iScience, Volume *24*

Supplemental information

Vascepa protects against high-fat diet-induced glucose intolerance, insulin resistance, and impaired β-cell function

Dana Al Rijjal, Ying Liu, Mi Lai, Youchen Song, Zahra Danaei, Anne Wu, Haneesha Mohan, Li Wei, Francisco J. Schopfer, Feihan F. Dai, and Michael B. Wheeler

Table S1. qPCR Primer sequences, Related to STAR Methods.

Gene Name	Forward Primer (5’ to 3’)	Reverse Primer (5’ to 3’)
PPAR-α	ATCACAGACACCCTCTCTCCA	GACACTCGATGTTCAGGGCA
Cyp4a31	GGGCGATCAGGGTATGGTTT	GCCGTTCCCATTTGTCTAGC
Cd36	TGGAGGCATTCTCATGCCAG	TTGCTGCTGTTCTTTGCCAC
Fabp5	AGGATCTCGAAGGGAAGTGG	GACCGTGATGTTGTTGCCATC
Cyp2c38	CACGGCCCATTGTTGTATTGC	TGAGTGTGAAACGTCTTGTCTCT

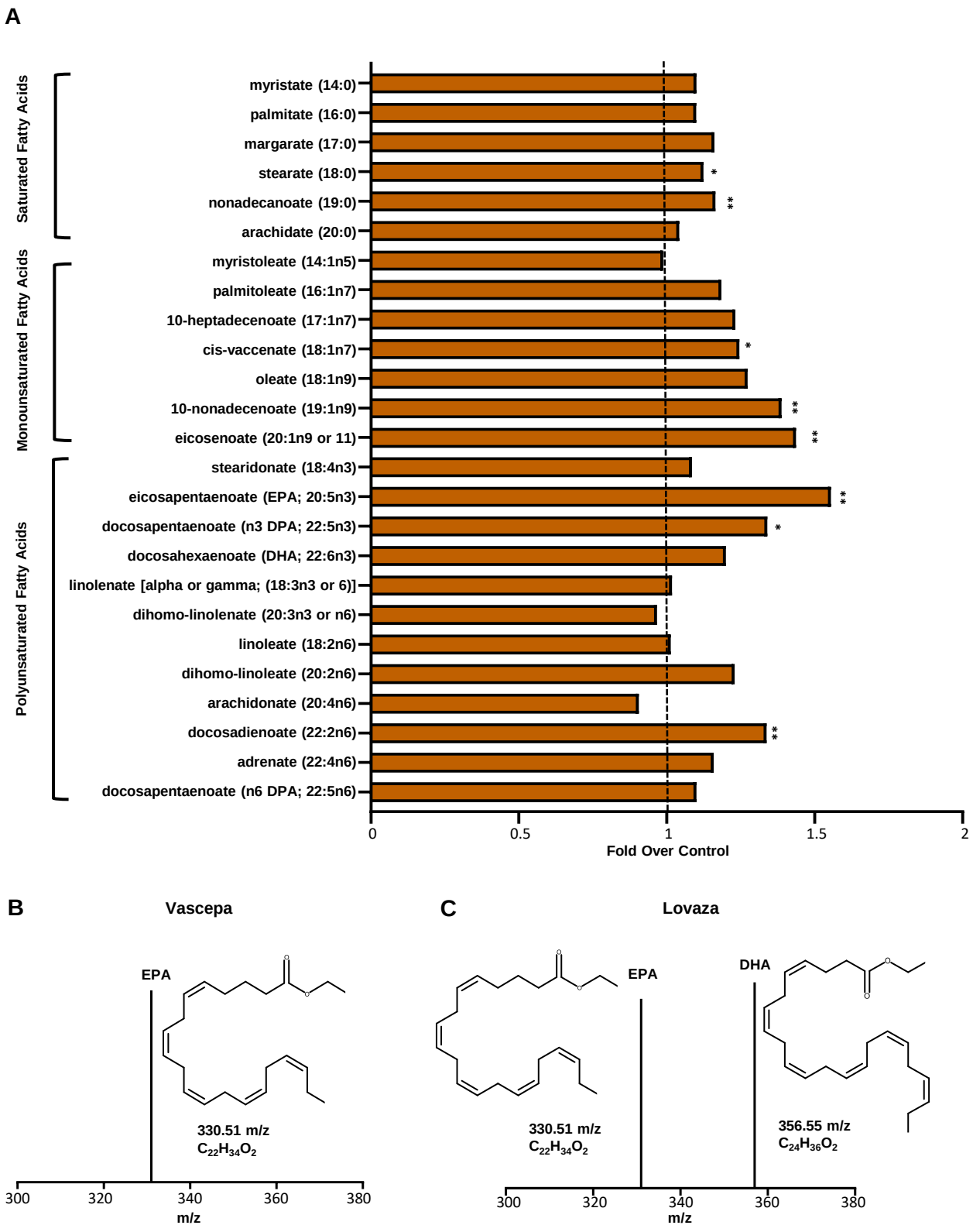

Figure S1. The omega-3 fatty acids, EPA and DPA, are elevated in patients with type 2 diabetes. A) Fatty acid analysis in patients with diabetes vs normal glucose tolerant (NGT) controls (n=25-28) B) Determination of the presence of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) ethyl esters in Vascepa or C) Lovaza pill. *P<0.05, **P<0.01, Related to Table 1.

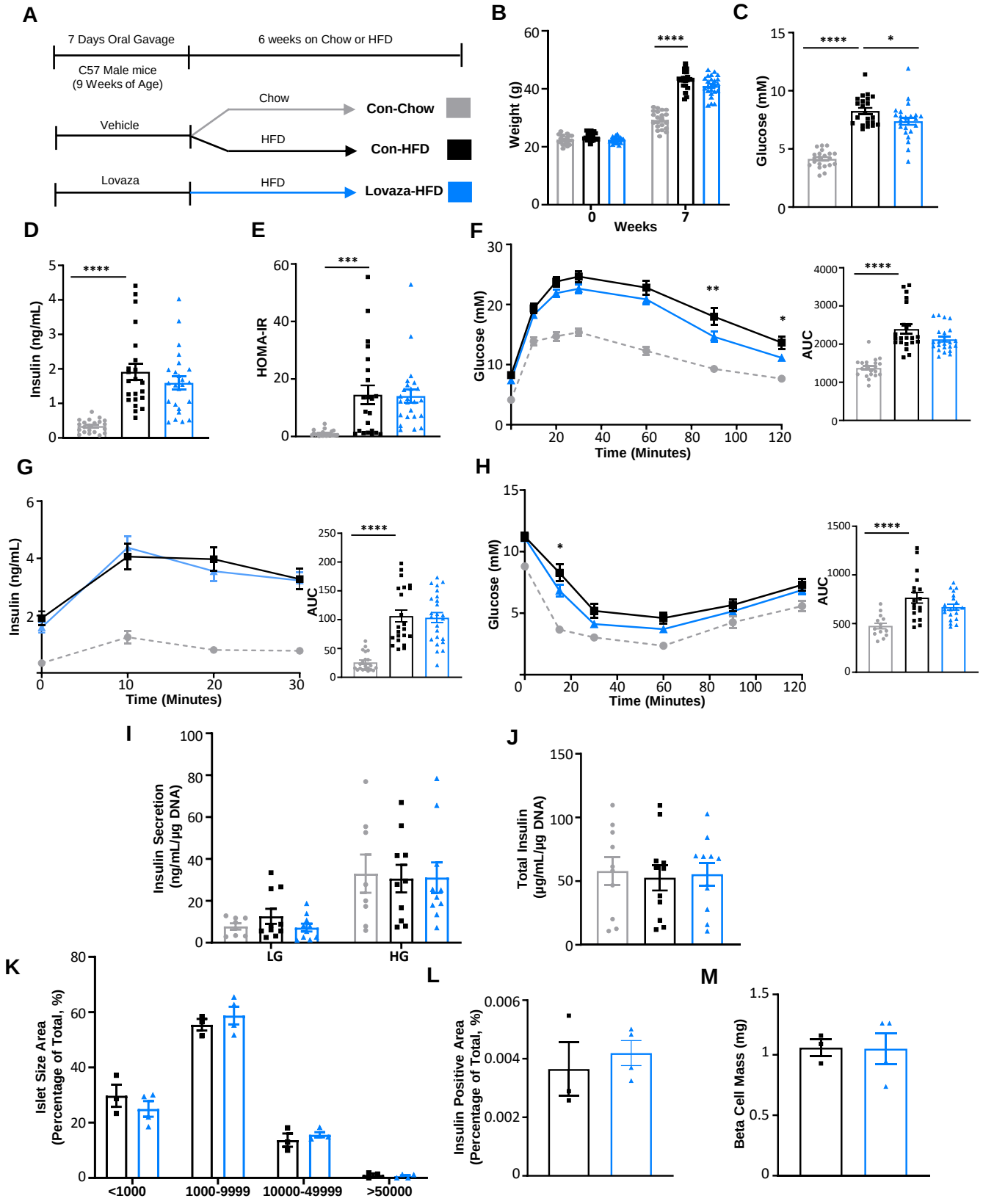

Figure S2. Lovaza does not affect HFD impaired glucose intolerance and insulin resistance. A) Schematic Diagram B) Weight C) Fasting blood glucose levels D) Fasting insulin levels E) Calculated HOMA-IR F) Oral glucose tolerance test with area under curve G) Insulin secretion during oral glucose tolerance test with area under curve H) Intraperitoneal insulin tolerance test with area under curve (n=21,22,24) I) Ex vivo glucose stimulated insulin secretion and J) total insulin content (n=8-10) K) Islet size distribution L) Total insulin positive area M) Beta cell mass (n=3-4). Con-Chow and con-HFD are the same controls used for Figure 1 and Figure 2. *P<0.05, ***P<0.001, ****P<0.0001 vs con-HFD. All error bars ±SEM, Related to Figure 1 and Figure 2.

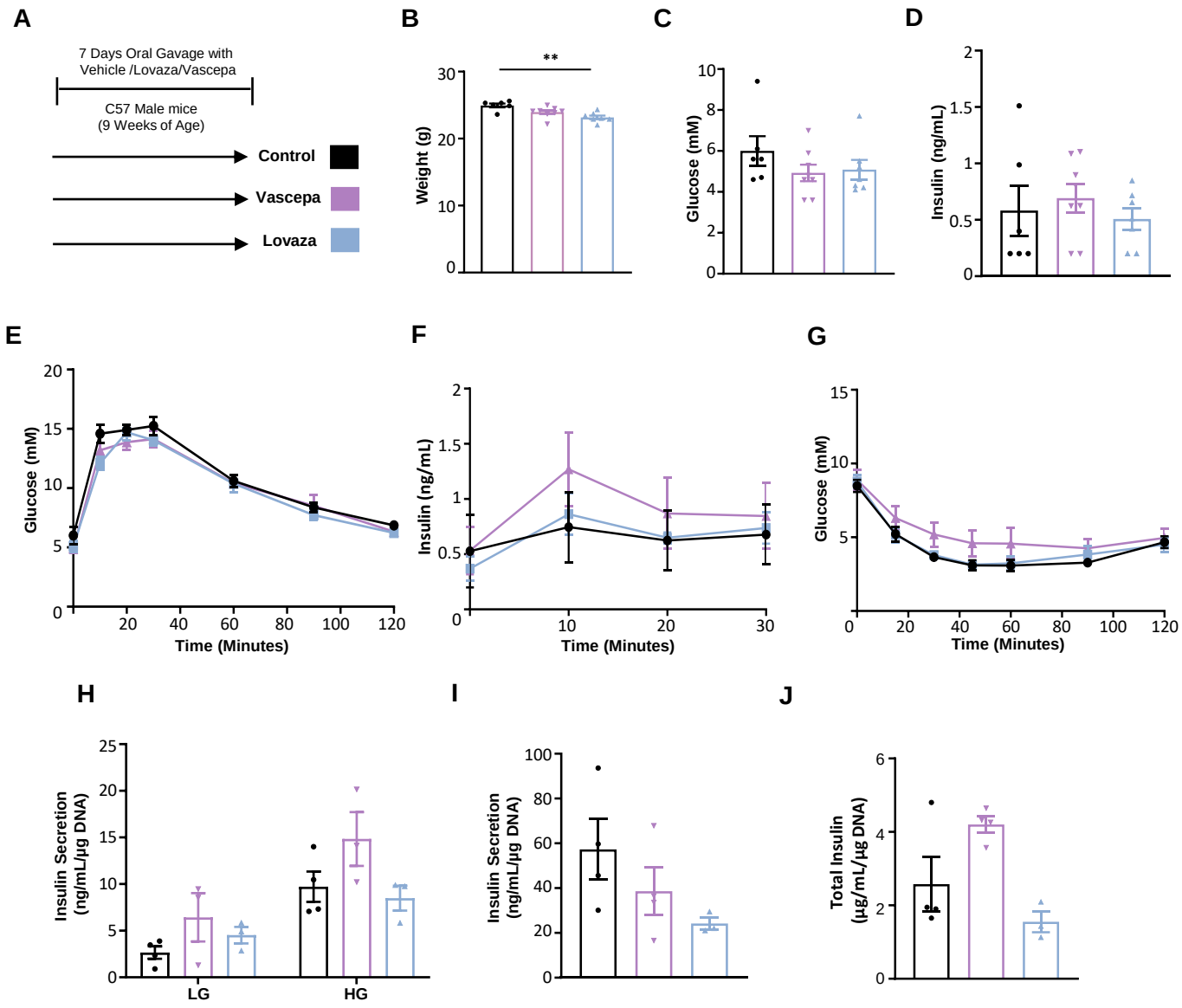

Figure S3. Treatment with Vascepa or Lovaza for 7 days does not improve glucose tolerance, insulin resistance or glucose stimulated insulin secretion. A) Schematic Diagram B) Weight C) Blood glucose levels and D) Serum insulin levels after overnight fasting E) Oral glucose tolerance test (n=6-8/group) F) Insulin secretion during oral glucose tolerance test (n=4/group) G) Intraperitoneal insulin tolerance test (n=6-8/group) H) Glucose stimulated insulin secretion I) KCl-Induced Insulin Secretion and J) Total insulin content (n=3-4/group). **p<0.01. All error bars ±SEM, Related to Figure 1.

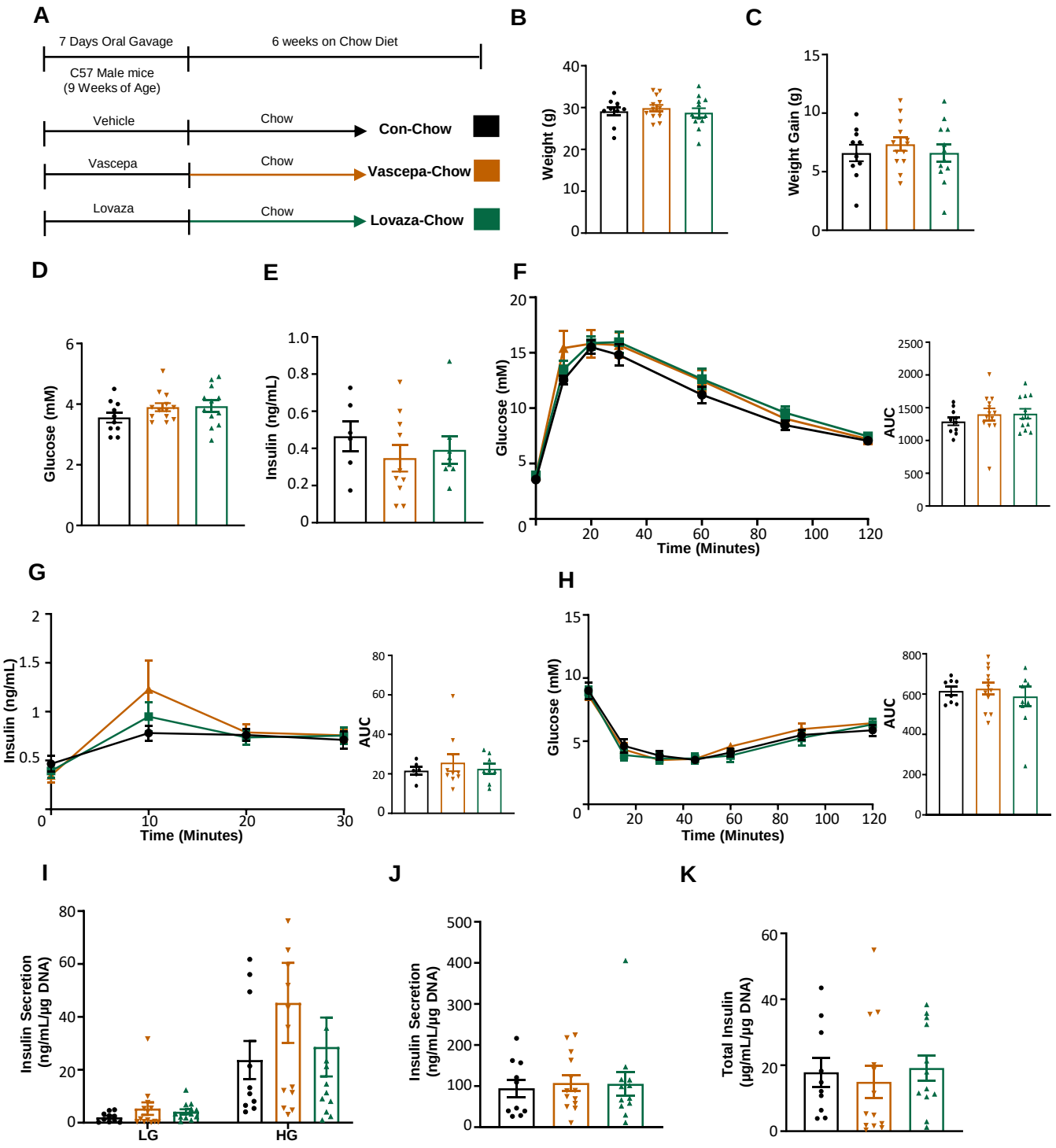

Figure S4. Vascepa or Lovaza does not improve glucose tolerance, insulin resistance or glucose stimulated insulin secretion 6 weeks after cessation of treatment in chow treated mice. A) Schematic Diagram B) Weight C) Weight Gain D) Blood glucose levels and E) Serum insulin levels after overnight fasting F) Oral glucose tolerance test with area under curve (10,12,13) G) Insulin secretion during oral glucose tolerance test with area under curve (n=6,10,8) H) Intraperitoneal insulin tolerance test with area under curve (n=9,12,13) I) Glucose stimulated insulin secretion and J) KCl-Induced Insulin Secretion K) Total insulin content (n=10,12,13). All error bars ±SEM, Related to Figure 1.

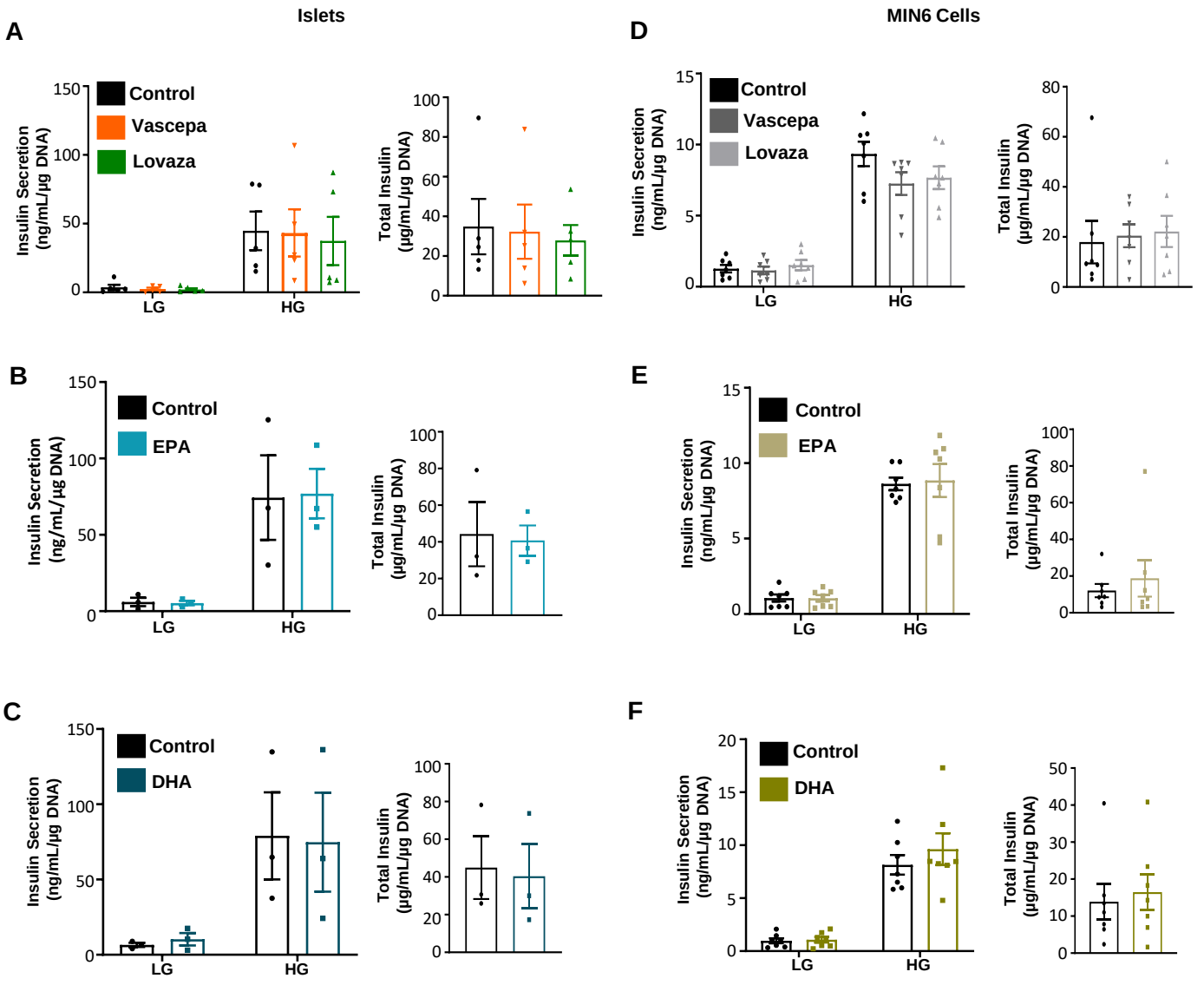

Figure S5. In Vitro treatment of Vascepa, Lovaza, EPA or DHA ethyl ester at an equivalent of 100µM EPA has no effect on glucose stimulated insulin secretion in primary mouse islets or MIN6K8 cells. Glucose stimulated insulin secretion and total insulin content of islets (n=3-5/group) treated for 24 hours with A) Lovaza or Vascepa (100 µM EPA ethyl ester) (n=5/group) B) 100µM EPA ethyl ester or C) 70µM DHA ethyl ester (n=3/group).Glucose stimulated insulin secretion and total insulin content of MIN6K8 cells (n=7/group) treated for 24 hours with D) Lovaza or Vascepa (100 µM EPA ethyl ester) E) 100µM EPA ethyl ester or F) 70µM DHA ethyl ester. All error bars ±SEM, Related to Figure 2.

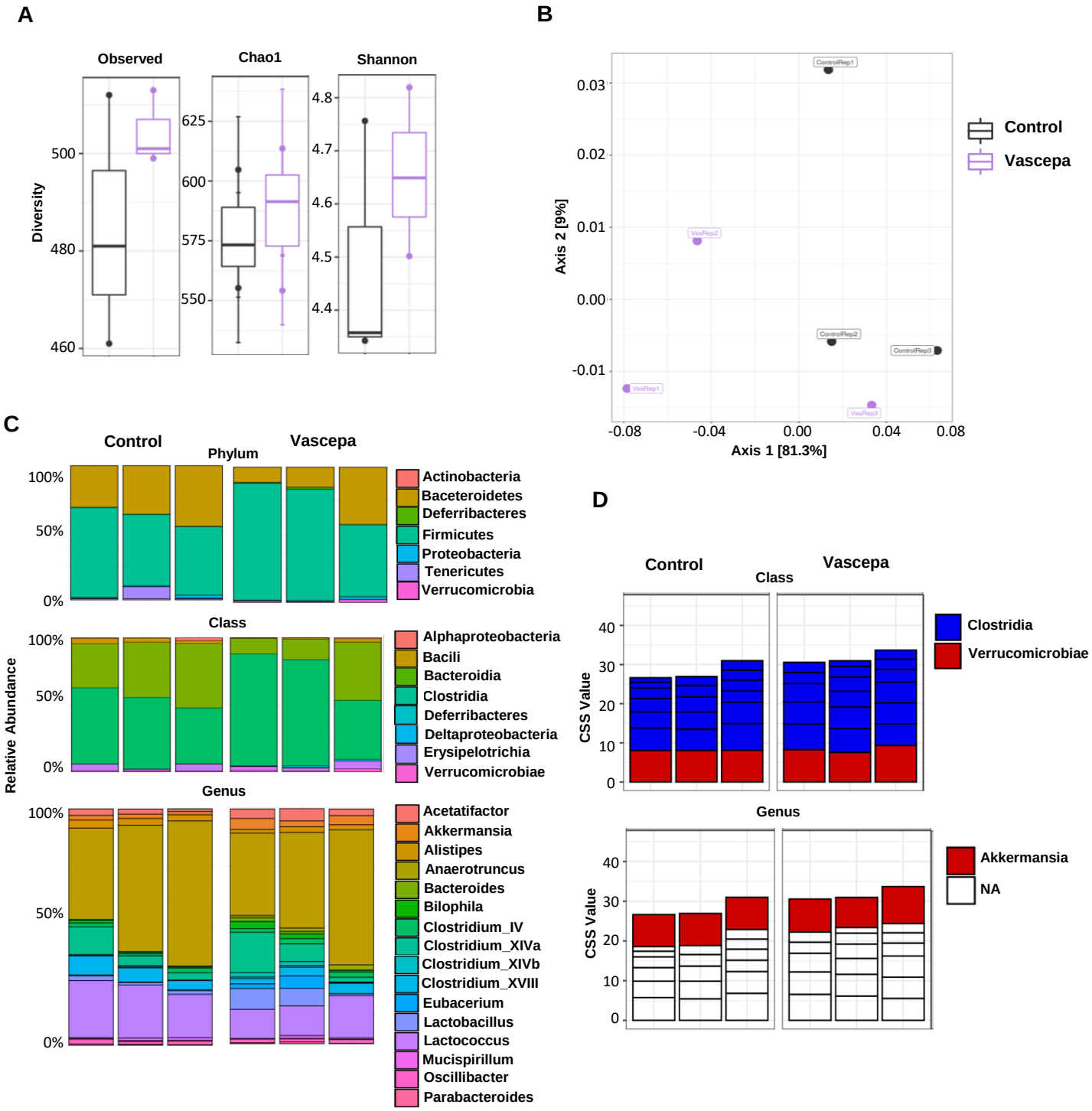

Figure S6. Vascepa treatment for 7 days does not induce changes on microbiota composition. A) Alpha diversity B) Beta diversity C) Relative abundance based on Phylum, Class and Genus D) Metagenomseq analysis showing cumulative sum scaling (CSS) abundances of species (n=3/group), Related to Figure 5.