SUPPLEMENTAL INFORMATION

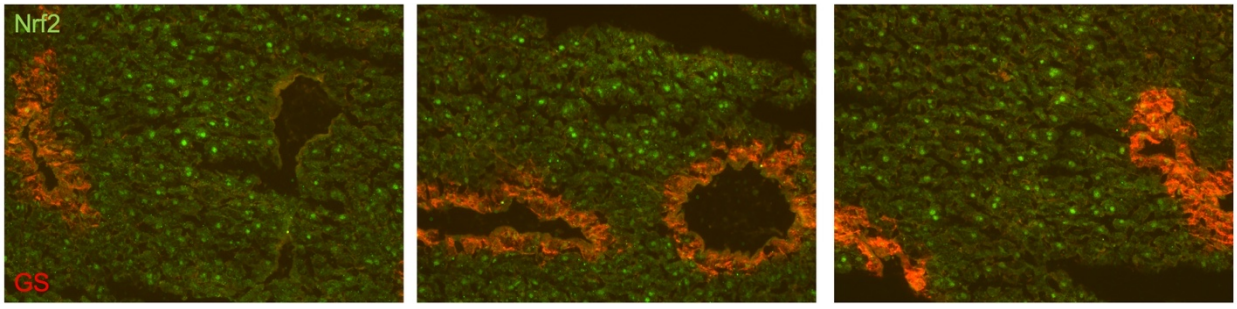

Figure S1. Zonal distribution of hepatic Nrf2 activation after LGG gavage (Related to Figure 3). Representative immunofluorescent images (20x) of liver tissues from LGG gavaged animals immunostained for Nrf2 (green) and glutamine synthetase (GS – red), a marker of pericentral hepatocytes.

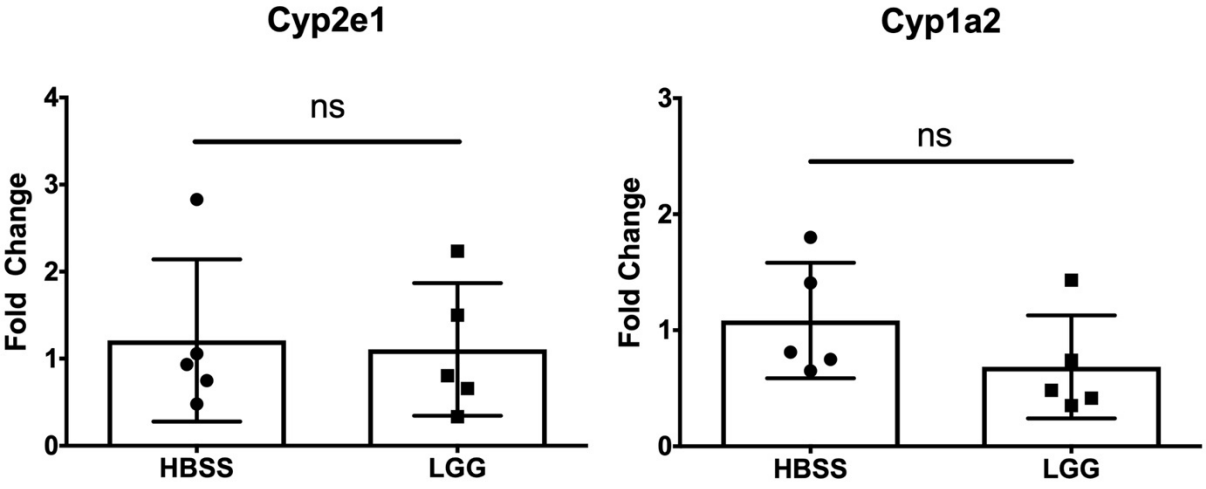

Figure S2. Steady-state mRNA levels of acetaminophen metabolizing enzymes (Related to Figure 5). RT-PCR for the mRNA levels of cytochrome P450 2e1 and 1a2 in liver tissue after 2

weeks of oral HBSS or LGG gavage. ns=not significant as determined by t-test. n=5 mice per group.

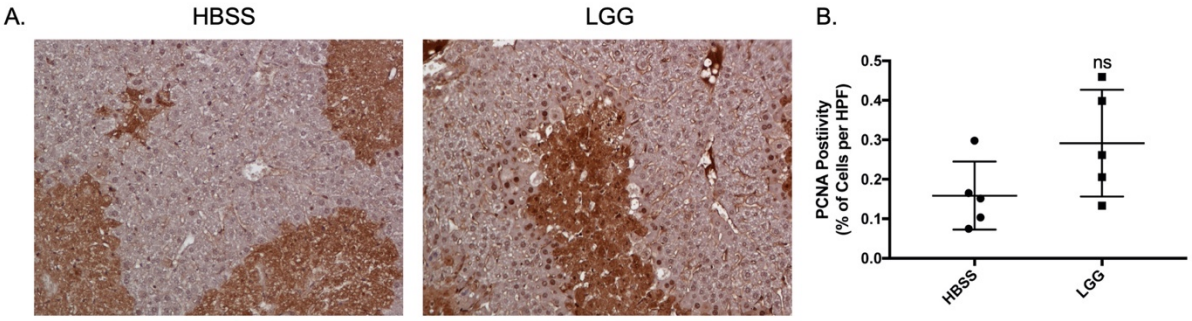

Figure S3. Hepatocyte proliferation 24 hours post-acetaminophen overdose (Related to Figure 5). **(A)** Representative immunohistochemical images of HBSS or LGG pretreated animals 24 hours after acetaminophen overdose for PCNA (a marker of hepatocyte proliferation). **(B)**

Quantification of percent PCNA positive cells per high powered field. ns=not significant as determined by t-test. n=5 mice per group.

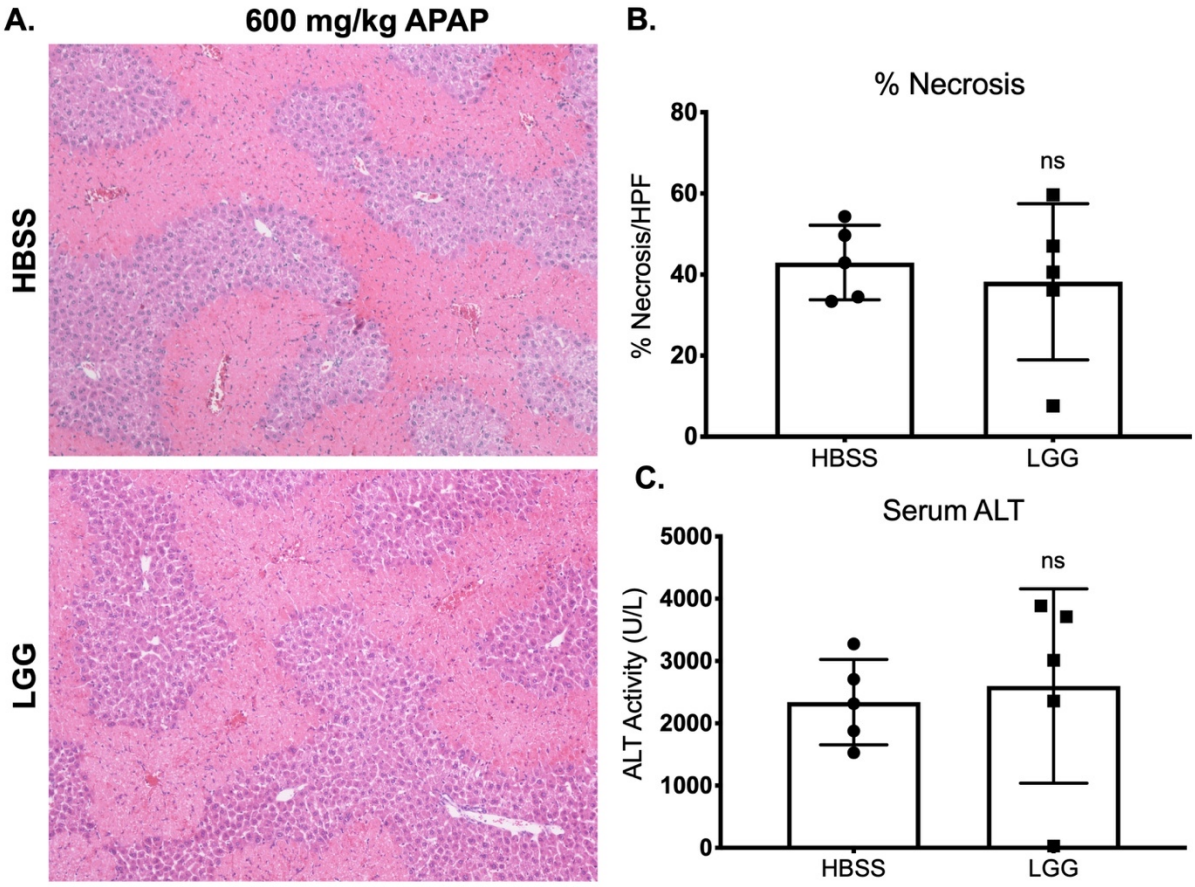

Figure S4. Effect of *Lactobacillus rhamnosus* GG administration on high dose acetaminophen hepatotoxicity (Related to Figure 5). (A) Representative H&E of mouse liver from HBSS or LGG pretreated animals 24 hours after oral overdose with 600 mg/kg acetaminophen**. (B)** Quantification of percent necrosis/HPF from histology in (A). **(C)** Serum ALT levels at 24 hours

post overdose of mice described in (A). ns=not significant as determined by t-test. n=5 mice per group.

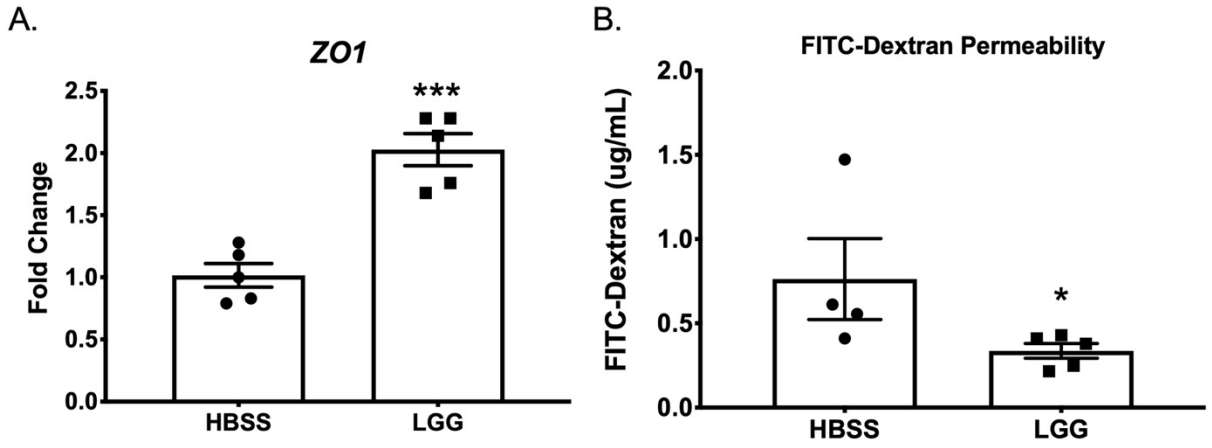

Figure S5. Effect of *Lactobacillus rhamnosus* GG on intestinal barrier function (Related to Figure 5). (A) RT-PCR for the steady state mRNA levels of the tight junction protein *ZO1* in colonic epithelium from animals treated by daily oral gavage with either HBSS (vehicle) or LGG.

(B) FITC-Dextran concentration in systemic serum 4 hours post gavage of FITC-Dextran from animals treated in (A). *p<0.05, **p<0.01, ***p<0.002 as determined by t-test. n=5

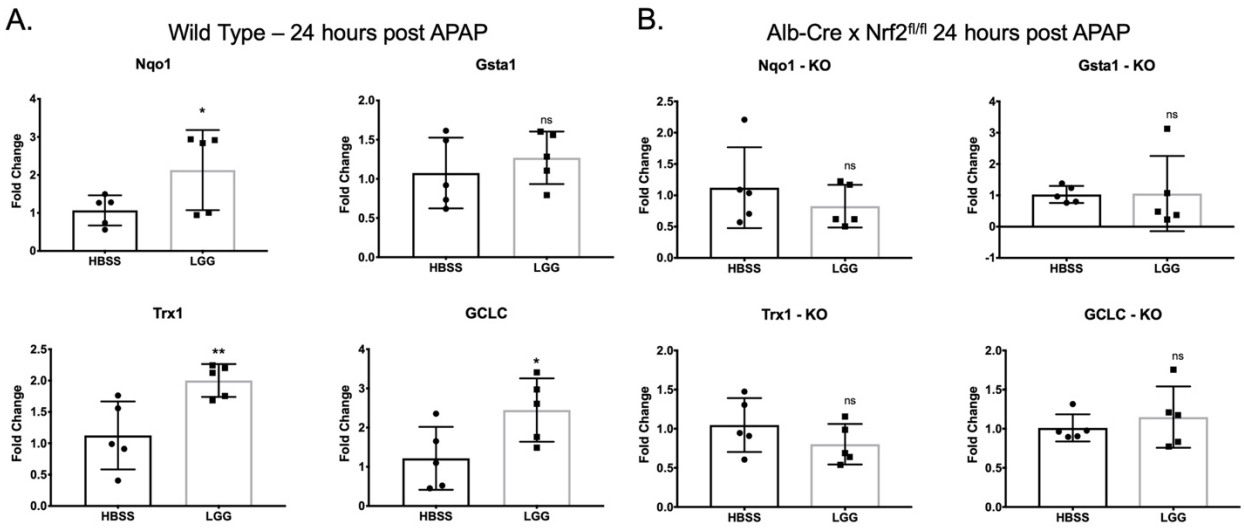

Figure S6. Effect of LGG on Nrf2 target transcripts after APAP overdose in WT and liver specific Nrf2 KO liver tissue (Related to Figures 5 and 6). (A) RT-PCR for the steady state mRNA levels of the Nrf2 target genes *Nqo1*, *Gsta1*, *Trx1*, and *Gclc* in liver tissue for HBSS (vehicle) or LGG pretreated WT mice 24 hours post oral overdose with 300 mg/kg APAP. **(B)** RT-

PCR for the same targets described in (A) after HBSS or LGG pretreatment and APAP overdose in Alb Cre x $Nrf2^{fl/fl}$ animals.

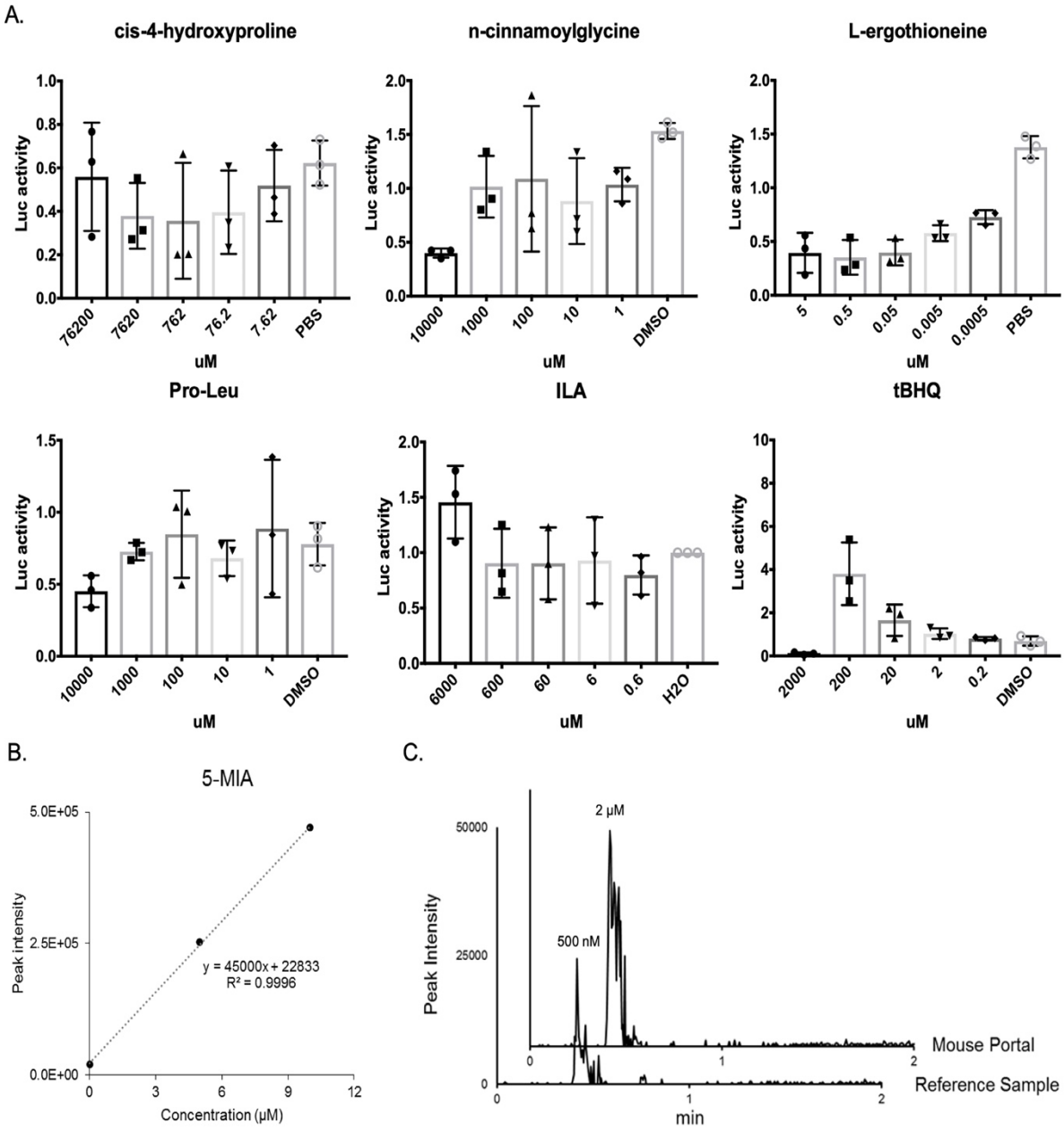

Figure S7. Characterization of compounds identified in the portal serum of LGG-treated mice (Related to Figure 7). (A) Luciferase activity in extracts of HepG2 cells which harbors a Nrf2 responsive promoter transcriptionally fused to *luc* upon exposure to the indicated

compounds for 12 hours. **(B)** Method of standards addition to determine concentration of 5-MIAA in plasma reference sample. **(C)** Reference standardization shows that 5-MIAA in mouse portal circulation after LGG administration is 2 uM.

Species	Gene	Primer	5' to 3'
Mouse	Actin	F	ACCTTCTACAATGAGCTGCG
		R	CTGGATGGCTACGTACATGG
	Nqo1	F	GGTAGCGGCTCCATGTACTC
		R	CGCAGGATGCCACTCTGAAT
	Gsta1	F	CCAGGACTCTCACTAGACCGT
		R	CAATCTCCACCATGGGCACT
	Trx1	F	AAGCTTGTCGTGGTGGACTT
		R	AACTCCCCCACCTTTTGACC
	Gclc	F	GGGAACGGACGGGACG
		R	CAACATGTACTCCACCTCGT
	Zo1	F	CCACAGCTGAAGGACTCACA
		R	ACTCCCACTTCCCCAAAAAC
	Cyp1a2	F	AACGTCATTGGTGCCATGTG
		R	ATACTGTTCTTGTTGAAGTCTTGGT
	Cyp2e1	F	GGAGAAGGAAAAACACAGCCAA
		R	CTCATGCACTACAGCGTCCA
Human	ACTIN	F	CCTGGCACCCAGCACAAT
		R	GCCGATCCACACGGAGTACT
	NQO1	F	ATCACAGGTAAACTGAAGGACCC
		R	ACTCGCTCAAACCAGCCTTT
	HMOX1	F	TTCAAGCAGCTCTACCGCTC
		R	GGGGCAGAATCTTGCACTTT
	GCLC	F	AAACAAGCACCCTCGCTTCA
		R	AGGCTTGGAATGTCACCTGG

Table S1. List and sequence for primers used for RT-PCR (Related to STAR methods section).