

Supplementary Table 1. Composition of control and high leucine diets.

	Control		High Leucine Diet	
	gm%	kcal%	gm%	kcal%
Protein	19.9	23.2	29.1	33.3
Carbohydrate	62.5	71.1	55.4	61.8
Fat	6.4	5.7	5.6	4.9
Total	3.52kcal/g	100%	3.59kcal/g	100%
Ingredient	Control		High Leucine Diet	
	gm	kcal	gm	kcal
Casein	200	820	200	820
L-Cystine	3	12.3	3	12.3
L-Leucine	15.8	64.8	158	648
Corn Starch	356	1460	356	1460
Maltodextrin 10	45	184.5	45	184.5
Dextrose	250	1025	250	1025
Cellulose (BW200)	75	0	75	0
Inulin	25	37.5	25	37.5
Soybean Oil	70	220	70	220
Mineral Mix S10026	10	0	10	0
Dicalcium Phosphate	13	0	13	0
Calcium Carbonate	5.5	0	5.5	0
Potassium Citrate, 1 H ₂ O	16.5	0	16.5	0
Vitamin Mix V10001	10	40	10	40
Choline Bitartrate	2	0	2	0
FD&C Blue Dye #1	0.025	0	-----	-----
FD&C Yellow Dye #5	0.025	0	0.025	0
FD&C Red Dye #40	-----	-----	0.025	0
Total	1096.85	3864.1	1239.05	4447.3

Supplementary Table 2. Plasma amino acid concentrations in *ob/ob* and wild-type control mice. (n=5)

Amino Acid	<u>+/+</u>		<u>ob/ob</u>		P value
	Mean	SD	Mean	SD	
Alanine	890.3 +/-	240.7	1106.1 +/-	307.1	0.25119
Arginine	74.8 +/-	43.3	53.8 +/-	35.0	0.42247
Asparagine	56.0 +/-	18.1	73.6 +/-	36.1	0.35943
Aspartic Acid	29.6 +/-	22.1	26.8 +/-	11.0	0.80726
Citrulline	94.4 +/-	18.5	99.4 +/-	14.7	0.65304
Cysteine	43.2 +/-	19.8	30.7 +/-	13.5	0.27594
Glutamic Acid	86.2 +/-	98.7	161.5 +/-	147.1	0.36973
Glutamine	798.7 +/-	210.7	865.7 +/-	119.1	0.55299
Glycine	367.0 +/-	120.2	340.4 +/-	130.1	0.74497
Histidine	80.2 +/-	15.0	102.0 +/-	23.0	0.11460
Isoleucine	114.5 +/-	28.4	181.9 +/-	27.6	<u>0.00526</u>
Leucine	195.8 +/-	39.4	324.1 +/-	63.6	<u>0.00497</u>
Lysine	320.3 +/-	59.4	340.3 +/-	54.4	0.59256
Methionine	47.7 +/-	5.0	93.1 +/-	22.8	<u>0.00244</u>
Ornithine	101.7 +/-	77.1	171.5 +/-	52.4	0.13237
Phenylalanine	84.8 +/-	17.5	140.5 +/-	24.4	<u>0.00324</u>
Proline	114.4 +/-	37.8	158.5 +/-	58.3	0.19361
Serine	132.5 +/-	25.6	160.6 +/-	51.6	0.30672
Taurine	1456.9 +/-	1354.7	2405.2 +/-	1562.8	0.33527
Threonine	152.6 +/-	27.9	163.8 +/-	28.7	0.54925
Tryptophan	22.4 +/-	3.2	44.2 +/-	7.0	<u>0.00023</u>
Tyrosine	73.6 +/-	14.4	99.5 +/-	25.1	0.07987
Urea	7494.7 +/-	1156.3	14106.6 +/-	644.0	<u>0.00000</u>
Valine	255.7 +/-	46.7	494.9 +/-	93.2	<u>0.00090</u>

Supplementary Table 3. Plasma amino acid concentrations in *db/db* and wild-type control mice. (n=5)

Amino Acid	<u>+/+</u>		<u>db/db</u>		P value
	Mean	SD	Mean	SD	
Alanine	798.1	+/- 197.0	1016.3	+/- 349.9	0.27271
Arginine	110.9	+/- 25.0	61.4	+/- 20.9	0.01583
Asparagine	56.3	+/- 16.3	55.7	+/- 14.9	0.95667
Aspartic Acid	22.3	+/- 3.8	21.9	+/- 4.4	0.88658
Citrulline	110.2	+/- 12.1	107.5	+/- 28.8	0.85104
Cysteine	53.3	+/- 14.9	31.6	+/- 6.2	0.03040
Glutamic Acid	67.9	+/- 41.0	57.2	+/- 20.6	0.65106
Glutamine	704.3	+/- 142.8	728.2	+/- 111.6	0.79248
Glycine	322.6	+/- 43.0	230.3	+/- 46.6	0.01764
Histidine	80.1	+/- 6.6	88.0	+/- 8.8	0.16342
Isoleucine	104.7	+/- 11.6	221.4	+/- 52.0	0.00166
Leucine	189.6	+/- 20.9	336.5	+/- 63.0	0.00163
Lysine	309.4	+/- 48.6	266.0	+/- 43.1	0.20435
Methionine	73.4	+/- 14.7	77.1	+/- 48.5	0.87456
Ornithine	70.2	+/- 12.1	98.8	+/- 55.0	0.28790
Phenylalanine	83.3	+/- 7.8	131.9	+/- 8.1	0.00004
Proline	117.7	+/- 23.9	120.0	+/- 53.9	0.93195
Serine	143.7	+/- 16.1	129.0	+/- 22.4	0.28639
Taurine	1169.0	+/- 616.8	1660.8	+/- 427.8	0.21965
Threonine	172.1	+/- 18.1	156.4	+/- 44.6	0.49308
Tryptophan	21.7	+/- 3.6	30.7	+/- 5.6	0.02127
Tyrosine	75.2	+/- 9.3	103.7	+/- 16.5	0.01324
Urea	8589.6	+/- 647.7	9291.7	+/- 1478.4	0.36674
Valine	268.3	+/- 21.8	507.0	+/- 127.9	0.00419

Supplementary Table 4. Plasma amino acid concentrations in $A^y/+$ and wild-type control mice. (n=5)

Amino Acid	$+/+$		$A^y/+$		P value
	Mean	SD	Mean	SD	
Alanine	904.7	+/- 176.0	1145.8	+/- 276.5	0.15362
Arginine	87.4	+/- 22.0	58.3	+/- 21.8	0.08855
Asparagine	68.9	+/- 25.8	70.0	+/- 14.5	0.94376
Aspartic Acid	19.0	+/- 3.0	26.5	+/- 14.7	0.29406
Citrulline	66.1	+/- 23.0	91.4	+/- 7.2	0.07432
Cysteine	36.3	+/- 9.7	20.9	+/- 14.5	0.09656
Glutamic Acid	114.3	+/- 88.5	231.8	+/- 94.2	0.09552
Glutamine	749.2	+/- 190.5	840.8	+/- 171.5	0.47907
Glycine	501.9	+/- 46.5	563.8	+/- 120.7	0.32202
Histidine	88.2	+/- 24.4	86.1	+/- 15.9	0.88980
Isoleucine	98.7	+/- 10.7	83.9	+/- 7.7	0.05355
Leucine	179.2	+/- 16.3	195.3	+/- 42.9	0.45943
Lysine	296.1	+/- 14.5	283.0	+/- 60.1	0.64719
Methionine	57.0	+/- 12.6	37.4	+/- 4.6	0.02183
Ornithine	69.9	+/- 25.9	107.1	+/- 61.2	0.25337
Phenylalanine	90.0	+/- 23.4	87.3	+/- 9.9	0.83481
Proline	117.8	+/- 18.6	96.7	+/- 19.1	0.13939
Serine	173.9	+/- 41.1	174.3	+/- 36.5	0.98972
Taurine	1595.8	+/- 645.4	3205.4	+/- 1202.9	0.03594
Threonine	163.7	+/- 26.9	158.1	+/- 47.9	0.82874
Tryptophan	22.4	+/- 9.9	21.9	+/- 7.5	0.94504
Tyrosine	92.1	+/- 25.1	82.9	+/- 24.5	0.60154
Urea	7467.4	+/- 539.8	8275.1	+/- 1594.1	0.31824
Valine	228.4	+/- 14.6	238.6	+/- 58.6	0.71423

Supplementary Table 5. Plasma amino acid concentrations in wild-type mice fed a high-fat diet compared to normal chow. (n=5)

Amino Acid	Control		HFD		P value
	Mean	SD	Mean	SD	
Alanine	565.0 +/-	293.9	969.2 +/-	106.6	0.04146
Arginine	66.5 +/-	14.8	77.8 +/-	43.5	0.63990
Asparagine	39.9 +/-	5.7	66.4 +/-	8.5	0.00207
Aspartic Acid	21.5 +/-	5.3	17.4 +/-	3.2	0.23116
Citrulline	73.1 +/-	3.2	87.4 +/-	23.2	0.26948
Cysteine	31.9 +/-	13.5	49.0 +/-	22.6	0.24149
Glutamic Acid	59.6 +/-	33.2	50.4 +/-	11.4	0.62032
Glutamine	629.0 +/-	131.4	758.0 +/-	167.0	0.27021
Glycine	338.6 +/-	73.7	374.6 +/-	63.4	0.48661
Histidine	65.6 +/-	4.8	77.9 +/-	4.6	0.01048
Isoleucine	83.2 +/-	26.4	87.7 +/-	17.8	0.78405
Leucine	154.8 +/-	33.6	163.4 +/-	40.5	0.75520
Lysine	213.0 +/-	39.9	321.3 +/-	25.6	0.00380
Methionine	37.1 +/-	18.6	45.2 +/-	4.6	0.42924
Ornithine	58.4 +/-	19.4	76.4 +/-	42.0	0.46712
Phenylalanine	69.4 +/-	14.2	69.7 +/-	14.1	0.97339
Proline	74.3 +/-	31.0	111.8 +/-	14.5	0.07050
Serine	97.6 +/-	19.4	154.8 +/-	21.5	0.00749
Taurine	978.1 +/-	503.5	1420.4 +/-	550.4	0.28057
Threonine	114.1 +/-	23.4	166.1 +/-	18.3	0.01293
Tryptophan	23.6 +/-	4.3	24.1 +/-	5.1	0.87813
Tyrosine	57.9 +/-	13.1	69.3 +/-	12.9	0.25996
Urea	8450.7 +/-	1111.0	7024.5 +/-	825.2	0.08493
Valine	214.0 +/-	34.9	216.2 +/-	34.6	0.93121

Supplementary Table 6. Plasma amino acid concentrations in Δ Gly-APN^{+/+}, Δ Gly-APN^{ob/ob} and wild-type mice. (n=10, 16, and 5, respectively)

Amino Acid	+/+		Δ Gly-APN ^{+/+}		Δ Gly-APN ^{ob/ob}		+/+ vs. Δ Gly-APN ^{+/+}	+/+ vs. Δ Gly-APN ^{ob/ob}	Δ Gly-APN ^{+/+} vs. Δ Gly-APN ^{ob/ob}
	Mean	SD	Mean	SD	Mean	SD	P value	P value	P value
Alanine	890.3 +/- 240.7		471.3 +/- 181.4		543.7 +/- 66.0		0.00925	0.00774	0.37962
Arginine	74.8 +/- 43.3		79.3 +/- 31.9		117.3 +/- 15.8		0.84843	0.05130	0.02601
Asparagine	56.0 +/- 18.1		92.1 +/- 62.0		81.2 +/- 10.3		0.24364	0.01724	0.68004
Aspartic Acid	29.6 +/- 22.1		19.7 +/- 7.3		11.8 +/- 1.7		0.32561	0.07905	0.02892
Citrulline	94.4 +/- 18.5		20.6 +/- 4.0		21.1 +/- 3.3		0.00000	0.00000	0.81780
Cysteine	43.2 +/- 19.8		ND		ND		ND	ND	ND
Glutamic Acid	86.2 +/- 98.7		27.7 +/- 14.4		24.7 +/- 4.0		0.22413	0.15741	0.50605
Glutamine	798.7 +/- 210.7		701.2 +/- 113.6		792.0 +/- 106.0		0.35163	0.94634	0.18288
Glycine	367.0 +/- 120.2		281.7 +/- 34.8		169.0 +/- 22.1		0.12843	0.00312	0.00005
Histidine	80.2 +/- 15.0		61.6 +/- 10.9		75.5 +/- 7.1		0.04139	0.50806	0.02639
Isoleucine	114.5 +/- 28.4		85.8 +/- 20.3		130.3 +/- 32.8		0.08162	0.42226	0.01788
Leucine	195.8 +/- 39.4		158.3 +/- 42.4		223.2 +/- 50.6		0.16665	0.35000	0.03682
Lysine	320.3 +/- 59.4		254.4 +/- 60.3		304.4 +/- 40.1		0.10286	0.60963	0.12199
Methionine	47.7 +/- 5.0		46.9 +/- 12.5		53.5 +/- 21.2		0.88739	0.57318	0.52678
Ornithine	101.7 +/- 77.1		50.7 +/- 19.0		41.6 +/- 8.0		0.14830	0.08718	0.30670
Phenylalanine	84.8 +/- 17.5		85.9 +/- 15.7		113.2 +/- 20.4		0.91505	0.03763	0.02698
Proline	114.4 +/- 37.8		66.7 +/- 27.6		77.0 +/- 33.6		0.05226	0.11567	0.59917
Serine	132.5 +/- 25.6		117.7 +/- 24.9		120.6 +/- 13.1		0.35615	0.34236	0.80415
Taurine	1456.9 +/- 1354.7		432.8 +/- 133.6		551.1 +/- 152.4		0.09563	0.13472	0.18353
Threonine	152.6 +/- 27.9		114.2 +/- 30.6		121.6 +/- 16.6		0.05974	0.04791	0.61361
Tryptophan	22.4 +/- 3.2		23.4 +/- 7.7		21.0 +/- 7.0		0.80663	0.68224	0.58782
Tyrosine	73.6 +/- 14.4		82.3 +/- 24.4		90.3 +/- 16.3		0.50222	0.10840	0.51862
Urea	7494.7 +/- 1156.3		6189.8 +/- 855.1		10087.2 +/- 1019.7		0.05959	0.00333	0.00003
Valine	255.7 +/- 46.7		179.6 +/- 34.1		268.5 +/- 43.3		0.01219	0.64998	0.00273

Supplementary Table 7. Plasma amino acid concentrations in wild-type mice fed a high-leucine diet compared to normal chow. (n=8)

Amino Acid	Post-Prandial			Post-Absorptive			Fasted		
	Control		P value	Control		P value	Control		P value
	Mean	SD		Mean	SD		Mean	SD	
Alanine	597.2 +/- 166.8	424.3 +/- 16.2	0.14854	666.9 +/- 42.8	641.8 +/- 92.5	0.69125	504.8 +/- 33.6	480.6 +/- 57.2	0.45775
Arginine	87.2 +/- 18.9	80.1 +/- 10.7	0.60154	154.4 +/- 66.3	190.8 +/- 127.0	0.68286	83.0 +/- 15.4	69.2 +/- 6.1	0.04623
Asparagine	81.2 +/- 32.3	59.0 +/- 4.6	0.30430	77.5 +/- 5.8	82.0 +/- 4.5	0.34793	55.4 +/- 17.8	60.2 +/- 6.1	0.48971
Aspartic Acid	15.9 +/- 3.7	10.4 +/- 1.8	0.08641	18.6 +/- 3.6	16.7 +/- 0.4	0.42491	30.8 +/- 12.2	23.8 +/- 5.5	0.18832
Citrulline	92.3 +/- 11.5	114.4 +/- 6.5	0.04393	89.3 +/- 12.8	77.0 +/- 7.3	0.21951	77.3 +/- 13.4	66.6 +/- 10.7	0.16280
Cysteine	43.0 +/- 23.3	30.6 +/- 12.0	0.45665	ND	ND	ND	35.3 +/- 15.4	27.0 +/- 7.1	0.22106
Glutamic Acid	38.1 +/- 12.1	31.1 +/- 6.2	0.41979	115.1 +/- 4.9	101.5 +/- 22.7	0.36836	61.9 +/- 31.9	51.9 +/- 12.8	0.44070
Glutamine	786.3 +/- 134.3	1066.0 +/- 48.3	0.02742	648.8 +/- 105.1	844.9 +/- 18.3	0.03344	773.1 +/- 121.6	737.8 +/- 80.9	0.55715
Glycine	258.0 +/- 32.7	198.1 +/- 18.9	0.05186	338.1 +/- 52.2	276.0 +/- 23.7	0.13431	324.4 +/- 28.4	321.3 +/- 28.5	0.86542
Histidine	98.4 +/- 27.0	83.2 +/- 5.6	0.39362	78.3 +/- 6.5	84.6 +/- 4.1	0.22646	73.7 +/- 8.3	76.6 +/- 5.6	0.47904
Isoleucine	121.7 +/- 63.6	133.0 +/- 28.0	0.79345	93.5 +/- 3.9	79.1 +/- 3.4	0.00867	64.7 +/- 16.0	88.3 +/- 16.2	0.03838
Leucine	216.7 +/- 108.9	2403.3 +/- 295.0	0.00027	167.4 +/- 18.0	478.1 +/- 55.2	0.00075	130.3 +/- 26.4	161.6 +/- 21.4	0.05071
Lysine	504.4 +/- 110.9	330.0 +/- 39.3	0.06209	605.3 +/- 16.2	505.3 +/- 59.7	0.04871	369.3 +/- 65.7	272.3 +/- 31.3	0.00516
Methionine	100.9 +/- 26.0	49.2 +/- 11.9	0.03549	105.8 +/- 10.2	86.4 +/- 9.2	0.07092	42.5 +/- 5.7	50.6 +/- 3.0	0.00795
Ornithine	55.8 +/- 16.5	53.8 +/- 3.0	0.85219	74.0 +/- 12.2	91.7 +/- 45.4	0.54977	49.5 +/- 5.0	45.7 +/- 11.9	0.55498
Phenylalanine	93.2 +/- 31.5	75.1 +/- 2.1	0.37743	79.7 +/- 3.6	86.3 +/- 1.4	0.04227	59.4 +/- 7.1	71.7 +/- 9.1	0.04148
Proline	269.5 +/- 154.5	150.4 +/- 10.8	0.25375	204.9 +/- 37.8	187.0 +/- 22.3	0.51915	82.5 +/- 21.2	79.5 +/- 11.9	0.75157
Serine	176.5 +/- 36.5	122.8 +/- 8.0	0.06761	194.1 +/- 10.8	167.2 +/- 11.8	0.04360	153.7 +/- 26.3	152.2 +/- 16.3	0.90487
Taurine	760.5 +/- 144.2	607.6 +/- 117.3	0.22724	1086.9 +/- 61.0	1006.2 +/- 141.3	0.41498	963.9 +/- 300.4	891.7 +/- 210.0	0.63493
Threonine	322.6 +/- 69.4	246.3 +/- 39.4	0.17261	328.2 +/- 30.2	250.4 +/- 10.3	0.01341	182.5 +/- 31.5	192.0 +/- 25.8	0.58648
Tryptophan	136.0 +/- 25.2	122.2 +/- 12.0	0.44063	128.5 +/- 17.6	124.0 +/- 22.2	0.79898	38.4 +/- 9.3	44.5 +/- 8.9	0.29854
Tyrosine	132.6 +/- 37.2	55.6 +/- 5.8	0.02394	148.5 +/- 25.8	93.3 +/- 8.4	0.02443	63.5 +/- 15.9	69.6 +/- 12.1	0.47254
Urea	10083.9 +/- 1607.8	12541.6 +/- 1452.2	0.12089	9690.9 +/- 267.0	13629.9 +/- 83.3	0.00002	9963.5 +/- 1685.2	12612.4 +/- 1621.8	0.02491
Valine	413.5 +/- 144.2	486.2 +/- 85.4	0.49409	309.1 +/- 25.6	240.0 +/- 27.9	0.03424	209.2 +/- 28.2	207.7 +/- 24.1	0.92667