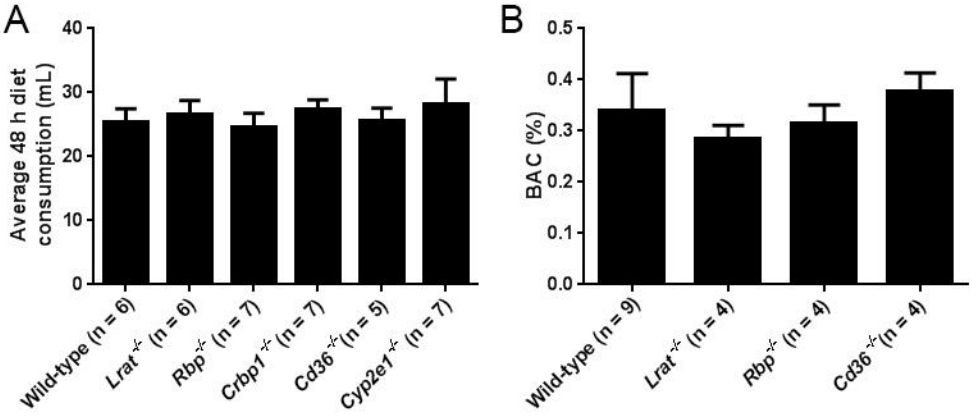
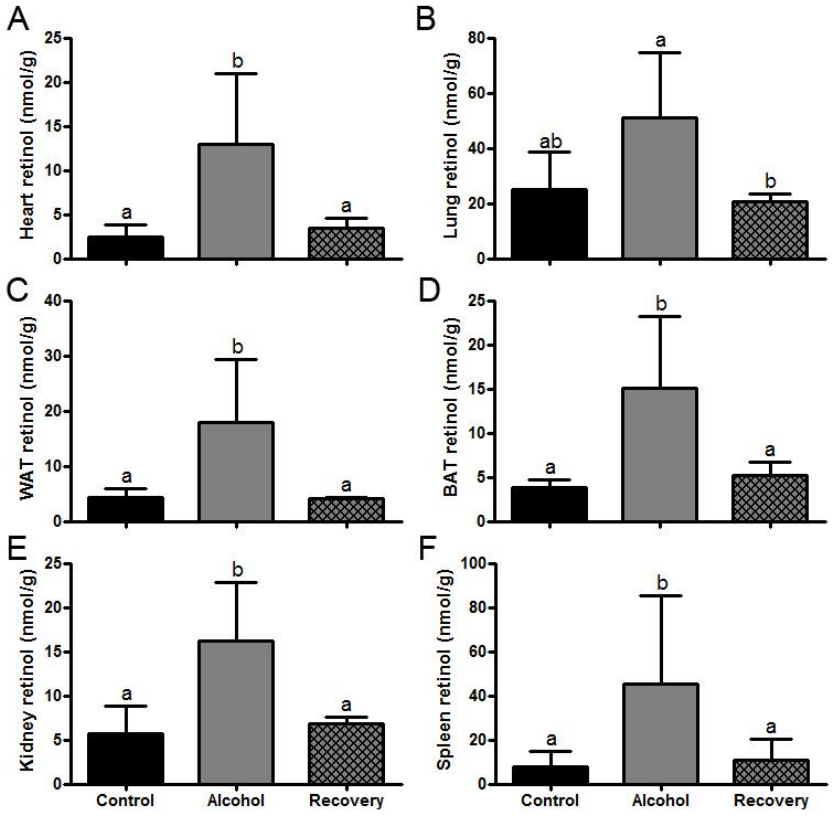
Supplemental data

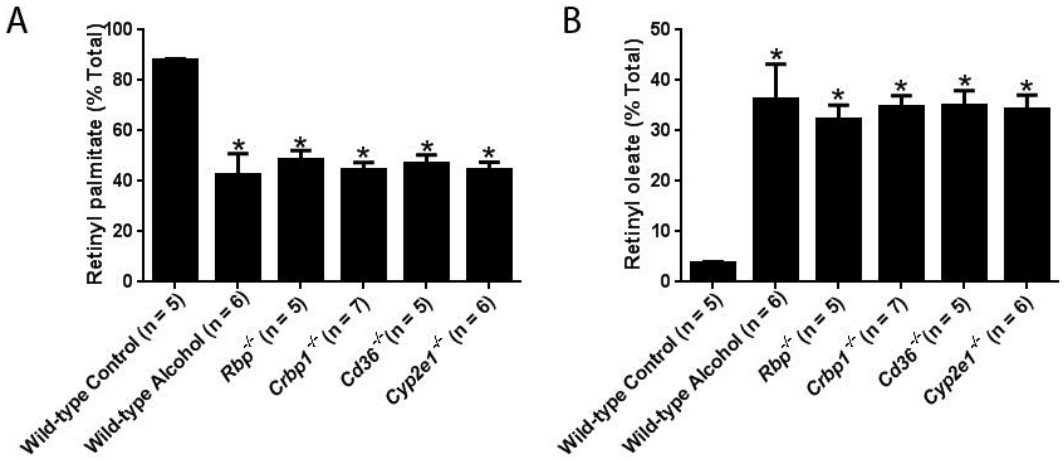


Supp. Fig. 1: Average liquid diet consumption and blood alcohol content is equal among different strains of experimental mice: Average liquid diet consumption over a 48 h period was not significantly different in different strains of experimental mice consuming 4.2% alcohol (A). Blood alcohol content (BAC) was not significantly different in WT, *Lrat*$^{-/-}$, *Rbp*$^{-/-}$, and *Cd36*$^{-/-}$ mice 4 h after an intraperitoneal injection of ethanol (3.5 mg/kg). One-way ANOVA, $p > 0.05$.



Supp. Fig. 2: The alcohol-induced increase in extrahepatic retinol levels is reversible following the cessation of alcohol consumption: Alcohol consumption is associated with increased levels of retinol in multiple extrahepatic tissues (n = 5-12), including the heart (A), Lung (B), WAT (C), BAT (D), kidney (E) and spleen (F); however, following

a recovery period of one month the levels of retinol in these extrahepatic tissues has returned to baseline. Columns that do not share a common letter are significantly different; one-way ANOVA, $p < 0.05$.



Supp. Figure 3: The alcohol-induced decrease in retinyl palmitate and compensatory increase in retinyl oleate is comparable in different strains of mice consuming alcohol. Alcohol has a profound effect on the acyl composition of hepatic retinyl esters. Here we show that the alcohol-induced change in hepatic retinyl ester acyl composition is identical in WT, *Rbp*$^{-/-}$, *Crbp1*$^{-/-}$, *Cd36*$^{-/-}$, and *Cyp2e1*$^{-/-}$ mice. No data is available for *Lrat*$^{-/-}$ mice because these mice have no hepatic retinyl ester stores. * $p < 0.05$ vs. wild-type control; one-way ANOVA.

Supp. Table 1: Body weight and liver weight in different strains of mice after the alcohol adaptation period. Chronic alcohol consumption is known to have an effect on body and liver weight; however, the majority of experiments described in this manuscript focused on the alcohol adaptation period where the greatest changes in hepatic retinoid metabolism were measured. At this early time, no significant effect of alcohol on body or liver weight was expected. Alcohol had no effect on body weight in WT, *Lrat*$^{-/-}$, *Rbp*$^{-/-}$, *Crbp1*$^{-/-}$ and *Cd36*$^{-/-}$ mice. In one experiment, alcohol was associated with decreased body weight in *Cyp2e1*$^{-/-}$ mice, but this effect was also observed in matching WT mice. Alcohol had no significant effect on liver weight in all strains of mice studied. In several cases, our analysis revealed genotypic differences in body and liver weight, such that *Crbp1*$^{-/-}$ and *Cyp2e1*$^{-/-}$ mice tended to be heavier than corresponding WT mice. Consistent with their phenotype, *Cd36*$^{-/-}$ mice tended to have a lower body weight and corresponding smaller livers.

	WT Control	**WT Alcohol**	***Lrat*$^{-/-}$ Control**	***Lrat*$^{-/-}$ Alcohol**	**2-way ANOVA**
Body weight (g)	26.6 ± 1.3	26.0 ± 1.6	27.4 ± 2.0	23.8 ± 3.5	Diet: $p > 0.05$ Genotype: $p > 0.05$
Liver weight (g)	1.2 ± 0.2	1.1 ± 0.1	1.2 ± 0.1	1.1 ± 0.2	Diet: $p > 0.05$ Genotype: $p > 0.05$
	WT Control	**WT Alcohol**	***Rbp*$^{-/-}$ Control**	***Rbp*$^{-/-}$ Alcohol**	
Body weight (g)	28.7 ± 3.0	29.0 ± 1.5	31.4 ± 2.8	28.8 ± 2.2	Diet: $p > 0.05$ Genotype: $p > 0.05$
Liver weight (g)	1.3 ± 0.2	1.4 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	Diet: $p > 0.05$ Genotype: $p > 0.05$
	WT Control	**WT Alcohol**	***Crbp1*$^{-/-}$ Control**	***Crbp1*$^{-/-}$ Alcohol**	
Body weight (g)	26.2 ± 2.3	23.3 ± 3.7	29.3 ± 1.3	29.1 ± 2.3	Diet: $p > 0.05$ Genotype: $p < 0.05$
Liver weight	*no data*	*no data*	*no data*	*no data*	

(g)					
	WT Control	**WT Alcohol**	***Cd36*$^{-/-}$ Control**	***Cd36*$^{-/-}$ Alcohol**	
Body weight (g)	34.6 ± 2.0	33.5 ± 2.0	27.1 ± 0.8	26.6 ± 0.9	Diet: p > 0.05 Genotype: p < 0.05
Liver weight (g)	1.7 ± 0.1	1.6 ± 0.1	1.3 ± 0.8	1.2 ± 0.7	Diet: p > 0.05 Genotype: p < 0.05
	WT Control	**WT Alcohol**	***Cyp2e1*$^{-/-}$ Control**	***Cyp2e1*$^{-/-}$ Alcohol**	
Body weight (g)	27.0 ± 2.8	24.0 ± 1.2	28.0 ± 1.5	25.5 ± 2.9	Diet: p < 0.05 Genotype: p > 0.05
Liver weight (g)	0.9 ± 0.2	0.8 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	Diet: p > 0.05 Genotype: p > 0.05

Supp. Table 2: Hepatic retinoid content in different strains of mice fed alcohol

	WT Control	**WT Alcohol**	***Lrat*$^{-/-}$ Control**	***Lrat*$^{-/-}$ Alcohol**	**2-way ANOVA**
Experiment: WT vs. Lrat*$^{-/-}$ *mice; end point: alcohol adaptation period					
Retinol (nmol/g)	34.2 ± 4.4	23.2 ± 4.6*	0.9 ± 0.1	1.7 ± 0.9	Diet: p < 0.05 Genotype: p < 0.05
Retinyl ester (nmol/g)	2174 ± 555	1883 ± 102	0.0 ± 0.0	0.0 ± 0.0	Diet: p > 0.05 Genotype: p < 0.05
Experiment: WT vs. Rbp*$^{-/-}$ *mice; end point: alcohol adaptation period					
	WT Control	**WT Alcohol**	***Rbp*$^{-/-}$ Control**	***Rbp*$^{-/-}$ Alcohol**	
Retinol (nmol/g)	51.9 ± 23.3	44.5 ± 15.4	41.0 ± 8.8	53.9 ± 9.1	Diet: p > 0.05 Genotype: p > 0.05
Retinyl ester (nmol/g)	2895 ± 954	1966 ± 465	3083 ± 328	2897 ± 641	Diet: p > 0.05 Genotype: p > 0.05
Experiment: WT vs. Rbp*$^{-/-}$ *mice; end point: 2 weeks 6.4% alcohol					
	WT Control	**WT Alcohol**	***Rbp*$^{-/-}$ Control**	***Rbp*$^{-/-}$ Alcohol**	
Retinol (nmol/g)	39.1 ± 14.6	38.1 ± 8.7	25.5 ± 4.7	20.7 ± 9.0	Diet: p > 0.05 Genotype: p < 0.05
Retinyl ester (nmol/g)	2570 ± 429	2203 ± 180	3061 ± 278	2079 ± 722*	Diet: p < 0.05 Genotype: p > 0.05
Experiment: WT vs. Crbp1*$^{-/-}$ *mice; end point: alcohol adaptation period					
	WT Control	**WT Alcohol**	***Crbp1*$^{-/-}$ Control**	***Crbp1*$^{-/-}$ Alcohol**	
Retinol (nmol/g)	49.1 ± 23.0	28.2 ± 10.6	47.0 ± 19.6	35.9 ± 17.7	Diet: p < 0.05 Genotype: p < 0.05
Retinyl ester (nmol/g)	6242 ± 839	6381 ± 1260	1713 ± 346	1590 ± 343	Diet: p > 0.05 Genotype: p < 0.05
Experiment: WT vs. Cd36*$^{-/-}$ *mice; end point: alcohol adaptation period					
	WT Control	**WT Alcohol**	***Cd36*$^{-/-}$ Control**	***Cd36*$^{-/-}$ Alcohol**	
Retinol (nmol/g)	43.5 ± 14.4	44.9 ± 5.3	53.6 ± 13.5	62.0 ± 10.8	Diet: p > 0.05 Genotype: p < 0.05
Retinyl ester (nmol/g)	3367 ± 461	3024 ± 176	3900 ± 424	3694 ± 414	Diet: p > 0.05 Genotype: p < 0.05
Experiment: WT vs. Cyp2e1*$^{-/-}$ *mice; end point: alcohol adaptation period					
	WT Control	**WT Alcohol**	***Cyp2e1*$^{-/-}$ Control**	***Cyp2e1*$^{-/-}$ Alcohol**	
Retinol (nmol/g)	88.3 ± 36.2	64.0 ± 22.5	69.5 ± 18.3	57.7 ± 9.2	Diet: p > 0.05 Genotype: p > 0.05

Retinyl ester (nmol/g)	5406 ± 1219	5390 ± 1528	5643 ± 784	5527 ± 688	Diet: p > 0.05 Genotype: p > 0.05
Experiment: WT vs. Cyp2e1$^{-/-}$ mice; end point: 2 weeks 6.4% alcohol					
	WT Control	**WT Alcohol**	***Cyp2e1$^{-/-}$* Control**	***Cyp2e1$^{-/-}$* Alcohol**	
Retinol (nmol/g)	134.7 ± 57.4	50.1 ± 8.2*	116.8 ± 36.7	106.1 ± 60.3	Diet: p < 0.05 Genotype: p > 0.05
Retinyl ester (nmol/g)	6435 ± 885	4840 ± 757*	6236 ± 599	5120 ± 455	Diet: p < 0.05 Genotype: p > 0.05

* P < 0.05 vs genotype control; 2-way ANOVA. The data for *Cd36*$^{-/-}$ and *Cyp2e1*$^{-/-}$ mice is also presented in graph form in figures 7 and 8, respectively.

Supp. Table 3: Serum retinol (µM) levels in different strains of mice at the end of the alcohol adaptation period

WT Control	**WT Alcohol**	***Lrat*$^{-/-}$ Control**	***Lrat*$^{-/-}$ Alcohol**	**2-way ANOVA**
1.08 ± 0.32	1.15 ± 0.36	1.33 ± 0.13	1.38 ± 0.25	Diet: p > 0.05 Genotype: p > 0.05
WT Control	**WT Alcohol**	***Rbp*$^{-/-}$ Control**	***Rbp*$^{-/-}$ Alcohol**	
1.73 ± 0.30	1.86 ± 0.18	0.08 ± 0.01	0.13 ± 0.05	Diet: p > 0.05 Genotype: p < 0.05
WT Control	**WT Alcohol**	***Crbp1*$^{-/-}$ Control**	***Crbp1*$^{-/-}$ Alcohol**	
1.57 ± 0.21	1.60 ± 0.40	1.30 ± 0.01	1.29 ± 0.29	Diet: p > 0.05 Genotype: p < 0.05
WT Control	**WT Alcohol**	***Cd36*$^{-/-}$ Control**	***Cd36*$^{-/-}$ Alcohol**	
1.56 ± 0.11	2.04 ± 0.15*	1.73 ± 0.25	2.01 ± 0.24	Diet: p < 0.05 Genotype: p > 0.05
WT Control	**WT Alcohol**	***Cyp2e1*$^{-/-}$ Control**	***Cyp2e1*$^{-/-}$ Alcohol**	
1.22 ± 0.04	1.55 ± 0.20	1.13 ± 0.10	1.45 ± 0.32	Diet: p < 0.05 Genotype: p > 0.05

* P < 0.05 vs genotype control; 2-way ANOVA

Supp. Table 4: Average threshold cycle (Ct) for PCR amplification of *18s*, *Crbp1* and *Crbp3*

	18s (Ct)	*Crbp1* (Ct)	*Crbp3* (Ct)
Liver	13.0	25.6	34.1
Kidney	12.8	26.4	30.2
Lung	10.2	25.7	28.6
Spleen	9.9	29.4	31.9
WAT	12.9	27.8	26.5
BAT	13.2	29.5	25.7

Ct = Threshold cycle

Supp. Table 5: Average threshold cycle (Ct) for PCR amplification of *18s*, *Cyp26a1* and *Cyp26b1* in the liver of control and alcohol-fed mice

	18s (Ct)	*Cyp26a1* (Ct)	*Cyp26b1* (Ct)
Control	11.8	30.4	28.3
Alcohol	11.8	25.5	26.2

Ct = Threshold cycle