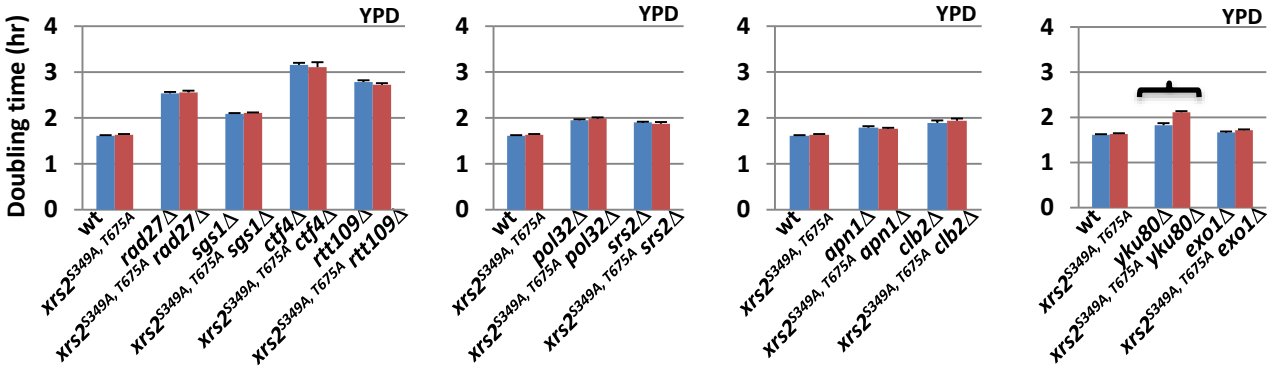
A.


Doubling time (hr)
YPD
wt
xrs2S349A, T675A
rad27Δ
xrs2S349A, T675A rad27Δ
sgs1Δ
xrs2S349A, T675A sgs1Δ
ctf4Δ
xrs2S349A, T675A ctf4Δ
rtt109Δ
xrs2S349A, T675A rtt109Δ
pol32Δ
xrs2S349A, T675A pol32Δ
srs2Δ
xrs2S349A, T675A srs2Δ
apn1Δ
xrs2S349A, T675A apn1Δ
clb2Δ
xrs2S349A, T675A clb2Δ
yku80Δ
xrs2S349A, T675A yku80Δ
exo1Δ
xrs2S349A, T675A exo1Δ

B.

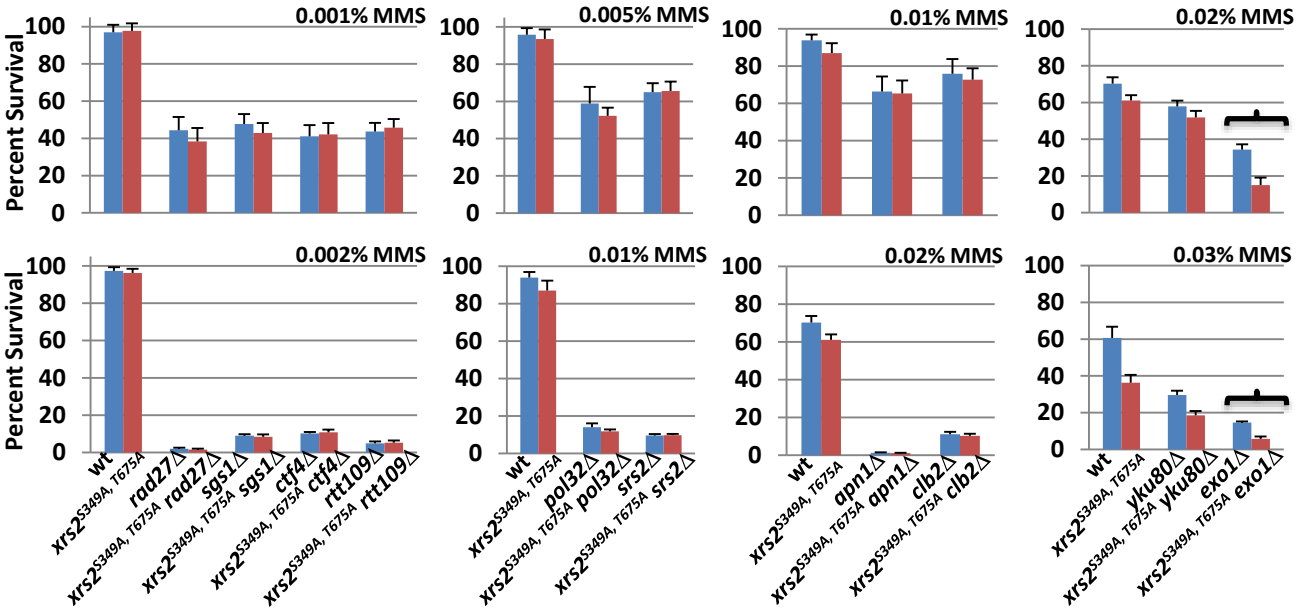

Percent Survival
0.001% MMS
0.005% MMS
0.01% MMS
0.02% MMS
0.002% MMS
0.01% MMS
0.02% MMS
0.03% MMS
wt
xrs2S349A, T675A
rad27Δ
xrs2S349A, T675A rad27Δ
sgs1Δ
xrs2S349A, T675A sgs1Δ
ctf4Δ
xrs2S349A, T675A ctf4Δ
rtt109Δ
xrs2S349A, T675A rtt109Δ
pol32Δ
xrs2S349A, T675A pol32Δ
srs2Δ
xrs2S349A, T675A srs2Δ
apn1Δ
xrs2S349A, T675A apn1Δ
clb2Δ
xrs2S349A, T675A clb2Δ
yku80Δ
xrs2S349A, T675A yku80Δ
exo1Δ
xrs2S349A, T675A exo1Δ

Figure S7. Screen for genetic interactions with *xrs2*$^{S349A,\ T675A}$ in the absence or presence of MMS. A) *xrs2*$^{S349A,\ T675A}$ *yku80*Δ showed enhanced growth defects as compared to *yku80*Δ in YPD. The doubling time of the wild type and mutant strains were measured and calculated as in Figure 2A. Three independent, PCR-confirmed gene knockout transformants of each genotype were assayed, and the error bars represent the standard deviation for the three isolates. **B) *xrs2*$^{S349A,\ T675A}$ *exo1*Δ showed enhanced MMS-sensitivity as compared to *exo1*Δ.** The log-phase wild type and mutant cells were serially diluted in PBS and spread onto YPD, YPD + MMS plates. Viable cells were determined as in Figure 2B. Three independent, PCR-confirmed gene knockout transformants of each strain were tested, and the error bars represent the standard deviation for the three isolates. The *xrs2*$^{S349A,\ T675A}$ *xxx*Δ strains that show significant genetic interactions were indicated with curly brackets and subjected to further assays shown in Figure 3B.