

Supplemental Figures and Tables

Supplemental Figures

Figure S1

Four replicate fluctuation tests, using resistance to 5-fluoroorotic acid, show an average fold increase of 20.8 (95% CI: 13.4 to 28.3) for the *mmr* strain.

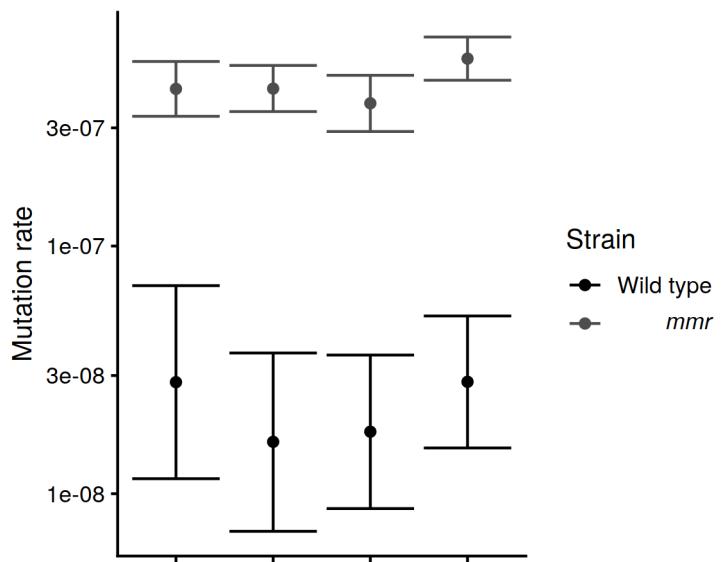


Figure S2

Histogram and QQ plot of fitness distributions for diploid strains. Panel **A** shows the results for the wild-type ($n=279$) strain and panel **B** for the *mmr* strain ($n=294$). As in Figure 3, the dashed line indicates the mean. The high fitness diploid *mmr* clone shaded in gray was removed from the data set for load calculations and is not shown on the histogram. Removal does not affect the calculation of the load, 0.3%, given rounding.

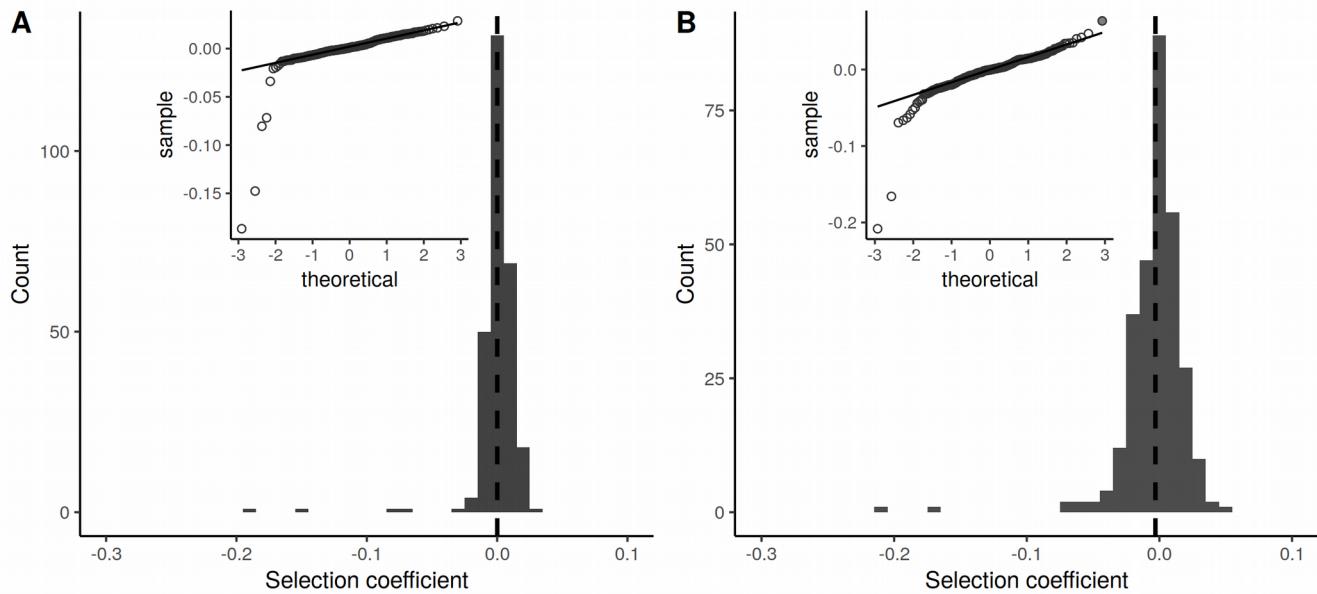
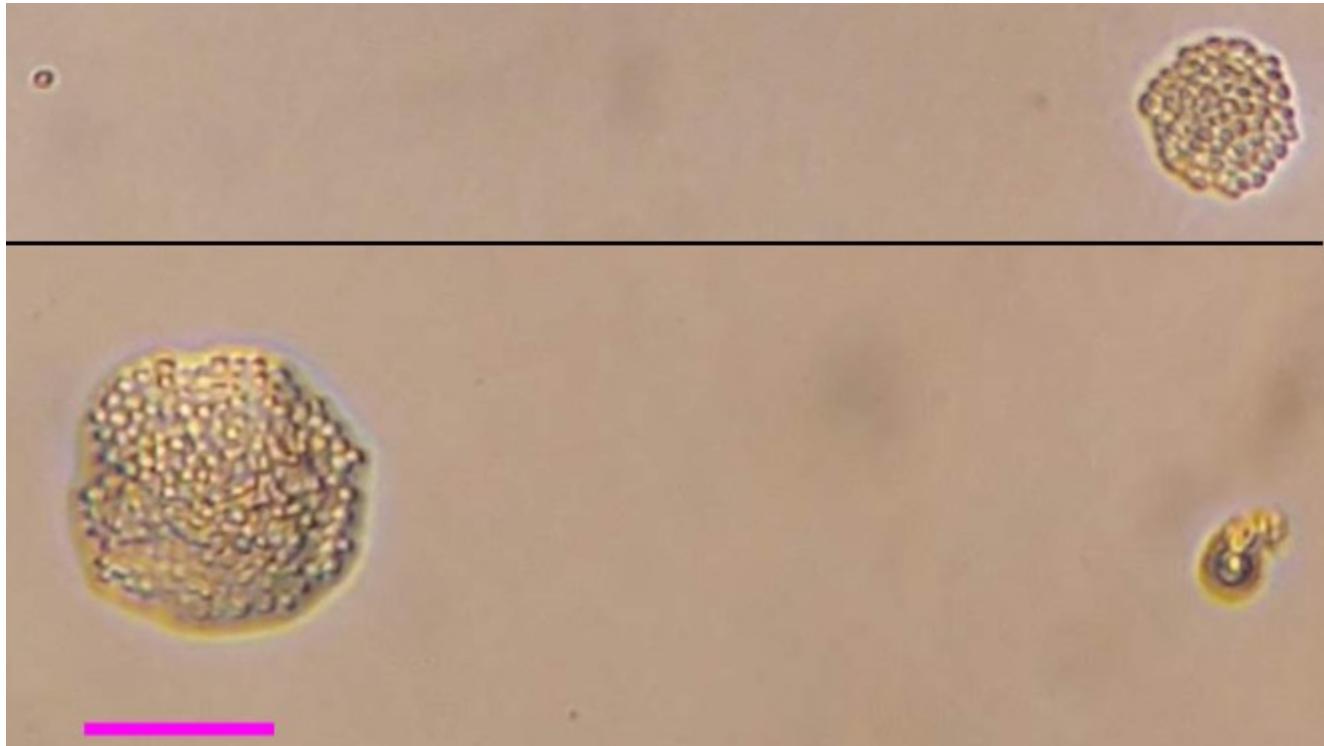


Figure S3

Photographs of two lethal events. Top: daughter is lethal, photo taken 27 hours after separation.
Bottom: mother is lethal, photo taken 29 hours after separation. Scale bar is ~40 microns.



Supplemental Tables

Table S1: Lethal events by mother/daughter.

	Wild type	<i>mmr</i>	Total
Mother	8	10	18
Daughter	6	23	29

Table S2: Lethal events by final microcolony size.

Final size (number of cells)	Number
1-2	15
3-30	25
31-100	3
100+	4
Total	47

Table S3: Lethal events by strain, size, and mother/daughter.

Wild-type

Final size	Mother	Daughter	Total
1-2	4	4	8
3-30	4	2	6
31-100	0	0	0
100+	0	0	0
Total	8	6	14

mmr

Final size	Mother	Daughter	Total
1-2	1	6	7
3-30	7	12	19
31-100	1	2	3
100+	1	3	4
Total	10	23	33

Table S4: Collected canavanine fluctuation tests for *S. cerevisiae*.

Author and year	Strain	Locus	Genotype	Rate	Fold increase
Lang & Murray 2008	W303	CAN1	WT	1.5E-07	n/a
Zeyl & de Visser 2001	Y55	CAN1	WT	3.2E-07	
Zeyl & de Visser 2001	Y55	CAN1	<i>msh2</i>	1.7E-05	53
Lang et al 2013	W303	CAN1	WT	8.0E-07	
Lang et al 2013	W303	CAN1	<i>msh2</i>	6.7E-06	8
Gammie et al 2007	W303	CAN1	WT	4.8E-07	
Gammie et al 2007	W303	CAN1	<i>msh2</i>	1.5E-05	31
Reenan & Kolodner 1992	SK1	CAN1	WT	4.0E-07	
Reenan & Kolodner 1992	SK1	CAN1	<i>msh2</i>	3.4E-05	85
Marsischky et al 1996	MGD	CAN1	WT	1.0E-07	
Marsischky et al 1996	MGD	CAN1	<i>msh2</i>	4.0E-06	40
Average of above		CAN1	WT	3.8E-07	
Average of above		CAN1	<i>msh2</i>	1.5E-05	44

Table S5: Homopolymer occurrence in coding sequences of *S. cerevisiae* and *E. coli*. p-values are given for the difference in per base rates; “***” indicates a p-value of less than 2.2×10^{-16} .**Homopolymeric repeats in coding sequences**

Repeat length	<i>S. cerevisiae</i>			<i>E. coli</i>			<i>S. cerevisiae / E. coli</i> ratio			
	Number	Per gene	Per base	Number	Per gene	Per base	Per coding genome	Per gene	Per base	p-value
3	331178	57.31	4.0E-02	141596	32.830	3.5E-02	2.3	1.7	1.2	***
4	102058	17.66	1.2E-02	35301	8.185	8.7E-03	2.9	2.2	1.4	***
5	31363	5.43	3.8E-03	10895	2.526	2.7E-03	2.9	2.1	1.4	***
6	9287	1.61	1.1E-03	2997	0.695	7.3E-04	3.1	2.3	1.5	***
7	3066	0.53	3.7E-04	564	0.131	1.4E-04	5.4	4.1	2.7	***
8	971	0.17	1.2E-04	97	0.022	2.4E-05	10.0	7.5	5.0	***
9	306	0.05	3.7E-05	9	0.002	2.2E-06	34.0	25.4	17.0	***
≥10	214	0.04	2.6E-05	0	0	0	n/a	n/a	n/a	***

References

- Gammie AE, Erdeniz N, Beaver J, Devlin B, Nanji A, Rose MD (2007) Functional Characterization of Pathogenic Human MSH2 Missense Mutations in *Saccharomyces cerevisiae*. *Genetics* 177: 707–721.
- Lang GI, Murray AW (2008) Estimating the per-base-pair mutation rate in the yeast *Saccharomyces cerevisiae*. *Genetics* 178: 67–82.

Lang GI, Parsons L, Gammie AE (2013) Mutation rates, spectra, and genome-wide distribution of spontaneous mutations in mismatch repair deficient yeast. *G3: Genes, Genomes, Genetics* 3: 1453–1465.

Marsischky GT, Filosi N, Kane MF, Kolodner R (1996) Redundancy of *Saccharomyces cerevisiae* MSH3 and MSH6 in MSH2-dependent mismatch repair. *Genes Dev* 10: 407–420.

Reenan RA, Kolodner RD (1992) Characterization of insertion mutations in the *Saccharomyces cerevisiae* MSH1 and MSH2 genes: Evidence for separate mitochondrial and nuclear functions. *Genetics* 132: 975–985.

Zeyl C, DeVisser JAGM (2001) Estimates of the Rate and Distribution of Fitness Effects of Spontaneous Mutation in *Saccharomyces cerevisiae*. *Genetics* 157: 53–61.