

**Additional Table 1 - Validation of the *Y. lipolytica* model**

Validation of the *Y. lipolytica* model with respect to experimental evidence of *Y. lipolytica* growth under different media conditions and gene knockouts. Expected Growth was obtained by the referenced literature. Simulated Growth was obtained using flux balance analysis (FBA), optimizing over the biomass function of our model, and converted to a qualitative phenotype/no phenotype value by thresholding. In both cases, the symbols represent ‘+’: growth; ‘-’:no growth; ‘n/a’: condition cannot be simulated with current model, but are provided for future model improvements. The “Result” column compares the two: TP/FP: True/False Positives, TN/FN: True/False Negatives. The simulated models shows a sensitivity of 0.68, a specificity of 0.61 and an accuracy (geometric mean between sensitivity and specificity) of 0.65.

Ref	Media	<i>Y. lipolytica</i> knocked locus	<i>S. cerevisiae</i> ortholog	Gene name	Exp. Growth	Simul. Growth	Result
[33]	YNBO	YALI0C06347g	YGL124C	<i>MON1</i>	+	n/a	n/a
[33]	YNBC16	YALI0C06347g	YGL124C	<i>MON1</i>	+	n/a	n/a
[33]	YNBT	YALI0C06347g	YGL124C	<i>MON1</i>	+	n/a	n/a
[33]	YNBD	YALI0D27126g	YDR353W YHR106W	<i>TRR1</i> <i>TRR2</i>	+	-	FN
[33]	YNBD	YALI0E14729g	YOR153W	<i>PDR5</i>	+	+	TP
[33]	YNBO	YALI0E14729g	YOR153W	<i>PDR5</i>	+	-	FN
[33]	YNBC10	YALI0E14729g	YOR153W	<i>PDR5</i>	+	+	TP
[33]	YNBC16	YALI0E14729g	YOR153W	<i>PDR5</i>	-	-	TN
[33]	YNBT	YALI0E14729g	YOR153W	<i>PDR5</i>	+	-	FN
[33]	YNBD	YALI0E09405g	YGL153W	<i>PEX14</i>	+	n/a	n/a
[33]	YNBO	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBC10	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBC16	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBD	YALI0D26081g	YLL051C YOL152W YOR381W YOR384W	<i>FRE3-7</i>	+	n/a	n/a
[33]	YNBO	YALI0D26081g	YLL051C YOL152W YOR381W YOR384W	<i>FRE3-7</i>	+	n/a	n/a
[33]	YNBC10	YALI0D26081g	YLL051C YOL152W YOR381W YOR384W	<i>FRE3-7</i>	-	n/a	n/a
[33]	YNBC16	YALI0D26081g	YLL051C YOL152W YOR381W YOR384W	<i>FRE3-7</i>	+	n/a	n/a
[33]	YNBT	YALI0D26081g	YLL051C YOL152W YOR381W YOR384W	<i>FRE3-7</i>	+	n/a	n/a
[33]	YNBD	YALI0F04095g	YDL066W	<i>IDP1</i>	-	+	FP
[33]	YNBO	YALI0F04095g	YDL066W	<i>IDP1</i>	-	-	TN
[33]	YNBT	YALI0F04095g	YDL066W	<i>IDP1</i>	-	-	TN
[33]	YNBD	YALI0E09405g	YGL153W	<i>PEX14</i>	+	n/a	n/a
[33]	YNBO	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBC10	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBC16	YALI0E09405g	YGL153W	<i>PEX14</i>	-	n/a	n/a
[33]	YNBT	YALI0E09405g	YGL153W	<i>PEX14</i>	+	n/a	n/a
[33]	YNBD	YALI0C21582g	YGL059W	<i>PKP2</i>	+	n/a	n/a
[33]	YNBO	YALI0C21582g	YGL059W	<i>PKP2</i>	-	n/a	n/a
[33]	YNBC10	YALI0C21582g	YGL059W	<i>PKP2</i>	-	n/a	n/a
[33]	YNBC16	YALI0C21582g	YGL059W	<i>PKP2</i>	+	n/a	n/a

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Ref	Media	<i>Y. lipolytica</i> knocked locus	<i>S. cerevisiae</i> ortholog	Gene name	Exp. Growth	Simul. Growth	Result
[33]	YNBD	YALI0E34672g	YJR095W	<i>ACR1</i>	+	+	TP
[33]	YNBO	YALI0E34672g	YJR095W	<i>ACR1</i>	-	-	TN
[33]	YNBC10	YALI0E34672g	YJR095W	<i>ACR1</i>	-	+	FP
[33]	YNBC16	YALI0E34672g	YJR095W	<i>ACR1</i>	-	-	TN
[33]	YNBT	YALI0E34672g	YJR095W	<i>ACR1</i>	-	-	TN
[33]	YNBD	YALI0B13970g	YIL155C	<i>GUT2</i>	+	+	TP
[33]	YNBC10	YALI0B13970g	YIL155C	<i>GUT2</i>	+	+	TP
[33]	YNBC16	YALI0B13970g	YIL155C	<i>GUT2</i>	+	-	FN
[33]	YNBD	YALI0E06831g		<i>PEX20</i>	+	n/a	n/a
[33]	YNBO	YALI0E06831g		<i>PEX20</i>	-	n/a	n/a
[33]	YNBC10	YALI0E06831g		<i>PEX20</i>	-	n/a	n/a
[33]	YNBC16	YALI0E06831g		<i>PEX20</i>	-	n/a	n/a
[33]	YNBT	YALI0E06831g		<i>PEX20</i>	+	n/a	n/a
[33]	YNBD	YALI0F18216g	YFL001W	<i>DEG1</i>	+	+	TP
[33]	YNBC16	YALI0F18216g	YFL001W	<i>DEG1</i>	+	-	FN
[33]	YNBT	YALI0F18216g	YFL001W	<i>DEG1</i>	+	-	FN
[33]	YNBD	YALI0E03058g	YPR128C	<i>PMP34</i>	+	+	TP
[33]	YNBO	YALI0E03058g	YPR128C	<i>PMP34</i>	+	-	FN
[33]	YNBC10	YALI0E03058g	YPR128C	<i>PMP34</i>	-	+	FP
[33]	YNBC16	YALI0E03058g	YPR128C	<i>PMP34</i>	+	-	FN
[33]	YNBT	YALI0E03058g	YPR128C	<i>PMP34</i>	+	-	FN
[33]	YNBD	YALI0C16885g	YER065C	<i>ICL1</i>	+	+	TP
[33]	YNBO	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[33]	YNBC10	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[33]	YNBC16	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[33]	YNBT	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[33]	YNBD	YALI0E14729g	YOL075C YNR070W YDR011W	<i>PDR5</i>	+	+	TP
[33]	YNBO	YALI0E14729g	YOL075C YNR070W YDR011W	<i>PDR5</i>	+	-	FN
[33]	YNBC10	YALI0E14729g	YOL075C YNR070W YDR011W	<i>PDR5</i>	+	+	TP
[33]	YNBC16	YALI0E14729g	YOL075C YNR070W YDR011W	<i>PDR5</i>	-	-	TN
[33]	YNBT	YALI0E14729g	YOL075C YNR070W YDR011W	<i>PDR5</i>	+	-	FN
[34]	Lactose	n/a, media only			-	n/a	n/a
[34]	D-Galactose	n/a, media only			-	+	FP
[35]	YNBD	YALI0A15972g	YLR377C	<i>FBP1</i>	+	+	TP
[35]	Ethanol	YALI0A15972g	YLR377C	<i>FBP1</i>	+	-	FN
[35]	Glycerol	YALI0A15972g	YLR377C	<i>FBP1</i>	+	-	FN

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Ref	Media	<i>Y. lipolytica</i> knocked locus	<i>S. cerevisiae</i> ortholog	Gene name	Exp. Growth	Simul. Growth	Result
[35]	Acetate	YALI0A15972g	YLR377C	<i>FBP1</i>	+	-	FN
[36]	YNBD	YALI0C24101g	YGL062W	<i>PYC1</i>	+	+	TP
[36]	Ethanol	YALI0C24101g	YGL062W	<i>PYC1</i>	+	+	TP
[36]	Aspartate	YALI0C24101g	YGL062W	<i>PYC1</i>	+	+	TP
[36]	Glutamate	YALI0C24101g	YGL062W	<i>PYC1</i>	+	+	TP
[36]	YNBD	YALI0C16885g	YER065C	<i>ICL1</i>	+	+	TP
[36]	Ethanol	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[36]	Aspartate	YALI0C16885g	YER065C	<i>ICL1</i>	+	+	TP
[36]	Glutamate	YALI0C16885g	YER065C	<i>ICL1</i>	+	+	TP
[36]	YNBD	YALI0C24101g YALI0C16885g	YGL062W YER065C	<i>ICL1</i> <i>PYC1</i>	-	+	FP
[36]	Ethanol	YALI0C24101g YALI0C16885g	YGL062W YER065C	<i>ICL1</i> <i>PYC1</i>	-	-	TN
[36]	Aspartate	YALI0C24101g YALI0C16885g	YGL062W YER065C	<i>ICL1</i> <i>PYC1</i>	+	+	TP
[36]	Glutamate	YALI0C24101g YALI0C16885g	YGL062W YER065C	<i>ICL1</i> <i>PYC1</i>	+	+	TP
[37]	YNBC10	YALI0E19514g	YCR077C	<i>PAT1</i>	-	n/a	n/a
[37]	YNBD	YALI0E19514g	YCR077C	<i>PAT1</i>	+	n/a	n/a
[37]	Glycerol	YALI0E19514g	YCR077C	<i>PAT1</i>	+	n/a	n/a
[38]	YNBD	YALI0D24431g YALI0E34793g		<i>ACL1</i>	+	+	TP
[38]	YNBO	YALI0D24431g YALI0E34793g		<i>ACL1</i>	+	-	FN
[39]	Acetate	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[39]	YNBO	YALI0C16885g	YER065C	<i>ICL1</i>	-	-	TN
[39]	YNBD	YALI0C16885g	YER065C	<i>ICL1</i>	+	+	TP
[39]	Acetate	YALI0E15708g	YNL117W	<i>MLS1</i>	+	+	TP
[39]	YNBO	YALI0E15708g	YNL117W	<i>MLS1</i>	+	-	FN
[39]	YNBD	YALI0E15708g	YNL117W	<i>MLS1</i>	+	+	TP
[39]	Acetate	YALI0E02684g	YCR005C YNR001C	<i>CIT2</i>	+	+	TP
[39]	YNBO	YALI0E02684g	YCR005C YNR001C	<i>CIT2</i>	+	-	FN
[39]	YNBD	YALI0E02684g	YCR005C YNR001C	<i>CIT2</i>	+	+	TP
[40]	YNBD	YALI0B13970g	YIL155C	<i>GUT2</i>	+	+	TP
[40]	Glycerol	YALI0B13970g	YIL155C	<i>GUT2</i>	-	+	FP
[40]	YNBO	YALI0B13970g	YIL155C	<i>GUT2</i>	+	-	FN
[40]	YNBD	YALI0B13970g YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>GUT2</i> <i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	+	+	TP

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Ref	Media	<i>Y. lipolytica</i> knocked locus	<i>S. cerevisiae</i> ortholog	Gene name	Exp. Growth	Simul. Growth	Result
[40]	Glycerol	YALI0B13970g YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>GUT2</i> <i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	-	+	FP
[40]	YNBO	YALI0B13970g YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>GUT2</i> <i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	-	-	TN
[40]	YNBD	YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	+	+	TP
[40]	Glycerol	YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	+	+	TP
[40]	YNBO	YALI0E32835g YALI0F10857g YALI0D24750g YALI0E27654g YALI0C23859g YALI0E06567g	YIL155C YGL205W	<i>POX1</i> <i>POX2</i> <i>POX3</i> <i>POX4</i> <i>POX5</i> <i>POX6</i>	-	-	TN
[41]	YNBD	YALI0D02629g	YOR222W YPL134C	<i>ODC1</i>	-	+	FP
[41]	YNBD+ pu- trescine	YALI0D02629g	YOR222W YPL134C	<i>ODC1</i>	+	+	TP
[42]	YNBD	YALI0B07667g	YDR007W	<i>TRP1</i>	-	+	FP
[42]	YNBD+ trypto- phane	YALI0B07667g	YDR007W	<i>TRP1</i>	+	+	TP
[32]	2-Keto-D- Gluconate	n/a, media only			-	n/a	n/a
[32]	a,a-Trehalose	n/a, media only			-	+	FP
[32]	Arbutin	n/a, media only			-	n/a	n/a
[32]	Butane 2,3 diol	n/a, media only			-	n/a	n/a
[32]	Cellobiose	n/a, media only			-	n/a	n/a
[32]	Citrate	n/a, media only			+	+	TP
[32]	D-Arabinose	n/a, media only			-	-	TN

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Ref	Media	<i>Y. lipolytica</i> knocked locus	<i>S. cerevisiae</i> ortholog	Gene name	Exp. Growth	Simul. Growth	Result
[32]	D-Galactonate	n/a, media only			-	n/a	n/a
[32]	D-Galactose	n/a, media only			-	+	FP
[32]	D-Galacturonate	n/a, media only			-	-	TN
[32]	D-glucarate	n/a, media only			-	n/a	n/a
[32]	D-Glucitol	n/a, media only			+	+	TP
[32]	D-Gluconate	n/a, media only			+	n/a	n/a
[32]	D-Glucono-1,5-lactone	n/a, media only			+	n/a	n/a
[32]	D-Glucosamine	n/a, media only			-	+	FP
[32]	D-Glucose	n/a, media only			+	+	TP
[32]	D-Glucuronate	n/a, media only			-	n/a	n/a
[32]	D-Mannitol	n/a, media only			+	n/a	n/a
[32]	D-Ribose	n/a, media only			-	+	FP
[32]	D-Xylose	n/a, media only			-	+	FP
[32]	DL-Lactate	n/a, media only			+	+	TP
[32]	Erythritol	n/a, media only			+	n/a	n/a
[32]	Ethanol	n/a, media only			+	+	TP
[32]	Galactitol	n/a, media only			-	n/a	n/a
[32]	Glycerol	n/a, media only			+	+	TP
[32]	Inulin	n/a, media only			-	n/a	n/a
[32]	L-Arabinitol	n/a, media only			-	-	TN
[32]	L-Arabinose	n/a, media only			-	-	TN
[32]	L-Rhamnose	n/a, media only			-	n/a	n/a
[32]	L-Sorbose	n/a, media only			-	-	TN
[32]	Lactose	n/a, media only			-	n/a	n/a
[32]	Maltose	n/a, media only			-	-	TN
[32]	Me-a-D-Glucoside	n/a, media only			-	n/a	n/a
[32]	Melezitose	n/a, media only			-	n/a	n/a
[32]	Melibiose	n/a, media only			-	-	TN
[32]	Methanol	n/a, media only			-	n/a	n/a
[32]	myo-Inositol	n/a, media only			-	-	TN
[32]	Propane 1,2 diol	n/a, media only			-	n/a	n/a
[32]	Quinic acid	n/a, media only			-	n/a	n/a
[32]	Raffinose	n/a, media only			-	n/a	n/a
[32]	Ribitol	n/a, media only			-	n/a	n/a
[32]	Salicin	n/a, media only			-	n/a	n/a
[32]	Starch	n/a, media only			-	n/a	n/a
[32]	Succinate	n/a, media only			+	+	TP
[32]	Sucrose	n/a, media only			-	+	FP
[32]	Xylitol	n/a, media only			-	+	FP
Overall results:					TP: 39, TN: 25, FN: 18, FP: 16; accuracy: 0.65		