

Diet	Energy Density (kcal/gram)	Carbohydrate (% kcals)	Protein (% kcals)	Fat (% kcals)	Fiber (%)	Ingredients
Chow	3.1	44.2	18.6	6.2	3-5 soluble, 14.7 insoluble	Ground wheat, ground corn, wheat middlings, dehulled soybean meal, corn gluten meal, soybean oil, calcium carbonate, dicalcium phosphate, brewers dried yeast, iodized salt, L-lysine, DL-methionine, choline chloride, kaolin, magnesium oxide, vitamin E acetate, menadione sodium bisulfite complex, manganous oxide, ferrous sulfate, zinc oxide, niacin, calcium pantothenate, copper sulfate, pyridoxine hydrochloride, riboflavin, thiamin mononitrate, vitamin A acetate, calcium iodate, vitamin B12 supplement, folic acid, biotin, vitamin D3 supplement, cobalt carbonate.
HFD	4.6	36	18	46	5.8 insoluble	Casein, L-cysteine, corn starch, maltodextrin, sucrose, cellulose, soybean oil, lard, mineral mixture, dicalcium phosphate, calcium carbonate, potassium citrate, vitamin mixture, choline bitartrate

**Table S1.** Macronutrient and fiber contents and ingredients of the chow diet and high fat diet (HFD).

Pathway	log2Fold Change	p-value
4-hydroxyphenylacetate degradation	2.722940251	0.002674464
arginine, ornithine and proline interconversion	-1.384700294	6.77E-11
biotin biosynthesis I	2.03664634	7.39E-11
catechol degradation to &beta;-keto adipate	1.976426813	0.041330499
pyruvate fermentation to butanoate	-1.019334009	0.00350156
chlorophyllide a biosynthesis I (aerobic, light-dependent)	-3.015328029	0.00012822
reductive acetyl coenzyme A pathway	1.549448186	0.002959629
creatinine degradation I	2.024905335	0.00212871
nitrate reduction I (denitrification)	3.258938311	0.00260768
glucose degradation (oxidative)	2.385286395	0.011254152
fatty acid &beta;-oxidation I	-1.099664009	0.007093604
superpathway of fatty acid biosynthesis initiation (E. coli)	2.875459736	1.53E-13
D-glucarate degradation I	-1.783936949	0.000455135
superpathway of glycolysis, pyruvate dehydrogenase, TCA, and glyoxylate bypass	-1.924801132	0.001179148
superpathway of glycerol degradation to 1,3-propanediol	-1.404546601	0.002731046
L-methionine biosynthesis I	1.555842437	1.10E-05
L-methionine biosynthesis III	1.747271836	7.93E-12
lactose and galactose degradation I	-3.483217437	7.14E-10
L-leucine degradation I	3.103418173	0.00598016
superpathway of S-adenosyl-L-methionine biosynthesis	1.386081458	1.72E-05
NAD salvage pathway II	-1.155657983	0.002374661
ectoine biosynthesis	2.250635238	0.017661111
TCA cycle IV (2-oxoglutarate decarboxylase)	-2.064043204	0.000508278
purine nucleobases degradation I (anaerobic)	-1.444221374	1.21E-12
octane oxidation	3.032493979	0.007291367
3-phenylpropanoate degradation	3.246273203	6.43E-05
superpathway of taurine degradation	1.905628947	0.040937688
formaldehyde assimilation I (serine pathway)	3.137366854	0.049175839
photorespiration	3.294765748	0.016560335
formaldehyde assimilation II (RuMP Cycle)	-1.365317593	0.001139863
L-lysine biosynthesis II	-1.712567672	1.76E-10
glycine betaine degradation I	3.218897669	0.019723566
S-methyl-5-thio-&alpha;-D-ribose 1-phosphate degradation	-2.237137674	0.010751073
creatinine degradation II	9.107201731	8.08E-12
urea cycle	1.144204435	0.00036105
biotin biosynthesis II	-2.030935198	3.76E-05
4-aminobutanoate degradation V	-1.157851201	0.013742876
L-histidine degradation II	2.69075977	0.003046278
L-glutamate degradation VIII (to propanoate)	3.90100551	0.001202568
toluene degradation III (aerobic) (via p-cresol)	-1.636149093	0.047095602
superpathway of sulfur oxidation (Acidianus ambivalens)	1.748728522	7.17E-05
superpathway of L-methionine biosynthesis (transsulfuration)	1.200467604	2.91E-05
catechol degradation III (ortho-cleavage pathway)	2.014920406	0.037626711

aromatic compounds degradation via $\beta$ -ketoacid pathway	2.014920406	0.037626711
adenosylcobalamin biosynthesis I (early cobalt insertion)	3.018808213	0.025790622
chlorophyllide a biosynthesis II (anaerobic)	-3.015328029	0.00012822
allantoin degradation to glyoxylate III	-1.832305282	0.000309966
ethylmalonyl-CoA pathway	3.34601404	0.00373592
2-methylcitrate cycle II	1.504297217	0.017107359
superpathway of menaquinol-9 biosynthesis	-1.223796802	0.024571513
superpathway of menaquinol-6 biosynthesis I	-1.293161028	0.019066006
ubiquinol-7 biosynthesis (prokaryotic)	1.36810042	0.013086171
ubiquinol-9 biosynthesis (prokaryotic)	1.36810042	0.013086171
ubiquinol-10 biosynthesis (prokaryotic)	1.36810042	0.013086171
superpathway of demethylmenaquinol-6 biosynthesis I	-1.316131373	0.019066006
superpathway of demethylmenaquinol-9 biosynthesis	-1.245888505	0.024571513
superpathway of menaquinol-10 biosynthesis	-1.293161028	0.019066006
superpathway of geranylgeranyldiphosphate biosynthesis I (via mevalonate)	-4.250014114	3.01E-13
superpathway of heme biosynthesis from glycine	1.468621901	0.037626711
palmitate biosynthesis II (bacteria and plants)	1.366443251	0.000787509
stearate biosynthesis II (bacteria and plants)	2.824725873	2.52E-13
superpathway of phenylethylamine degradation	-2.337473071	0.001202568
superpathway of salicylate degradation	1.991861057	0.039785754
4-methylcatechol degradation (ortho cleavage)	2.194358799	0.02058022
superpathway of menaquinol-8 biosynthesis II	1.766596167	3.33E-06
palmitoleate biosynthesis I (from (5Z)-dodec-5-enoate)	2.839965233	1.53E-13
8-amino-7-oxononanoate biosynthesis I	2.241557343	2.74E-11
chondroitin sulfate degradation I (bacterial)	2.407376551	8.78E-09
superpathway of L-phenylalanine biosynthesis	-1.216058261	0.003649799
superpathway of L-tyrosine biosynthesis	-1.208269537	0.003744832
superpathway of sulfolactate degradation	3.164294449	0.00692912
ubiquinol-8 biosynthesis (prokaryotic)	1.36810042	0.013086171
methylaspartate cycle	2.673723213	0.021892741
glycerol degradation to butanol	-1.807175936	6.84E-05
L-1,2-propanediol degradation	-1.004292045	0.014317426
UDP-2,3-diacetamido-2,3-dideoxy- $\alpha$ -D-mannuronate biosynthesis	1.26046917	0.013289115
chlorophyllide a biosynthesis III (aerobic, light independent)	-3.015328029	0.00012822
pyrimidine deoxyribonucleotide phosphorylation	1.012978979	0.000215599
inosine-5-phosphate biosynthesis III	-1.399939073	4.73E-05
myo-, chiro- and scillo-inositol degradation	1.699882168	0.000246312
ergothioneine biosynthesis I (bacteria)	2.04725852	0.03566568
superpathway of UDP-N-acetylglucosamine-derived O-antigen building blocks biosynthesis	1.013985946	0.001945406
1,4-dihydroxy-6-naphthoate biosynthesis II	1.893429092	5.85E-06
1,4-dihydroxy-6-naphthoate biosynthesis I	2.553752453	7.22E-07
taxadiene biosynthesis (engineered)	-1.24676871	0.003344638

L-methionine salvage cycle III	-2.809609141	0.000536568
methanol oxidation to carbon dioxide	3.72103984	7.61E-06
oleate biosynthesis IV (anaerobic)	2.791812448	1.21E-13
mevalonate pathway I	-4.28556232	3.61E-13
anhydromuropeptides recycling	1.746622623	0.000164026
superpathway of heme biosynthesis from uroporphyrinogen-III	1.554975457	0.00226536
tRNA processing	1.37059828	0.037413831
methylphosphonate degradation I	1.632203133	0.002090436
phenylacetate degradation I (aerobic)	-2.463902139	0.014310413
allantoin degradation IV (anaerobic)	2.500968789	0.004569686
2-methylcitrate cycle I	1.782774777	0.013742876
(5Z)-dodec-5-enoate biosynthesis	2.827637127	1.53E-13
mycolate biosynthesis	2.77734563	1.21E-13
formaldehyde oxidation I	-1.290305426	0.001292646
superpathway of glyoxylate bypass and TCA	-1.956921099	0.001899903
superpathway of L-threonine metabolism	-1.910292755	0.041487753
L-tyrosine degradation I	2.212701998	0.031660005
superpathway of ubiquinol-8 biosynthesis (prokaryotic)	1.381865246	0.013086171
L-valine degradation I	2.402497172	0.001832754

**Table S2.** Cecum microbiome functional pathways differentially regulated in HFD-fed rats compared to chow-fed rats.

Pathway	log2Fold Change	p-value
4-hydroxyphenylacetate degradation	1.640510084	0.016271615
reductive acetyl coenzyme A pathway	1.239847462	0.030770187
fucose degradation	1.002479255	0.01462439
D-galactarate degradation I	-3.124348945	0.036469733
superpathway of D-glucarate and D-galactarate degradation	-3.124348945	0.036469733
superpathway of glycol metabolism and degradation	1.331005884	0.038133365
superpathway of glycolysis, pyruvate dehydrogenase, TCA, and glyoxylate bypass	1.690739782	0.017630708
glyoxylate cycle	1.613055786	0.020340651
heme biosynthesis II (anaerobic)	1.199928772	0.0188208
ketogluconate metabolism	1.526470517	0.042829735
lactose and galactose degradation I	2.074399734	0.003617119
methanogenesis from acetate	1.717898827	0.003617119
TCA cycle IV (2-oxoglutarate decarboxylase)	1.520429124	0.026734258
adenosylcobalamin biosynthesis II (late cobalt incorporation)	2.456817138	0.019521238
myo-inositol degradation I	2.074851639	0.001510231
formaldehyde assimilation II (RuMP Cycle)	1.014622558	0.032861765
peptidoglycan biosynthesis II (staphylococci)	5.630046228	0.020340651
sucrose degradation IV (sucrose phosphorylase)	1.283024969	0.003617119
allantoin degradation to glyoxylate III	1.276639249	0.032203122
superpathway of geranylgeranyldiphosphate biosynthesis I (via mevalonate)	2.035902146	0.006072323
superpathway of phenylethylamine degradation	3.516360365	0.000202308
norspermidine biosynthesis	2.665631856	0.012125915
superpathway of L-phenylalanine biosynthesis	1.050863775	0.019521238
superpathway of L-tyrosine biosynthesis	1.044549517	0.019521238
fatty acid salvage	2.021690738	0.020340651
inosine-5-phosphate biosynthesis III	1.76453324	3.53E-07
mevalonate pathway I	2.061169423	0.006145873
tRNA processing	1.979960696	0.009894679
allantoin degradation IV (anaerobic)	2.526361723	0.014893373
formaldehyde oxidation I	1.003003957	0.030381929
superpathway of glyoxylate bypass and TCA	1.86651564	0.014893373
superpathway of L-threonine metabolism	4.586857116	3.53E-07

**Table S3.** Cecum microbiome functional pathways differentially regulated in HFD-fed rats supplemented with OFS compared to HFD-fed rats.



