**Generic Model**

**Recon3D Model with the following modifications:**

- Artificial sinks and drug modules were removed

- Resulting blocked reactions and the respective genes and metabolites that end up with no reaction associated due to this removal.

- Gene ‘8041’ was removed as it no longer is in the entrez database. However, the corresponding reaction was not removed as, according to annotation, it is necessary for modelling.

**Original Recon3D model vs consistent Recon3D model:**

|  |  |  |
| --- | --- | --- |
|  | **Original** | **Consistent** |
| **Nº Reactions** | 10600 | 10284 |
| **Nº Unique Metabolites** | 5835 |  |
| **Nº of Unique Genes** | 1884 | 1870 |

**Units:** mmol gDW-1 h-1 -> mmol of metabolite per gram of dry weight of cell per hour

**Biomasses**

**To generate the T-Cells models:**

Compare models reconstructed with different biomasses:

- *biomass\_reaction* from Recon3D model;

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.505626 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.35926 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.279425 |
| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.352607 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 20.704451 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020401 |
| clpn\_hs[c] | Cardiolipin[cytoplasm] | 0.011658 |
| ctp[c] | Cytidine triphosphate[cytoplasm] | 0.039036 |
| cys\_L[c] | L-Cysteine[cytoplasm] | 0.046571 |
| datp[c] | Deoxyadenosine triphosphate[cytoplasm] | 0.013183 |
| dctp[c] | dCTP[cytoplasm] | 0.009442 |
| dgtp[c] | dGTP[cytoplasm] | 0.009898 |
| dttp[c] | Thymidine 5'-triphosphate[cytoplasm] | 0.013091 |
| g6p[c] | Glucose 6-phosphate[cytoplasm] | 0.275194 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.325996 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.385872 |
| gly[c] | Glycine[cytoplasm] | 0.538891 |
| gtp[c] | Guanosine triphosphate[cytoplasm] | 0.036117 |
| h2o[c] | Water[cytoplasm] | 20.650823 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.126406 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.286078 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.545544 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.592114 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.153018 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.023315 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.154463 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.055374 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.002914 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.259466 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.412484 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.005829 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.392525 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] | 0.017486 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.31269 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.013306 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.159671 |
| utp[c] | Uridine triphosphate[cytoplasm] | 0.053446 |
| val\_L[c] | L-Valine[cytoplasm] | 0.352607 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | adp[c] | ADP[cytoplasm] | 20.650823 |
| h[c] | Hydrogen Ion[cytoplasm] | 20.650823 |
| pi[c] | Phosphate[cytoplasm] | 20.650823 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

- *biomass\_maintenance* from Recon3D model;

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.50563 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.35926 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.27942 |
| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.35261 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 20.7045 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020401 |
| clpn\_hs[c] | Cardiolipin[cytoplasm] | 0.011658 |
| ctp[c] | Cytidine triphosphate[cytoplasm] | 0.039036 |
| cys\_L[c] | L-Cysteine[cytoplasm] | 0.046571 |
| g6p[c] | Glucose 6-phosphate[cytoplasm] | 0.27519 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.326 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.38587 |
| gly[c] | Glycine[cytoplasm] | 0.53889 |
| gtp[c] | Guanosine triphosphate[cytoplasm] | 0.036117 |
| h2o[c] | Water[cytoplasm] | 20.6508 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.12641 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.28608 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.54554 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.59211 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.15302 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.023315 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.15446 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.055374 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.002914 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.25947 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.41248 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.005829 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.39253 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] | 0.017486 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.31269 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.013306 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.15967 |
| utp[c] | Uridine triphosphate[cytoplasm] | 0.053446 |
| val\_L[c] | L-Valine[cytoplasm] | 0.35261 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | adp[c] | ADP[cytoplasm] | 20.6508 |
| h[c] | Hydrogen Ion[cytoplasm] | 20.6508 |
| pi[c] | Phosphate[cytoplasm] | 20.6508 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

- *R\_biomass\_mac* from iAB-AMØ-1410 model (a macrophage model, built from Recon1 model), also added to the generic model Recon3D

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.396559456 |
| alpa\_hs[c] | Lysophosphatidic Acid [cytoplasm] | 0.011499127 |
| amp[c] | Adenosine monophosphate [cytoplasm] | 0.048664064 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.325724532 |
| asn\_L[c] | L-Asparagine[cytoplasm] | 0.215407845 |
| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.282759085 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 25.17352552 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020930954 |
| cmp[c] | Cytidine monophosphate[cytoplasm] | 0.042373167 |
| cys\_L[c] | L-Cysteine[cytoplasm] | 0.127154496 |
| dag\_hs[c] | Diglyceride[cytoplasm] | 0.0036682 |
| damp[c] | Deoxyadenosine monophosphate[cytoplasm] | 0.021495345 |
| dcmp[c] | dCMP[cytoplasm] | 0.014937443 |
| dgmp[c] | 2'-Deoxyguanosine 5'-monophosphate[cytoplasm] | 0.014937443 |
| dtmp[c] | 5-Thymidylic acid[cytoplasm] | 0.021495345 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.280436629 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.424428935 |
| gly[c] | Glycine[cytoplasm] | 0.366948135 |
| glygn2[c] | Glycogen, Structure 2 (Glycogenin-1,6-{7[1,4-Glc], 4[1,4-Glc]}) [cytoplasm] | 0.528027894 |
| gmp[c] | Guanosine monophosphate[cytoplasm] | 0.043710887 |
| h2o[c] | Water[cytoplasm] | 25.17352552 |
| hdca[c] | Palmitic acid[cytoplasm] | 0.004850777 |
| hdcea[c] | Palmitoleic acid[cytoplasm] | 0.001222285 |
| his\_L[c] | L-Histidine[cytoplasm] | 0.153862747 |
| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.25953452 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.580614138 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.351852168 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.126573882 |
| ocdca[c] | Stearic acid[cytoplasm] | 0.004736708 |
| ocdcea[c] | Oleic acid[cytoplasm] | 0.003853116 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.003741686 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.031527146 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.021107135 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.008918017 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.214246617 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.346626641 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.001024655 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.476684207 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] | 0.007049706 |
| tag\_hs[c] | Triglyceride[cytoplasm] | 0.002742439 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.303661194 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.069673697 |
| ttdca[c] | Myristic acid[cytoplasm] | 0.00136164 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.156185203 |
| ump[c] | Uridine 5'-monophosphate[cytoplasm] | 0.04602478 |
| val\_L[c] | L-Valine[cytoplasm] | 0.347207255 |
| **Products** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | apd[c] | ADP[cytoplasm] | 25.17352552 |
| h[c] | Hydrogen Ion[cytoplasm] | 25.17352552 |
| pi[c] | Phosphate[cytoplasm] | 25.17352552 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |

**To generate the cancer models:**

- *biomass\_reaction* from Recon3D model

|  |  |  |  |
| --- | --- | --- | --- |
| **Reactants** | **Metabolite ID** | **Metabolite Name** | **Stoichiometry** |
|  | ala\_L[c] | L-Alanine [cytoplasm] | 0.505626 |
| arg\_L[c] | L-Arginine[cytoplasm] | 0.35926 |
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| asp\_L[c] | L-Aspartic acid[cytoplasm] | 0.352607 |
| atp[c] | Adenosine triphosphate[cytoplasm] | 20.704451 |
| chsterol[c] | Cholesterol[cytoplasm] | 0.020401 |
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| ctp[c] | Cytidine triphosphate[cytoplasm] | 0.039036 |
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| datp[c] | Deoxyadenosine triphosphate[cytoplasm] | 0.013183 |
| dctp[c] | dCTP[cytoplasm] | 0.009442 |
| dgtp[c] | dGTP[cytoplasm] | 0.009898 |
| dttp[c] | Thymidine 5'-triphosphate[cytoplasm] | 0.013091 |
| g6p[c] | Glucose 6-phosphate[cytoplasm] | 0.275194 |
| gln\_L[c] | L-Glutamine[cytoplasm] | 0.325996 |
| glu\_L[c] | L-Glutamic acid[cytoplasm] | 0.385872 |
| gly[c] | Glycine[cytoplasm] | 0.538891 |
| gtp[c] | Guanosine triphosphate[cytoplasm] | 0.036117 |
| h2o[c] | Water[cytoplasm] | 20.650823 |
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| ile\_L[c] | L-Isoleucine[cytoplasm] | 0.286078 |
| leu\_L[c] | L-Leucine[cytoplasm] | 0.545544 |
| lys\_L[c] | L-Lysine[cytoplasm] | 0.592114 |
| met\_L[c] | L-Methionine[cytoplasm] | 0.153018 |
| pail\_hs[c] | 1-Phosphatidyl-1D-Myo-Inositol[cytoplasm] | 0.023315 |
| pchol\_hs[c] | Phosphatidylcholine[cytoplasm] | 0.154463 |
| pe\_hs[c] | Phosphatidylethanolamine[cytoplasm] | 0.055374 |
| pglyc\_hs[c] | Phosphatidylglycerol[cytoplasm] | 0.002914 |
| phe\_L[c] | L-Phenylalanine[cytoplasm] | 0.259466 |
| pro\_L[c] | L-Proline[cytoplasm] | 0.412484 |
| ps\_hs[c] | Phosphatidylserine[cytoplasm] | 0.005829 |
| ser\_L[c] | L-Serine[cytoplasm] | 0.392525 |
| sphmyln\_hs[c] | Sphingomyelin[cytoplasm] | 0.017486 |
| thr\_L[c] | L-Threonine[cytoplasm] | 0.31269 |
| trp\_L[c] | L-Tryptophan[cytoplasm] | 0.013306 |
| tyr\_L[c] | L-Tyrosine[cytoplasm] | 0.159671 |
| utp[c] | Uridine triphosphate[cytoplasm] | 0.053446 |
| val\_L[c] | L-Valine[cytoplasm] | 0.352607 |
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|  | adp[c] | ADP[cytoplasm] | 20.650823 |
| h[c] | Hydrogen Ion[cytoplasm] | 20.650823 |
| pi[c] | Phosphate[cytoplasm] | 20.650823 |
| **Lower Bound** | 0 | | |
| **Upper Bound** | 1000 | | |