

Table S2

Mutant	Simulation result	Predicted phenotype	Observed phenotype (Ref.)
<i>cdk1Δ</i>	No formation of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc}	Lethal. No budding and DNA replication	Lethal. The cells arrest as unbudded cells ⁽¹⁾
<i>clb5Δ clb6Δ cdk1Δ</i>	No formation of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc}	Lethal. No budding and DNA replication	Lethal ⁽²⁾
<i>cln1Δ cln2Δ clb5Δ clb6Δ</i>	No formation of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc}	Lethal. No budding and DNA replication	Lethal. The cells arrest in G ₁ phase ⁽³⁾
CLB5 stabilized	Wild type level of Cdk1-Cln1,2 _{cyt} , and slight increase of the Cdk1-Clb5,6 _{nuc} level	Viable. Budding like wild type, and slight anticipation of DNA replication	Viable. The strain rescues the replication defect of the <i>clb5Δ</i> strain ⁽⁴⁾
OE-CLB5 and stabilized	Decrease of the Cdk1-Cln1,2 _{cyt} level, and very high level (about 10X) of Cdk1-Clb5,6 _{nuc}	Decrease of budding, and abnormal increase of DNA replication. Possibly lethal	Lethal ⁽⁵⁾
<i>cln1Δ cln2Δ</i> OE-SIC1 OE-CLN2	Increase of the Cdk1-Cln1,2 _{cyt} level, and similar timing of Cdk1-Clb5,6 _{nuc} formation	Viable. Increase of budding, and DNA replication comparable to wild type	Viable. The strain suppresses the defects of the <i>cln1Δ cln2Δ</i> OE-SIC1 strain ⁽⁶⁾
<i>cln1Δ cln2Δ</i> OE-WHI5	No formation of Cdk1-Cln1,2 _{cyt} , and very strong decrease of the Cdk1-Clb5,6 _{nuc} level (four orders of magnitude)	Lethal. No budding and DNA replication	Lethal. Severely delayed growth ⁽⁷⁾
<i>cln1Δ cln2Δ</i> OE-CLN2	Increased of the Cdk1-Cln1,2 _{cyt} level (about 15X), similar timing, but overall reduction (about 1/3) of Cdk1-Clb5,6 _{nuc} formation	Viable. Slight anticipation of budding, DNA replication should be ca. normal	Viable. The cells go through START immediately after cytokinesis ⁽⁸⁾
<i>cln1Δ cln2Δ cln3Δ</i>	No formation of Cdk1-Cln1,2 _{cyt} , and very strong decrease of the Cdk1-Clb5,6 _{nuc} level (three/four orders of magnitude)	Lethal. No budding and DNA replication	Lethal. The cells arrest the growth in G ₁ phase ⁽⁹⁾
<i>cln1Δ cln2Δ cln3Δ</i> OE-CDK1	No formation of Cdk1-Cln1,2 _{cyt} , and very strong decrease of the Cdk1-Clb5,6 _{nuc} level (three orders of magnitude)	No budding and very strong delay in DNA replication. Lethal	Lethal. The phenotype of the triple cyclins mutant is not recovered ⁽¹⁰⁾

<i>cln1Δ cln2Δ cln3Δ</i> OE-CLN2	Early formation of Cdk1-Cln1,2 _{cyt} , and decrease of the Cdk1-Clb5,6 _{nuc} level (one order of magnitude)	Viable. Anticipation of budding, and delay in DNA replication	Viable ⁽¹¹⁾
<i>cln1Δ cln2Δ cln3Δ</i> CLN2 stabilized	Strong decrease of the Cdk1-Cln1,2 _{cyt} level, and decrease of the Cdk1-Clb5,6 _{nuc} level (one order of magnitude)	Viable. Decrease of budding, and delay in DNA replication	Viable. The phenotype of the triple cyclins mutant is recovered ⁽¹²⁾
<i>cln3Δ</i> OE-WHI5	Very strong decrease of the Cdk1-Cln1,2 _{cyt} level, and very strong decrease of the Cdk1-Clb5,6 _{nuc} level (three orders of magnitude)	Lethal. No budding, and very strong delay in DNA replication	Lethal. The cells arrest as unbudded cells ⁽¹³⁾
CLN2 stabilized	Slight increase of the Cdk1-Cln1,2 _{cyt} level, and similar timing of Cdk1-Clb5,6 _{nuc} formation	Viable. Increased budding, and DNA replication comparable to wild type	Viable ⁽¹⁴⁾
CLN3 stabilized <i>NOTE. Lack of agreement on cell size likely originates from the fact that stable Cln3 mutants are more stable at the end of the cycle. The net result may thus be a larger Cln3 level in new-born cells, synthesis then proceeding as in wild type</i>	Level and timing of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc} formation like wild type	Viable. Budding and DNA replication comparable to wild type	Viable. No arrest of the cell cycle in G ₁ phase, and small cell size ⁽¹⁵⁾
<i>far1Δ sic1Δ</i>	Slight anticipation of the Cdk1-Cln1,2 _{cyt} level, and decrease of the Cdk1-Clb5,6 _{nuc} level (one order of magnitude)	Viable. Slight anticipation of budding, and delay in DNA replication	Viable ⁽¹⁶⁾
OE-SIC1 and stabilized	Wild type level of Cdk1-Cln1,2 _{cyt} , and very strong decrease of the Cdk1-Clb5,6 _{nuc} level (three orders of magnitude)	Lethal. Budding like wild type, and very strong delay in DNA replication	Lethal. The cells arrest in G ₁ phase ⁽¹⁷⁾
OE-SIC1 OE-CLN2	Increase of the Cdk1-Cln1,2 _{cyt} level, and similar timing of Cdk1-Clb5,6 _{nuc} formation	Viable. Increase of budding, and slight delay in DNA replication	Viable. OE-CLN2 suppresses the toxicity of the OE-SIC1 strain ⁽¹⁸⁾
<i>sbfΔ mbfΔ</i>	No formation of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc}	Lethal. No budding and DNA replication	Lethal ⁽¹⁹⁾
<i>sbfΔ mbfΔ</i> OE-CLN2	Early formation of Cdk1-Cln1,2 _{cyt} , and no	Viable. Anticipation of budding, DNA	Viable. The strain rescues the <i>sbfΔ</i>

<i>NOTE. To get agreement with experimental data, we must assume that synthesis of Clb3,4 (not included in the model) must start at some point</i>	Cdk1-Clb5,6 _{nuc} formation	replication delayed because synthesis of Clb3,4 (not included in the model) would be required to get (delayed) S phase	lethal phenotype ⁽²⁰⁾
OE-SBF <i>NOTE. SBF and MBF are not differentiated in our model, and we consider OE-SBF increasing the rate of CLN1,2 transcription</i>	Strong increase of Cdk1-Cln1,2 _{cyt} level, and slight anticipation of Cdk1-Clb5,6 _{nuc} formation	Viable. Strong anticipation of budding, and slight anticipation in DNA replication	Viable. The overexpression results in small cell size ⁽²¹⁾
<i>sbfΔ mbfΔ sic1Δ</i>	No formation of Cdk1-Cln1,2 _{cyt} and Cdk1-Clb5,6 _{nuc}	Lethal. No budding and DNA replication	Lethal ⁽²²⁾
<i>sbfΔ mbfΔ sic1Δ OE-CLN2</i>	Early formation of Cdk1-Cln1,2 _{cyt} , and no Cdk1-Clb5,6 _{nuc} formation	Viable. Anticipation of budding, DNA replication delayed because synthesis of Clb3,4 (not included in the model) would be required to get (delayed) S phase	Viable ⁽²³⁾
OE-MBF <i>NOTE. SBF and MBF are not differentiated in our model, and we consider OE-MBF increasing the rate of CLB5,6 transcription</i>	Early formation of Cdk1-Cln1,2 _{cyt} , and very high level of Cdk1-Clb5,6 _{nuc}	Lethal. Anticipation of budding, and abnormal increase of DNA replication	Lethal ⁽²⁴⁾

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