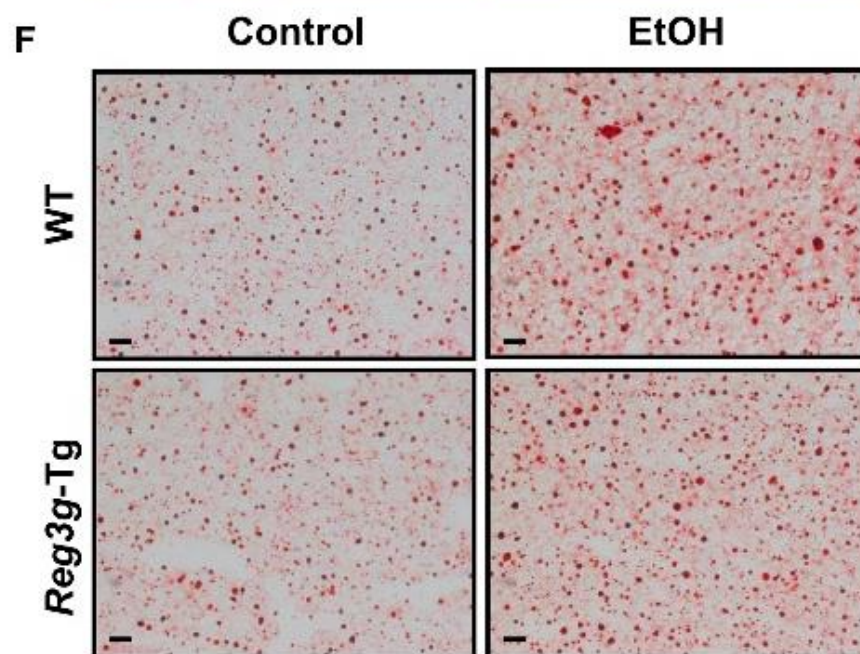
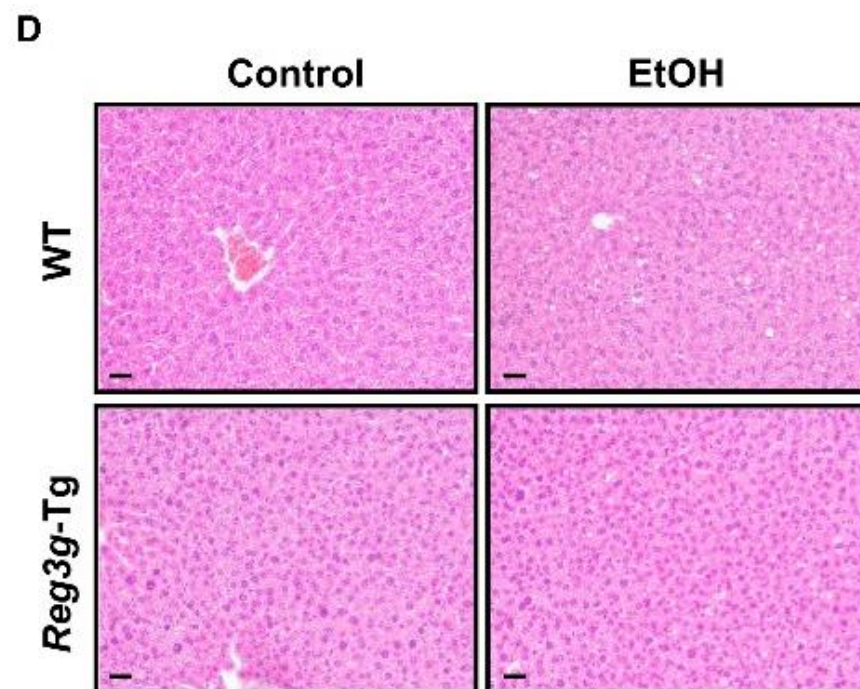
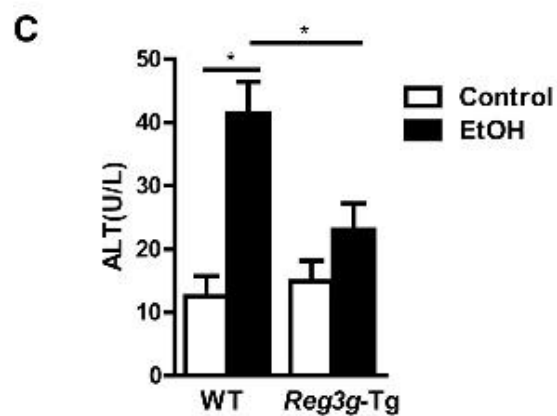
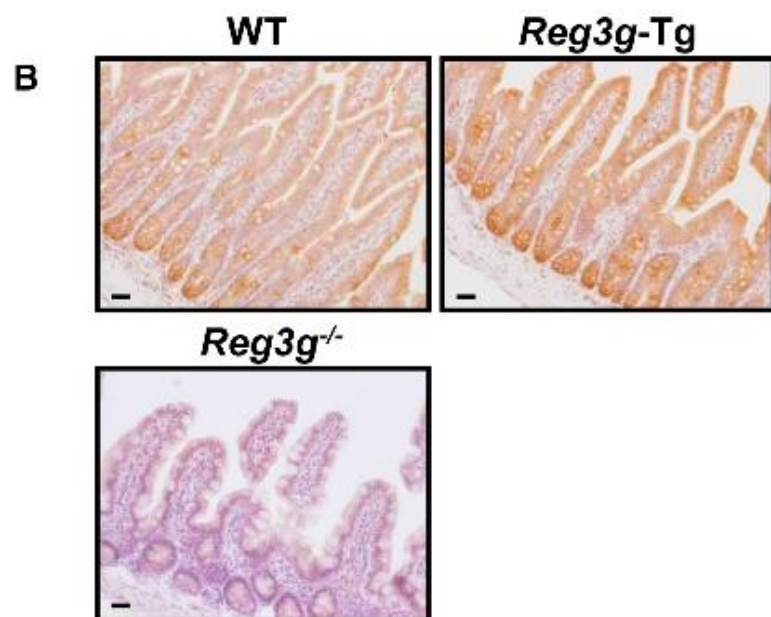
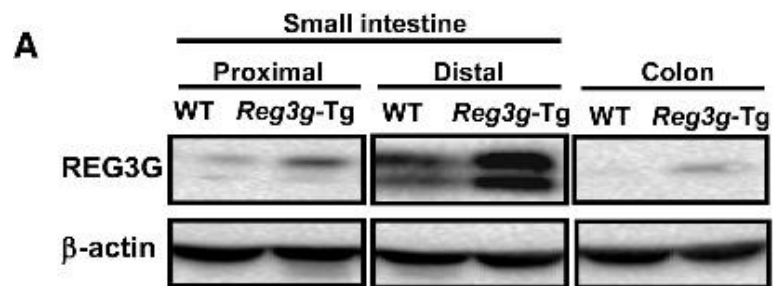


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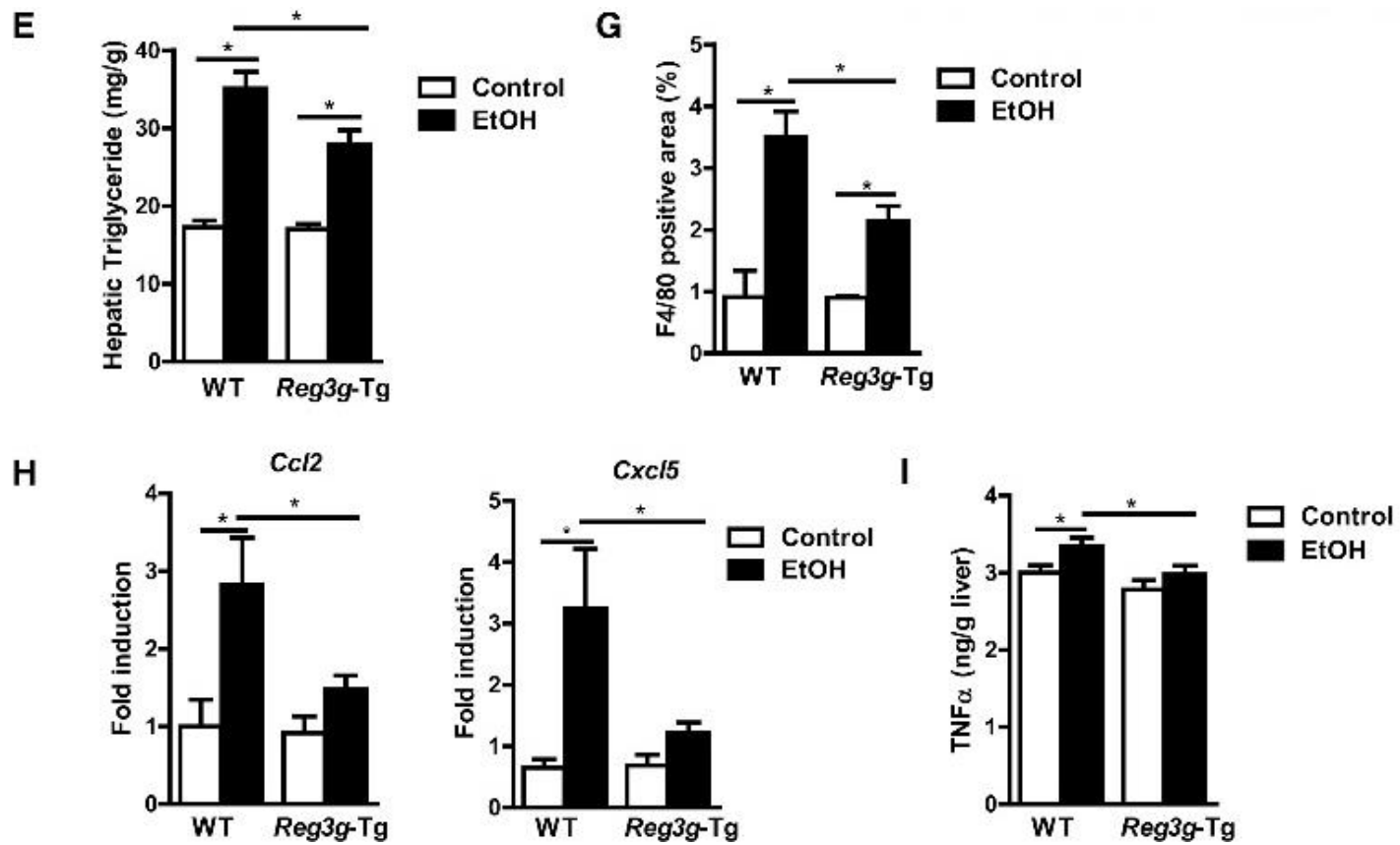


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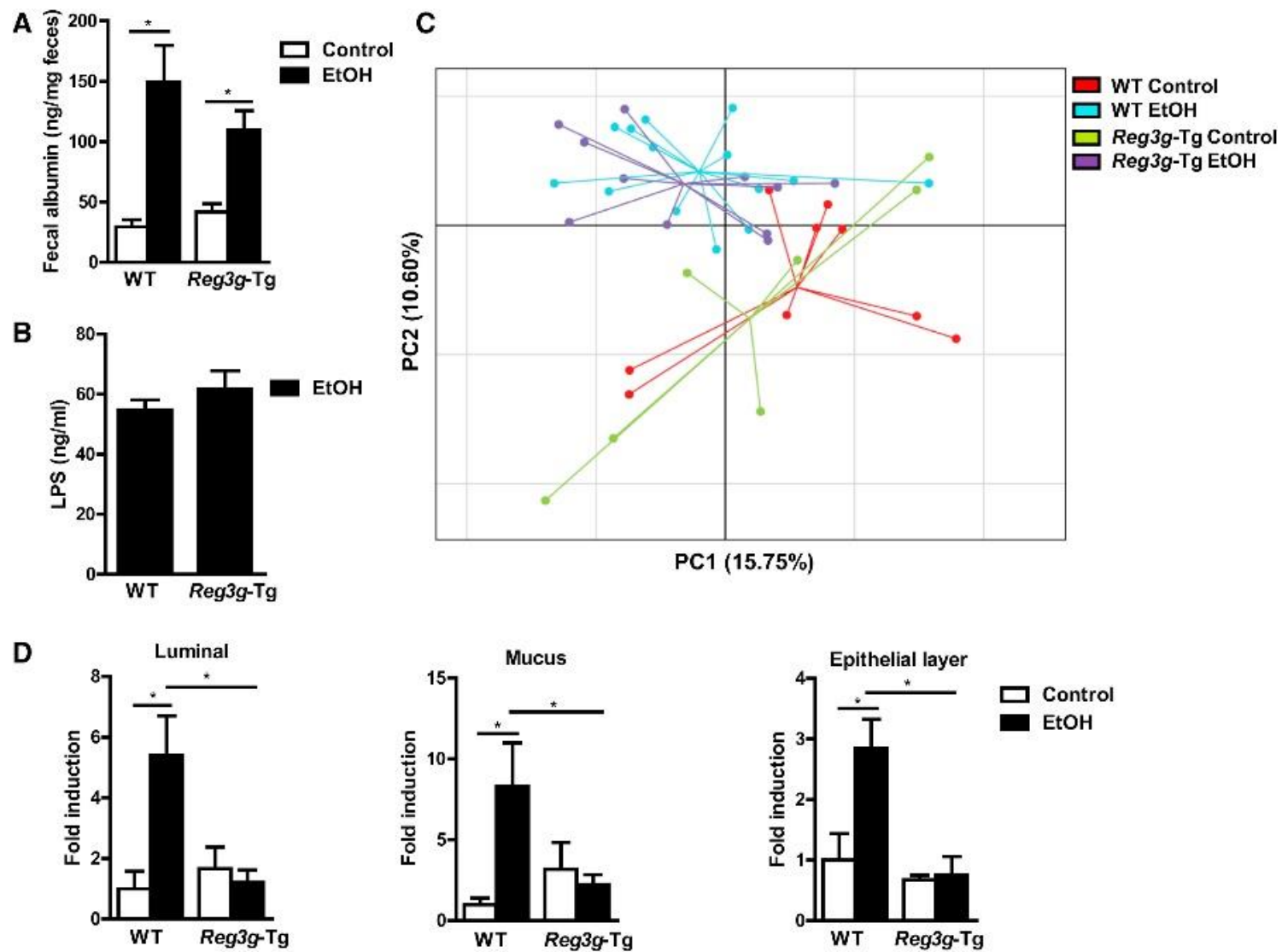


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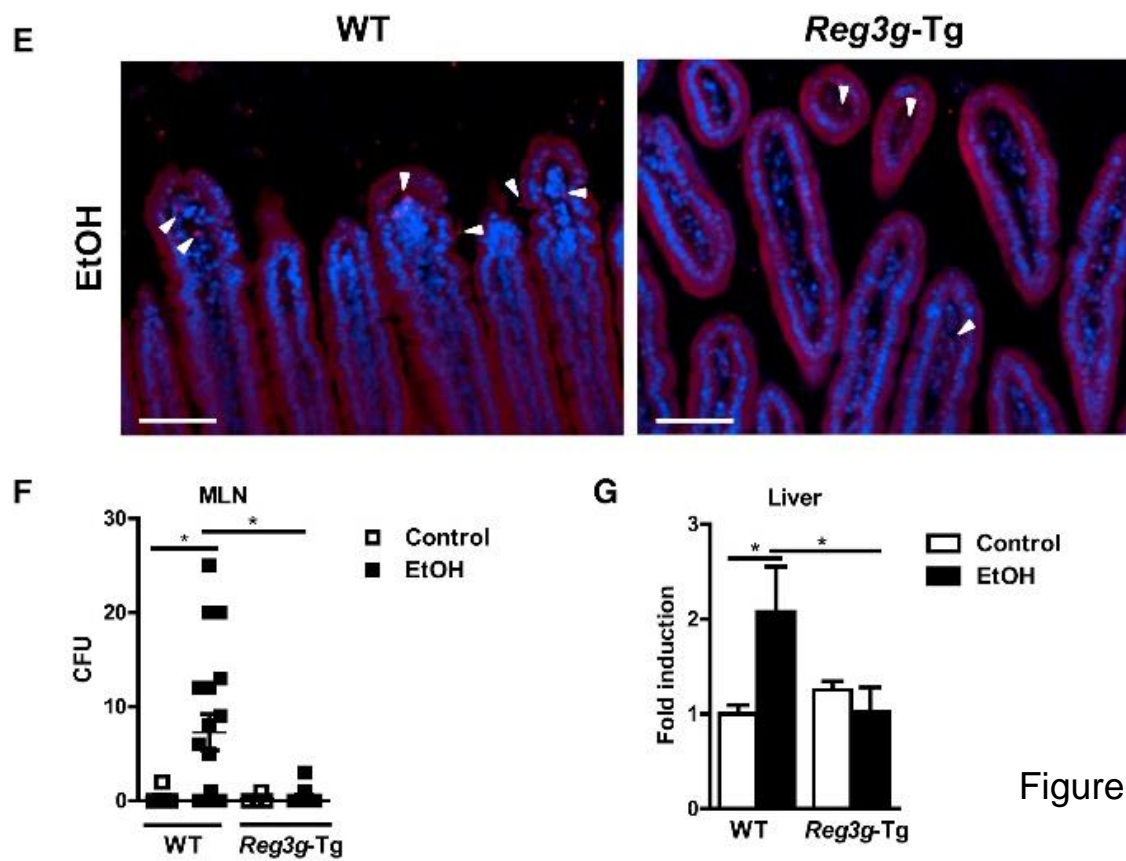
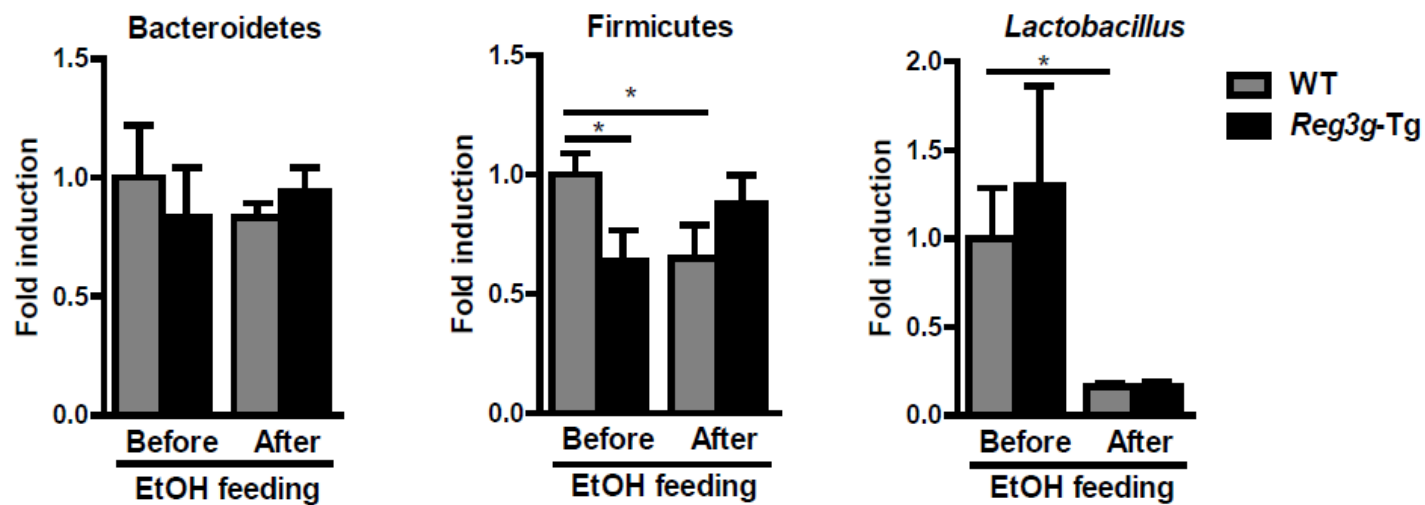
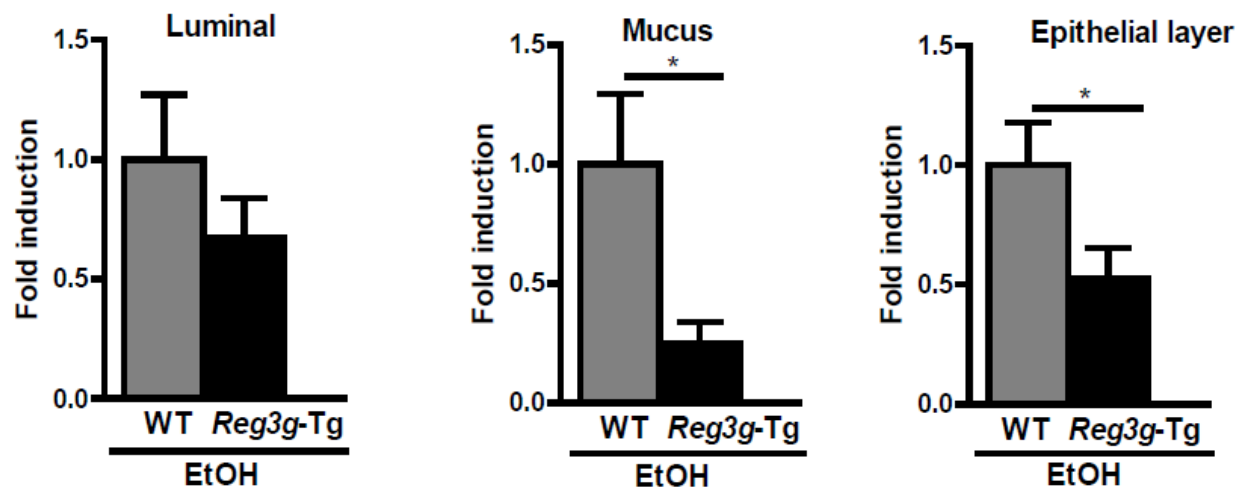
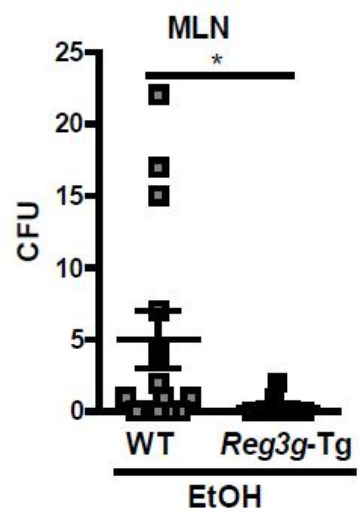
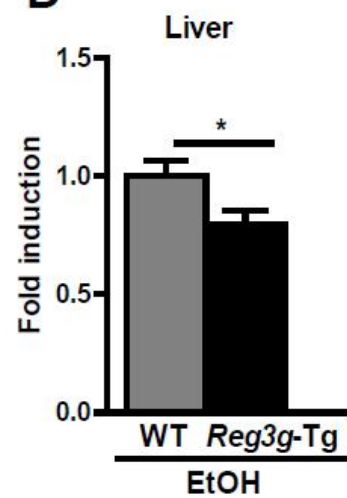
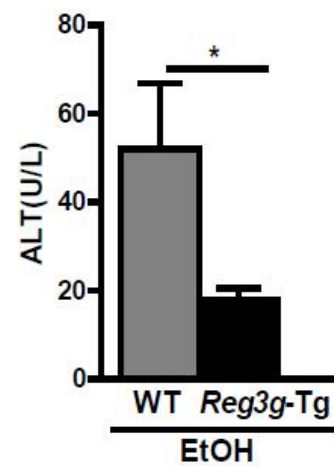
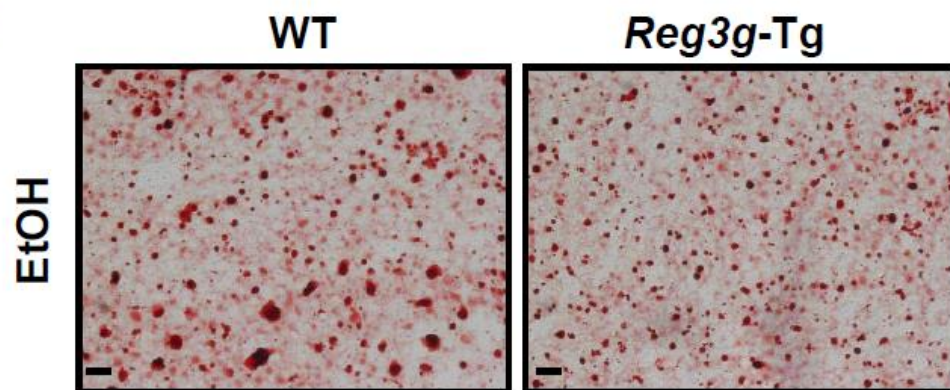
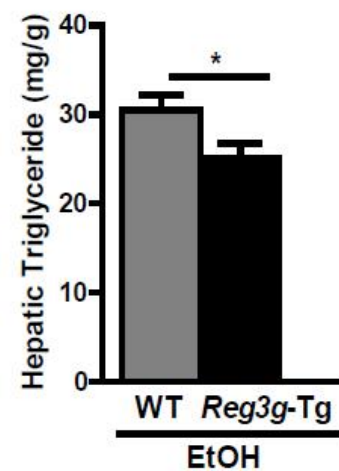


Figure 6

A**B**

C**D****E****F****G**

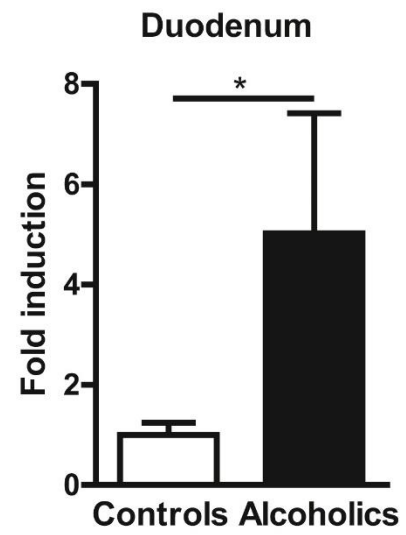
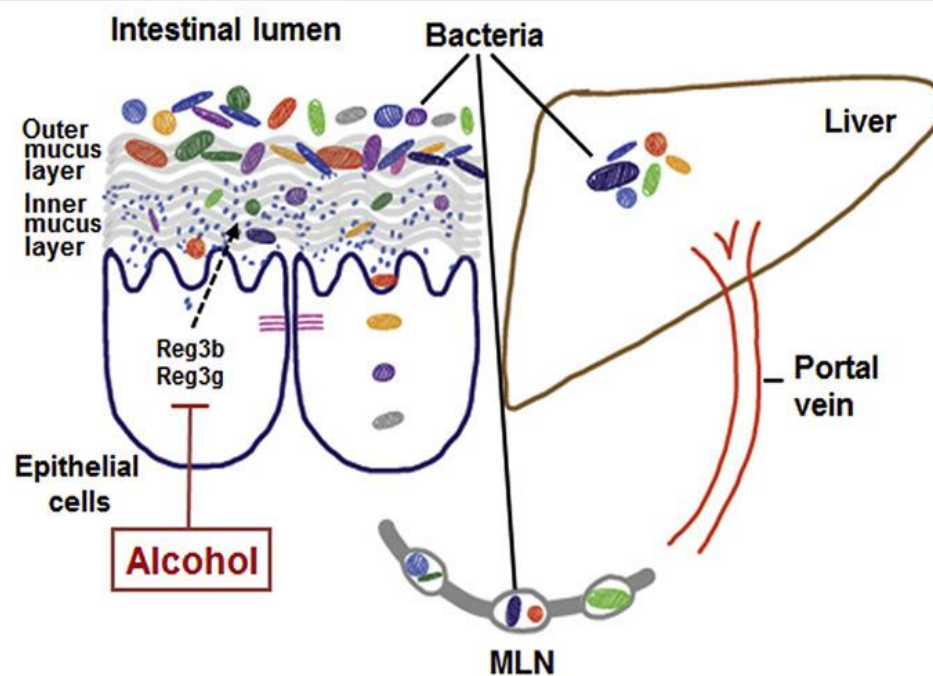
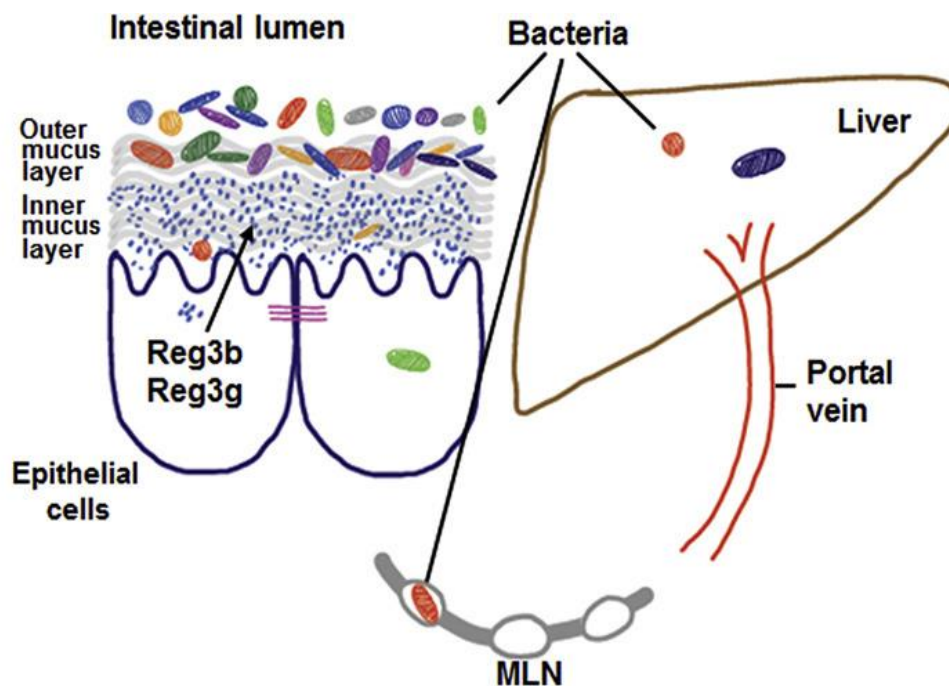


Figure 7



ORIGINAL ARTICLE

Changes in gut toll-like receptor-4 and nod-like receptor family pyrin domain containing-3 innate pathways in liver cirrhosis rats with bacterial translocation

Ling Liu^a, Chiqian Zhang^b, Yanyan Hu^c, Li Zhou^b,
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Experimental model:

Feeding with a HF/LP diet:

- 79.5% maize flour
- 20% lard
- 0.5% cholesterol

Liver damage induced by:

- CCl₄ in oil solution s.c. twice a week for 10 weeks.
- Alcohol (100mL/L) in drinking water.

Table 1 Biochemical differences among normal control (NC) and liver cirrhosis rats with BT-negative and BT-positive bacterial cultures from the mesenteric lymph nodes.

Group	NC (n = 10)	BT-negative (n = 8)	BT-positive (n = 18)
Alt (U/L)	46.31 ± 7.36	129.00 ± 39.32 ^a	138.67 ± 31.40 ^a
Ast (U/L)	151.75 ± 7.50	296.46 ± 65.59 ^a	369.80 ± 85.72 ^a
Tp (g/L)	68.89 ± 3.04	59.33 ± 1.52 ^a	58.27 ± 5.81 ^a
Alb (g/L)	37.41 ± 0.81	33.28 ± 0.29 ^a	29.27 ± 2.21 ^{a,b}
Glb (g/L)	31.49 ± 2.98	26.05 ± 1.36	29.00 ± 3.81
Tbil (umol/L)	2.32 ± 0.44	5.460 ± 1.56	7.95 ± 2.54 ^a
Dbil (umol/L)	0.36 ± 0.20	2.653 ± 1.15 ^a	4.11 ± 1.54 ^a
Ibil (umol/L)	1.95 ± 0.25	2.807 ± 0.43	3.39 ± 1.07 ^a
Urea (mmol/L)	4.16 ± 1.07	5.75 ± 1.14	5.27 ± 1.96
Crea (umol/L)	44.88 ± 2.94	48.34 ± 2.10	44.77 ± 1.13
Amm (umol/L)	102.69 ± 22.22	134.81 ± 29.92	188.21 ± 16.40 ^{a,b}

^a Compared with the normal control group, $P < 0.05$.

^b Compared with the bacterial translocation-negative group, $P < 0.05$.

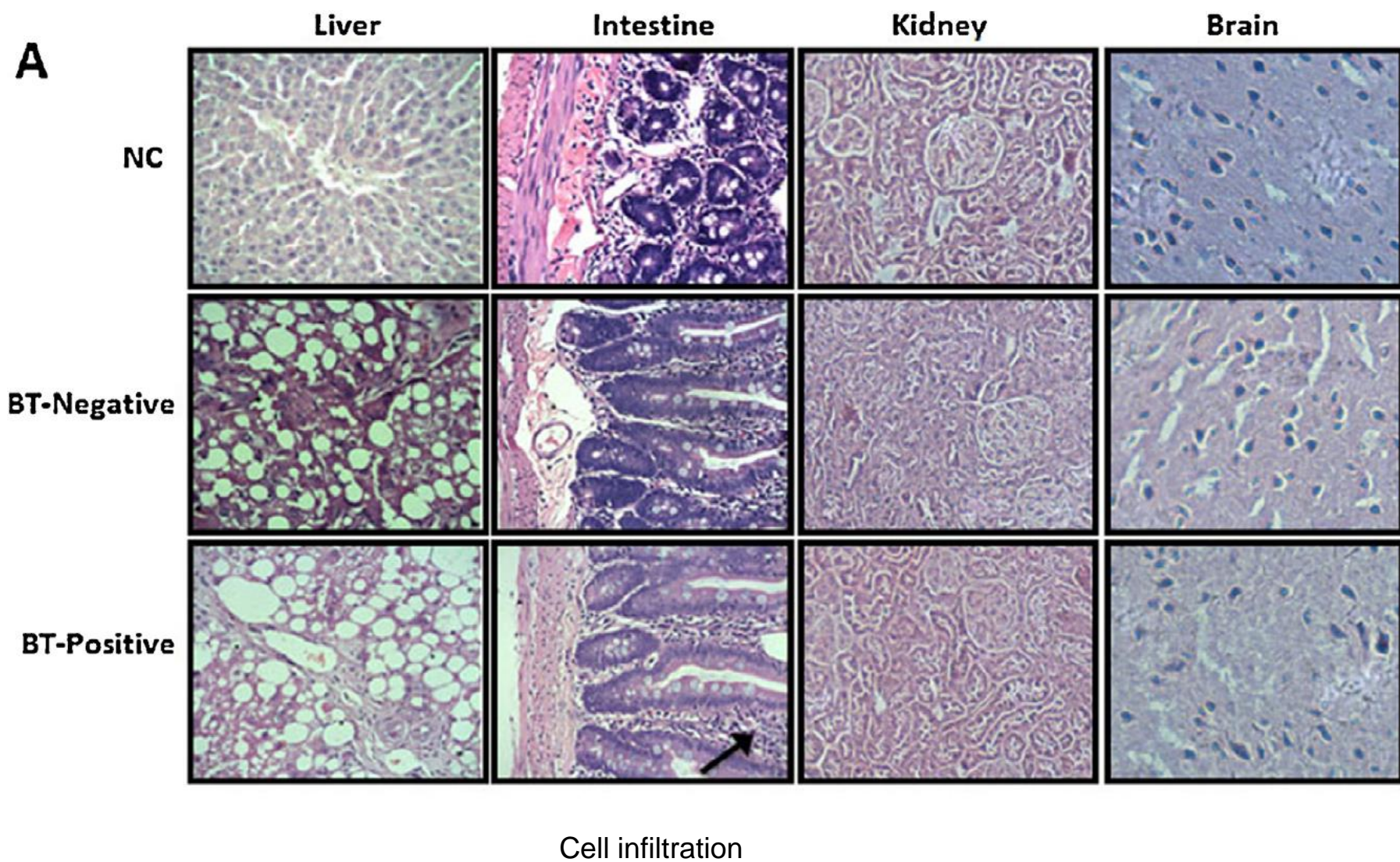
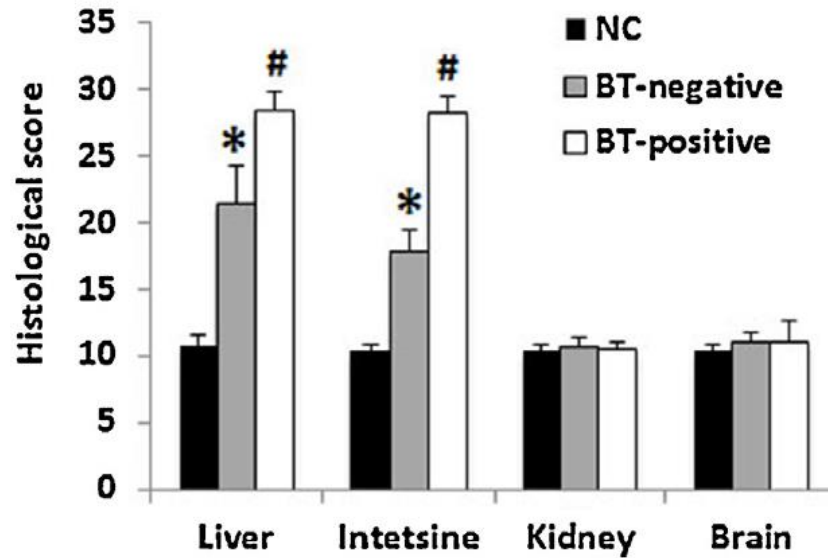
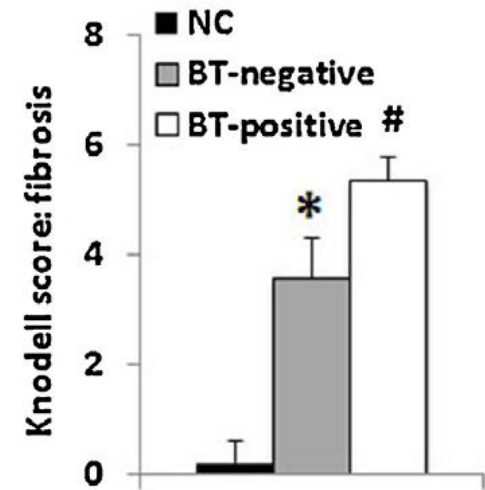


Figure 1

B**C**

The histological score is based on area of inflammatory lesions:

- The sum of the scores from 10 different microscopy fields
 - $< 1/3$ total area \rightarrow 1 point
 - $1/3 - 2/3$ total area \rightarrow 2 points
 - $> 2/3$ total area \rightarrow 3 points

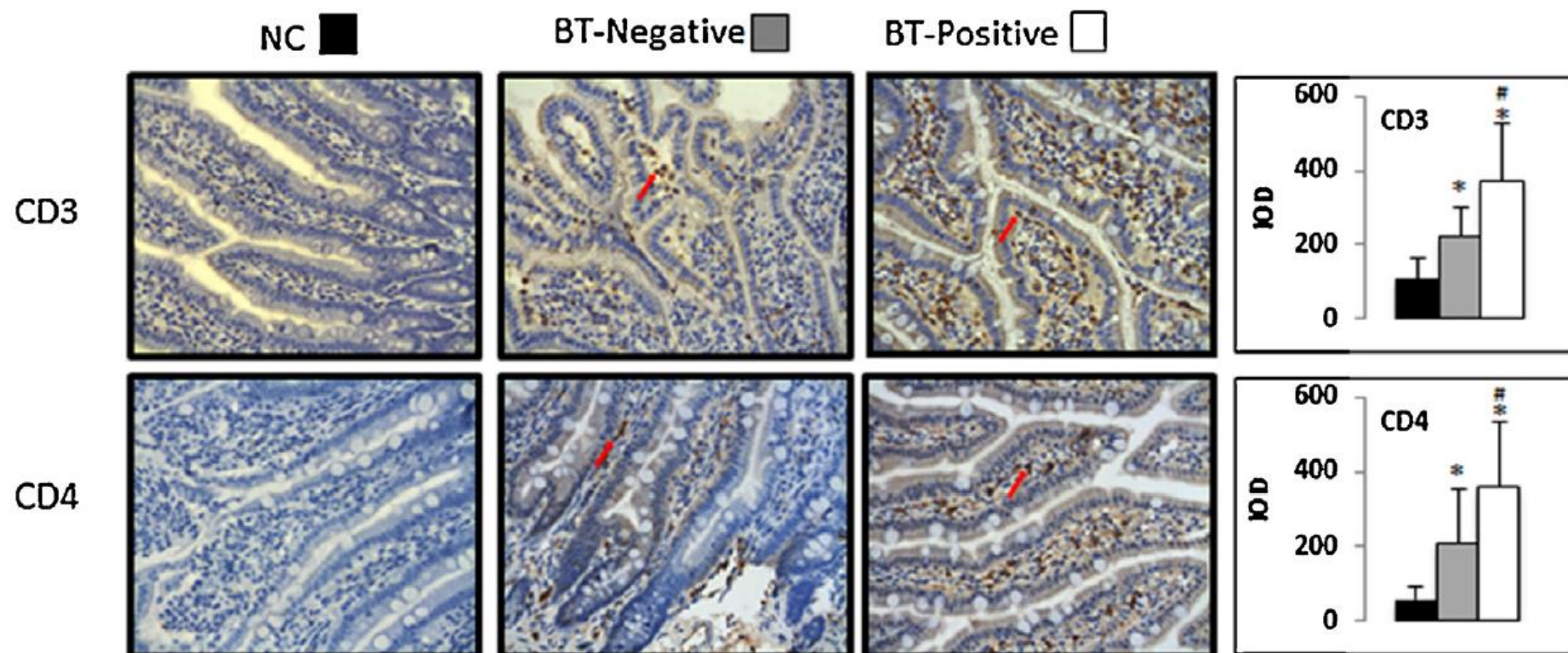
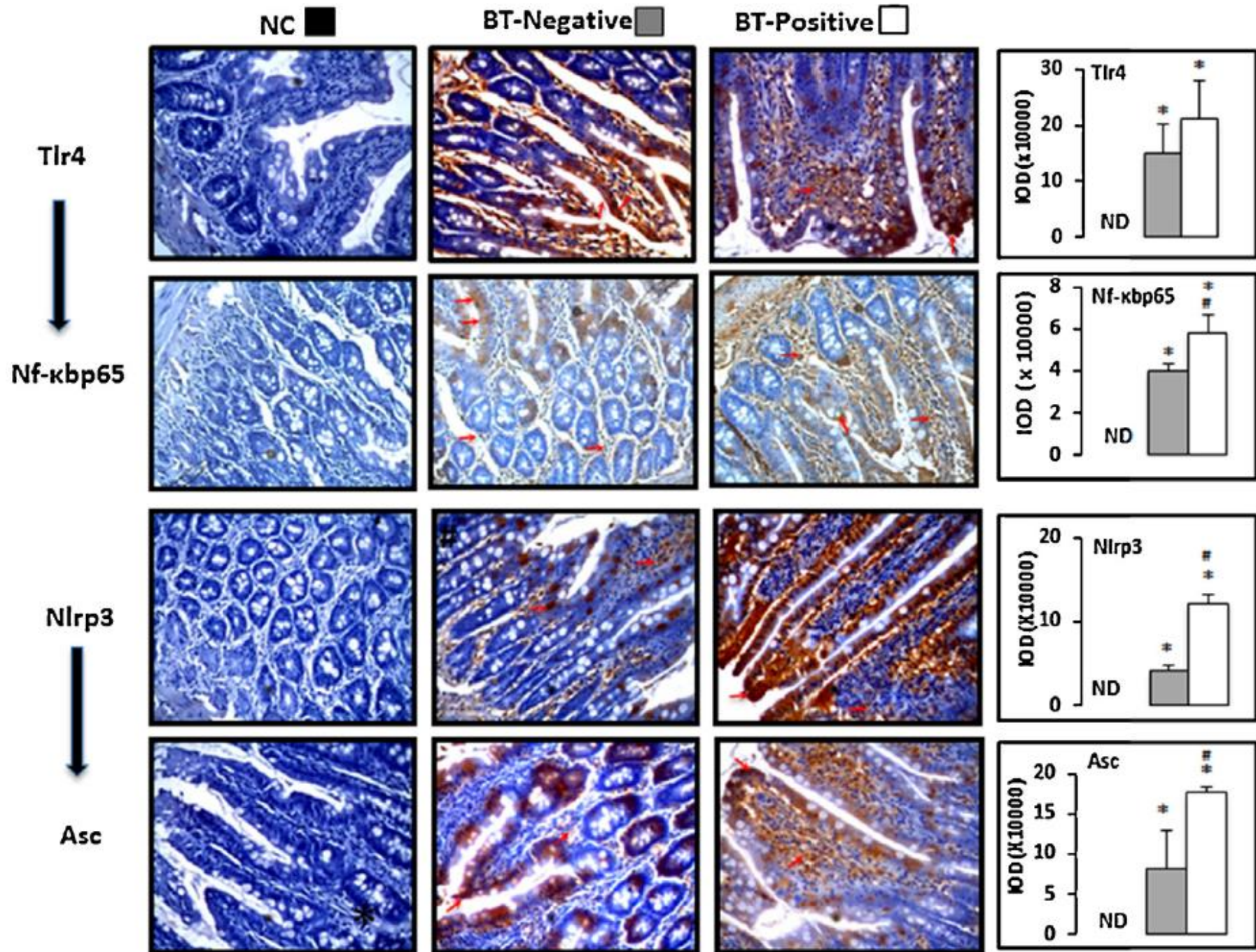


Figure 2



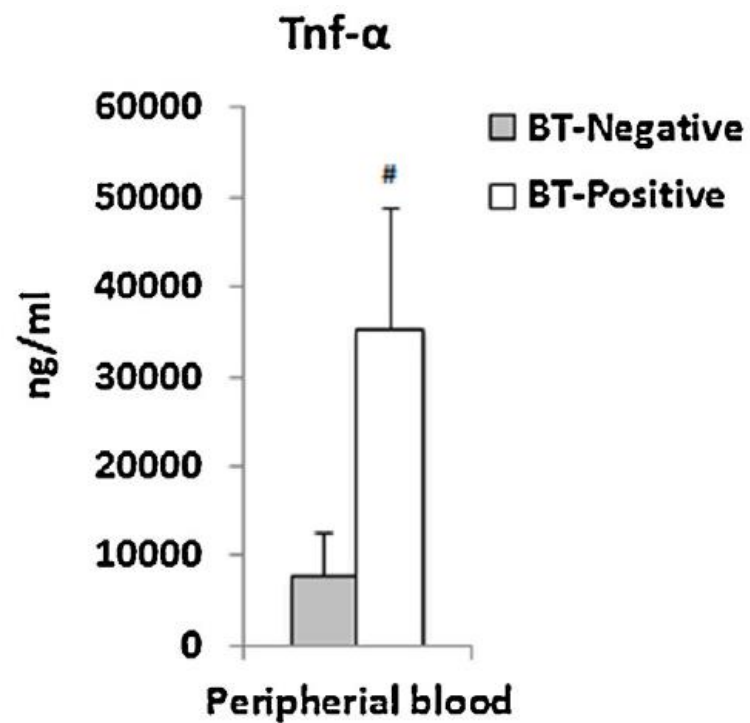
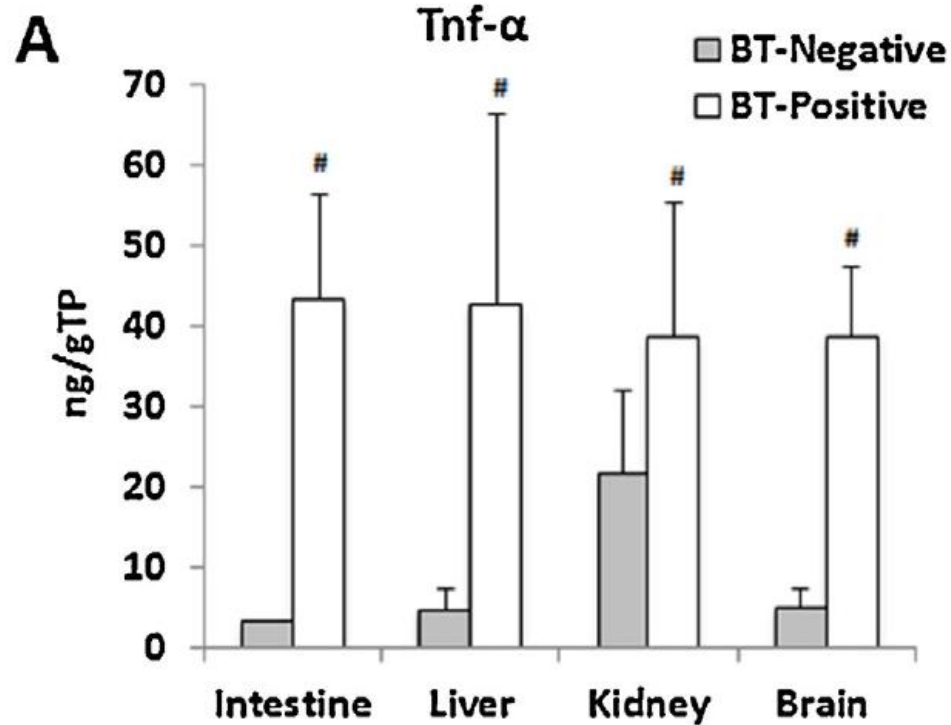


Figure 4

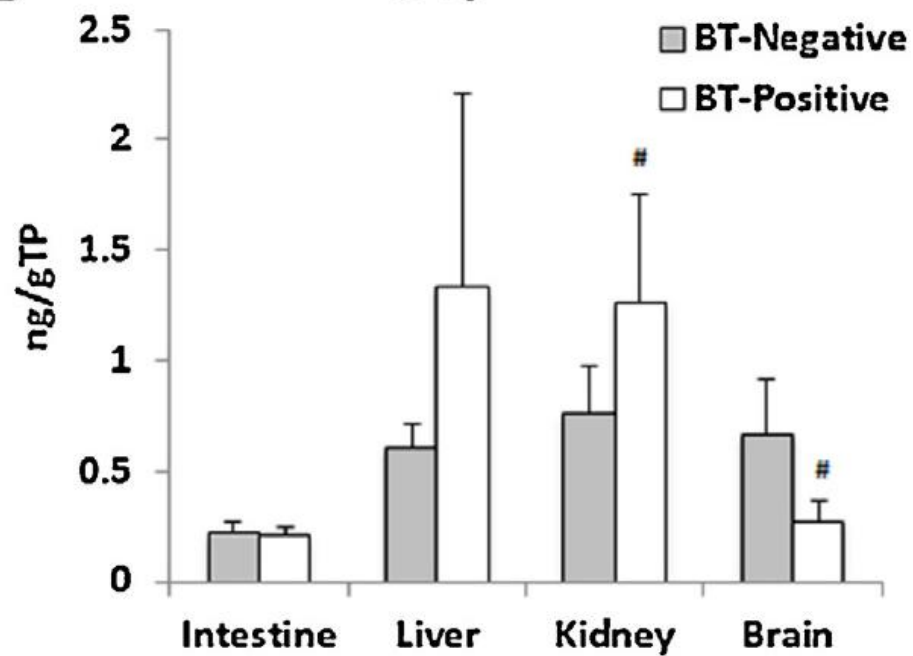
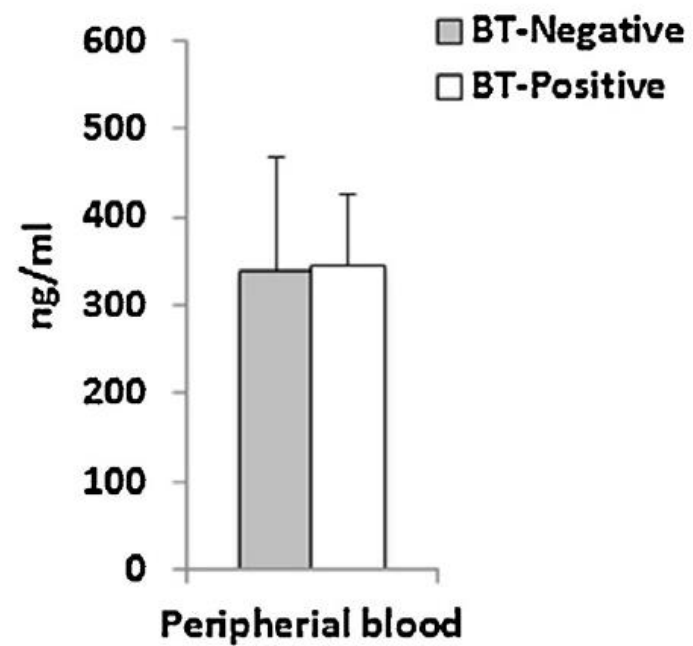
B**IL-1 β** **IL-1 β** 

Figure 4

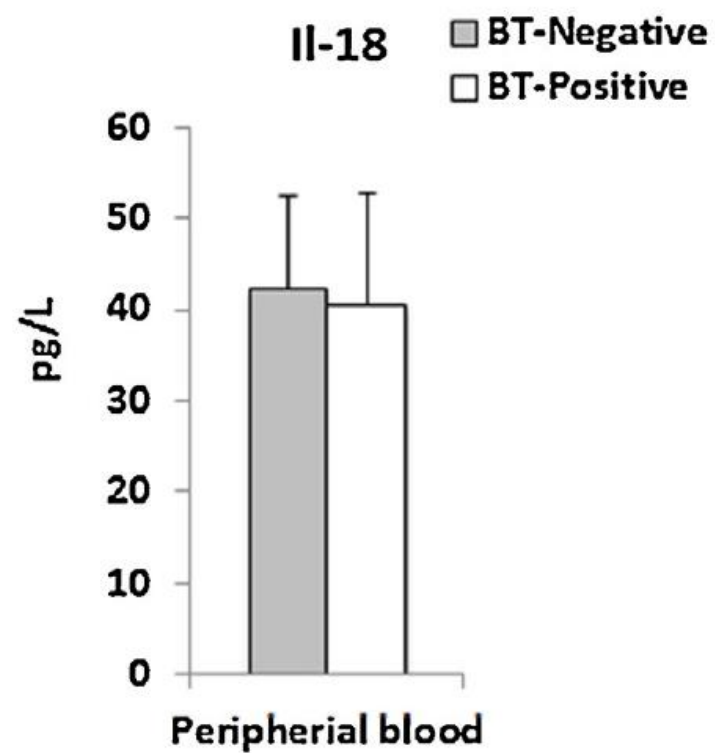
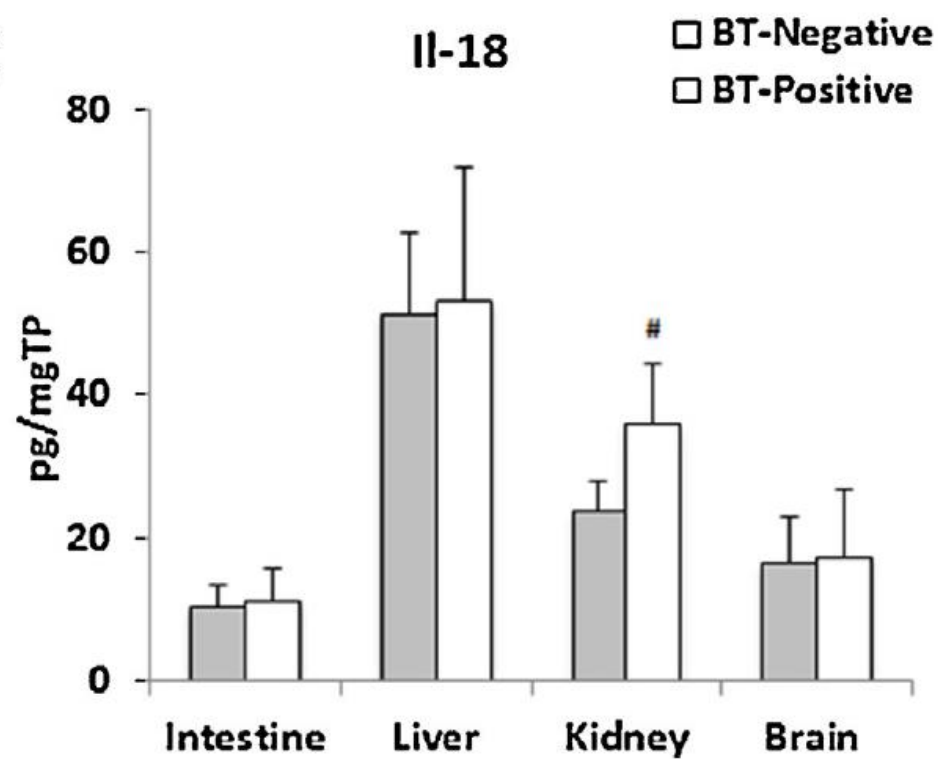
C

Figure 4

Summary:

- BT positive rats:
 - showed an increased liver injury.
 - Increased intestinal edema and cell infiltration.
 - Showed strong NFkB activation and TNF-a but not TLR4 activation suggesting an abnormal TLR4 signal transduction in these animals.
 - NLRP3/ASC activation did not correlate with IL1b/IL-18 production
→ Abnormal NLRP3 and Pro-IL1b/18 proteasomal degradation