

Figure S1. Feature-based molecular networking of L8 radiated mutants.

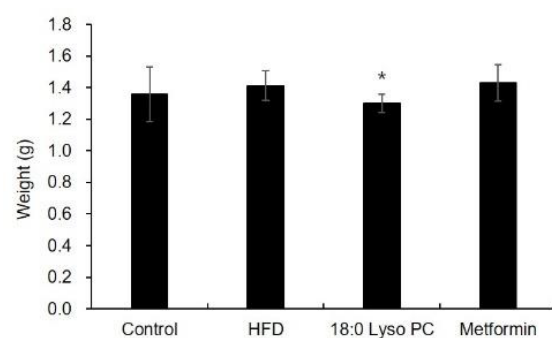


Figure S2. Effect of 18:0 Lyso PC on liver weigh in high-fat diet-fed mice after 8 weeks. The results are presented as mean \pm SD ($n = 6$). Significant difference was identified at $*p < 0.05$, the high fat diet group vs the treatment group.

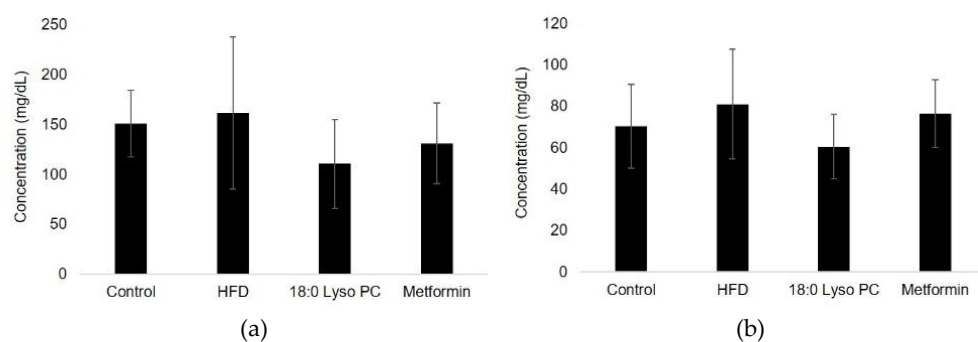


Figure S3. Effect of 18:0 Lyso PC on **(a)** the concentrations of aspartate transaminase and **(b)** alanine transaminase in serum of high fat diet-fed mice. Significant differences were not observed.

Normal Diet



| Product # | D12450B | |
|---------------------------------------|---------|-------|
| | gm% | kcal% |
| Protein | 19.2 | 20.0 |
| Carbohydrate | 67.3 | 70.0 |
| Fat | 4.3 | 10.0 |
| Total | | 100.0 |
| kcal/gm | 3.85 | |
| Ingredient | gm | kcal |
| Casein, 30 Mesh | 200 | 800 |
| L-Cystine | 3 | 12 |
| | | |
| Corn Starch | 315 | 1260 |
| Maltodextrin 10 | 35 | 140 |
| Sucrose | 350 | 1400 |
| | | |
| Cellulose, BW200 | 50 | 0 |
| | | |
| Soybean Oil | 25 | 225 |
| Lard | 20 | 180 |
| | | |
| Mineral Mix S10026 | 10 | 0 |
| DiCalcium Phosphate | 13 | 0 |
| Calcium Carbonate | 5.5 | 0 |
| Potassium Citrate, 1 H ₂ O | 16.5 | 0 |
| | | |
| Vitamin Mix V10001 | 10 | 40 |
| Choline Bitartrate | 2 | 0 |
| | | |
| FD&C Yellow Dye #5 | 0.05 | 0 |
| FD&C Red Dye #40 | 0 | 0 |
| FD&C Blue Dye #1 | 0 | 0 |
| | | |
| Total | 1055.05 | 4057 |

High Fat Diet



| Product # | D12451 | |
|---------------------------------------|--------|-------|
| | gm% | kcal% |
| Protein | 24 | 20.0 |
| Carbohydrate | 41 | 35.0 |
| Fat | 24 | 45.0 |
| Total | | 100.0 |
| kcal/gm | 4.73 | |
| Ingredient | gm | kcal |
| Casein, 30 Mesh | 200 | 800 |
| L-Cystine | 3 | 12 |
| | | |
| Corn Starch | 72.8 | 291 |
| Maltodextrin 10 | 100 | 400 |
| Sucrose | 172.8 | 691 |
| | | |
| Cellulose, BW200 | 50 | 0 |
| | | |
| Soybean Oil | 25 | 225 |
| Lard | 177.5 | 1598 |
| | | |
| Mineral Mix S10026 | 10 | 0 |
| DiCalcium Phosphate | 13 | 0 |
| Calcium Carbonate | 5.5 | 0 |
| Potassium Citrate, 1 H ₂ O | 16.5 | 0 |
| | | |
| Vitamin Mix V10001 | 10 | 40 |
| Choline Bitartrate | 2 | 0 |
| | | |
| FD&C Red Dye #40 | 0.05 | 0 |
| FD&C Blue Dye #1 | 0 | 0 |
| | | |
| Total | 858.15 | 4057 |

Figure S4. Information of the compositions of the normal diet and the high-fat diet.

Table S1. Annotated molecular node by Global Natural Product Social Molecular Networking library in feature-based molecular networking applied with a L8 control and 100 radiated mutant samples.

| Group | Observed <i>m/z</i> | Matched library ID | Class | | |
|-------|------------------------------------|--|--------------------------------|---|--------------------------|
| A | 277.2157 /277.2161 | 9,12-Octadecadiynoic Acid | Fatty acid derivative | | |
| | 293.2108 | 9(S)-HpOTrE | | | |
| | 279.2318 /281.2473 | Linolenic acid | | | |
| | 315.2531 | 12,13-DiHOME | | | |
| | 277.2162 | 9-Oxo-10E,12Z-octadecadienoic acid | | | |
| | 353.2685 /353.2687 /357.2999 | Monolinolenin (9c,12c,15c) | | | |
| | 300.2896 | Palmitoyl ethanolamide | | | |
| | 324.2898 /324.2896 | Linoleoyl ethanolamide | | | |
| | 295.2262 | 13-Keto-9Z,11E-octadecadienoic acid | | | |
| | 297.2424 /315.2531 | 9,10-Dihydroxy-12Z-octadecenoic acid | | | |
| | 326.3053 | N-Oleoylethanolamine | | | |
| | 331.2848 | 1-Hexadecanoyl-sn-glycerol | | | |
| | B | 786.6004 | | 1-Stearoyl-2-linoleoyl-sn-glycero-3-phosphocholine (18:0/18:2 Lyso PC) | Phosphatidylcholine |
| | C | 420.1866 | | Phenylmethyl-6-O-[(2R,3R,4R)-tetrahydro-3,4-dihydroxy-4-(hydroxymethyl)-2-furanyl]-beta-D-Glucopyranoside | Carbohydrate |
| | | 325.1130 | | 4-O-beta-Galactopyranosyl-D-mannopyranose | |
| | | 360.1502 | | Isomaltulose | |
| D | 291.0865 | Catechin | Flavonoid | | |
| | 453.1394 | (2R,3R,4S,5S,6R)-2-[[2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-3,4-dihydro-2H-chromen-3-yl]oxy]-6-(hydroxymethyl)oxane-3,4,5-triol | | | |
| E | 518.3212 | 1-Hexadecanoyl-sn-glycero-3-phosphocholine (16:0 Lyso PC) | Phosphatidylcholine | | |
| | 544.3371 | 1-(9Z-Octadecenoyl)-sn-glycero-3-phosphocholine (18:1 Lyso PC) | | | |
| F | 175.1188 | Arginine | Amino acid derivative | | |
| G | 518.3328 | 1-(9Z,12Z,15Z-octadecatrienoyl)-sn-glycero-3-phosphocholine (18:3 Lyso PC) | Phosphatidylcholine | | |
| | 482.3247 | 1-Pentadecanoyl-sn-glycero-3-phosphocholine (15:0 Lyso PC) | | | |
| | 524.3717 | 1-Stearoyl-2-hydroxy-sn-glycero-3-phosphocholine (18:0 Lyso PC) | | | |
| | 522.3559 | 1-(9Z-Octadecenoyl)-sn-glycero-3-phosphocholine (18:1 Lyso PC) | | | |
| | 468.3089 | 1-Myristoyl-sn-glycero-3-phosphocholine (14:0 Lyso PC) | | | |
| | H | 480.3086 | | 1-(9Z-Octadecenoyl)-sn-glycero-3-phosphoethanolamine (18:1 Lyso PE) | Phosphatidylethanolamine |
| I | 247.1442 | Lenticin | Aromatic amino acid derivative | | |
| J | 328.1392 | N-(1-Deoxy-1-fructosyl)phenylalanine | Aromatic amino acid derivative | | |
| K | 757.2191 | 5,7-Dihydroxy-2-[4-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyphenyl]-3-[(2S,3R,4S,5S,6R)-3,4,5-trihydroxy-6-[[[(2R,3R,4R,5R,6S)-3,4,5-trihydroxy-6-methyloxan-2-yl]oxymethyl]oxan-2-yl]oxychromen-4-one | Flavonoid glycoside | | |

| | | | |
|---|----------|---|--------------------------------|
| L | 387.2015 | (4S)-4-Hydroxy-3,5,5-trimethyl-4-[(E)-3-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxybut-1-enyl]cyclohex-2-en-1-one | Terpenoid glycoside |
| M | 205.0972 | L-Tryptophan | Aromatic amino acid derivative |
| N | 182.0813 | L-Tyrosine | Aromatic amino acid derivative |
| O | 579.1501 | Procyanidin B3 | Procyanidin |
| P | 255.0652 | 7,4'-Dihydroxyflavone | Flavonoid |

Table S2. Significant differences p values for the effect of 18:0 Lyso PC on changes in body weight during the entire experimental period.

| | Days | | | | | | | | |
|---------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| | 0 | 7 | 14 | 21 | 28 | 35 | 42 | 49 | 56 |
| Control vs HFD | 0.337225 | 0.800899 | 0.295365 | 0.006532 | 0.002758 | 0.003044 | 0.000005 | 0.000003 | 0.000002 |
| HFD vs 18:0 Lyso PC | 0.417169 | 0.389523 | 0.077717 | 0.000657 | 0.006785 | 0.039776 | 0.003320 | 0.003589 | 0.001395 |
| HFD vs metformin | 0.529554 | 0.655448 | 0.108034 | 0.003841 | 0.129756 | 0.072521 | 0.004325 | 0.002096 | 0.004165 |