Supplemental Table 1. Diet Formulation

	LF		HF		HF-EP		HF-NEP		HF-EP+NEP		HF-GP	
Ingredient	**gm**	**kcal**	**gm**	**kcal**	**gm**	**kcal**	**gm**	**kcal**	**gm**	**kcal**	**gm**	**kcal**
Casein	190	758	234	936	234	935	233	933	233	932	233	933
L-Cystine	2.8	11	3.5	14	3.5	14	3.5	14	3.5	14	3.5	14
Corn Starch	480	1919	86	343	86	342	85	341	85	341	89	358
Maltodextrin 10	118	474	110	440	110	439	110	438	109	438	110	438
Fructose	0.0	0.0	26	102	26	102	26	102	26	102	0.0	0.0
Dextrose, anhydrous	0.0	0.0	26	102	26	102	26	102	26	102	0.0	0.0
Sucrose	65	261	163	651	162	650	162	648	162	647	162	648
Cellulose, BW200	47	0.0	47	0.0	47	0.0	47	0.0	47	0.0	47	0.0
Soybean Oil	24	213	57	514	57	513	57	512	57	511	57	512
Butter	0.0	0.0	52	471	52	470	52	469	52	469	52	469
Lard	19	171	41	371	41	371	41	370	41	369	41	370
Shortening	0.0	0.0	65	585	65	585	65	583	65	583	65	583
Beef Tallow	0.0	0.0	24	214	24	214	24	213	24	213	24	213
Mineral Mix, S10026	9.5	0.0	12	0.0	12	0.0	12	0.0	12	0.0	12	0.0
DiCalcium Phosphate	12	0.0	15	0.0	15	0.0	15	0.0	15	0.0	15	0.0
Calcium Carbonate	5.2	0.0	6.4	0.0	6.4	0.0	6.4	0.0	6.4	0.0	6.4	0.0
Potassium Citrate	16	0.0	19	0.0	19.3	0.0	19	0.0	19	0.0	19	0.0
Vitamin Mix, V10001	9.5	40	12	40	12	40	12	40	12	40	12	40
Choline Bitartrate	1.9	0.0	2.3	0.0	2.3	0.0	2.3	0.0	2.3	0.0	2.3	0.0
NEP Grape Fraction	0.0	0.0	0.0	0.0	0.0	0.0	3.5	0.0	3.5	0.0	0.0	0.0
EP Grape Fraction	0.0	0.0	0.0	0.0	1.1	0.0	0.0	0.0	1.1	0.0	0.0	0.0
Grape Powder	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	50	161
FD&C Yellow Dye #5	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0
FD&C Red Dye #40	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.0
FD&C Blue Dye #1	0.0	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total	1000	3847	1000	4783	1000	4778	1000	4767	1000	4761	1000	4741
total fat, kcals%		10		44		44		44		44		44
sat. fat, kcal%		2.2		16		16		16		16		16
monounsat. fat, kcal%		3.0		17		17		17		17		17
polyunsat. fat, kcal%		4.7		11		11		11		11		11
total sugars, kcal%		7.8		19		19		19		19		19

*Numbers have been rounded up or down to optimize space constraints; LF, low fat control; HF, high fat sugar control; EP, extractable polyphenol fraction; NEP, non-extractable polyphenol fraction; GP, grape powder. EP and NEP are calorie free. GP contains 90% sugar w/w.

Supplemental Table 2. Phenolic Composition of Grape Powder, Extractable Polyphenol (EP), and Non-Extractable (NEP) Fraction

Assay	grape powder	EP	NEP
Weight percentage (%)	100	2.26	6.91
Total phenolics[1]	9.13	180.0 ± 1.3	10.5 ± 1.02
Total anthocyanins[2]	0.33	37.8 ± 1.8	ND
Total proanthocyanidins[3]	3.05	305.5 ± 7.0	ND

[1]Total phenolics, mg/g DM as gallic acid equivalent (Folin Ciocaleau assay)

[2]Total anthocyanins, mg/g DM as cyaniding-3-*O*- glucoside equivalent (pH differential assay)

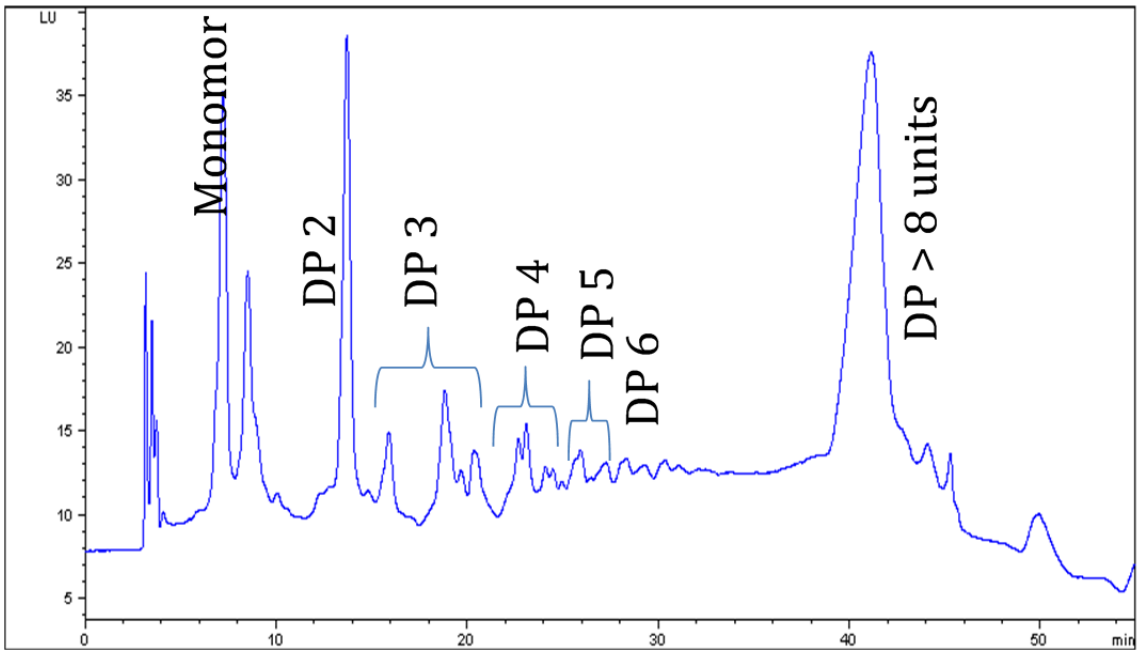
[3]Total proanthocyanidins, mg/g DM as procyanidin B2 equivalent (DMAC assay)

ND = not detectable

Supplemental Table 3. Principal Component Analysis of OTUs between Dietary Groups.

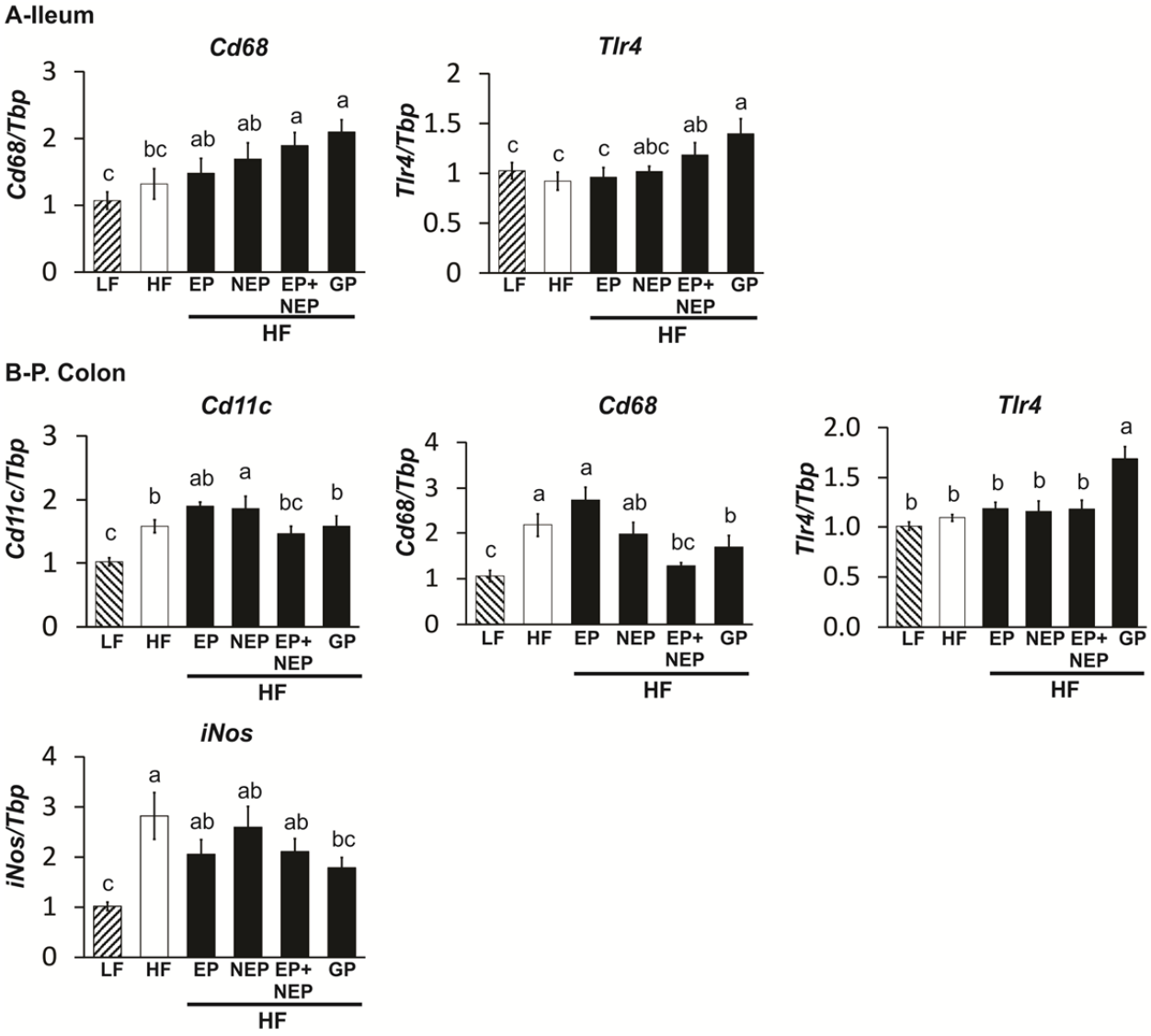
HF vs HF+EP	
PC1	**Correlation**
Firmicutes; Bacilli; Lactobacillales; Lactobacillaceae; Lactobacillus	0.67
Firmicutes; Clostridia; Clostridiales; Peptococcaceae; rc4-4	-0.77
PC2	
Actinobacteria; Actinobacteria; Bifidobacteriales; Bifidobacteriaceae; Bifidobacterium	-0.65
Firmicutes; Bacilli; Lactobacillales; Lactobacillaceae; Lactobacillus	-0.63
Firmicutes; Clostridia; Clostridiales; Other; Other	0.79
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae; Oscillospira	0.74
Firmicutes; Erysipelotrichi; Erysipelotrichales; Erysipelotrichaceae; Allobaculum	-0.71
HF vs HF+NEP	
PC1	
Bacteria; Verrucomicrobia; Verrucomicrobiae; Verrucomicrobiales; Verrucomicrobiaceae; Akkermansia	-0.88
PC2	
Bacteroidetes; Bacteroidia; Bacteroidales; S24-7	0.61
Firmicutes; Bacilli; Lactobacillales; Lactobacillaceae; Lactobacillus	-0.71
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae	0.92
Firmicutes; Erysipelotrichi; Erysipelotrichales; Erysipelotrichaceae; Allobaculum	-0.69
HF vs HF+EP-NEP	
PC1	
Actinobacteria; Actinobacteria; Bifidobacteriales; Bifidobacteriaceae; Bifidobacterium	-0.73
Bacteroidetes; Bacteroidia; Bacteroidales; S24-7	0.71
Firmicutes; Clostridia; Clostridiales; Clostridiaceae	0.65
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae	0.88
Firmicutes; Erysipelotrichi; Erysipelotrichales; Erysipelotrichaceae; Allobaculum	-0.91
PC2	
Actinobacteria; Actinobacteria; Bifidobacteriales; Bifidobacteriaceae; Bifidobacterium	0.68
Firmicutes; Clostridia; Clostridiales; Other; Other	-0.88
HF vs HF+Grape	
PC1	
Firmicutes; Clostridia; Clostridiales; Ruminococcaceae	0.67
Firmicutes; Clostridia; Clostridiales	0.65
PC2	
Firmicutes; Clostridia; Clostridiales;Lachnospiraceae; Ruminococcus; gnavus	0.74
Firmicutes; Clostridia; Clostridiales; Clostridiaceae	0.8
Firmicutes; Erysipelotrichi; Erysipelotrichales; Allobaculum	-0.6

Supplemental Figure 1



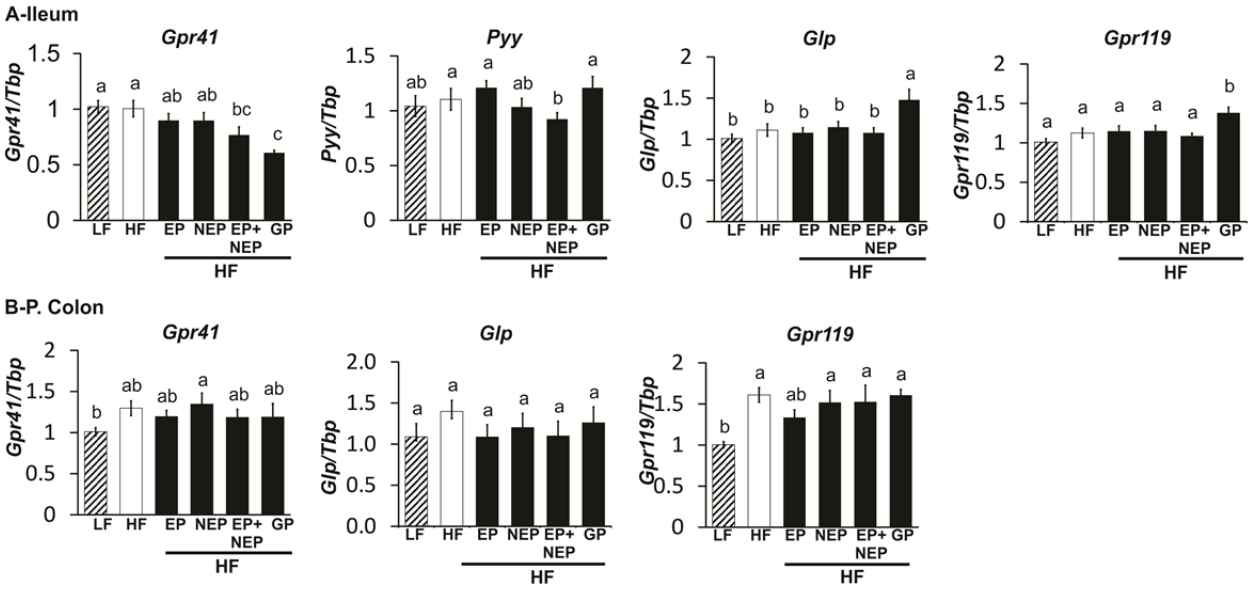
Supplemental Figure 1. Proanthocyanin degree of polymerization in EP fraction. NP-HPLC-FLD chromatogram (excitation 230 nm, emission 320 nm) for proanthocyanidins showing degree of polymerization (DP) in extractable polyphenol (EP) from grapes.

Supplemental Figure 2



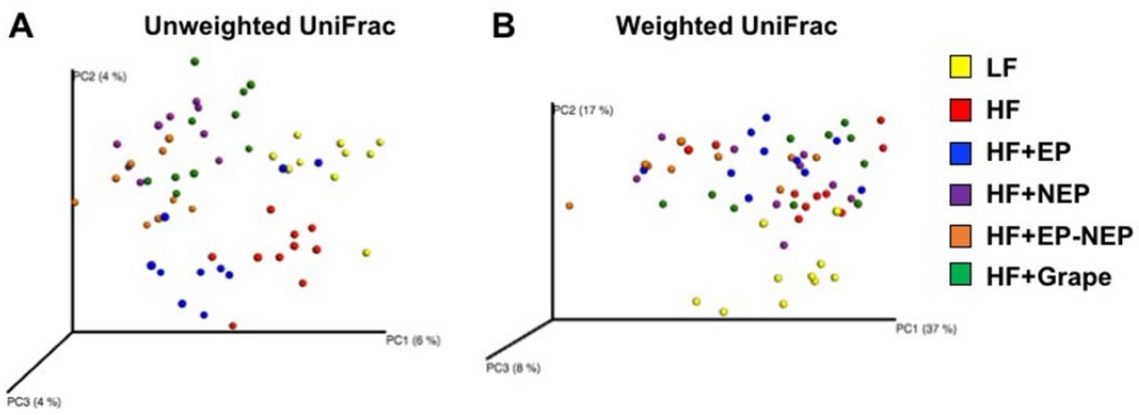
Supplemental Figure 2. The expression of markers of inflammation in the (A) ileum and (B) proximal colon of C57BL/6J mice fed a low fat (LF), high fat (HF) diet, or a HF diet containing extractable (HF-EP) or non-extractable (HF-NEP) polyphenols, an equal combination of the EP and NEP fractions (HF-EP+NEP), or grape powder (HF-GP) for 16 weeks. qPCR was conducted to measure mRNA abundance of genes associated with inflammation.. Means ± SEM (n=9-10) without a common lowercase letter differ ($p<0.05$) using one-way ANOVA and Student's t test.

Supplemental Figure 3



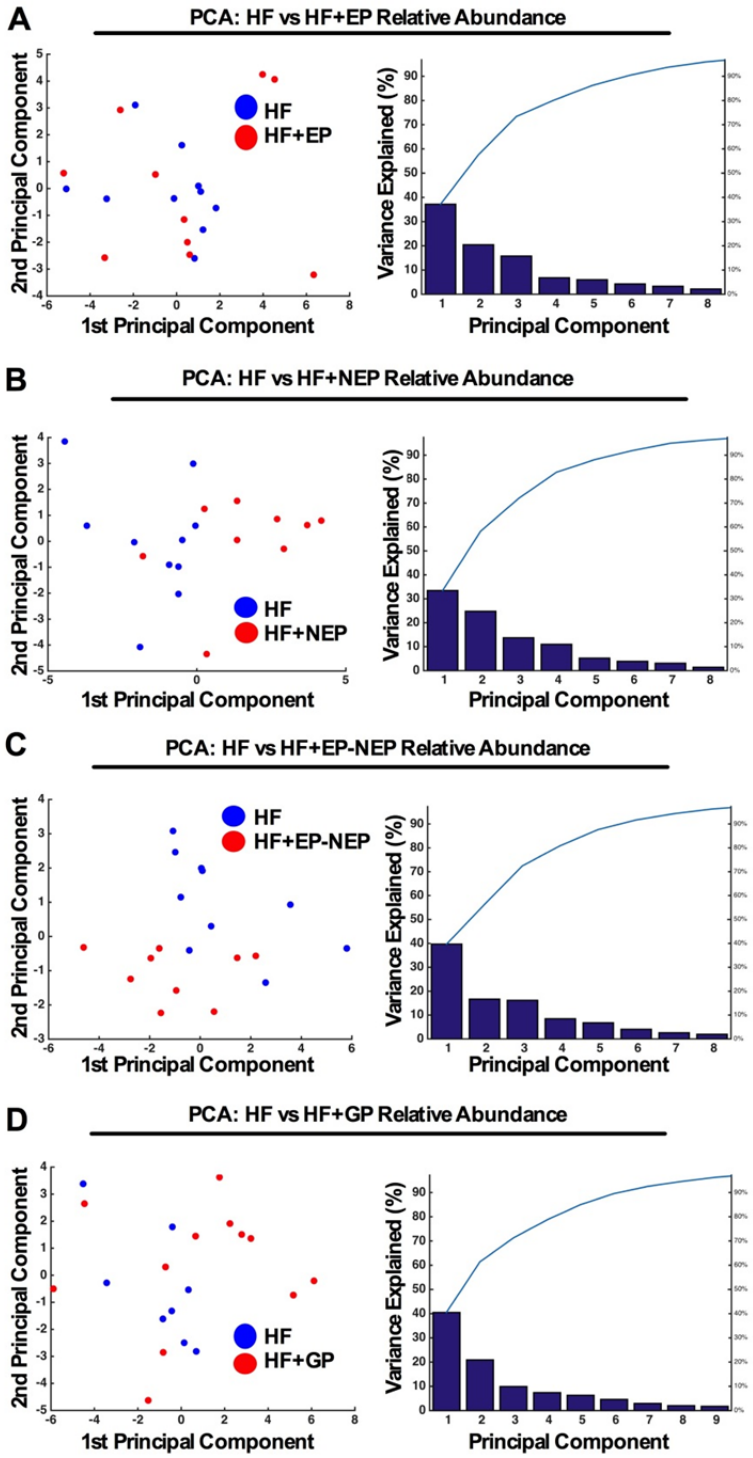
Supplemental Figure 3. The expression of G-protein receptors (*Gpr*) *41* and *119*, peptide YY (*Pyy*), and glucagon like protein (*Glp*) were measured as markers of SCFA regulation in the (A) ileum and (B) proximal colon mucosa of C57BL/6J mice fed a low fat (LF), high fat (HF) diet, or a HF diet containing extractable (HF-EP) or non-extractable (HF-NEP) polyphenols, an equal combination of the EP and NEP fractions (HF-EP+NEP), or grape powder (HF-GP) for 16 weeks. qPCR was conducted to measure mRNA abundance of genes associated with regulation of energy intake in ileum mucosa and proximal colon mucosa. Means ± SEM (n=9-10) without a common lowercase letter differ ($p<0.05$) using one-way ANOVA and Student's test.

Supplemental Figure 4.



Supplemental Figure 4. PCoA plots of unweighted (A) and weighted (B) UniFrac distances of C57BL/6J mice fed a low fat (LF), high fat (HF) diet, or a HF diet containing extractable (HF-EP) or non-extractable (HF-NEP) polyphenols, an equal combination of the EP and NEP fractions (HF-EP+NEP), or grape powder (HF-GP) for 16 weeks.

Supplemental Figure 5.



Supplemental Figure 5. The microbial relative abundances of C57BL/6J mice fed a low fat (LF), high fat (HF) diet, or a HF diet containing extractable (HF-EP) or non-extractable (HF-NEP) polyphenols, an

equal combination of the EP and NEP fractions (HF-EP+NEP), or grape powder (HF-GP) for 16 weeks. (A) Top Left - PCA plot between low fat (LF), high fat + extactable polyphenols (HF-EP), high fat + non-extractable polyphenols (HF-NEP), high fat + extactable and nonextractable polyphenols (HF-EP+NEP), and HF+Grape Powder (HF-GP). A) Left Side – PCA plot showing percentage of variance in Relative Abundances across diets explained by principal components. Right Side – Pareto plot showing percentage of variance explained by principal components. (B) Same as A, but showing PCA of HF vs HF-EP groups; (C) HF vs HF-NEP, and (D) HF vs HF-EP+NEP.