

# Supplementary Materials: Effect of High-Carbohydrate Diet on Plasma Metabolome in Mice with Mitochondrial Respiratory Chain Complex III Deficiency

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**Table S1.** One-way ANOVA analysis for Plasma metabolomics.

Metabolites	<i>f</i> Value	<i>p</i> Value	Log <i>p</i>	FDR	Fisher's LSD
Ornithine	49.494	$6.94 \times 10^{-11}$	10.159	$7.01 \times 10^{-9}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Carnitine	44.053	$2.47 \times 10^{-10}$	9.6079	$1.25 \times 10^{-8}$	CO SD-GG SD; CO HCD-GG SD; CO SD-GG HCD; CO HCD-GG HCD; CO SD-CO HCD
Arginine	32.735	$5.57 \times 10^{-9}$	8.2545	$1.87 \times 10^{-7}$	CO SD-GG SD; CO HCD-GG SD; CO SD-GG HCD; CO HCD-GG HCD
Glutamine	27.743	$2.91 \times 10^{-8}$	7.5363	$7.34 \times 10^{-7}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
CholicAcid	26.017	$5.43 \times 10^{-8}$	7.2652	$1.10 \times 10^{-6}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD
DimethylGlycine	23.703	$1.32 \times 10^{-7}$	6.8802	$2.22 \times 10^{-6}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO HCD
Glycine	19.92	$6.48 \times 10^{-7}$	6.1882	$9.36 \times 10^{-6}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Propionylcarnitine	19.462	$7.97 \times 10^{-7}$	6.0985	$9.96 \times 10^{-6}$	CO SD-GG SD; CO SD-GG HCD; CO SD-CO HCD
Phenylalanine	19.191	$9.02 \times 10^{-7}$	6.0446	$9.96 \times 10^{-6}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Sucrose	18.998	$9.86 \times 10^{-7}$	6.006	$9.96 \times 10^{-6}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Cytidine	18.172	$1.45 \times 10^{-6}$	5.8377	$1.33 \times 10^{-5}$	CO SD-GG SD; CO SD-GG HCD; CO SD-CO HCD
5-Hydroxyindole-3-aceticacid	17.48	$2.03 \times 10^{-6}$	5.6926	$1.71 \times 10^{-5}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
Glyceraldehyde	17.241	$2.28 \times 10^{-6}$	5.6416	$1.77 \times 10^{-5}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
NAD	16.722	$2.95 \times 10^{-6}$	5.5295	$2.13 \times 10^{-5}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Asparagine	15.817	$4.70 \times 10^{-6}$	5.3283	$3.16 \times 10^{-5}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
SymmetriS Dimethylarginine	15.581	$5.31 \times 10^{-6}$	5.2746	$3.35 \times 10^{-5}$	GG HCD-GG SD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
2-Aminoisobutyricacid	14.841	$7.89 \times 10^{-6}$	5.1031	$4.69 \times 10^{-5}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Acetylcarnitine	14.725	$8.40 \times 10^{-6}$	5.0756	$4.71 \times 10^{-5}$	CO SD-GG SD; CO SD-GG HCD; CO SD-CO HCD
KynurenicAcid	14.029	$1.23 \times 10^{-5}$	4.9087	$6.56 \times 10^{-5}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
Serine	13.916	$1.31 \times 10^{-5}$	4.8811	$6.64 \times 10^{-5}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD

Table S1. Cont.

Metabolites	<i>f</i> Value	<i>p</i> Value	Log <i>p</i>	FDR	Fisher's LSD
Creatinine	13.723	$1.47 \times 10^{-5}$	4.8337	$7.05 \times 10^{-5}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
L-5-Hydroxytryptophan	12.998	$2.23 \times 10^{-5}$	4.6519	$9.98 \times 10^{-5}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Leucine	12.965	$2.27 \times 10^{-5}$	4.6437	$9.98 \times 10^{-5}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Tyrosine	11.99	$4.08 \times 10^{-5}$	4.3895	$1.72 \times 10^{-4}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
2-deoxyuridine	11.725	$4.81 \times 10^{-5}$	4.3182	$1.94 \times 10^{-4}$	CO HCD-GG SD; CO HCD-GG HCD; CO HCD-CO SD
Alanine	10.299	$1.2 \times 10^{-4}$	3.9199	$4.67 \times 10^{-4}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Histidine	10.105	$1.37 \times 10^{-4}$	3.8636	$5.12 \times 10^{-4}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
4-PyridoxicAcid	8.9863	$2.97 \times 10^{-4}$	3.5273	$1.071 \times 10^{-3}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
Citrulline	8.7693	$3.47 \times 10^{-4}$	3.4597	$1.208 \times 10^{-3}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD
Lysine	8.6957	$3.66 \times 10^{-4}$	3.4366	$1.23 \times 10^{-3}$	GG SD-CO SD; GG HCD-CO SD; CO HCD-CO SD
Isobutyrylcarnitine	8.6157	$3.88 \times 10^{-4}$	3.4114	$1.23 \times 10^{-3}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD; CO SD-CO HCD
L-Methionine	8.6088	$3.9 \times 10^{-4}$	3.4092	$1.23 \times 10^{-3}$	GG SD-CO SD; GG HCD-CO SD; CO HCD-CO SD
Proline	7.8377	$6.91 \times 10^{-4}$	3.1605	$2.115 \times 10^{-3}$	GG SD-CO SD; GG HCD-CO SD; GG HCD-CO HCD
AminodipicAcid	7.7256	$7.53 \times 10^{-4}$	3.1234	$2.236 \times 10^{-3}$	GG SD-CO SD; GG HCD-CO SD; CO HCD-CO SD
Normetanephrene	7.6403	$8.03 \times 10^{-4}$	3.0951	$2.318 \times 10^{-3}$	GG HCD-GG SD; CO SD-GG SD; CO HCD-GG SD
Valine	7.0742	$1.249 \times 10^{-3}$	2.9034	$3.504 \times 10^{-3}$	GG SD-CO SD; GG HCD-CO SD; CO HCD-CO SD
Cystathionine	6.8357	$1.511 \times 10^{-3}$	2.8208	$4.124 \times 10^{-3}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
L-Kynurenine	6.1515	$2.648 \times 10^{-3}$	2.5771	$7.038 \times 10^{-3}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Asymmetric-Dimethylarginine	6.1017	$2.761 \times 10^{-3}$	2.5589	$7.15 \times 10^{-3}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD
Allantoin	5.7268	$3.796 \times 10^{-3}$	2.4207	$9.585 \times 10^{-3}$	GG SD-CO HCD; GG HCD-CO SD; GG HCD-CO HCD; CO SD-CO HCD
PantothenicAcid	5.5058	$4.595 \times 10^{-3}$	2.3377	$1.132 \times 10^{-2}$	GG HCD-GG SD; CO HCD-GG SD; GG HCD-CO SD
cAMP	5.4261	$4.926 \times 10^{-3}$	2.3075	$1.1846 \times 10^{-2}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
Isoleucine	5.3479	$5.276 \times 10^{-3}$	2.2777	$1.2393 \times 10^{-2}$	GG SD-CO SD; GG HCD-CO SD
L-GlutamicAcid	5.1635	$6.21 \times 10^{-3}$	2.2069	$1.4256 \times 10^{-2}$	CO SD-GG SD; CO HCD-GG SD; CO HCD-GG HCD
GABA	4.9664	$7.408 \times 10^{-3}$	2.1303	$1.6626 \times 10^{-2}$	GG SD-CO SD; GG HCD-CO SD; GG HCD-CO HCD
3-Hydroxy-DL-kynurenine	4.9305	$7.651 \times 10^{-3}$	2.1163	$1.68 \times 10^{-2}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Adenosine	4.8552	$8.19 \times 10^{-3}$	2.0867	$1.7601 \times 10^{-2}$	GG HCD-CO SD; GG HCD-CO HCD
Succinate	4.2698	$1.4064 \times 10^{-2}$	1.8519	$2.9593 \times 10^{-2}$	CO SD-GG SD; CO HCD-GG SD; CO SD-GG HCD; CO HCD-GG HCD
deoxycytidine	3.8474	$2.1037 \times 10^{-2}$	1.677	$4.2039 \times 10^{-2}$	CO SD-GG SD; CO SD-CO HCD
TaurochenodeoxycholicAcid	3.8413	$2.1162 \times 10^{-2}$	1.6744	$4.2039 \times 10^{-2}$	GG SD-CO SD; GG SD-CO HCD
GlycocholicAcid	3.8381	$2.1227 \times 10^{-2}$	1.6731	$4.2039 \times 10^{-2}$	GG SD-GG HCD; GG SD-CO HCD; CO SD-CO HCD

**Table S1.** *Cont.*

Metabolites	<i>f</i> Value	<i>p</i> Value	Log <i>p</i>	FDR	Fisher's LSD
Myoinositol	3.7122	$2.3984 \times 10^{-2}$	1.6201	$4.6585 \times 10^{-2}$	GG SD-CO HCD; CO SD-CO HCD
Cotinine	3.6899	$2.4512 \times 10^{-2}$	1.6106	$4.6711 \times 10^{-2}$	GG HCD-GG SD; CO SD-GG SD; CO HCD-GG SD
TaurocholicAcid	3.6485	$2.5525 \times 10^{-2}$	1.593	$4.7741 \times 10^{-2}$	GG SD-CO SD; GG SD-CO HCD; GG HCD-CO SD
Niacinamide	3.6226	$2.6179 \times 10^{-2}$	1.582	$4.8074 \times 10^{-2}$	CO HCD-GG SD; CO HCD-CO SD
ChenodeoxycholicAcid	3.5855	0.02715	1.5662	$4.8967 \times 10^{-2}$	GG SD-GG HCD; GG SD-CO SD
Trimethylamine- <i>N</i> -Oxide	3.3463	$3.4397 \times 10^{-2}$	1.4635	$6.095 \times 10^{-2}$	CO SD-GG SD; CO SD-GG HCD
Uracil	3.2606	$3.7474 \times 10^{-2}$	1.4263	$6.5257 \times 10^{-2}$	CO SD-GG SD; CO HCD-GG SD
Xanthine	3.2286	$3.8696 \times 10^{-2}$	1.4123	$6.6241 \times 10^{-2}$	CO SD-GG SD; CO HCD-GG SD; CO SD-GG HCD; CO HCD-GG HCD
Adenine	3.1326	$4.2622 \times 10^{-2}$	1.3704	$7.1747 \times 10^{-2}$	GG HCD-GG SD; GG HCD-CO SD; GG HCD-CO HCD
NicotinicAcid	3.1126	$4.3492 \times 10^{-2}$	1.3616	$7.2012 \times 10^{-2}$	GG SD-GG HCD; GG SD-CO SD; GG SD-CO HCD
Hexanoylcarnitine	3.0808	$4.4914 \times 10^{-2}$	1.3476	$7.3167 \times 10^{-2}$	CO SD-GG HCD; CO SD-CO HCD

FDR—False discovery rate; LSD—Least significant difference; GG—homozygous mice; CO—control mice; SD—standard diet; HCD—High carbohydrate diet; NAD—Nicotinamide adenine dinucleotide; GABA— $\gamma$ -Aminobutyric acid.

**Table S2.** Result of quantitative enrichment analysis between Control and homozygous mice on standard diet.

Metabolic Pathways	Total Cmpd	Hits	Statistic <i>q</i>	Expected <i>q</i>	Raw <i>p</i>	Holm <i>p</i>	FDR
Glycolysis	21	1	89.092	5.8824	$4.14 \times 10^{-9}$	$2.57 \times 10^{-7}$	$8.56 \times 10^{-8}$
Glycerol phosphate shuttle	8	1	89.092	5.8824	$4.14 \times 10^{-9}$	$2.57 \times 10^{-7}$	$8.56 \times 10^{-8}$
Gluconeogenesis	27	1	89.092	5.8824	$4.14 \times 10^{-9}$	$2.57 \times 10^{-7}$	$8.56 \times 10^{-8}$
Arginine and proline metabolism	26	8	46.435	5.8824	$5.81 \times 10^{-9}$	$3.43 \times 10^{-7}$	$9.00 \times 10^{-8}$
Urea cycle	20	7	49.351	5.8824	$1.07 \times 10^{-8}$	$6.21 \times 10^{-7}$	$1.33 \times 10^{-7}$
Ketone body metabolism	10	2	45.295	5.8824	$2.40 \times 10^{-8}$	$1.37 \times 10^{-6}$	$2.48 \times 10^{-7}$
Glutamate metabolism	18	7	44.937	5.8824	$9.29 \times 10^{-8}$	$5.20 \times 10^{-6}$	$8.23 \times 10^{-7}$
Ammonia recycling	18	8	61.363	5.8824	$1.07 \times 10^{-7}$	$5.87 \times 10^{-6}$	$8.27 \times 10^{-7}$
Glycine, serine and threonine metabolism	26	9	38.756	5.8824	$1.75 \times 10^{-7}$	$9.44 \times 10^{-6}$	$1.20 \times 10^{-6}$
Methionine metabolism	24	9	38.177	5.8824	$4.25 \times 10^{-7}$	$2.25 \times 10^{-5}$	$2.64 \times 10^{-6}$
Glucose-alanine cycle	12	2	68.551	5.8824	$5.42 \times 10^{-7}$	$2.82 \times 10^{-5}$	$3.06 \times 10^{-6}$
Protein biosynthesis	19	14	58.955	5.8824	$8.10 \times 10^{-7}$	$4.13 \times 10^{-5}$	$4.05 \times 10^{-6}$
Malate-aspartate shuttle	8	3	46.562	5.8824	$8.50 \times 10^{-7}$	$4.25 \times 10^{-5}$	$4.05 \times 10^{-6}$
Citric acid cycle	23	2	59.415	5.8824	$1.51 \times 10^{-6}$	$7.41 \times 10^{-5}$	$6.25 \times 10^{-6}$
Mitochondrial electron transport chain	15	2	59.415	5.8824	$1.51 \times 10^{-6}$	$7.41 \times 10^{-5}$	$6.25 \times 10^{-6}$
Nicotinate and nicotinamide metabolism	13	3	42.225	5.8824	$2.65 \times 10^{-6}$	$1.25 \times 10^{-4}$	$1.03 \times 10^{-5}$
Glutathione metabolism	10	4	37.882	5.8824	$2.83 \times 10^{-6}$	$1.3 \times 10^{-4}$	$1.03 \times 10^{-5}$
Glycerolipid metabolism	13	1	74.897	5.8824	$3.51 \times 10^{-6}$	$1.58 \times 10^{-4}$	$1.15 \times 10^{-5}$
Pyrimidine metabolism	36	6	36.69	5.8824	$3.54 \times 10^{-6}$	$1.58 \times 10^{-4}$	$1.15 \times 10^{-5}$
Porphyryn metabolism	22	1	74	5.8824	$4.68 \times 10^{-6}$	$2.01 \times 10^{-4}$	$1.45 \times 10^{-5}$
Lysine degradation	13	2	69.046	5.8824	$5.19 \times 10^{-6}$	$2.18 \times 10^{-4}$	$1.53 \times 10^{-5}$
Tyrosine metabolism	38	4	33.987	5.8824	$6.41 \times 10^{-6}$	$2.63 \times 10^{-4}$	$1.81 \times 10^{-5}$
Bile acid biosynthesis	49	7	41.706	5.8824	$7.81 \times 10^{-6}$	$3.12 \times 10^{-4}$	$2.10 \times 10^{-5}$
Oxidation of branched chain fatty acids	14	2	65.742	5.8824	$1.07 \times 10^{-5}$	$4.18 \times 10^{-4}$	$2.77 \times 10^{-5}$
Phenylalanine and tyrosine metabolism	13	4	37.466	5.8824	$1.13 \times 10^{-5}$	$4.3 \times 10^{-4}$	$2.80 \times 10^{-5}$
Valine, leucine and isoleucine degradation	36	3	46.168	5.8824	$1.41 \times 10^{-5}$	$5.2 \times 10^{-4}$	$3.35 \times 10^{-5}$
Tryptophan metabolism	34	5	39.984	5.8824	$2.88 \times 10^{-5}$	$1.037 \times 10^{-3}$	$6.62 \times 10^{-5}$
Biotin metabolism	4	1	67.34	5.8824	$3.02 \times 10^{-5}$	$1.057 \times 10^{-3}$	$6.69 \times 10^{-5}$
Catecholamine biosynthesis	5	1	65.975	5.8824	$4.23 \times 10^{-5}$	$1.437 \times 10^{-3}$	$9.04 \times 10^{-5}$
Betaine metabolism	10	5	29.452	5.8824	$4.63 \times 10^{-5}$	$1.527 \times 10^{-3}$	$9.57 \times 10^{-5}$
Sphingolipid metabolism	15	2	35.992	5.8824	$7.38 \times 10^{-5}$	$2.361 \times 10^{-3}$	$1.48 \times 10^{-4}$
Propanoate metabolism	18	1	63.429	5.8824	$7.66 \times 10^{-5}$	$2.373 \times 10^{-3}$	$1.48 \times 10^{-4}$
Beta oxidation of very long chain fatty acids	14	1	61.872	5.8824	$1.08 \times 10^{-4}$	$3.24 \times 10^{-3}$	$2.03 \times 10^{-4}$
Histidine metabolism	11	4	32.538	5.8824	$3.86 \times 10^{-4}$	$1.1186 \times 10^{-2}$	$7.03 \times 10^{-4}$
Aspartate metabolism	12	3	40.198	5.8824	$4.05 \times 10^{-4}$	$1.1344 \times 10^{-2}$	$7.18 \times 10^{-4}$
Purine metabolism	45	12	20.47	5.8824	$9.15 \times 10^{-4}$	$2.4705 \times 10^{-2}$	$1.576 \times 10^{-3}$
Alanine metabolism	6	1	48.009	5.8824	$1.434 \times 10^{-3}$	$3.7285 \times 10^{-2}$	$2.403 \times 10^{-3}$
Starch and sucrose metabolism	14	3	26.402	5.8824	$1.503 \times 10^{-3}$	$3.7572 \times 10^{-2}$	$2.452 \times 10^{-3}$
Cysteine metabolism	8	2	38.202	5.8824	$1.611 \times 10^{-3}$	$3.8652 \times 10^{-2}$	$2.56 \times 10^{-3}$

Table S2. Cont.

Metabolic Pathways	Total Cmpd	Hits	Statistic $q$	Expected $q$	Raw $p$	Holm $p$	FDR
Taurine and hypotaurine metabolism	7	1	36.903	5.8824	$7.496 \times 10^{-3}$	0.1724	$1.1618 \times 10^{-2}$
Galactose metabolism	25	4	20.806	5.8824	$1.3267 \times 10^{-2}$	0.29187	$2.0062 \times 10^{-2}$
Pantothenate and CoA biosynthesis	10	1	32.18	5.8824	$1.408 \times 10^{-2}$	0.29567	$2.0784 \times 10^{-2}$
Beta-alanine metabolism	13	4	16.541	5.8824	$3.4087 \times 10^{-2}$	0.68175	$4.9149 \times 10^{-2}$
Pentose phosphate pathway	18	1	20.231	5.8824	$6.1094 \times 10^{-2}$	1	$8.6087 \times 10^{-2}$
Intracellular signalling through adenosine receptor A2A and adenosine  intracellular signalling through adenosine receptor A2B and adenosine	7	2	13.071	5.8824	$1.1236 \times 10^{-1}$	1	$1.5481 \times 10^{-1}$
Vitamin b6 metabolism	10	2	10.316	5.8824	$1.7526 \times 10^{-1}$	1	$2.3623 \times 10^{-1}$
Excitatory neural signalling through through 5-hydroxytryptamine receptor (HTR) 4 and serotonin  excitatory neural signalling through 5-HTR 7 and serotonin  excitatory neural signalling through 5-HTR 6 and serotonin	5	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Corticotropin activation of cortisol production	5	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Vasopressin regulation of water homeostasis	5	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Intracellular signalling through FSH receptor and follicle stimulating hormone  intracellular signalling through LHCGR receptor and luteinizing hormone/ choriogonadotropin	4	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Intracellular signalling through histamine H2 receptor and histamine	5	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Intracellular signalling through PGD2 receptor and prostaglandin D2	5	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Intracellular signalling through prostacyclin receptor and prostacyclin	6	1	8.424	5.8824	$2.4266 \times 10^{-1}$	1	$2.8387 \times 10^{-1}$
Folate and pterine biosynthesis	17	2	8.0943	5.8824	$2.6581 \times 10^{-1}$	1	$3.0045 \times 10^{-1}$
Fructose and mannose degradation	18	1	7.6504	5.8824	$2.6653 \times 10^{-1}$	1	$3.0045 \times 10^{-1}$
Butyrate metabolism	9	1	1.4981	5.8824	$6.285 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$
One carbon pool by folate	8	1	1.4576	5.8824	$6.3322 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$

Table S2. Cont.

Metabolic Pathways	Total Cmpd	Hits	Statistic <i>q</i>	Expected <i>q</i>	Raw <i>p</i>	Holm <i>p</i>	FDR
Inositol metabolism	19	2	2.6146	5.8824	$6.5431 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$
Insulin signalling	19	3	3.4459	5.8824	$6.6305 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$
RNA transcription	9	1	1.1743	5.8824	$6.6864 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$
Phospholipid biosynthesis	19	1	1.1693	5.8824	$6.693 \times 10^{-1}$	1	$6.8028 \times 10^{-1}$
Nucleotide sugars metabolism	9	1	0.73929	5.8824	$7.3444 \times 10^{-1}$	1	$7.3444 \times 10^{-1}$

Table S3. Result of quantitative enrichment analysis between homozygous mice on standard and high carbohydrate diet.

Metabolic Pathways	Total Cmpd	Hits	Statistic <i>q</i>	Expected <i>q</i>	Raw <i>p</i>	Holm <i>p</i>	FDR
Glycerolipid metabolism	13	1	56.974	9.0909	0.004545	0.28179	0.17675
Betaine metabolism	10	5	27.483	9.0909	0.008893	0.54247	0.17675
Tyrosine metabolism	38	4	27.407	9.0909	0.009369	0.56214	0.17675
Tryptophan metabolism	34	5	24.445	9.0909	0.012649	0.74632	0.17675
Pantothenate and coa biosynthesis	10	1	46.273	9.0909	0.01492	0.86537	0.17675
Glycine, serine and threonine metabolism	26	9	23.588	9.0909	0.017105	0.97498	0.17675
Methionine metabolism	24	9	22.21	9.0909	0.020219	1	0.17908
Phenylalanine and tyrosine metabolism	13	4	26.169	9.0909	0.024551	1	0.19027
Purine metabolism	45	12	19.265	9.0909	0.04478	1	0.26012
Urea cycle	20	7	19.057	9.0909	0.048986	1	0.26012
Catecholamine biosynthesis	5	1	33.157	9.0909	0.050081	1	0.26012
Bile acid biosynthesis	49	7	20.48	9.0909	0.050346	1	0.26012
Starch and sucrose metabolism	14	3	20.349	9.0909	0.063278	1	0.26596
Porphyrin metabolism	22	1	29.309	9.0909	0.069088	1	0.26596
Galactose metabolism	25	4	19.865	9.0909	0.0857	1	0.26596
Nicotinate and nicotinamide metabolism	13	3	18.557	9.0909	0.10065	1	0.26596
Protein biosynthesis	19	14	17.883	9.0909	0.10079	1	0.26596
Excitatory neural signalling through 5- hydroxytryptamine receptor (HTR) 4 and serotonin excitatory neural signalling through 5-HTR 7 and serotonin excitatory neural signalling through 5-HTR 6 and serotonin	5	1	24.36	9.0909	0.10295	1	0.26596
Corticotropin activation of cortisol production	5	1	24.36	9.0909	0.10295	1	0.26596
Vasopressin regulation of water homeostasis	5	1	24.36	9.0909	0.10295	1	0.26596
Intracellular signalling through FSH receptor and follicle stimulating hormone intracellular signalling through lhcg receptor and luteinizing hormone/ choriogonadotropin	4	1	24.36	9.0909	0.10295	1	0.26596
Intracellular signalling through histamine H2 receptor and histamine	5	1	24.36	9.0909	0.10295	1	0.26596
Intracellular signalling through PGD2 receptor and prostaglandin D2	5	1	24.36	9.0909	0.10295	1	0.26596
Intracellular signalling through prostacyclin receptor and prostacyclin	6	1	24.36	9.0909	0.10295	1	0.26596

Table S3. Cont.

Metabolic Pathways	Total Cmpd	Hits	Statistic <i>q</i>	Expected <i>q</i>	Raw <i>p</i>	Holm <i>p</i>	FDR
Beta-alanine metabolism	13	4	18.972	9.0909	0.10911	1	0.27059
Arginine and proline metabolism	26	8	15.267	9.0909	0.11716	1	0.27939
Ammonia recycling	18	8	16.561	9.0909	0.13267	1	0.29522
Glutathione metabolism	10	4	16.468	9.0909	0.13694	1	0.29522
Lysine degradation	13	2	19.026	9.0909	0.13809	1	0.29522
Intracellular signalling through adenosine receptor A2A and adenosine I intracellular signalling through adenosine receptor A2B and adenosine	7	2	18.655	9.0909	0.14435	1	0.29832
Valine, leucine and isoleucine degradation	36	3	15.254	9.0909	0.16817	1	0.33257
Pyrimidine metabolism	36	6	13.547	9.0909	0.17424	1	0.33257
Cysteine metabolism	8	2	16.869	9.0909	0.17701	1	0.33257
Glutamate metabolism	18	7	13.584	9.0909	0.18558	1	0.33432
Histidine metabolism	11	4	14.319	9.0909	0.19149	1	0.33432
Insulin signalling	19	3	14.45	9.0909	0.19412	1	0.33432
Vitamin B6 metabolism	10	2	14.872	9.0909	0.20242	1	0.33918
Phospholipid biosynthesis	19	1	14.933	9.0909	0.21467	1	0.35025
Inositol metabolism	19	2	13.088	9.0909	0.23776	1	0.37071
Biotin metabolism	4	1	13.545	9.0909	0.23917	1	0.37071
RNA transcription	9	1	12.541	9.0909	0.25873	1	0.39125
Sphingolipid metabolism	15	2	9.9573	9.0909	0.34635	1	0.50254
Fructose and mannose degradation	18	1	8.8205	9.0909	0.34853	1	0.50254
Alanine metabolism	6	1	6.7891	9.0909	0.41339	1	0.5825
Nucleotide sugars metabolism	9	1	6.4467	9.0909	0.42585	1	0.5835
Glycolysis	21	1	5.3214	9.0909	0.47071	1	0.5835
Glycerol phosphate shuttle	8	1	5.3214	9.0909	0.47071	1	0.5835
Gluconeogenesis	27	1	5.3214	9.0909	0.47071	1	0.5835
Aspartate metabolism	12	3	7.2703	9.0909	0.47252	1	0.5835
Butyrate metabolism	9	1	5.2206	9.0909	0.47506	1	0.5835
Glucose-alanine cycle	12	2	6.0553	9.0909	0.47998	1	0.5835
Malate-aspartate shuttle	8	3	5.1521	9.0909	0.54929	1	0.64473
Ketone body metabolism	10	2	5.271	9.0909	0.56027	1	0.64473
One carbon pool by folate	8	1	3.4804	9.0909	0.56154	1	0.64473
Beta oxidation of very long chain fatty acids	14	1	3.0204	9.0909	0.58907	1	0.66404
Citric acid cycle	23	2	3.7354	9.0909	0.63647	1	0.6923
Mitochondrial electron transport chain	15	2	3.7354	9.0909	0.63647	1	0.6923
Folate and pterine biosynthesis	17	2	2.9161	9.0909	0.72298	1	0.77284
Propanoate metabolism	18	1	1.1408	9.0909	0.74111	1	0.77879
Pentose phosphate pathway	18	1	0.5445	9.0909	0.81972	1	0.84704
Oxidation of branched chain fatty acids	14	2	1.5711	9.0909	0.84347	1	0.85729
Taurine and hypotaurine metabolism	7	1	0.075561	9.0909	0.93242	1	0.93242

**Table S4.** Diet composition of Standard and High carbohydrate diet.

<b>Standard Diet (SD)</b>			<b>High Carbohydrate Diet (HCD)</b>		
<b>(Teklad Global 18% Rodent Diet-2018)</b>			<b>(60% Dextrose Diet, Orange—TD.05256)</b>		
Crude Protein	%	18.6	Casein	g/kg	207
Fat	%	6.2	Lard	g/kg	50
Carbohydrate	%	44.2	Dextrose, monohydrate	g/kg	658
Crude Fiber	%	3.5	Cellulose	g/kg	21.81
Neutral Detergent fiber	%	14.7			
Ash	%	5.3			
Energy Density	kcal/g	3.1			
Calories from Protein	%	24	Calories from Protein	% kcal	20.2
Calories from Fat	%	18	Calories from Fat	% kcal	12.9
Calories carbohydrate	%	58	Calories carbohydrate	% kcal	66.8
			Food color	g/kg	0.15
<b>Minerals</b>			<b>Mineral Mix, Rogers-Harper (170760)-50 g/kg</b>		
Calcium	%	1	Calcium Carbonate	g/kg	292.955
Phosphorus	%	0.7	Calcium Phosphate, dibasic, dihydrate	g/kg	4.3
Non-Phytate Phosphorus	%	0.4	Ammonium Paramolybdate, tetrahydrate	g/kg	0.025
Sodium	%	0.2	Sodium Chloride	g/kg	250.6
Potassium	%	0.6	Potassium Phosphate, monobasic	g/kg	343.1
Chloride	%	0.4	Zinc Chloride	g/kg	0.2
Magnesium	%	0.2	Magnesium Sulfate, heptahydrate	g/kg	99.8
Zinc	mg/kg	70	Zinc Carbonate	g/kg	0.04
Manganese	mg/kg	100	Manganese Sulfate, monohydrate	g/kg	1.21
Copper	mg/kg	15	Cupric Sulfate	g/kg	1.56
Iodine	mg/kg	6	Potassium Iodide	g/kg	0.005
Iron	mg/kg	200	Ferric Citrate	g/kg	6.23
Selenium	mg/kg	0.23	Sodium Selenite	g/kg	0.015
<b>Vitamins</b>			<b>Vitamin Mix, Teklad (40060)-10 g/kg</b>		
Vitamin A	IU/g	15	Vitamin A Palmitate (500,000 IU/g)	g/kg	3.9648
Vitamin D3	IU/g	1.5	Vitamin D3, cholecalciferol (500,000 IU/g)	g/kg	0.4405
Vitamin E	IU/kg	110	Vitamin E, DL- $\alpha$ tocopheryl acetate (500 IU/g)	g/kg	24.2291
Vitamin K3	mg/kg	50	Vitamin K3, menadione	g/kg	4.9559
Vitamin B1	mg/kg	17	Thiamin (81%)	g/kg	2.2026
Vitamin B2	mg/kg	15	Riboflavin	g/kg	2.2026
Niacin (Nicotinic acid)	mg/kg	70	Niacin	g/kg	9.9119
Vitamin B6	mg/kg	18	Pyridoxine HCl	g/kg	2.2026
Pantothenic Acid	mg/kg	33	Calcium Pantothenate	g/kg	6.6079
Vitamin B12	mg/kg	0.08	Vitamin B12 (0.1% in mannitol)	g/kg	2.9736
Biotin	mg/kg	0.4	Biotin	g/kg	0.0441
Folate	mg/kg	4	Folic Acid	g/kg	0.1982
Choline	mg/kg	1200	Choline Dihydrogen Citrate	g/kg	349.6916
			Vitamin C, (~97.5%)	g/kg	101.6604
			Inositol	g/kg	11.0132
			p-Aminobenzoic Acid	g/kg	11.0132
			Corn Starch	g/kg	466.687



Table S4. Cont.

Standard Diet (SD)			High Carbohydrate Diet (HCD)		
<b>Amino Acids</b>					
Aspartic Acid	%	1.4			
Glutamic Acid	%	3.4			
Alanine	%	1.1			
Glycine	%	0.8			
Threonine	%	0.7			
Proline	%	1.6			
Serine	%	1.1			
Leucine	%	1.8			
Isoleucine	%	0.8			
Valine	%	90%			
Phenylalanine	%	1			
Tyrosine	%	0.6			
Methionine	%	0.4	DL-Methionine	g/kg	3
Cystine	%	0.3			
Lysine	%	0.9			
Histidine	%	0.4			
Arginine	%	1			
Tryptophan	%	0.2			
<b>Fatty Acids</b>					
Palmitic	%	0.7			
Stearic	%	0.2			
Oleic	%	1.2			
Linoleic	%	3.1			
Linolenic	%	0.3			
Total Saturated	%	0.9			
Total Monounsaturated	%	1.3			
Total Polyunsaturated	%	3.4			