

| Flux number | Flux description  | PHH (μM/day) | HEPG2/C3A (μM/day) |
|-------------|---|--------------|--------------------|
| 1           | Glucose + Pi ↔ Glucose 6-P + H2O  | 3.61         | 24.015             |
| 2           | Glucose 6-P ↔ Fructose 6-P  | 4.157575     | 36.079558          |
| 3           | Fructose 6-P + Pi ↔ Fructose 1,6-P2 + H2O   | 4.157575     | 36.079558          |
| 4           | Fructose 1,6-P2 ↔ 2 Glyceraldehyde 3-P  | 4.157575     | 36.079558          |
| 5           | Glyceraldehyde 3-P + NAD+ + Pi + ADP ↔ Phosphoenolpyruvate + NADH + H+ + ATP  | 8.286208     | 72.107116          |
| 6           | Phosphoenolpyruvate + ADP → Pyruvate + ATP  | 8.286252     | 72.107116          |
| 7           | Pyruvate + CoA + NAD+ → Acetyl-CoA + CO2 + NADH   | 4.045443     | 16.270876          |
| 8           | Lactate + NAD+ ↔ Pyruvate + NADH + H+   | -2.79        | -42.794            |
| 9           | Acetyl-CoA + Oxaloacetate + H2O → Citrate + CoA + H+  | 2.885885     | -5.788956          |
| 10          | Citrate + NAD+ ↔ 2-oxo-glutarate + NADH + CO2   | 2.897834     | -5.788956          |
| 11          | 2-oxo-glutarate + NAD+ + CoA → Succinyl-CoA + NADH + CO2 + H+   | 5.415694     | -6.75215           |
| 12          | Succinyl-CoA + Pi + GDH + FDH ↔ Fumarate + GTP + FADH2 + CoA  | 5.725443     | -6.006258          |
| 13          | Fumarate + H2O ↔ Malate   | 6.641521     | -20.328852         |
| 14          | Malate + NAD+ ↔ Oxaloacetate + NADH + H+  | 6.653425     | -20.328852         |
| 15          | Arginine + H2O → Ornithine + Urea   | 0.838        | 0.040952           |
| 16          | Ornithine + CO2 + NH4+ + 2 ATP + H2O ↔ Citrulline + 2 ATP + 2 Pi + 3 H+   | 0.786184     | -14.61             |
| 17          | Citrulline + Aspartate + ATP → Arginine + Fumarate + AMP + P Pi   | 0.762267     | -14.61             |
| 18          | Arginine uptake   | 0.12         | 14.663             |
| 19          | Ammonia Uptake  | 0            | -22.515666         |
| 20          | Ornithine Output  | 0.05         | 0.077              |
| 21          | Alanine + 0.5 NAD+ + 0.05 NADP+ + H2O → Pyruvate + NH4+ + 0.5 NADH + 0.5 NADPH + H+   | -1.333337    | -12.413622         |
| 22          | Alanine Uptake  | -1.3         | -12.383            |
| 23          | Serine → Pyruvate + NH4+  | -0.129045    | -0.732036          |
| 24          | Serine Uptake   | -0.073       | -0.599             |
| 25          | Cysteine + 0.5 NAD+ + 0.5 NADP+ + H2O + SO3 2- → Pyruvate + Thiosulfate + NH4+ + 0.5 NADH + 0.5 NADPH + H+  | 0.011529     | 0.103418           |
| 26          | Cysteine Uptake   | 0            | 0                  |
| 27          | Threonine + NAD+ → Glycine + Acetyl-CoA + NADH  | 0.059491     | 0.292434           |
| 28          | Glycine + NAD+ + H4folate ↔ N5, N10-CH2H4folate + NADH + CO2 + NH4+ + H+  | 0.131643     | 0.0289             |
| 29          | Glycine Uptake  | 0.09         | -0.255             |
| 30          | Tryptophan + 3 H2O + 3 O2 + CoA + 3 NAD+ + FAD → 3 CO2 + FADH2 + 3 NADH + 4 H+ + NH4+ + Acetoacetyl-CoA   | -0.012453    | -0.000502          |
| 31          | Propionyl-CoA + CO2 + ATP → Succinyl-CoA + AMP + P Pi   | 0.297889     | 0.745892           |
| 32          | Lysine + 3 H2O + 5 NAD+ + FAD + CoA → 2 NH4+ + 5 NADH + 5 H+ + FADH2 + 2 CO2 + Acetoacetyl-CoA  | 0.098457     | 0.521394           |
| 33          | Phenylalanine + H4biopterin + O2 → Tyrosine + H2biopterin + H2O   | 0.049432     | 0.210948           |
| 34          | Tyrosine + 0.5 NAD+ + 0.5 NADP+ + H2O + 2 O2 → NH4+ + CO2 + 0.5 NADH + 0.5 NADPH + H+ + Fumarate + Acetoacetate                                   | 0.141907     | 0.287406           |
| 35          | Tyrosine Uptake   | 0.1          | 0.087              |
| 36          | Glutamate + 0.5 NAD+ + 0.5 NADP+ + H2O ↔ NH4+ + 2-oxo-glutarate + 0.5 NADH + 0.5 NADPH + H+   | 2.505956     | -0.963194          |
| 37          | Glutamate Uptake  | -0.091       | -1.723             |
| 38          | Glutamine + H2O → Glutamate + NH4+  | 2.699234     | -9.63755           |
| 39          | Ornithine + NAD+ + NADP+ + H2O → Glutamate + NH4+ + NADH + NADPH + H+   | -0.010264    | 14.573952          |
| 40          | Proline + 0.5 O2 + 0.5 NAD+ + 0.5 NADP+ → Glutamate + 0.5 NADH + 0.5 NADPH + H+   | -0.080684    | -4.241452          |
| 41          | Histidine + H4folate + 2 H2O → NH4+ + N5-formiminoH4folate + Glutamate  | 0.008744     | 0.09347            |
| 42          | Methionine + ATP + Serine + NAD+ + CoA → P Pi + Pi + Adenosine + Cysteine + NADH + Propionyl-CoA + CO2 + NH4+                                     | 0.03574      | 0.120988           |
| 43          | Aspartate + 0.5 NAD+ + 0.5 NADP+ + H2O ↔ Oxaloacetate + NH4+ + 0.5 NADH + 0.5 NADPH + H+  | -3.779488    | 14.539896          |
| 44          | Aspartate Uptake  | -2.97        | 0.147              |
| 45          | Asparagine + H2O → Aspartate + NH4+   | -0.035967    | -0.20104           |
| 46          | 8 Acetyl-CoA + 7 ATP + 14 NADPH + 14 H+ → Palmitate + 8 CoA + 6 H2O + 7 ADP + 7 Pi + 14 NADP+   | 0.082415     | -0.013             |
| 47          | 2 Acetyl-CoA ↔ Acetoacetyl-CoA + CoA  | 0.254804     | 11.416814          |
| 48          | Acetoacetyl-CoA + H2O → Acetoacetate + CoA  | 0.340808     | 11.937706          |
| 49          | Acetoacetate Output   | 0.48         | 10.804             |
| 50          | Acetoacetate + NADH + H+ ↔ β-hydroxybutyrate + NAD+   | 0.135        | 1.885              |
| 51          | NADH + H+ + 0.5 O2 + 3 ADP → NAD+ + H2O + 3 ATP   | 24.637286    | 29.553518          |
| 52          | FADH2 + 0.5 O2 + 2 ADP → FAD + H2O + 2 ATP  | 6.194067     | -4.396574          |
| 53          | O2 Uptake   | 15.9         | 11.54              |
| 54          | Glucose 6-P + 12 NADP+ + 7 H2O → 6 CO2 + 12 NADPH + 12 H+ + Pi  | 0.228279     | -1.109464          |
| 55          | Valine + 0.5 NADP+ + CoA + 2 H2O + 3.5 NAD+ + FAD → NH4+ + Propionyl-CoA + 3.5 NADH + 0.5 NADPH + 3 H+ + FADH2 + 2 CO2                            | 0.119517     | 0.32543            |
| 56          | Isoleucine + 0.5 NADP+ + H2O + 2.5 NAD+ + FAD + 2 CoA → NH4+ + Propionyl-CoA + Acetyl-CoA + 2.5 NADH + 0.5 NADPH + 3 H+ + FADH2 + CO2             | 0.115195     | 0.273474           |
| 57          | Leucine + 0.5 NADP+ + H2O + 1.5 NAD+ + FAD + ATP + CoA → NH4+ + 1.5 NADH + 0.5 NADPH + 2 H+ + FADH2 + ADP + Pi + Acetoacetate + Acetyl-CoA        | 0.132286     | 0.463888           |
| 58          | Threonine uptake  | 0.083        | 0.309              |
| 59          | Lysine Uptake   | 0.141        | 0.548              |
| 60          | Phenylalanine Uptake  | 0.0588       | 0.224              |
| 61          | Glutamine Uptake  | 2.72         | -9.625             |
| 62          | Proline Uptake  | -0.07        | -4.226392          |
| 63          | Histidine Uptake  | 0.026        | 0.101              |
| 64          | Methionine Uptake   | 0.038        | 0.124              |
| 65          | Asparagine Uptake   | -0.017       | -0.191             |
| 66          | Valine Uptake   | 0.132        | 0.343              |
| 67          | Isoleucine Uptake   | 0.12         | 0.28               |
| 68          | Leucine Uptake  | 0.164        | 0.492              |
| 69          | Albumin Synthesis   | 0.000351     | 0.000502           |
| 70          | Triglyceride ↔ Glycerol + 3 Palmitate   | -0.028899    | -0.052             |
| 71          | Triglyceride Uptake   | -0.027       | -0.052             |
| 72          | Glycerol Uptake   | 0            | 0                  |
| 73          | Palmitate Uptake  | 0.0049       | 0.169              |
| 74          | Glucose-6-P + UTP + H2O ↔ Glycogen + 2 Pi + UDP   | -0.775854    | -10.955093         |
| 75          | Glycerol + NAD+ ↔ Glyceraldehyde 3-P + NADH + H+  | -0.028943    | -0.052             |
| 76          | 18 Acetyl-CoA + 255 NADPH + NADH + 26 H+ + 18 ATP + 11 O2 → Cholesterol + 25 NADP+ + NAD+ + 18 ADP + 6 Pi + P Pi + 8 CO2 + 6 H2O + 18 CoA + HCOOH | 0.016534     | 0.02               |
| 77          | Cholesterol + 5 NADPH + H+ + 3 O2 + ATP + 2 CoA + FAD ↔ Choloyl-CoA + 5 NADP+ + 2 H2O + ADP + P Pi + FADH2 + Propionil-CoA                        | 0.015666     | 0.026              |
| 78          | Cholesterol Output  | -0.000016    | -0.006             |
| 79          | Bile Output   | 0.0031       | 0.026              |
| 80          | CO2 output  | 13.6         | 13.5               |

| <b>Gene Name</b> | <b>Forward</b>             | <b>Reverse</b>           |
|------------------|----------------------------|--------------------------|
| COX2             | TAGACAGCGTAAACTGCGCCT      | TGCCCCACAGCAAACCGTAG     |
| CPT1             | GAAGAAGAAAATCTTATGCAGCCTTG | CTTGGCTTACGTCGTAGACAGGTC |
| CPT2             | TTTGGGTCAGGATTGAAAGC       | TGGTTGCTCTGGACAAACAG     |
| UCP2             | GAACGGGACACCTTTAGAGAAG     | CAGCAACAAGACGACATAGAGG   |
| HMGCS2           | CCCAGTGGTAATGCTCGTCCC      | TGGGTACTCCGAGGCCAAAT     |
| HMGCR            | GATGGGAGGCCACAAAGAG        | TTCGGTGGCCTCTAGTGAGA     |
| SREBP1c          | GCTGTCCACAAAAGCAAATCT      | GTCAGTGTGTCCTCCACCTCA    |
| CYP2E1           | CTGACCACCCTCCGGAATA        | ATGTAGGCTATGACGTTGCA     |
| FAS              | TGCAGAAGATGTAGATTGTGTGATGA | GGGTCCGGGTGCAGTTTATT     |