Table S1.

Subject Characteristics

	Gender	Age		MELD score	
Controls n=14	F:36%(5)	46.4±3.4	F:46.8±9.4	NA	
	M:64%(9)		M:46.4±2.3		
Alcoholic cirrhosis n=28	F:21%(6)	45.7±1.4	F:44.5±2.6	<9	56.6% (15)
				10–19	35.7% (10)
	M:79%(22)		M:46±1.7	20–29	7.1% (2)
				30–39	3.6% (1)
Hepatitis B cirrhosis n=43	F:23%(10)	49.6±1.6	F:49.3±2.9	<9	67.4% (29)
				10–19	27.9% (12)
	M:77%(33)		M:49.7±1.9	20–29	4.7% (2)
				30–39	0

MELD=Model for end stage liver disease, M=male, F=female, NA=not applicable

Table S2.

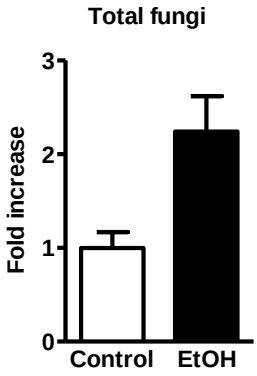
Subject Characteristics

	Gender	Age		Alcoholic liver disease
Controls n=8	F:16%(2)	41.2±4.2	F:54±3	NA
	M:84%(6)		M:37±4.3	
Non-progressive alcoholic liver disease n=10	F:20%(2)	50.9±3.2	F:55±2	No liver disease (2) Mild liver disease (8)
	M:80%(8)		M:49.9±4	
Alcoholic hepatitis n=6	F:50%(3)	52.7±3.5	F:53±6.8	MELD 22±1.6
	M:50%(3)		M:52.3±4.3	
Alcoholic cirrhosis n=4	F:33%(1)	47.5±6.8	F:54	Child Pugh A (2) Child Pugh C (2)
	M:67%(3)		M:45±9.1	

MELD=Model for end stage liver disease, M=male, F=female, NA=not applicable
Mild liver disease: AST/ALT elevation and/or hepatic steatosis on imaging

Figure S1

A



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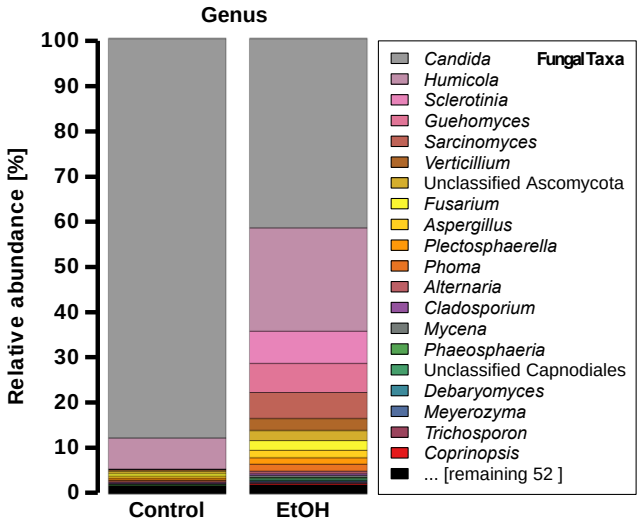

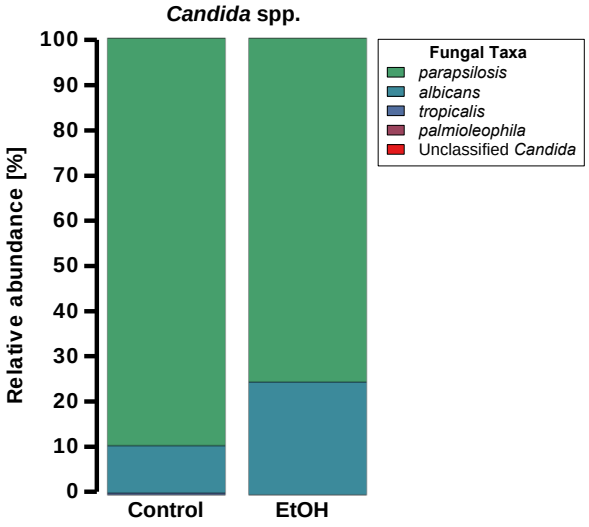

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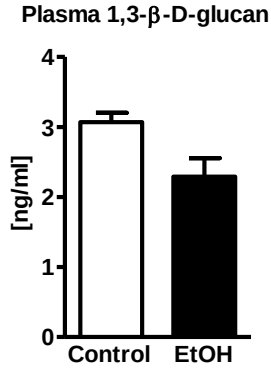

Figure S1

Figure S1. Changes in the intestinal mycobiota and translocation of fungal products following chronic alcohol feeding. (A and C) C57BL/6 mice were fed an oral control diet (n=4–5) or ethanol diet (n=4–14) for 5 weeks. Total fungi in feces were assessed by qPCR (A), and mean plasma levels of 1,3-β-D-glucan were measured by ELISA (C). (B) ITS sequencing of fecal samples from C57BL/6 mice that were fed an oral control diet (n=9) or ethanol diet (n=9) for 8 weeks. The graph demonstrates the average relative abundance of sequence reads in each fungal genus (left panel) and *Candida* species (right panel) for control and for ethanol-fed mice. Unpaired Student *t* test.

Figure S2

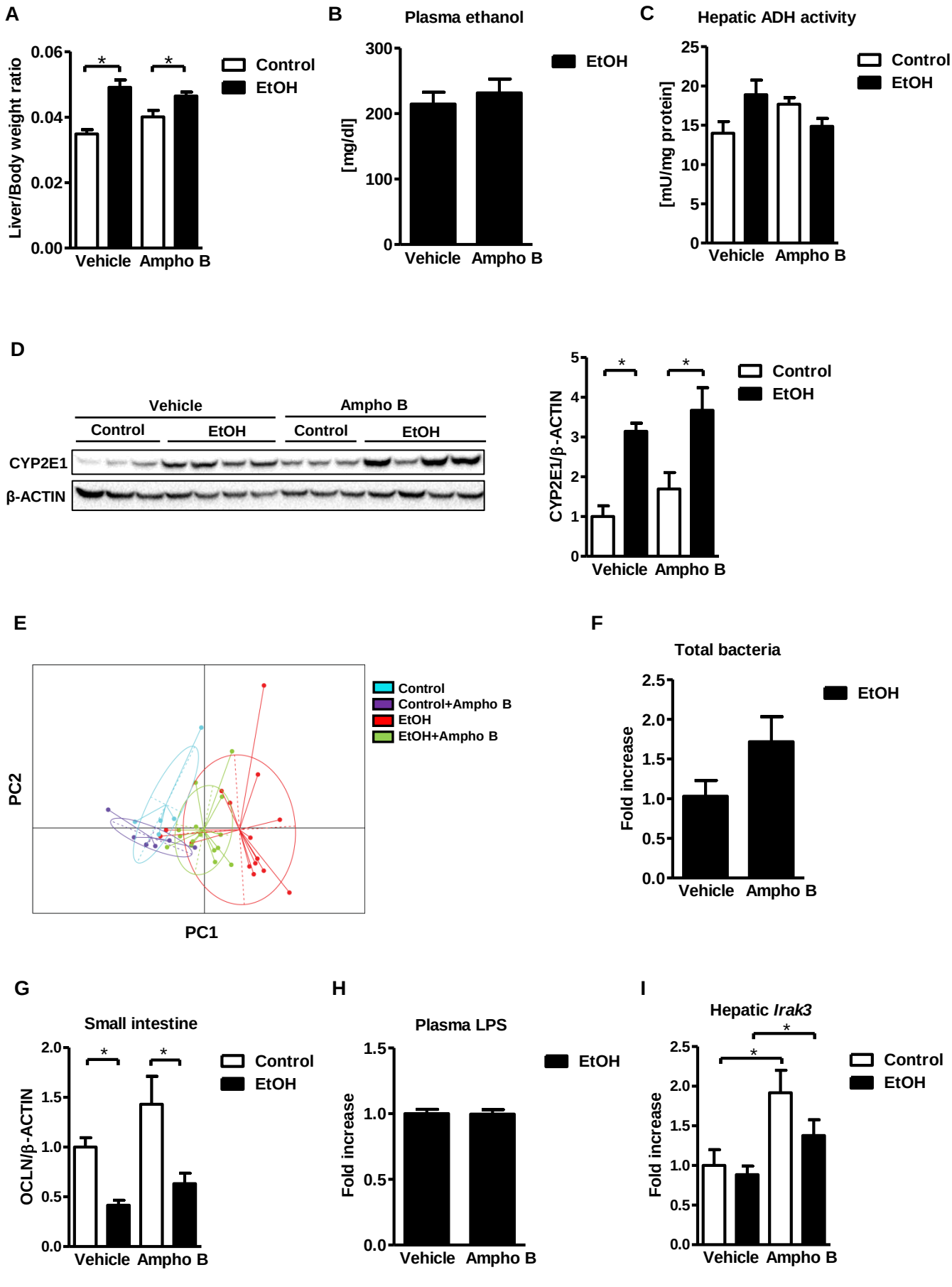
A
Liver/Body weight ratio
0.06
0.04
0.02
0.00
*
*
Vehicle
Ampho B
Control
EtOH
B
Plasma ethanol
[mg/dl]
300
200
100
0
Vehicle
Ampho B
EtOH
C
Hepatic ADH activity
[mU/mg protein]
25
20
15
10
5
0
Vehicle
Ampho B
Control
EtOH
D
Vehicle
Ampho B
Control
EtOH
Control
EtOH
CYP2E1
β-ACTIN
CYP2E1/β-ACTIN
5
4
3
2
1
0
*
*
Vehicle
Ampho B
Control
EtOH
E
PC2
PC1
Control
Control+Ampho B
EtOH
EtOH+Ampho B
F
Total bacteria
Fold increase
2.5
2.0
1.5
1.0
0.5
0.0
Vehicle
Ampho B
EtOH
G
Small intestine
OCLN/β-ACTIN
2.0
1.5
1.0
0.5
0.0
*
*
Vehicle
Ampho B
Control
EtOH
H
Plasma LPS
Fold increase
1.5
1.0
0.5
0.0
Vehicle
Ampho B
EtOH
I
Hepatic Irak3
Fold increase
2.5
2.0
1.5
1.0
0.5
0.0
*
*
Vehicle
Ampho B
Control
EtOH

Figure S2

Figure S2. Absorption and hepatic metabolism of ethanol. C57BL/6 mice were fed an oral control diet (n=5–6) or ethanol diet (n=12–15), and also given vehicle or amphotericin B (Ampho B). (A) Ratio of liver to body weight. (B) Plasma level of ethanol at time of harvesting. (C) Hepatic ADH activity. (D) Immunoblot analysis of hepatic CYP2E1 (n=5 for mice fed a control diet, n=8 for mice fed an ethanol diet). (E) Principal component analysis (PCA) of bacterial microbiomes. (F) Total bacteria in feces were assessed by qPCR. (G) Immunoblot analysis of OCLN (occludin) in the small intestine (n=5 in each group). (H) Plasma LPS. (I) Hepatic expression of *Irak3* mRNA. Unpaired Student t test. *P<.05.

Figure S3

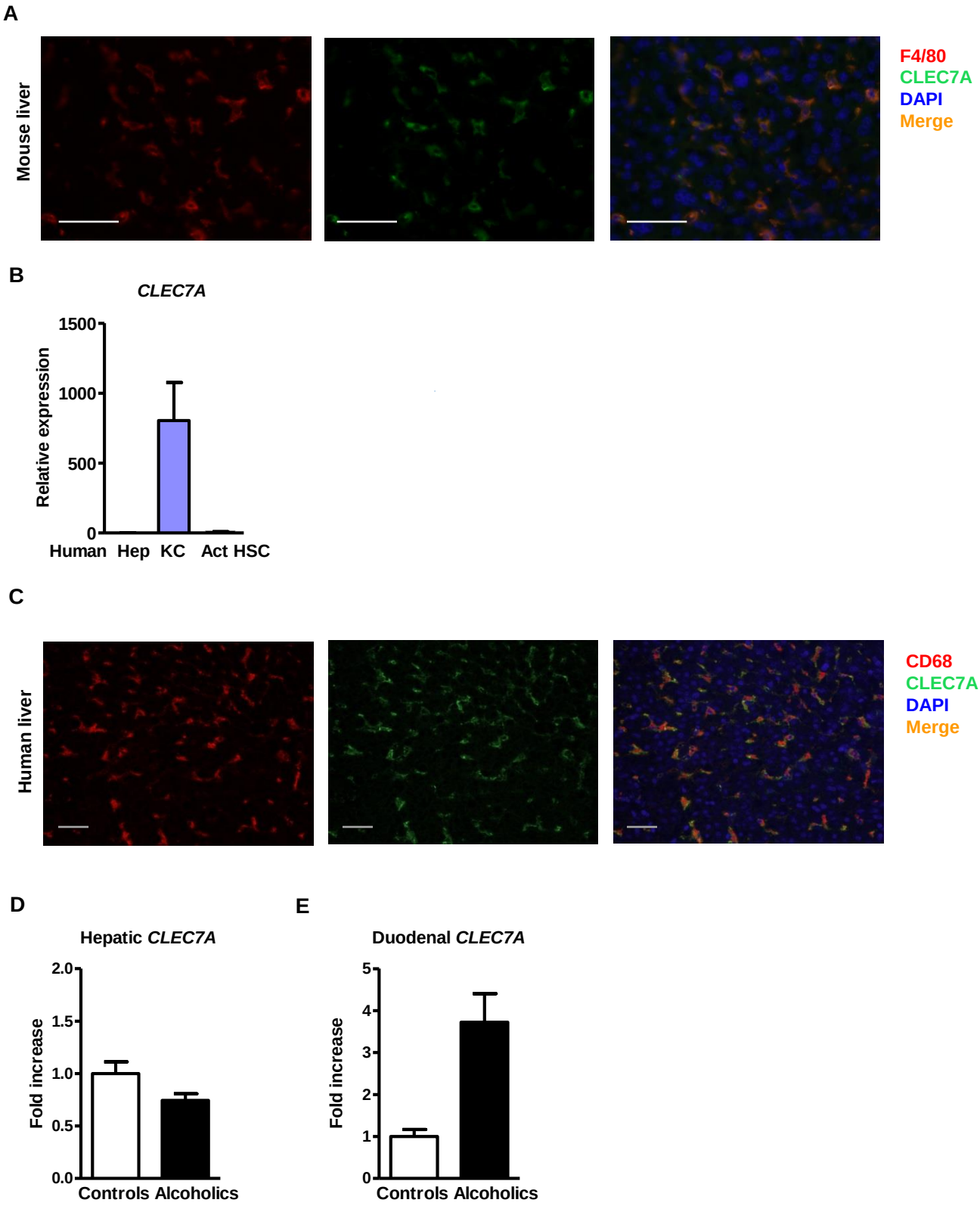
A
Mouse liver
F4/80
CLEC7A
DAPI
Merge
B
CLEC7A
Relative expression
1500
1000
500
0
Human
Hep
KC
Act HSC
C
Human liver
CD68
CLEC7A
DAPI
Merge
D
Hepatic CLEC7A
Fold increase
2.0
1.5
1.0
0.5
0.0
Controls
Alcoholics
E
Duodenal CLEC7A
Fold increase
5
4
3
2
1
0
Controls
Alcoholics

Figure S3

Figure S3. Expression of CLEC7A. (A) Immunofluorescence analysis of F4/80 (red) and CLEC7A (green) in non-diseased mouse liver (representative liver sections); nuclei are blue. (B) Expression of *Clec7a* in primary human hepatocytes (Hep), Kupffer cells (KC), and activated hepatic stellate cells (Act HSC) was measured by qPCR (n=2 independent experiments). (C) Immunofluorescence analysis of CD68 (red) and CLEC7A (green) in non-diseased human liver (representative liver sections); nuclei are blue. (D) Expression of *CLEC7A* mRNA in hepatic biopsies from controls without alcohol dependency (n=9) and alcohol-dependent patients (n=65). (E) Expression of *CLEC7A* mRNA in duodenal biopsies from controls without alcohol dependency (n=12) and alcohol-dependent patients (n=110). Scale bars, 50μm. Unpaired Student t test. *P<.05.

Figure S4

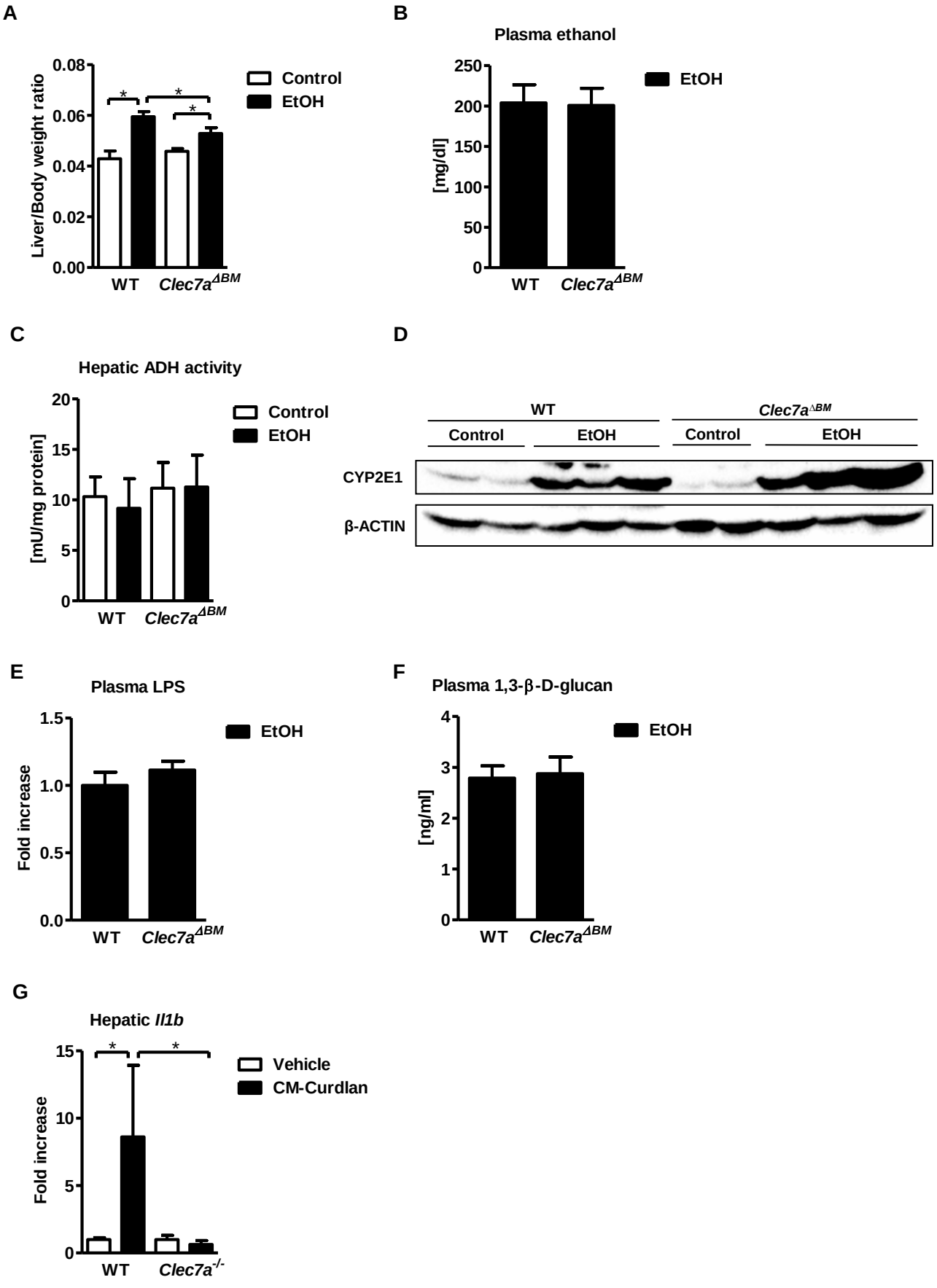
A
Liver/Body weight ratio
0.08
0.06
0.04
0.02
0.00
Control
EtOH
WT
Clec7a ΔBM
B
Plasma ethanol
[mg/dl]
250
200
150
100
50
0
EtOH
WT
Clec7a ΔBM
C
Hepatic ADH activity
[mU/mg protein]
20
15
10
5
0
Control
EtOH
WT
Clec7a ΔBM
D
WT
Clec7a ΔBM
Control
EtOH
Control
EtOH
CYP2E1
β-ACTIN
E
Plasma LPS
Fold increase
1.5
1.0
0.5
0.0
EtOH
WT
Clec7a ΔBM
F
Plasma 1,3-β-D-glucan
[ng/ml]
4
3
2
1
0
EtOH
WT
Clec7a ΔBM
G
Hepatic Il1b
Fold increase
15
10
5
0
Vehicle
CM-Curdlan
WT
Clec7a -/-

Figure S4

Figure S4. Absorption and hepatic metabolism of ethanol. C57BL/6 mice were transplanted with bone-marrow from WT (WT) or *Clec7a*$^{-/-}$ mice (*Clec7a*$^{\Delta BM}$) and fed an oral control diet (n=4–5) or ethanol diet (n=6–10). (A) Ratio of liver to body weight. (B) Plasma level of ethanol at time of harvesting. (C) Hepatic ADH activity. (D) Immunoblot analysis of hepatic CYP2E1. (E) Plasma LPS. (F) Plasma 1,3-β-D-glucan. (G) Hepatic expression of *Il1b* mRNA in WT (n=6) and *Clec7a*$^{-/-}$ mice (n=3) 2hrs after intraperitoneal injections with carboxymethyl-β-1,3-D-glucan (2mg/mouse). Unpaired Student *t* test (A–C, E–G). Mann-Whitney U-statistic test (H). **P*<.05.

Figure S5

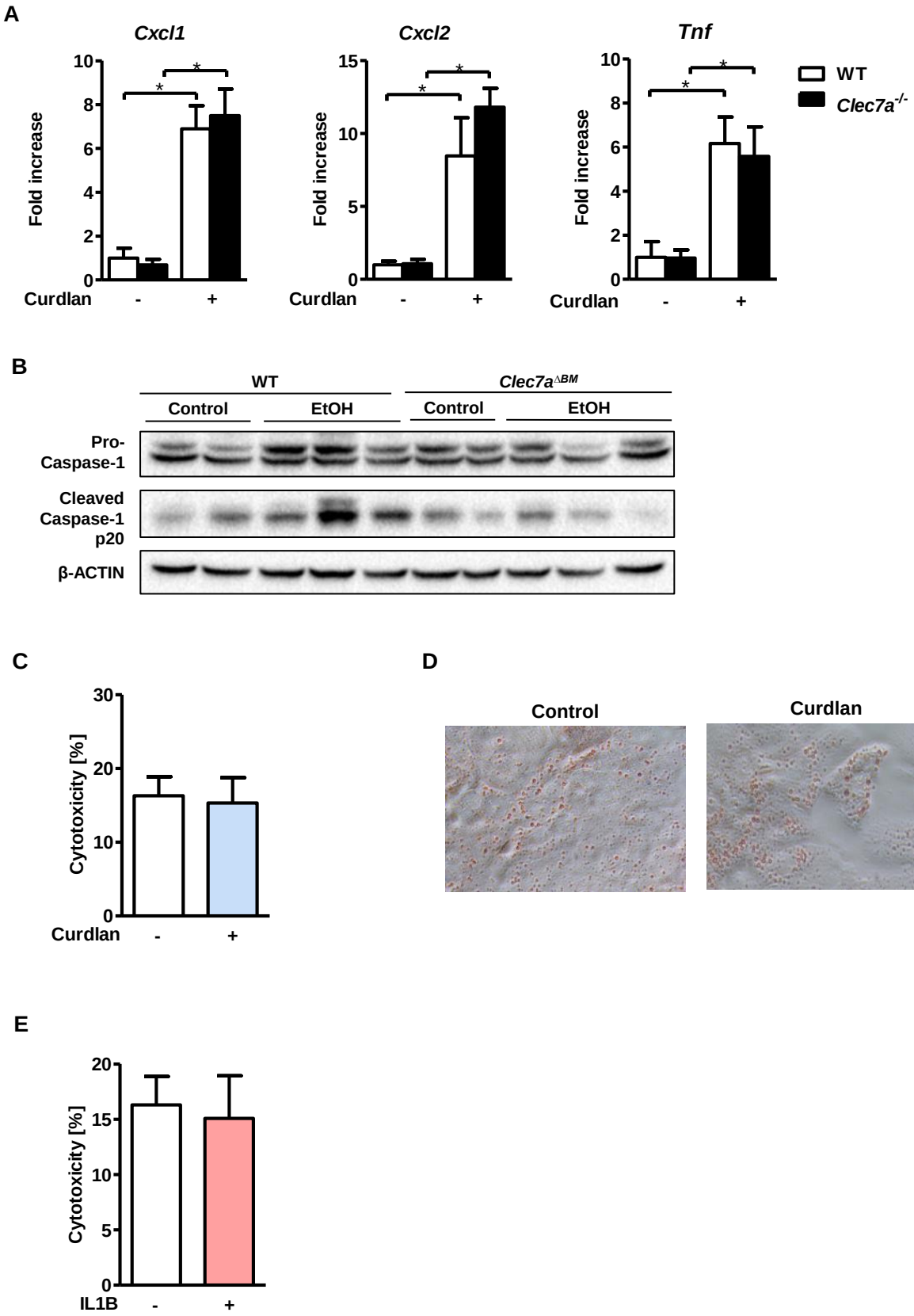
A
Cxcl1
Cxcl2
Tnf
Fold increase
Curdlan
WT
Clec7a-/-
B
WT
Clec7aΔBM
Control
EtOH
Pro-Caspase-1
Cleaved Caspase-1 p20
β-ACTIN
C
Cytotoxicity [%]
D
Control
Curdlan
E
IL1B

Figure S5

Figure S5. Curdlan does not induce hepatocyte death or steatosis. (A) Primary mouse WT and *Clec7a*$^{-/-}$ Kupffer cells were stimulated with curdlan; graphs show expression of *Cxcl1, Cxcl2* and *Tnf* mRNA (n=4–6 independent experiments). (B) C57BL/6 mice were transplanted with WT (WT) or *Clec7a*$^{-/-}$ bone-marrow (*Clec7a*$^{\Delta BM}$) and fed an oral control diet or ethanol diet. Hepatic caspase-1, cleaved caspase-1 and β-actin protein. (C–D) Hepatocytes were stimulated with curdlan. Hepatocyte cytotoxicity (C) and lipid accumulation as determined by Oil Red O-staining (D); n=3 independent experiments. (E) Hepatocytes were stimulated with IL1B and hepatocyte cytotoxicity measured; n=3 independent experiments. Unpaired Student t test. **P*<.05.

Figure S6

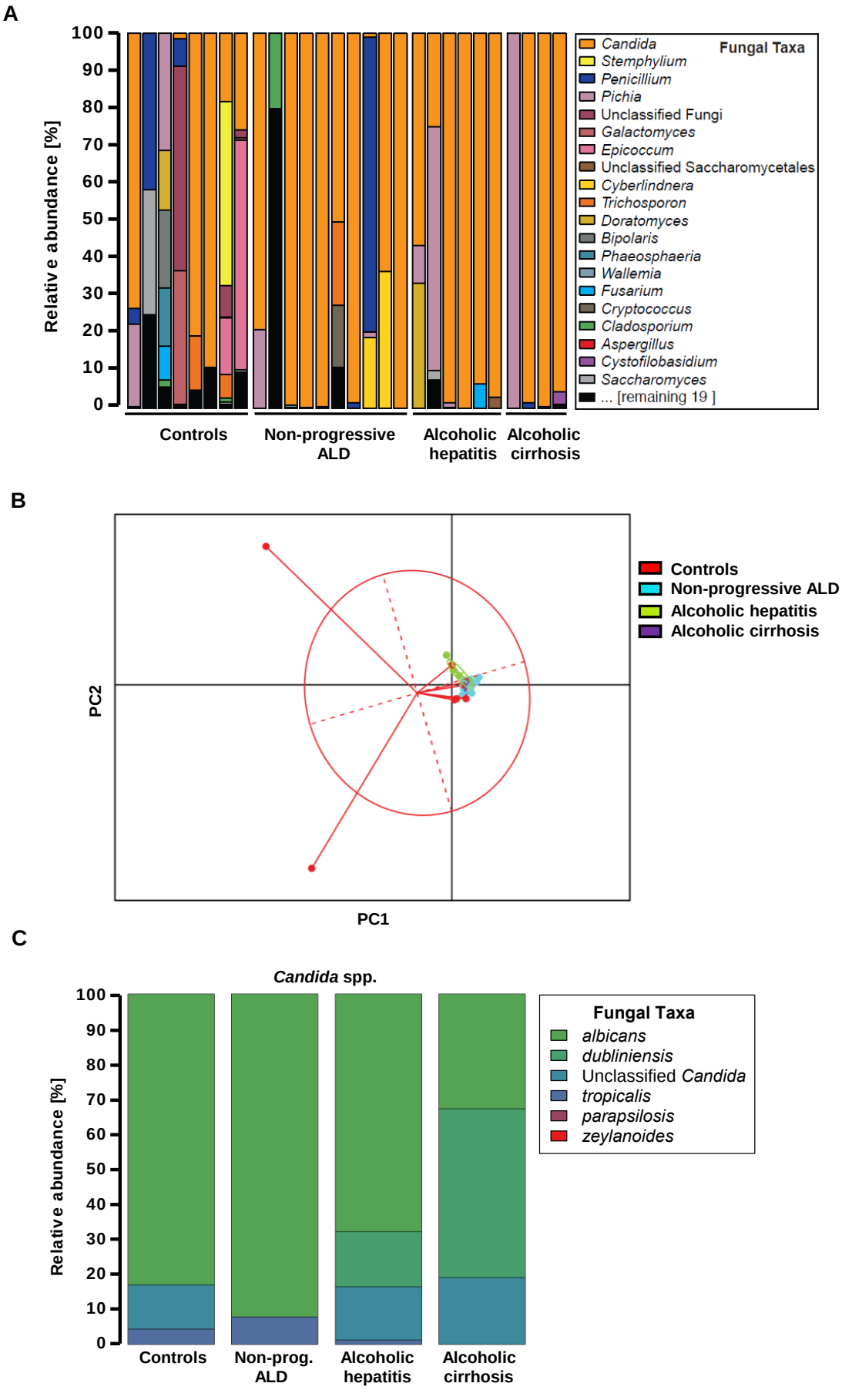
A
Relative abundance [%]
100
90
80
70
60
50
40
30
20
10
0
Fungal Taxa
Candida
Stemphylium
Penicillium
Pichia
Unclassified Fungi
Galactomyces
Epicoccum
Unclassified Saccharomycetales
Cyberlindnera
Trichosporon
Doratomyces
Bipolaris
Phaeosphaeria
Wallemia
Fusarium
Cryptococcus
Cladosporium
Aspergillus
Cystofilobasidium
Saccharomyces
... [remaining 19]
Controls
Non-progressive ALD
Alcoholic hepatitis
Alcoholic cirrhosis
B
PC2
PC1
Controls
Non-progressive ALD
Alcoholic hepatitis
Alcoholic cirrhosis
C
Candida spp.
Relative abundance [%]
100
90
80
70
60
50
40
30
20
10
0
Fungal Taxa
albicans
dubliniensis
Unclassified Candida
tropicalis
parapsilosis
zeylanoides
Controls
Non-prog. ALD
Alcoholic hepatitis
Alcoholic cirrhosis

Figure S6

Figure S6. Intestinal fungal dysbiosis in patients with alcohol abuse. ITS sequencing of fecal samples from controls (controls, n=8) or alcohol-dependent patients with non-progressive alcoholic liver disease (non-progressive ALD, n=10), alcoholic hepatitis (alcoholic hepatitis, n=6), or alcoholic cirrhosis (alcoholic cirrhosis, n=4). (A) The graph demonstrates the relative abundance of sequence reads in each genus for each individual person. (B) PCA of mycobiomes. (C) *Candida* species composition of human fungal ITS sequences from Fig. 6A divided into four groups: (controls; n=8), alcohol-dependent patients with non-progressive alcoholic liver disease (non-prog. ALD; n=10), alcoholic hepatitis (alcoholic hepatitis; n=6), or alcoholic cirrhosis (alcoholic cirrhosis; n=4).