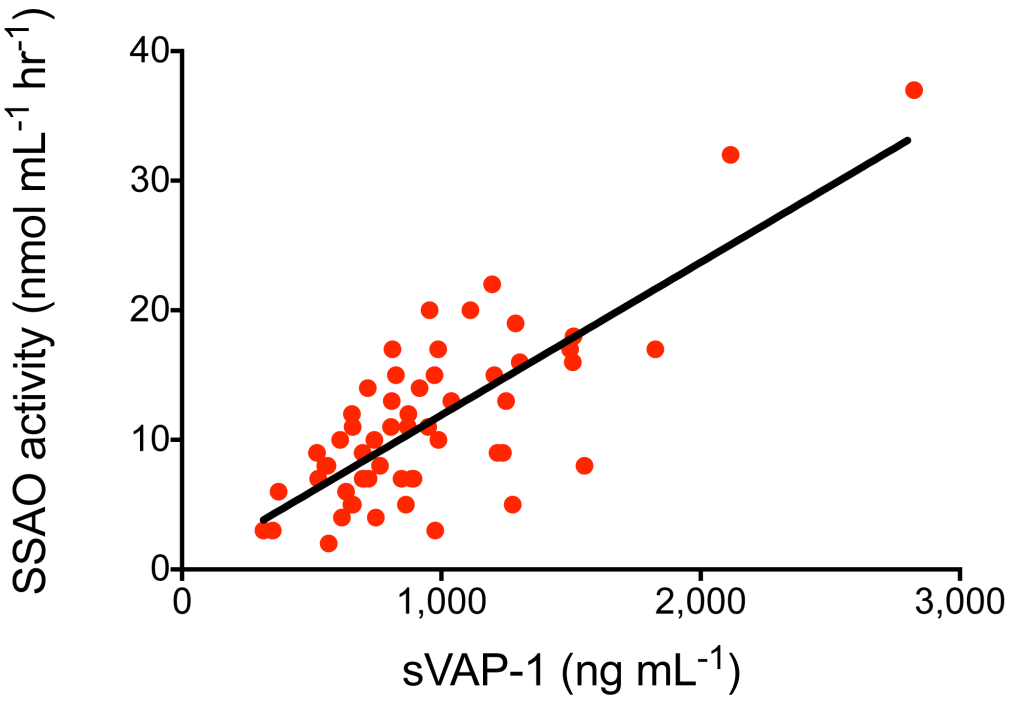
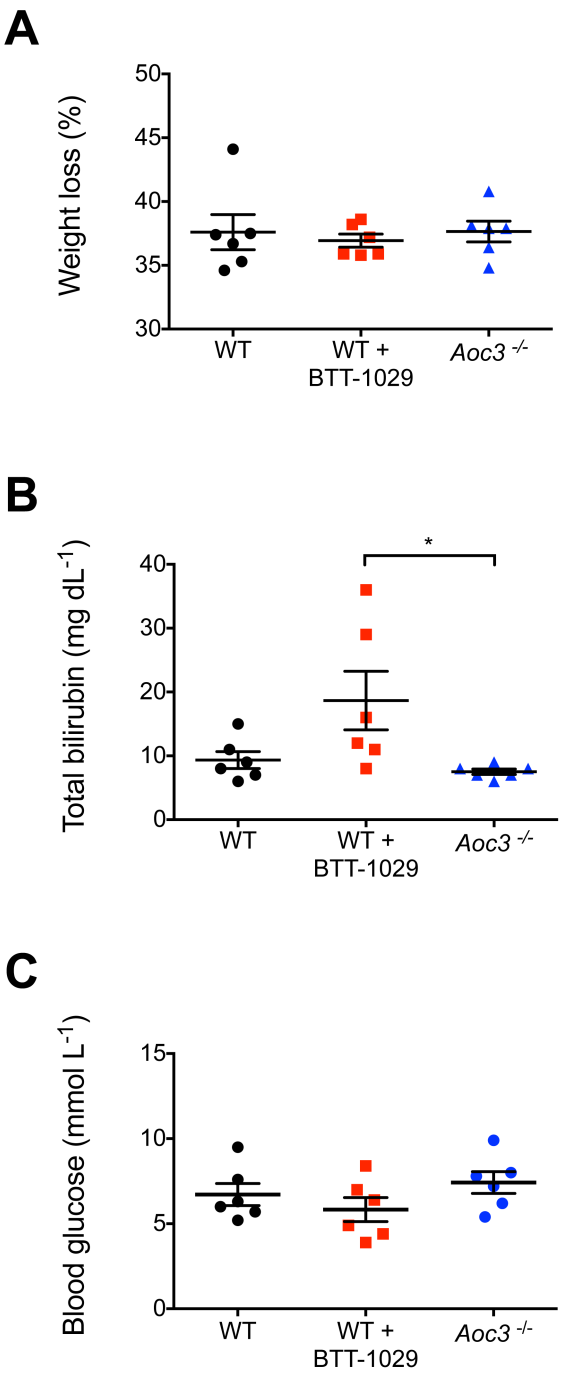
Supplementary Fig 1



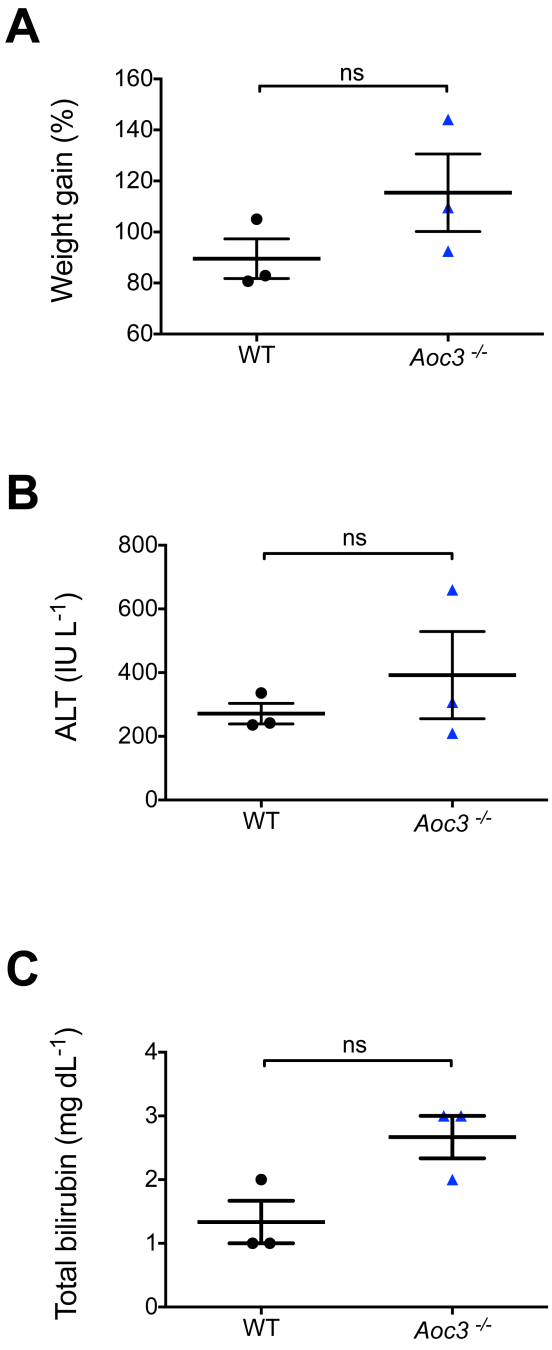
Supplementary Figure 1: Soluble VAP-1 levels in serum taken from patients in the NAFLD cohort correlated with the amine oxidase (SSAO) activity. Patient sVAP-1 levels (n=57) were measured by time-resolved fluorescence and amine oxidase activity was determined by Amplex Red based methodology. Pearson rank correlation coefficient = 0.77, $p<0.0001$.

Supplementary Fig 2



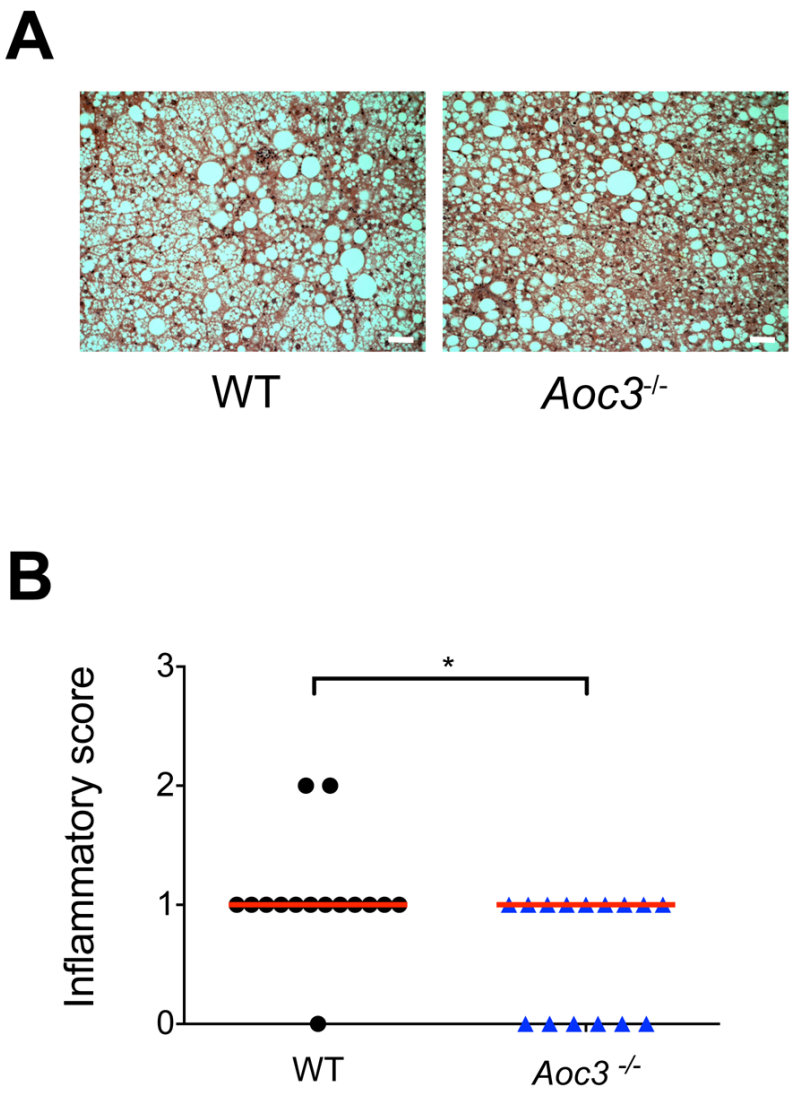
Supplementary Figure 2: Physical (body weight) and biochemical properties (bilirubin, blood glucose) of *Aoc3*$^{-/-}$ and WT mice that received anti-VAP-1 antibody BTT-1029 did not differ greatly from WT animals when MCD diet for 6 weeks. 6 animals/group. Statistical test: One way ANOVA with Tukey's *post hoc* test. * $p<0.05$.

Supplementary Fig 3



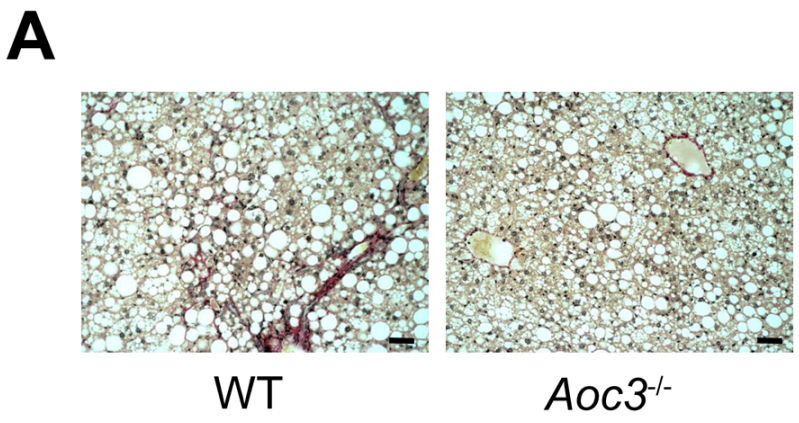
Supplementary Figure 3: Physical (body weight) and biochemical properties (ALT, bilirubin) of *Aoc3*$^{-/}$ mice did not differ from WT animals when fed a high fat diet for 18 weeks. 3 animals/group. Statistical test: Mann-Whitney test, ns – not significant.

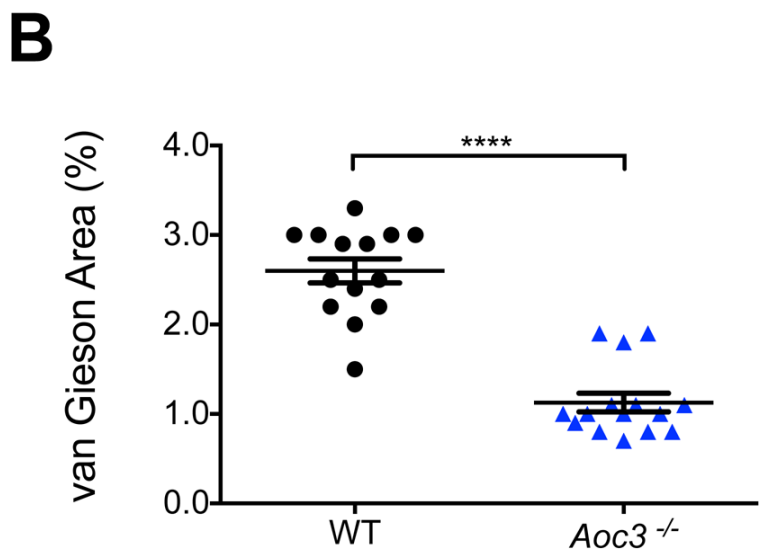
Supplementary Fig 4



Supplementary Figure 4: Liver sections taken from WT mice fed HFD had significantly higher inflammatory scores than those taken from *Aoc3*$^{-/-}$ animals. (a) Haematoxylin and Eosin staining of liver tissue sections. Scale bar: 50 μm. (b) Inflammatory score based on the number of inflammatory foci per field of view. 3 animals/group, 5 fields per animal. Statistical test: Mann-Whitney test. * $p<0.05$.

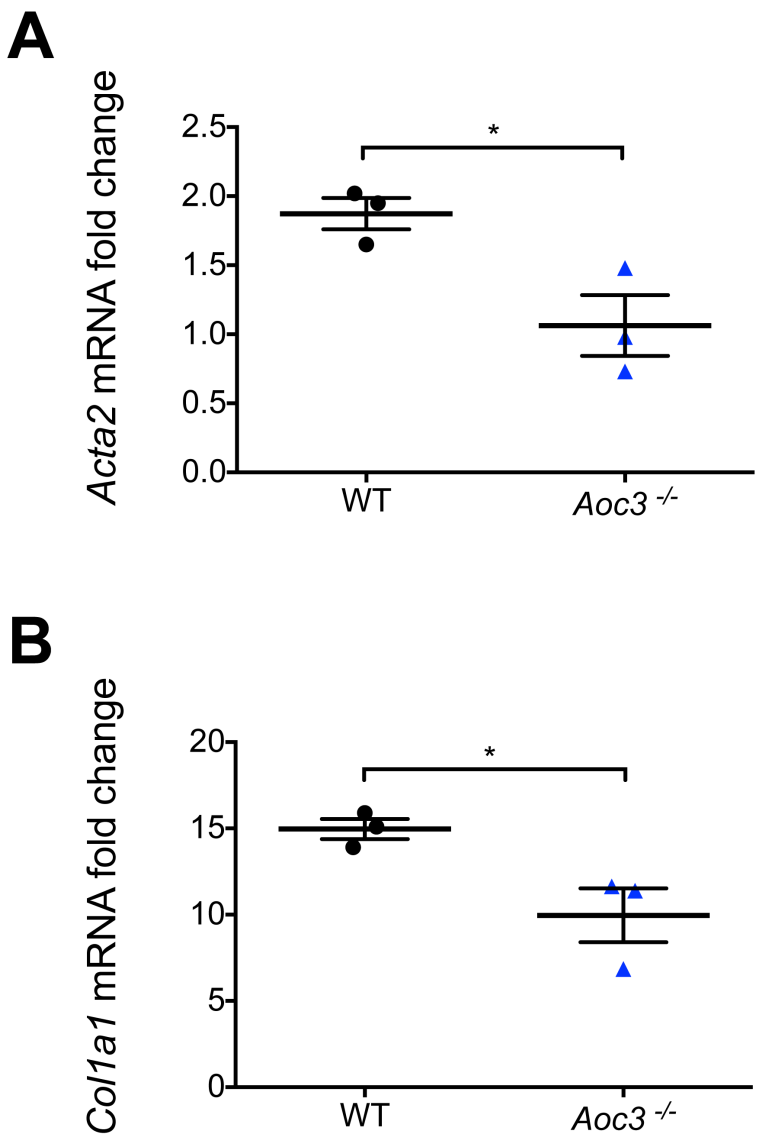
Supplementary Fig 5





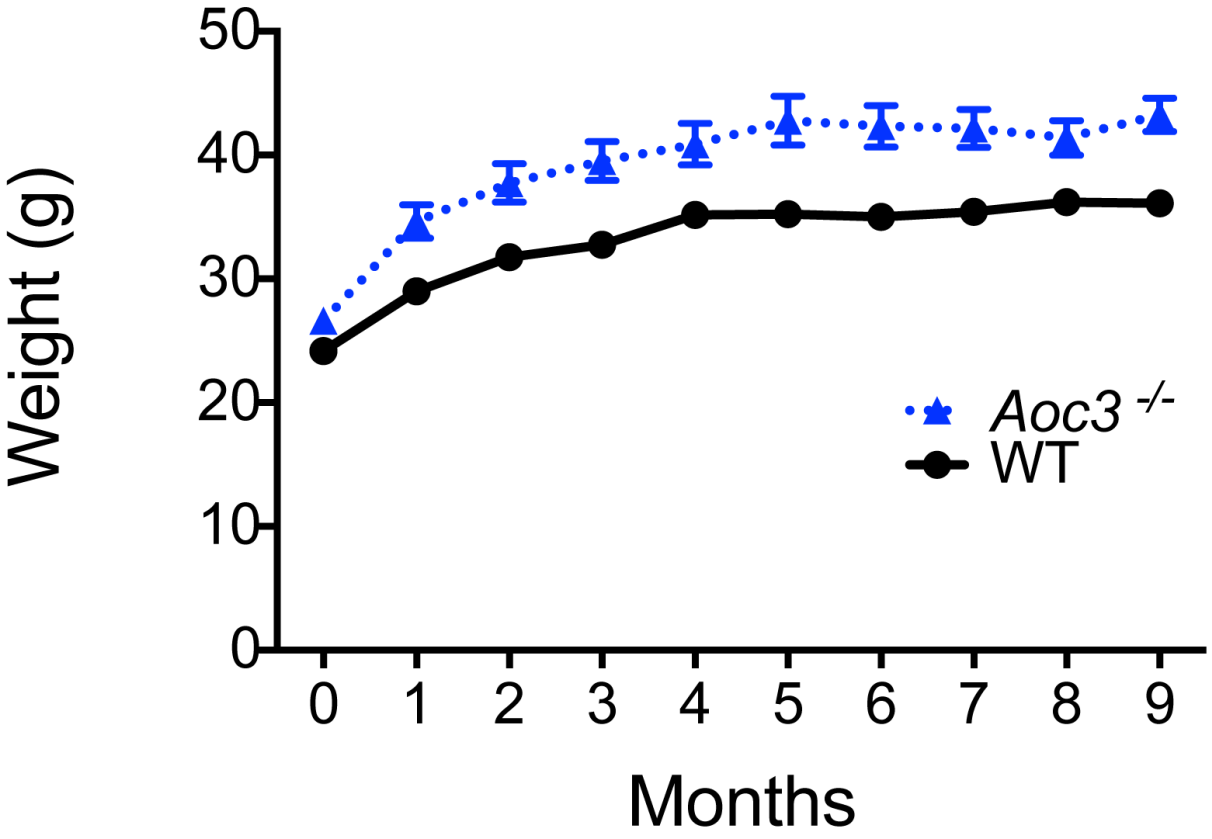
Supplementary Figure 5: WT mice fed HFD developed significantly more hepatic fibrosis than *Aoc3*$^{-/-}$ mice on the same diet as measured by van Gieson staining for collagens. Scale bar: 50 μm. 3 animals/group, 4-5 fields/animal. Statistical test: Mann-Whitney test. **** p<0.0001.

Supplementary Fig 6



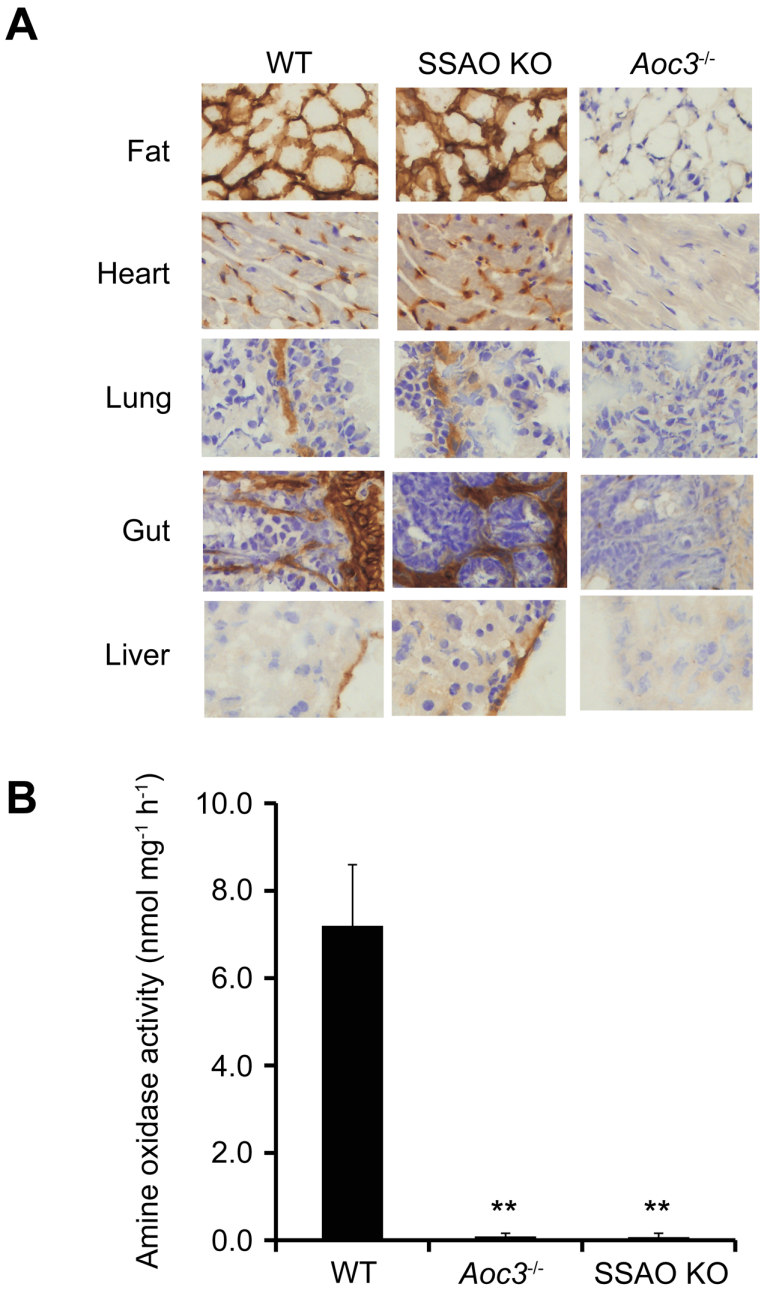
Supplementary Figure 6: The expression levels of *Acta2* and *Col1a1* were significantly higher in WT mice fed HFD compared to *Aoc3*$^{-/-}$ animals. 3 animals/group. Statistical test: Unpaired t-test. * $p<0.05$.

Supplementary Fig 7



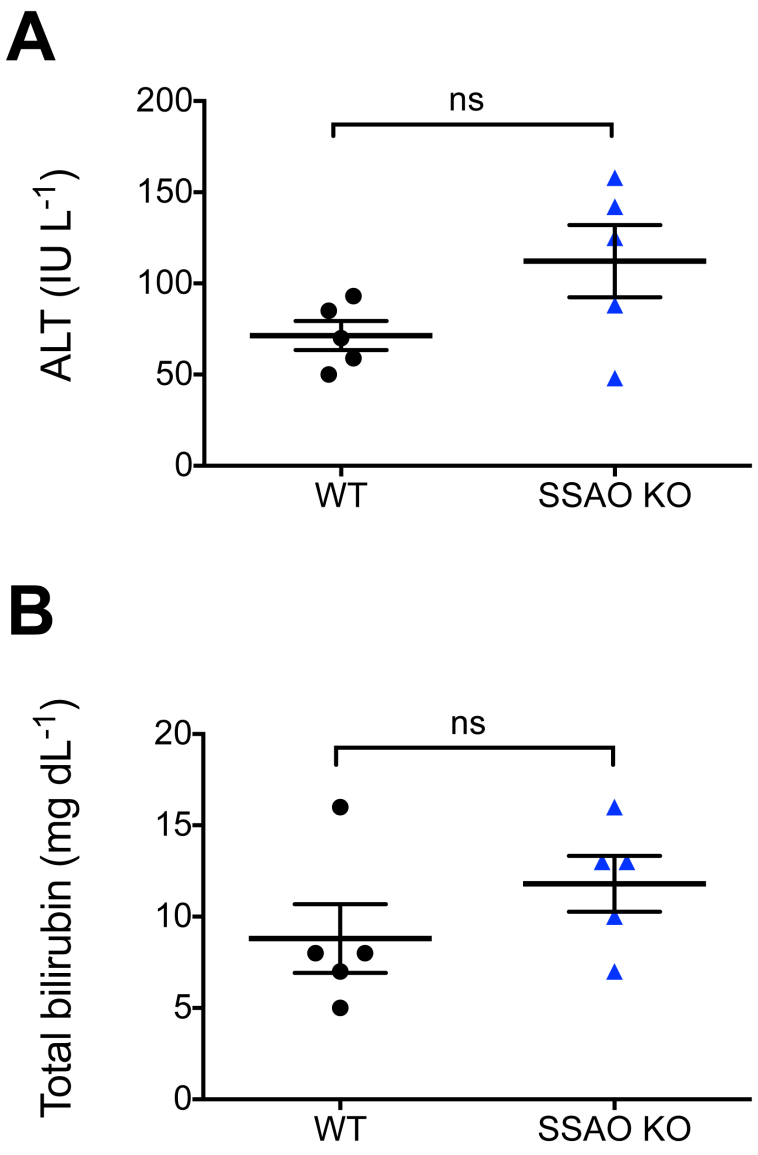
Supplementary Figure 7: *Aoc3*$^{-/-}$ animals had an increased body weight compared to WT animals when maintained on WLM. 2-way ANOVA with Sidak test, $p<0.01$ for months 1-9 (8 animals/group). No significant difference in body weight was observed at time zero (prior to being placed on the diet).

Supplementary Fig 8



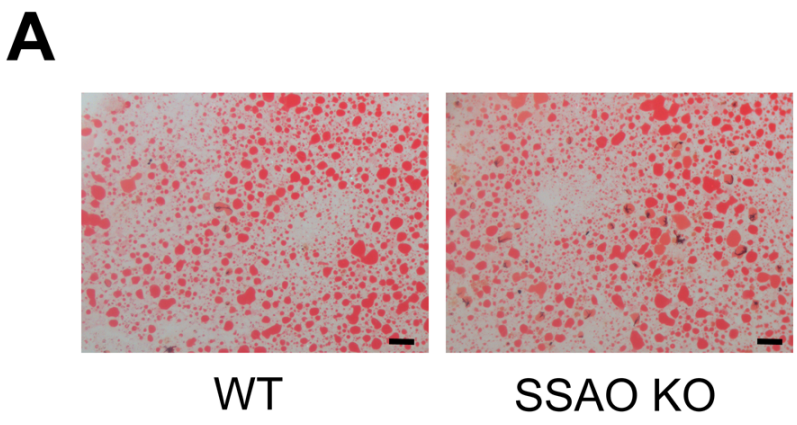
Supplementary Figure 8: The tissue expression pattern of VAP-1 protein in animals harbouring a mutation in the active site of the enzyme was similar to that of the native protein. (A) Immunohistochemistry was used to detect the expression of VAP-1 in murine tissues isolated from WT, SSAO KO and *Aoc3*$^{-/-}$ animals. The staining patterns for VAP-1 in WT and SSAO KO animals were similar, whereas the protein was absent in all tissues harvested from *Aoc3*$^{-/-}$ mice. (B) The catalytic activity of VAP-1 was undetectable in fat tissue lysates isolated from both SSAO KO and *Aoc3*$^{-/-}$ animals. 5 animals/group. Statistical test: Mann-Whitney test, ** p<0.01.

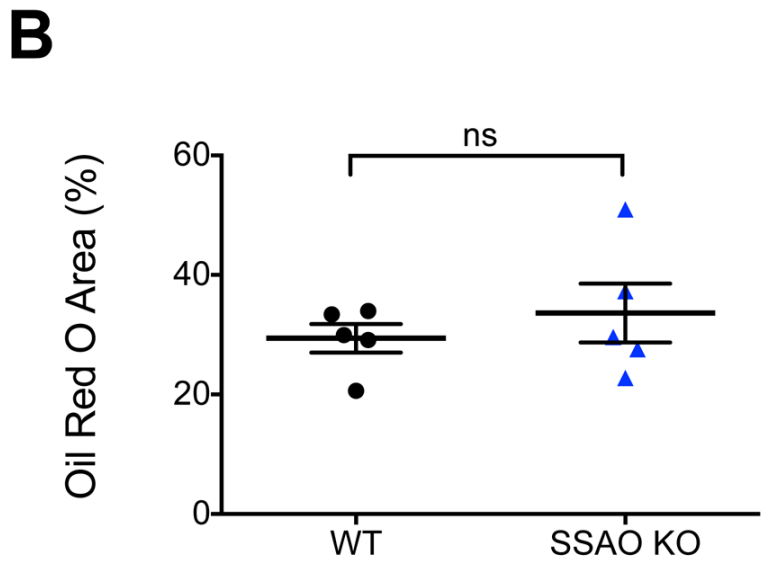
Supplementary Fig 9



Supplementary Figure 9: There were no significant differences in serum markers of liver injury in WT and SSAO KO animals fed MCD diet. Serum levels of ALT and bilirubin were not significantly different between WT and SSAO KO animals following 4.5 weeks of MCD diet. 5 animals/group. Statistical test: Mann-Whitney test, ns – not significant.

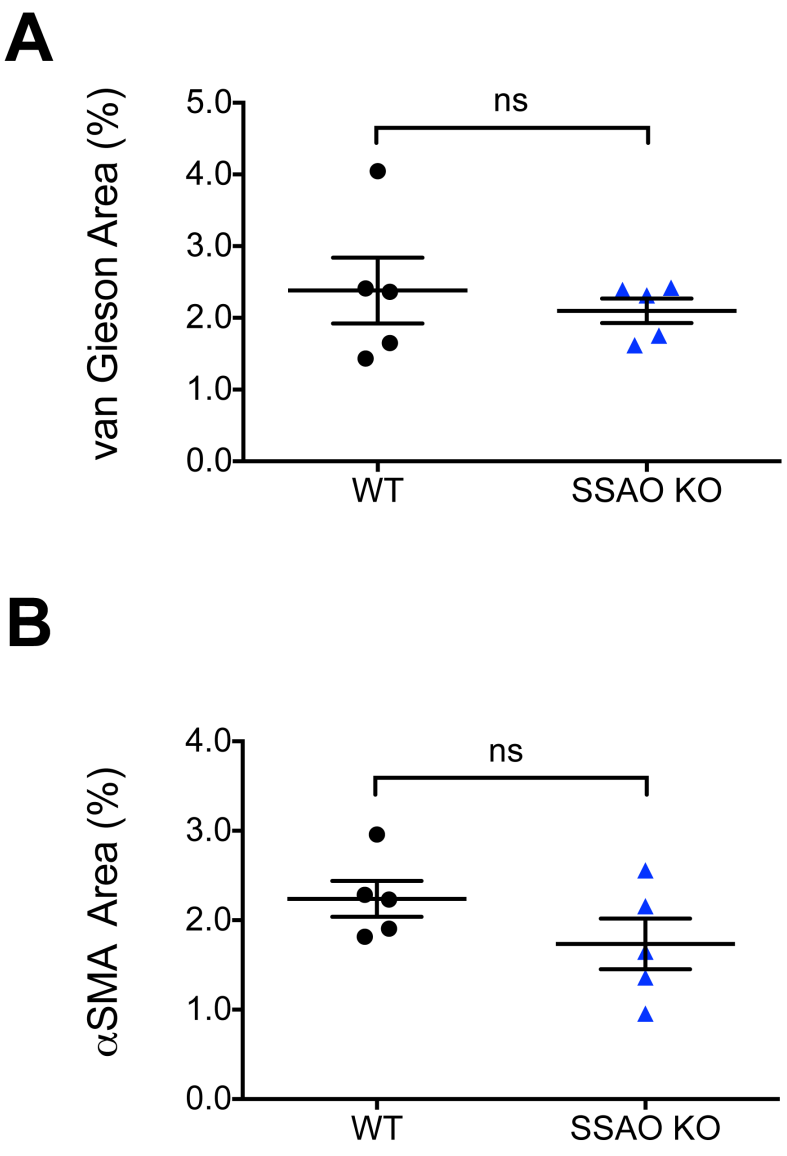
Supplementary Fig 10





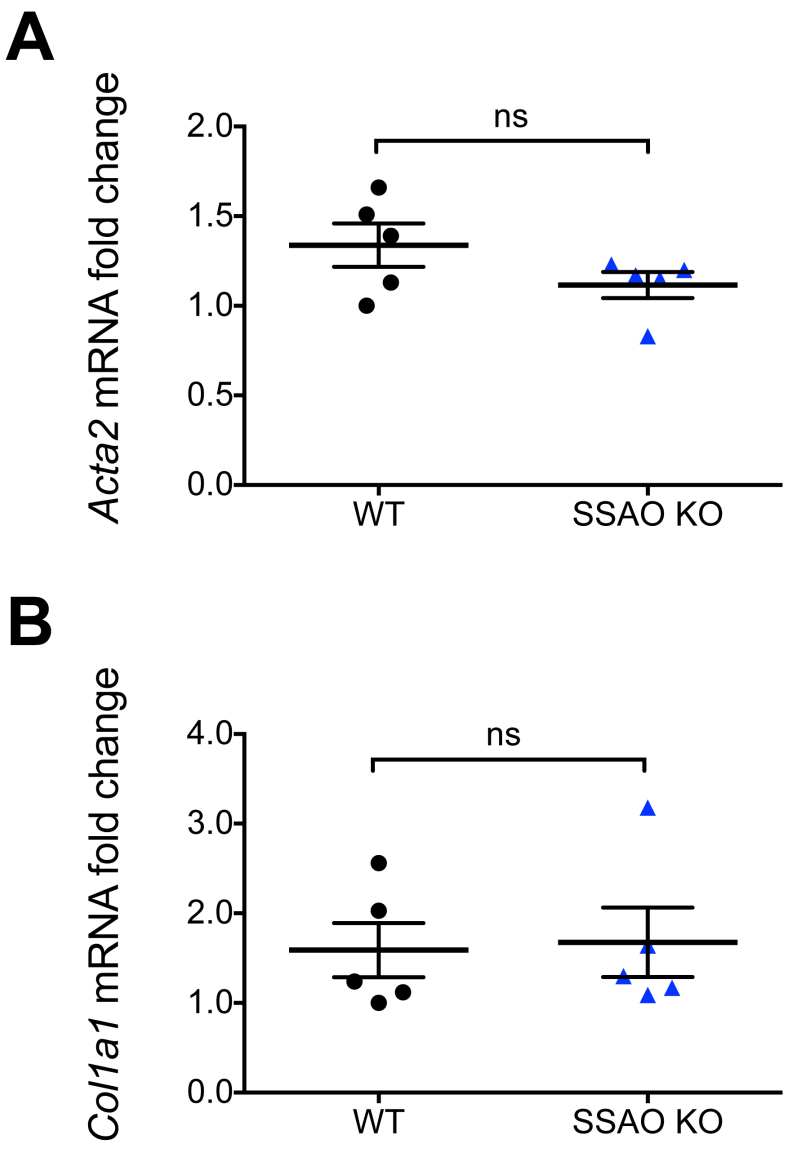
Supplementary Figure 10: WT and SSAO KO animals developed similar levels of hepatic steatosis following 4.5 weeks MCD diet. The surface area covered by the oil red O stain (a) was determined for 3-5 random fields with 5 animals per group (b). There was no significant difference between the two groups of animals. Scale bar: 50 μm. Statistical test: Mann-Whitney test, ns – not significant.

Supplementary Fig 11



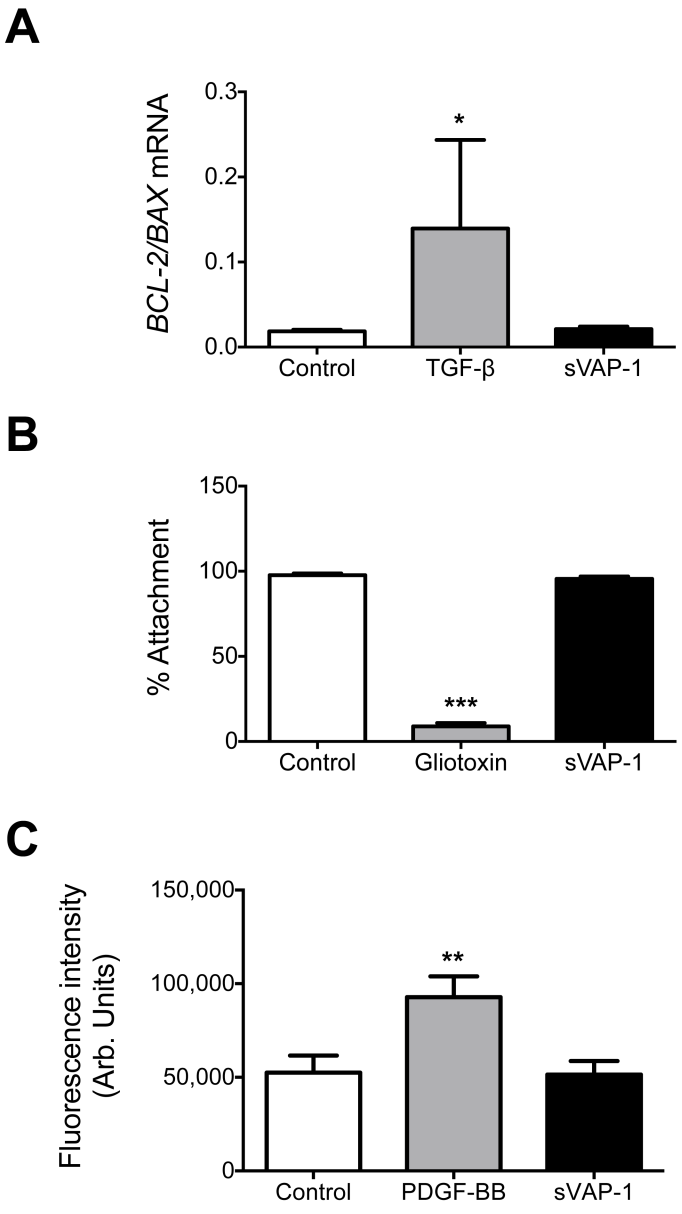
Supplementary Figure 11: WT and SSAO KO animals exhibited similar levels of hepatic fibrosis following 4.5 weeks MCD diet. The surface area covered by van Gieson stain (a) or immunohistochemistry for α-SMA (b) did not differ significantly between WT and SSAO KO animals. 3-5 random fields for 5 animals per group. Statistical test: Mann-Whitney test, ns – not significant.

Supplementary Fig 12



Supplementary Figure 12: There were no significant differences in the expression of two fibrotic gene transcripts in WT and SSAO KO animals fed MCD diet for 4.5 weeks. The expression of *Acta2* and *Col1a1* were not significantly different between WT and SSAO KO animals. 5 animals/group. Statistical test: Mann-Whitney test, ns – not significant.

Supplementary Fig 13



Supplementary Figure 13: Soluble VAP-1 does not affect proliferation or apoptosis of aHSC. Treatment of human aHSC with 500 ng mL^{-1} sVAP-1 did not alter: apoptosis (*BCL2*/*BAX* mRNA) (A), detachment (B), or proliferation (C). Responses to TGF-β (10 ng mL^{-1}), gliotoxin (1.5 μM) and PDGF-BB (10ng mL^{-1}) shown as positive controls. Statistical test: Mann-Whitney test, * $p<0.05$, ** $p<0.01$, *** $p<0.001$ (n=3 independent isolates).

Supplementary Table 1: Parameters which independently correlated with sVAP-1 concentration following univariate analysis.

Variable	r_s value	*p* value
Fibrosis stage	0.39	0.000003
Lobular inflammation	0.35	0.00005
Diabetes	0.32	0.0002
AST/ALT	0.32	0.0005
Age	0.27	0.002
Platelets	-0.27	0.002
Albumin	-0.24	0.006
Steatosis grade	0.21	0.02
HOMA-IR	0.3	0.03
AST	0.15	0.1
Hypertension	0.12	0.2
BMI	0.1	0.3
ALT	-0.075	0.4
Bilirubin	0.061	0.5
GGT	0.056	0.5
Total cholesterol	-0.033	0.7
Triglycerides	-0.026	0.7
Ferritin	-0.019	0.8
Total cholesterol/HDL	-0.010	0.9

Supplementary Table 2: Parameters which independently correlated with significant fibrosis (Kleiner score F≥2) following univariate analysis.

Variable	r_s value	Odds ratio (95% CI)	*p* value
Lobular inflammation	0.638	27.853 (9.653-80.368)	0.0000001
sVAP-1 (continuous)	0.361	1.003 (1.001-1.004)	0.00002
Diabetes	0.357	4.607 (2.168-9.789)	0.00003
AST/ALT ratio	0.301	6.144 (1.625-24.756)	0.001
Steatosis	0.280	2.307 (1.372-3.870)	0.002
Age (per year)	0.249	1.041 (1.010-1.072)	0.004
Hypertension	0.236	2.628 (1.265-5.458)	0.01

Supplementary Table 3: Primer/Probe mixes for qRT-PCR used in this study.

	Roche UPL		*Life Technologies*
Target	**Probe**	**Primers**	**Taqman Assay ID**
AOC3	49	5′-caatgagaccattgctggaa-3′ 5′-tgtcctctgcatgtgggata-3′	-
BCL2	2	5′-gcacctgcacacctggat-3′ 5′-agggccaaactgagcaga-3′	-
BAX	69	5′-gaaccatcatgggctgga-3′ 5′-cgtcccaaagtaggagagga-3′	-
PBGD	-	Catalogue # 05 046 149 001	-
Col1a1	15	5′-gacatgttcagctttgtggac-3′ 5′-gcagctgacttcagggatg-3′	-
Acta2	56	5′-ccgccatgtatgtggctatt-3′ 5′-cagttgtacgtccagaggcata-3′	-
Gapdh	-	Catalogue # 05 046 211 001	-
Actb	-	Catalogue # 05 046 190 001	-
AOC3	-	-	Hs00186647_m1
COL1A1	-	-	Hs00164004_m1
PDGFRB	-	-	Hs01019589_m1
LOXL2	-	-	Hs00158757_m1
18S (human)	-	-	Hs99999901_s1
Col1a1	-	-	Mm00801666_g1
Acta2	-	-	Mm01546733_m1
Aoc3	-	-	Mm00839624_m1
18S (mouse)	-	-	Mm03928990_g1