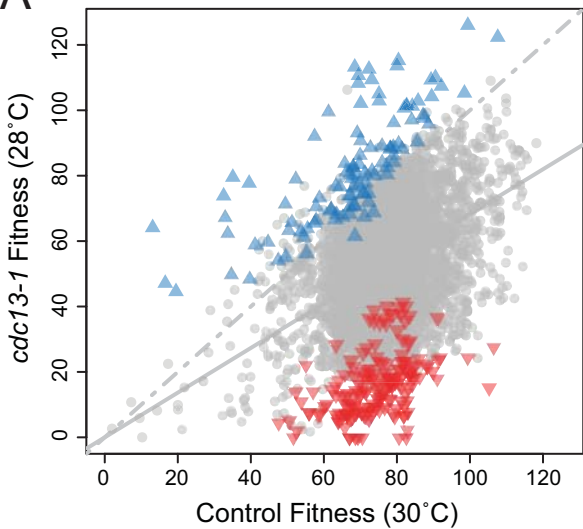
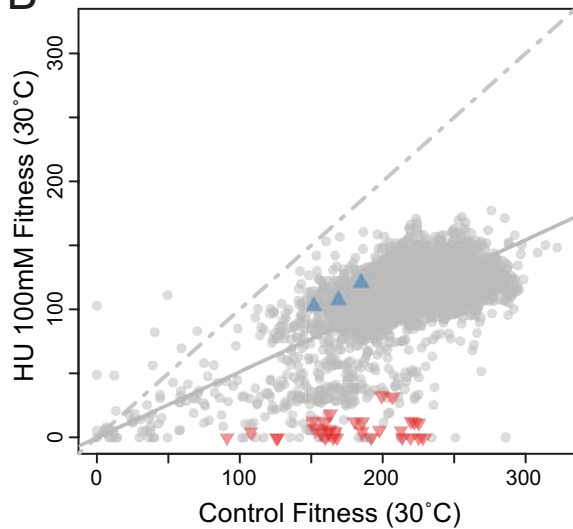


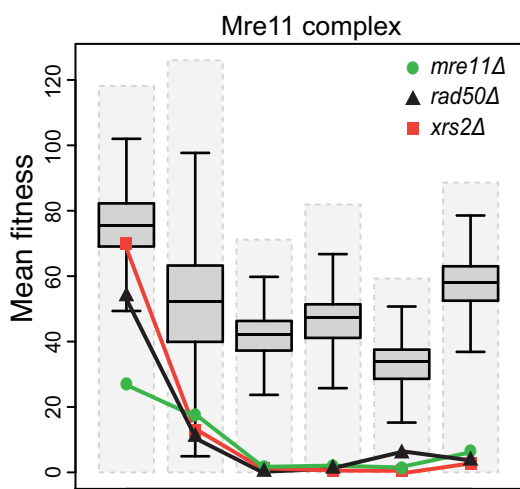
A



B



C

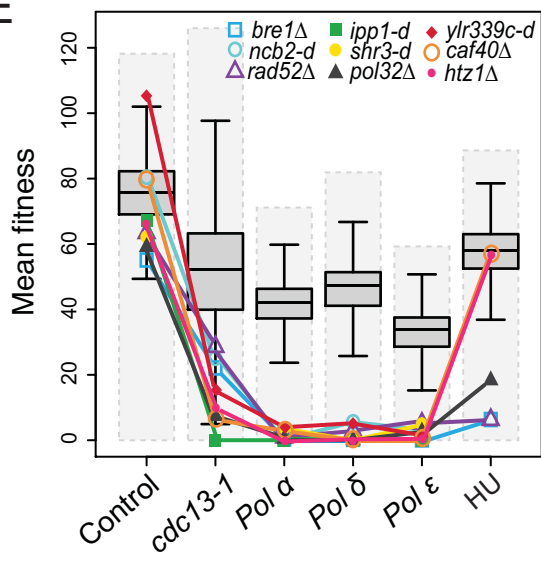


D

Distance (D) to the target mutant:

RAD24	D	Rank	Description
<i>RAD24</i>	0	1	Checkpoint protein, clamp loader of the Rad17-Mec3-Ddc1
<i>RAD17</i>	9.8	2	Checkpoint protein, forms a clamp with Ddc1 and Mec3
<i>DDC1</i>	17.4	3	Checkpoint protein, forms a clamp with Rad17 and Mec3
<i>RAD9</i>	51.8	4	DNA damage checkpoint protein

E



F

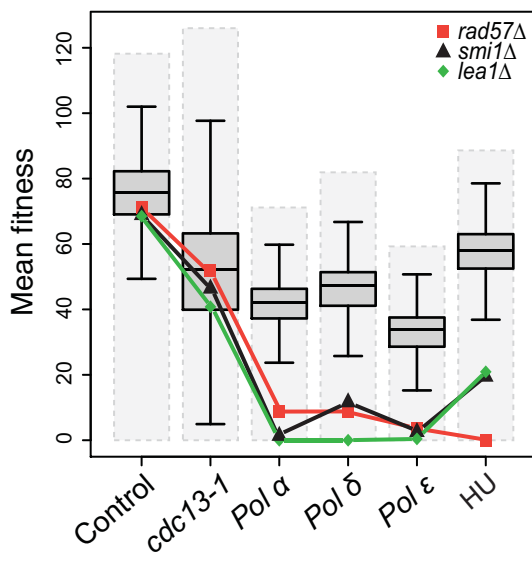


Figure S5: Fitness profiles of regulators of DNA replication

A) QFA fitness plot comparing *cdc13-1* strains at 28°C with a *lyp1Δ* control strain at 30°C. Positive (blue upward triangles), negative (red downward triangles) and neutral (grey dot) genetic interactions are presented. The solid grey line is a linear regression through all points and the dashed line is the line of equal fitness. **B)** QFA Fitness plot comparing mutants from the deletion library growing on complete synthetic media (CSM) supplemented with 100mM HU with strains growing on CSM (Andrew *et al.* 2013). **C)** Fitness profiles of gene deletions affecting *mre11Δ*, *rad50Δ* and *xrs2Δ* (Mre11 complex). **D)** List of the top four gene deletions/DAmP mutations that show similar profiles to *rad24Δ* when combined with control (*lyp1Δ*), *cdc13-1*, *pol1-4*, *pol2-12* and *cdc2-2* mutations and in presence of 100mM HU. **E-F)** Fitness profiles of *yfgΔ-d* that negatively affect Pol α , Pol δ and Pol ϵ mutations (Table 1). **E)** Fitness profiles of *yfgΔ-d* that negatively affect the fitness of *cdc13-1* mutants and the three DNA polymerase mutants. **F)** Fitness profiles of *yfgΔ-d* that do not affect the fitness of *cdc13-1* mutants.