

Supplementary Table S1. Lipid profile comparison among the three mice strains: BKS

Wild Type, BKS db/db, and BKS db/db mice treated with Semaglutide. The values are expressed as median (CI). BKS WT vs BKS db/db: #p < 0.05, ##p < 0.01, ###p < 0.001. BKS db/db vs BKS db/db + Semaglutide: *p < 0.05, **p < 0.01, ***p < 0.001.

Fatty Acid	BKS WT	BKS db/db	BKS db/db + Semaglutide
C12:0 (µg/mg)	0.0104 (0.0079 - 0.0254)	0.0204 (0.0180 - 0.0319)	0.0161 (0.0079 - 0.0275)
C14:0 (µg/mg)	0.1063 (0.072 - 0.1491)	0.5645 (0.5212 - 0.5831) ###	0.1419 (0.1238 - 0.3771) ***
C15:0 (µg/mg)	0.0189 (0.0153 - 0.0265)	0.0316 (0.0296 - 0.0512) #	0.0287 (0.0233 - 0.0545)
C16:0 (µg/mg)	3.920 (2.568 - 5.474)	18.870 (10.660 - 20.460) ###	3.659 (2.341 - 6.529) ***
C16:1n7 (µg/mg)	0.8818 (0.4489 - 1.308)	2.901 (2.414 - 3.194) ##	0.4227 (0.2859 - 0.8364) ***
C17:0 (µg/mg)	0.0209 (0.0184 - 0.0246)	0.0502 (0.0478 - 0.0799) ###	0.0606 (0.0372 - 0.0898)
C18:0 (µg/mg)	0.3219 (0.2868 - 0.3842)	1.580 (1.424 - 1.774) ###	0.7114 (0.4873 - 1.240) ***
C18:1n9cis (µg/mg)	6.254 (3.512 - 8.895)	39.620 (27.730 - 42.490) ###	5.967 (3.846 - 15.85) ***
C18:2n6cis (µg/mg)	2.083 (1.124 - 3.623)	4.045 (3.397 - 4.333)	3.648 (2.656 - 6.045)
C18:3n3 (µg/mg)	0.0448 (0.0343 - 0.0741)	0.1007 (0.0856 - 0.1116) ##	0.1575 (0.0987 - 0.1721)
C20:0 (µg/mg)	0.0274 (0.0077 - 0.0355)	0.0183 (0.0146 - 0.0285)	0.0285 (0.0113 - 0.0644)
C20:1n9 (µg/mg)	3.920 (2.568 - 5.474)	18.87 (10.660 - 20.460) ###	3.659 (2.341 - 6.529) ***
C20:2n6 (µg/mg)	0.0326 (0.0235 - 0.0510)	0.0502 (0.0437 - 0.1011)	0.1072 (0.0686 - 0.1336)
C20:3n6 (µg/mg)	0.0868 (0.0560 - 0.1263)	0.0513 (0.0482 - 0.0847)	0.1093 (0.0901 - 0.1497) *
C20:4n6 (µg/mg)	0.1651 (0.0775 - 0.2080)	0.0740 (0.0638 - 0.1124) #	0.1594 (0.1312 - 0.2436) *
C20:5n3 (µg/mg)	0.0054 (0.0024 - 0.0076)	0.0040 (0.0029 - 0.0056)	0.0192 (0.0100 - 0.0370) ***
C22:1n9 (µg/mg)	0.8818 (0.4489 - 1.3080)	2.9010 (2.4140 - 3.1940) ###	0.4227 (0.2859 - 0.8364) ***
C24:0 (µg/mg)	0.0104 (0.0079 - 0.0254)	0.0204 (0.018 - 0.0319)	0.0161 (0.0079 - 0.0275) **
C22:6n3 (µg/mg)	0.0628 (0.0317 - 0.0879)	0.0351 (0.0324 - 0.0654)	0.1239 (0.1040 - 0.2413) ***

Supplementary Figure S1. Experimental design. Leptin receptor-deficient mice (BKS db/db, 12-week-old males) were randomized to untreated and semaglutide-treated (25 $\mu\text{g/kg/week}$ for 2 weeks followed by 100 $\mu\text{g/kg/week}$ for 8 weeks). BKS wild-type mice (BKS WT) littermates served as controls. Mice at 23 weeks-old were sacrificed (euthanized).

