**Supplementary Material 11 – Knockout Candidates derived using MOMA**

**Table 1 - Knockout candidates for HSA overproduction**

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| --- | --- | --- | --- | --- |
|  | **Deleted Gene** | **Final Biomass [g/L]** | **Final HSA [g/L]** | **Reaction(s) Name(s)** |
| **1** | PAS\_chr2-2\_0094 | 11,81 | 0,91 | Chitin synthase |
| **2** | PAS\_chr1-4\_0194 | 11,41 | 0,84 | Putrescine and Spermidine transport |
| **3** | PAS\_chr4\_0836 | 11,41 | 0,84 | Putrescine and Spermidine transport |
| **4** | RPPA11109 | 10,74 | 0,63 | ribulose 5-phosphate 3-epimerase |
| **5** | RPPA11110 | 10,74 | 0,63 | ribulose 5-phosphate 3-epimerase |
| **6** | PAS\_chr2-2\_0330 | 10,20 | 0,62 | Phosphoryl ceramide syntase |
| **7** | PAS\_chr2-2\_0044 | 8,59 | 0,30 | CDP-Diacylglycerol synthetase, yeast-specific |
| **8** | PAS\_chr4\_0210 | 8,84 | 0,29 | ADP/ATP transporter, mitochondrial |
| **9** | PAS\_chr4\_0212 | 8,84 | 0,29 | ribose-5-phosphate isomerase |
| **10** | PAS\_chr3\_0604 | 14,05 | 0,23 | Deoxyribokinase and ribokinase |
| **11** | PAS\_chr4\_0408 | 15,33 | 0,22 | phosphoethanolamine cytidyltransferase |
| **12** | PAS\_chr1-1\_0418 | 16,02 | 0,21 | Acetate transporter |
| **13** | PAS\_chr1-3\_0220 | 15,88 | 0,19 | Methylenetetrahydrofolate dehydrogenase NAD |
| **14** | PAS\_chr1-4\_0487 | 14,85 | 0,17 | Succinate Dehydrogenase |
| **15** | PAS\_chr2-2\_0278 | 14,85 | 0,17 | Peptide alpha-N-acetyltransferase |
| **16** | PAS\_chr3\_1110 | 14,85 | 0,17 | Tyrosyl-tRNA synthetase, mitochondrial |
| **17** | PAS\_chr4\_0733 | 14,85 | 0,17 | Succinate Dehydrogenase |
| **18** | PAS\_chr3\_0646 | 14,04 | 0,14 | Phospholipase D, yeast-specific |
| **19** | PAS\_chr3\_0471 | 15,44 | 0,12 | aspartate-semialdehyde dehydrogenase, irreversible |
| **20** | PAS\_chr2-1\_0657 | 13,40 | 0,12 | phosphoglycerate dehydrogenase |
| **21** | PAS\_chr4\_0284 | 13,40 | 0,12 | ribonucleoside-diphosphate reductase |
| **22** | PAS\_chr4\_0877 | 16,73 | 0,05 | malate, succinate and fumarate transport, mitochondrial |
| **23** | PAS\_chr3\_0176 | 16,53 | 0,05 | N-acteylglutamate synthase and ornithine transacetylase , mitochondrial |
| **24** | PAS\_chr1-1\_0050 | 9,78 | 0,05 | Pyruvate dehydrogenase |
| **25** | PAS\_chr1-4\_0254 | 9,78 | 0,05 | Ppyruvate dehydrogenase |
| **26** | PAS\_chr1-4\_0593 | 9,78 | 0,05 | Pyruvate dehydrogenase, tetrahydrofolate aminomethyltransferase |
| **27** | PAS\_chr2-2\_0288 | 9,78 | 0,05 | Arginase |
| **28** | PAS\_chr3\_0649 | 16,26 | 0,03 | Thiamine transport in via proton symport |
| **29** | PAS\_chr2-2\_0127 | 17,10 | 0,03 | Cytochrome c peroxidase, mitochondrial |
| **30** | PAS\_chr1-4\_0659 | 17,10 | 0,03 | Hydrogen peroxide reductase thioredoxin, peroxisomal |
| **31** | PAS\_chr2-1\_0547 | 16,70 | 0,03 | 3',5'-bisphosphate nucleotidase |
| **32** | PAS\_chr3\_0462 | 17,14 | 0,03 | Alanyl-tRNA synthetase |

**Table 2 - Reactions and pathways associated to the deletion candidates**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Deleted Gene** | **Reactions** | **Pathway** |
| **1** | PAS\_chr2-2\_0094 | udpacgam[c] => h[c] + udp[c] + chitin[c] | Glutamate metabolism |
| **2** | PAS\_chr1-4\_0194 | h[c] + ptrc[e] => h[e] + ptrc[c]  h[c] + spmd[e] => h[e] + spmd[c] h[c] + sprm[e] => h[e] + sprm[c] | Transport, Extracellular |
| **3** | PAS\_chr4\_0836 | h[c] + ptrc[e] => h[e] + ptrc[c]  h[c] + spmd[e] => h[e] + spmd[c] h[c] + sprm[e] => h[e] + sprm[c] | Transport, Extracellular |
| **4** | RPPA11109 | ru5p-D[c] <=> xu5p-D[c] | Pentose Phosphate Pathway |
| **5** | RPPA11110 | ru5p-D[c] <=> xu5p-D[c] | Pentose Phosphate Pathway |
| **6** | PAS\_chr2-2\_0330 | ptd1ino\_PP[c] + cer1\_24[c] => 12dgr\_PP[c] + ipc124\_PP[c] | Sphingolipid Metabolism |
| **7** | PAS\_chr2-2\_0044 | h[c] + pa\_PP[c] + ctp[c] <=> ppi[c] + cdpdag\_PP[c]  h[m] + ctp[m] + pa\_PP[m] <=> ppi[m] + cdpdag\_PP[m] | Phospholipid Biosynthesis |
| **8** | PAS\_chr4\_0210 | h[c] + adp[c] + atp[m] => h[m] + atp[c] + adp[m] | Transport, Mitochondrial |
| **9** | PAS\_chr4\_0212 | r5p[c] <=> ru5p-D[c] | Pentose Phosphate Pathway |
| **10** | PAS\_chr3\_0604 | atp[c] + rib-D[c] => h[c] + adp[c] + r5p[c] | Pentose Phosphate Pathway |
| **11** | PAS\_chr4\_0408 | h[c] + ctp[c] + ethamp[c] => ppi[c] + cdpea[c] | Phospholipid Biosynthesis |
| **12** | PAS\_chr1-1\_0418 | ac[e] <=> ac[c] | Transport, Extracellular |
| **13** | PAS\_chr1-3\_0220 | nad[c] + mlthf[c] => nadh[c] + methf[c] | Folate Metabolism |
| **14** | PAS\_chr1-4\_0487 | fad[m] + succ[m] <=> fadh2[m] + fum[m]  q6[m] + succ[m] <=> q6h2[m] + fum[m]  q6[m] + fadh2[m] <=> q6h2[m] + fad[m] | Citric Acid Cycle/Oxydative Phosphorilation |
| **15** | PAS\_chr2-2\_0278 | accoa[c] + pepd[c] => h[c] + coa[c] + apep[c] | Other Amino Acid Metabolism |
| **16** | PAS\_chr3\_1110 | atp[m] + tyr-L[m] + trnatyr[m] => amp[m] + ppi[m] + tyrtrna[m] | tRNA charging |
| **17** | PAS\_chr4\_0733 | fad[m] + succ[m] <=> fadh2[m] + fum[m]  q6[m] + succ[m] <=> q6h2[m] + fum[m]  q6[m] + fadh2[m] <=> q6h2[m] + fad[m] | Citric Acid Cycle/Oxydative Phosphorilation |
| **18** | PAS\_chr3\_0646 | h2o[c] + pc\_PP[c] => h[c] + pa\_PP[c] + chol[c] | Phospholipid Metabolism |
| **19** | PAS\_chr3\_0471 | h[c] + nadph[c] + 4pasp[c] => pi[c] + nadp[c] + aspsa[c] | Alanine and Aspartate Metabolism |
| **20** | PAS\_chr2-1\_0657 | nad[c] + 3pg[c] => h[c] + nadh[c] + 3php[c] | Glycine and Serine Metabolism |
| **21** | PAS\_chr4\_0284 | 19 Reactions | Nucleotide Salvage Pathway |
| **22** | PAS\_chr4\_0877 | pi[m] + mal-L[c] <=> pi[c] + mal-L[m] | Transport, Mitochondrial |
| **23** | PAS\_chr3\_0176 | accoa[m] + glu-L[m] => h[m] + coa[m] + acglu[m]  glu-L[m] + acorn[m] => acglu[m] + orn[m] | Arginine and Proline Metabolism |
| **24** | PAS\_chr1-1\_0050 | nad[m] + coa[m] + pyr[m] => nadh[m] + co2[m] + accoa[m] | Glycolysis/Gluconeogenesis |
| **25** | PAS\_chr1-4\_0254 | nad[m] + coa[m] + pyr[m] => nadh[m] + co2[m] + accoa[m] | Glycolysis/Gluconeogenesis |
| **26** | PAS\_chr1-4\_0593 | udpacgam[c] => h[c] + udp[c] + chitin[c] | Glycolysis/Gluconeogenesis |
| **27** | PAS\_chr2-2\_0288 | h[c] + ptrc[e] => h[e] + ptrc[c]  h[c] + spmd[e] => h[e] + spmd[c] h[c] + sprm[e] => h[e] + sprm[c] | Arginine and Proline Metabolism |
| **28** | PAS\_chr3\_0649 | h[c] + ptrc[e] => h[e] + ptrc[c]  h[c] + spmd[e] => h[e] + spmd[c] h[c] + sprm[e] => h[e] + sprm[c] | Transport, Extracellular |
| **29** | PAS\_chr2-2\_0127 | ru5p-D[c] <=> xu5p-D[c] | Oxidative Phosphorylation |
| **30** | PAS\_chr1-4\_0659 | ru5p-D[c] <=> xu5p-D[c] | Other |
| **31** | PAS\_chr2-1\_0547 | ptd1ino\_PP[c] + cer1\_24[c] => 12dgr\_PP[c] + ipc124\_PP[c] | Cysteine Metabolism |
| **32** | PAS\_chr3\_0462 | h[c] + pa\_PP[c] + ctp[c] <=> ppi[c] + cdpdag\_PP[c]  h[m] + ctp[m] + pa\_PP[m] <=> ppi[m] + cdpdag\_PP[m] | tRNA charging |