Cell-specific discrimination of desmosterol and desmosterol mimetics confers selective regulation of LXR and SREBP pathways in macrophages

Supplementary Figure 1. ***Effect of DHCR24-ASO administration in mouse liver and macrophage.*** **A.** For in vivo studies, mice received biweekly intraperitoneal (i.p.) injections of ASO for 3 weeks prior to sacrifice. **B.** Treatment of mice with 2 separate DHCR24 specific ASOs (ASO 805, ASO 873) and scramble control ASO (SCR ASO) was well tolerated throughout the course of the study without body weight changes among groups (n = 6 for all groups). **C**. Gene expression changes in Dhcr24, Abca1, and Abcg1 in liver and macrophage of animals treated with DHCR24 ASO. **D**. Desmosterol concentrations in plasma, liver and macrophage as measured by LC-MS after DHCR24 ASO (* $p < 0.005$).

Supplementary Figure 2. ***Purification of Kupffer cells.*** Successive gating strategy for isolation of Kupffer cells from labeled non-parenchymal cells using cell sorting. Kupffer cells were defined at CD45+, F4/80 high, CD11b intermediate, CD146-, single particles, FixVia NIR- (not shown), and Tim4+.

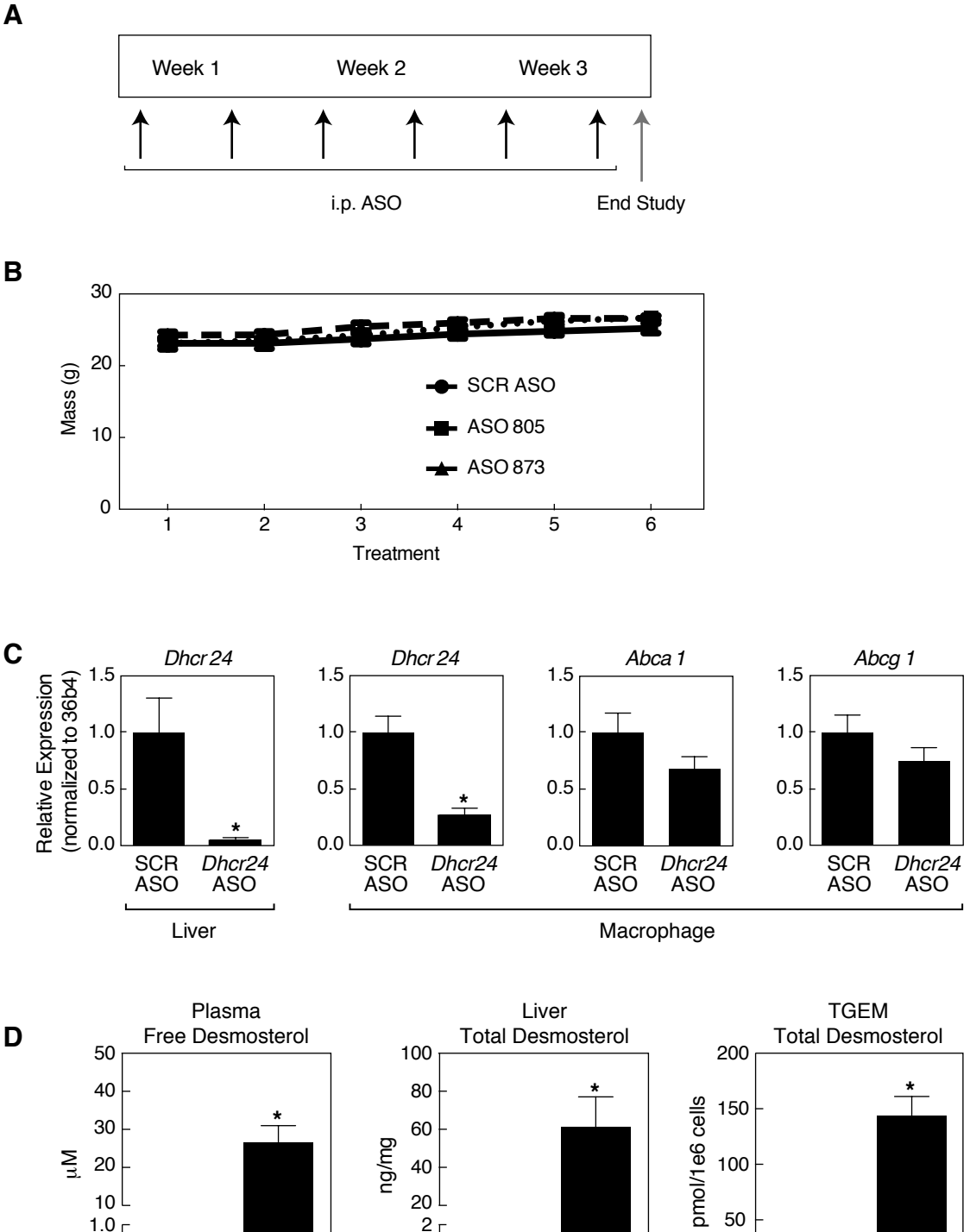
A
Week 1
Week 2
Week 3
i.p. ASO
End Study
B
Mass (g)
30
20
10
0
1
2
3
4
5
6
Treatment
SCR ASO
ASO 805
ASO 873
C
Relative Expression
(normalized to 36b4)
Dhcr 24
Dhcr 24
Abca 1
Abcg 1
1.5
1.0
0.5
0.0
*
SCR ASO
Dhcr24 ASO
Liver
Macrophage
D
Plasma
Free Desmosterol
µM
50
40
30
20
10
1.0
0.5
0.0
Liver
Total Desmosterol
ng/mg
100
80
60
40
20
2
1
0
TGEM
Total Desmosterol
pmol/1e6 cells
200
150
100
50
0

Figure S1

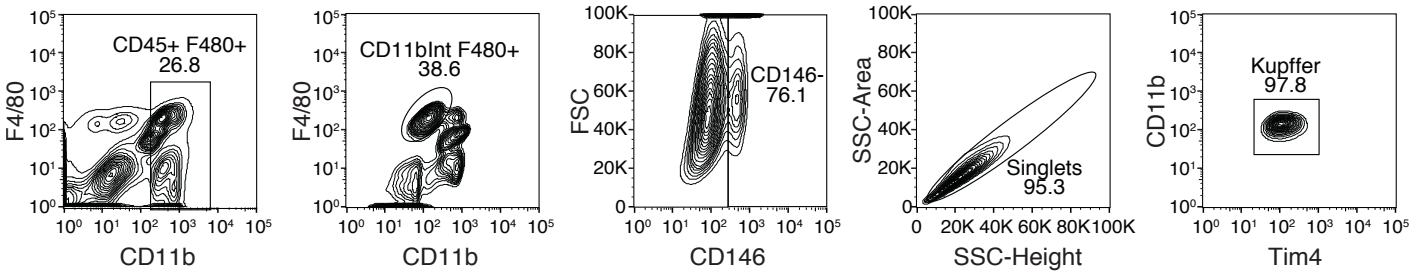
CD45+ F480+
26.8
F4/80
CD11b
CD11bInt F480+
38.6
F4/80
CD11b
CD146-
76.1
FSC
CD146
SSC-Area
Singlets
95.3
SSC-Height
Kupffer
97.8
CD11b
Tim4

Figure S2