Description of specific changes, reaction additions and reaction direction constraint changes, introduced to *Yarrowia lipolytica* genome-scale model iNL895:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **rxn\_id** | **reaction** | **modified lb** | **iNL895 lb** | **modified ub** | **iNL895 ub** |
| r\_010\_xxx | glycinamide ribonucleotide transformylase | 0 | -Inf | Inf | Inf |
| r\_39\_exchange | bicarbonate exchange | 0 | -Inf | Inf | Inf |
| r\_0125 | acetyl-CoA hydrolase | -Inf | -Inf | 0 | Inf |
| r\_0127 | acetyl-CoA synthatase [cytosol] | -Inf | -Inf | 0 | Inf |
| r\_0128 | acetyl-CoA synthatase [mitochondrion] | -Inf | -Inf | 0 | Inf |
| r\_0129 | acetyl-CoA synthatase [nuclear] | -Inf | -Inf | 0 | Inf |
| r\_019\_xxx | phosphoribosylpyrophosphate synthetase | 0 | -Inf | Inf | Inf |
| r\_0350 | D-arabinono-1,4-lactone oxidase | 0 | -Inf | Inf | Inf |
| r\_0371 | Diacylglycerol pyrophosphate phosphatase |  |  |  |  |
| r\_0455 -r\_0467 | fatty-acyl-ACP synthase | 0 | -Inf | 0 | Inf |
| r\_0477 | ubiquinone-coupled formate dehydrogenase | 0 | -Inf | 0 | Inf |
| r\_0743 | NADH kinase | 0 | -Inf | Inf | Inf |
| r\_0744 | NADH kinase mitochondrial | 0 | -Inf | Inf | Inf |
| r\_0746 | NADP phosphatase | 0 | -Inf | Inf | Inf |
| r\_0747 | NADP phosphatase | 0 | -Inf | Inf | Inf |
| r\_128\_exchange | oxygen exchange | 0 | 0 | Inf | 10 |
| r\_2000 | decane exchange | -Inf | -Inf | 0 | Inf |
| r\_2003 | hexadecane exchange | -Inf | -Inf | 0 | Inf |
| r\_2009 | tributyrin exchange | -Inf | -Inf | 0 | Inf |

**rxn\_id comment on the modification of bound**

r\_010\_xxx Would generate ATP if allowed to go to backward direction

r\_39\_exchange Removed mitochondrial fatty-acyl-ACP synthase reactions for longer than C8 fatty acids as in the yeast 7.6 model

r\_0125 Shouldn't be able to make acetyl-CoA from acetate without energy as in this reaction. Directionality restricted as in the yeast 7.6 model

r\_0127 All acetyl-CoA to be made via the ATP citrate lyase

r\_0128 All acetyl-CoA to be made via the ATP citrate lyase

r\_0129 All acetyl-CoA to be made via the ATP citrate lyase

r\_019\_xxx Shouldn’t be able to generate energy by breaking PRPP. Directionality restricted as in the yeast 7.6 model

r\_0350 Reaction is favoured towards D-arabinono-1,4-lactone

r\_0371 Diacylglycerol pyrophosphate phosphatase moved from cytocol to ER as in the yeast 7.6 model: r\_0371 was removed and a corresponding reaction added to ER.

Diacylglycerol acetyltransferase in endoplasmic reticulum and triglyceride transport from ER to cytosol were added as in yeast 7.6.

r\_0477 Removed as in the yeast 7.6 model

r\_0743 Directionality restricted as in the yeast 7.6 model

r\_0744 Directionality restricted as in the yeast 7.6 model

r\_0746 Directionality restricted as in the yeast 7.6 model

r\_0747 Directionality restricted as in the yeast 7.6 model

r\_128\_exchange Free oxygen (O2) uptake allowed

r\_2000 Only methanol allowed as a carbon source

r\_2003 Only methanol allowed as a carbon source

r\_2009 Only methanol allowed as a carbon source

**Methanol-related reactions added to the model:**

**Methanol dehydrogenase (EC 1.1.1.244)**

 methanol + NAD <=> formaldehyde + NADH

**Methanol and formaldehyde export and transport reactions**

 <=> methanol\_external

 methanol\_cytosolic <=> methanol\_external

 <=> formaldehyde\_external

 formaldehyde\_cytosolic <=> formaldehyde\_external

**XuMP pathway**

 **formaldehyde transketolase (EC 2.2.1.3)**

 formaldehyde + xylulose-5p <=> glycerone + glyceraldehyde-3p

**RuMP pathway**

 **3-hexulose-6-phosphate synthase (EC 4.1.2.43)**

 formaldehyde + ribulose-5p <=> 3-hexulose-6-phosphate

 **6-phospho-3-hexuloisomerase (EC 5.3.1.27)**

 3-hexulose-6-phosphate <=> fructose-6-phosphate

**Serine cycle**

 **formaldehyde to methylenetetrahydrofolate**

formaldehyde + tetrahydrofolate <=> 5,10 -methylenetetrahydrofolate

**serine-glyoxylate aminotransferase**

 glyoxylate + serine <=> glycine + hydroxypyruvate

 **hydroxypyruvate reductase**

hydroxypyruvate + NADP <=> glycerate + NADPH

 **glycerate kinase**

glycerate + ATP <=> 3-phosphoglycerate + ADP

 **phosphoenolpyruvate carboxylase**

phosphate + oxaloacetate = phosphoenolpyruvate + HCO3-

 **malate-Coa ligase**

malate + ATP + coenzyme A <=> Malyl-CoA + phosphate + ADP

 **malyl-Coa lyase**

malyl-CoA <=> acetyl-CoA + glyoxylate