

Supplementary table S1 - General and case-study specific modifications applied to the Yeast 6.06 model

General modifications		
Modification	Details	Source/Justification
Added reaction r_4039	acetate_m + succinyl_CoA_m <----> succinate_m + acetyl_CoA_m	imported from Yeast 7.11 (more recent consensus model)
Modified r_0718	NADP_m + S_malate_m <----> NADPH_m + pyruvate_m + carbon_dioxide_m	updated according to Yeast 7.11 (more recent consensus model)
Modified r_0773	NADH_m + H_m + ubiquinone_6_m <----> NAD_m + ubiquinol_6_m	updated according to Yeast 7.11 (more recent consensus model)
Modified r_0226	4 H_c + 1 ADP_m + 1 phosphate_m <----> 3 H_m + 1 H2O_m + 1 ATP_m	updated according to Yeast 7.11 (more recent consensus model)
Modified r_2129	H_m <----> H_c	updated according to Yeast 7.11 (more recent consensus model)
Modified r_1110	ADP_c + ATP_m <----> ATP_c + ADP_m	updated according to Yeast 7.11 (more recent consensus model)
Modified r_0470	NAD_c + H2O_c + L_glutamate_c <----> H_c + NADH_c + ammonium_c + 2_oxoglutarate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0303	citrate_c <----> H2O + cis_aconitate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0338	ubiquinone_6_m + S_dihydroorotate_c <----> ubiquinol_6_m + orotate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0339	oxygen_c + S_dihydroorotate_c <----> hydrogen_peroxide_c + orotate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_2127	NAD_c + S_dihydroorotate_c <----> NADH_c + orotate_c	updated according to Yeast 7.11 (more recent consensus model)
Modified r_1254	H_e + pyruvate_e <----> H_c + pyruvate_c	updated according to Yeast 7.11 (more recent consensus model)
Gene rule update r_0530	(YPL252C AND YDR376W) or (YPL252C AND YDR376W AND YER141W)	updated according to Yeast 7.11 (more recent consensus model)
Updated biomass reaction r_4041	Add 1.0E-6 * chitin_c and 1.0E-6 * heme_a_m to reactants	updated according to Yeast 7.11 (more recent consensus model)
gene rule update r_0076	(YER037W or YGL224C)	updated according to Yeast 7.11 (more recent consensus model)
gene rule update r_0078	(YER037W or YGL224C)	updated according to Yeast 7.11 (more recent consensus model)
gene rule update r_1619	YER037W	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0333	phosphate_c + 2_deoxyuridine_c <----> uracil_c + 2_deoxy_D_ribofuranose_1_phosphate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0944	phosphate_c + adenosine_c <----> alpha_D_ribose_1_phosphate_c + adenine_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0945	phosphate_m + adenosine_m <----> adenine_m + alpha_D_ribose_1_phosphate_m	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0946	phosphate_c + 2_deoxyadenosine_c <----> 2_deoxy_D_ribofuranose_1_phosphate_c + adenine_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0947	phosphate_c + 2_deoxyguanosine_c <----> guanine_c + 2_deoxy_D_ribofuranose_1_phosphate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0948	phosphate_c + 2_deoxyinosine_c <----> hypoxanthine_c + 2_deoxy_D_ribofuranose_1_phosphate_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_0952	phosphate_c + xanthosine_c <----> alpha_D_ribose_1_phosphate_c + 9H_xanthine_c	updated according to Yeast 7.11 (more recent consensus model)
Removed r_1044	phosphate_c + thymidine_c <----> 2_deoxy_D_ribofuranose_1_phosphate_c + thymine_c	updated according to Yeast 7.11 (more recent consensus model)
Added reaction r_4045	H2O_c + uridine_c <----> uracil_c + D_ribose_c	imported from Yeast 7.11 (more recent consensus model)
gene rule update r_0888	(YMR105C or YKL127W)	updated according to Yeast 7.11 (more recent consensus model)
gene rule update r_0907	((YMR278W or YMR105C) or YKL127W)	updated according to Yeast 7.11 (more recent consensus model)
Modified r_0110	H_c + coenzyme_A_c + acetate_c <----> H2O_c + acetyl_CoA_c	As corrected in Pereira R, Nielsen J, Rocha I (2016) Improving the flux distributions simulated with genome-scale metabolic models of <i>Saccharomyces cerevisiae</i> . <i>Metab Eng Commun</i> 3: 153–163. doi:10.1016/j.meteno.2016.05.002.
Added reaction r_0234x	NAD_c + zymosterol_intermediate_1c_c <----> H_c + NADH_c + carbon_dioxide_c + zymosterol_intermediate_2_c	As corrected in Pereira R, Nielsen J, Rocha I (2016) Improving the flux distributions simulated with genome-scale metabolic models of <i>Saccharomyces cerevisiae</i> . <i>Metab Eng Commun</i> 3: 153–163. doi:10.1016/j.meteno.2016.05.002.
Added reaction r_0939x	prephenate_c + NAD_c <----> NADH_c + 3_4_hydroxyphenylpyruvate_c + carbon_dioxide_c	As corrected in Pereira R, Nielsen J, Rocha I (2016) Improving the flux distributions simulated with genome-scale metabolic models of <i>Saccharomyces cerevisiae</i> . <i>Metab Eng Commun</i> 3: 153–163. doi:10.1016/j.meteno.2016.05.002.
Inactivated r_1840	3_hydroxy_3_methylglutaryl_CoA_c <----> 3_hydroxy_3_methylglutaryl_CoA_m	No data supporting such reaction
Modified r_1117	H_c + L_aspartate_c <----> H_m + L_aspartate_m	As corrected in Pereira R, Nielsen J, Rocha I (2016) Improving the flux distributions simulated with genome-scale metabolic models of <i>Saccharomyces cerevisiae</i> . <i>Metab Eng Commun</i> 3: 153–163. doi:10.1016/j.meteno.2016.05.002.
Modifications for PHB production		
Added reaction R_phaA	2 acetyl_CoA_c <----> coenzyme_A_c + acetoacetyl_CoA_c	Acetoacetyl-CoA thiolase from <i>Ralstonia eutropha</i>
Added reaction R_phaB	H_c + NADPH_c + acetoacetyl_CoA_c <----> 3hbcoa_c + NADP_c	Acetoacetyl-CoA reductase from <i>Ralstonia eutropha</i>
Added reaction R_phaC	3hbcoa_c <----> phb_c + coenzyme_A_c	PHB synthase from <i>Ralstonia eutropha</i>
Added reaction R_EX_phb_e	phb_c <---->	PHB drain reaction required for simulation purposes
Modifications for 3-HP production		
Added reaction R_MCR	2* H_c + 2* NADPH_c + 1* malonyl_CoA_c <----> 1* coenzyme_A_c + 2* NADP_c + 1* 3hp_c	Malonyl-CoA reductase from <i>Chloroflexus aurantiacus</i>
Added reaction R_EX_3hp_e	M_3hp_c <---->	3-HP drain reaction required for simulation purposes
Added reaction R_gapN	glyceraldehyde_3_phosphate_c + H2O_c + NADP_c <----> H_c + NADPH_c + 3_phosphoglycerate_c	Glyceraldehyde-3-phosphate dehydrogenase from <i>Streptococcus mutans</i>
Modifications for santalene production		
Added reaction R_SANSYN	farnesyl_diphosphate_c <----> diphosphate_c + santalene_c	Santalene synthase from <i>Clausena lansium</i>
Added reaction R_EX_santalene_e	santalene_c <---->	santalene drain reaction required for simulation purposes