

## Materials and Methods

### Strains and plasmids

Wild *S. cerevisiae* isolates were obtained from genetic stock centers or were the generous gifts of investigators and consortia indicated in the supplementary information. RM, BY, and their genotyped meiotic segregants have been described previously (1) and were kindly provided by L. Kruglyak.

Strains were inoculated in triplicate into 384-well plates containing 40  $\mu$ L YPD per well and grown to saturation at 23°C (typically 48 h). After re-suspension, QRep polypropylene 384-well pin replicators (Genetix) were used to transfer cells (200-500 nL) to new 384-well plates in duplicate. These new plates were used to assess different growth conditions (Table S2) and also contained 40  $\mu$ L media per well. The conditions were chosen to cause a measurable growth defect in yeast based either on previous studies or on pilot investigations in BY, RM, segregants from the BY $\times$ RM cross, or selected strains from Table S1. All plates were incubated at 23°C, covered and in a humidified chamber unless otherwise noted. Growth was measured approximately every 20 hours by OD<sub>600</sub> with a Tecan Sapphire2 plate reader (after re-suspension by gentle agitation). Permutation of the positions strains occupied within the plate had no effect on growth. This eliminated the possibility that position effects would be responsible for the traits we observed. In parallel, strains were analogously treated in 384-well plates containing each condition with Hsp90 inhibition (5  $\mu$ M Rad or GdA). As controls, strains were also grown in control medium (YPD) alone, and in control medium with

Hsp90 inhibitors alone (5  $\mu$ M Rad or GdA). Rad and GdA stocks (50 mM) were made in molecular biology grade dimethyl sulfoxide (DMSO).

MIC concentrations for Rad and GdA were determined by serial 1.5-fold dilutions of a 200  $\mu$ M starting concentration of each inhibitor in YPD. These measurements were carried out as above, in 384-well microplates with 40  $\mu$ L YPD per well. Growth was measured by OD<sub>600</sub> 66 h post-inoculation in a Tecan Sapphire plate reader. Four replicate measurements were performed for each strain.

*NDII* overexpression was achieved by transforming the *NDII*-containing clone from the Flexgene overexpression library (2) under the control of a galactose-inducible promoter. Plasmid-containing strains were grown in synthetic medium lacking uracil with either 2% glucose as a carbon source (as a control) and or 2% galactose as a carbon source (to induce expression). Strains were treated with 5 mM CDNB for 24 hours and 100  $\mu$ L of a 10,000-fold dilution was plated on synthetic medium lacking uracil. Images are shown after 3 days of incubation at 30°C.

### **Data analysis**

Growth yield of BYxRM segregants was measured by OD<sub>600</sub> in a Tecan Sapphire plate reader. Values for growth in each condition with Hsp90 inhibitors were compared to growth in the same condition without Hsp90 inhibitors. At these concentrations, the Hsp90 inhibitors themselves did not affect growth. However, Hsp90 inhibition altered growth of certain segregants in the selective conditions. A variety of patterns emerged. For example, strains with average growth in some conditions (e.g. in Fig. 1C-F, strain 1

in rapamycin and deoxycholate) were sensitive (CDNB) or resistant (HU) in others. Similarly, strains strongly affected by Hsp90 inhibition in some conditions were unaffected in others (e.g. in Fig. 1, strain 1 in hydroxyurea and CDMB vs. rapamycin and deoxycholate). The difference in growth in each condition elicited by Hsp90 inhibition with Rad was used for linkage analysis using R/qtl (3). Growth of the segregants in control media (containing DMSO) was used as an additive covariate where appropriate to eliminate the effects of carrier solvent. Linkage analysis was performed using several algorithms within R/qtl (standard maximum likelihood/EM, nonparametric, and binary models). To test significance, growth in each condition was randomly permuted among the segregants and genome-wide mapping was re-performed using the same algorithm. After 200 such permutations and mappings across all conditions, QTL were discarded if their LOD scores did not fall above the top 5% of those obtained by chance for each trait. Based on these empirical permutation tests, 3.2 of the QTL we identified (or less than 1%) would be expected to occur by chance.

The location of the QTL within the genome was defined by calculating approximate Bayesian credible intervals (to 95% confidence) in R/qtl. Virtually all Hsp90-contingent traits could be mapped to one or more QTL. However, we were unable to do so in several cases (Trichostatin A, iodoacetate, and chlorhexidine. It might be that too many genetic determinants contributed under these conditions, obscuring the effects of individual loci. However, trichostatin A and iodoacetate perturb histone modification (4, 5). Thus, it seems likely that epigenetic variation operates on these traits.

Published genotypic correlation among sequenced strains was obtained from refs. (6) and (7). Phenotypic correlations among the strains were determined by linear regression across the conditions in Table S2. Neighbor-joining trees were constructed in PHYLIP ([evolution.genetics.washington.edu/phylip.html](http://evolution.genetics.washington.edu/phylip.html)) from distance matrices derived from these correlations.

### **Allele replacement**

Allele replacement was performed as described in (8) and depicted in fig. S5 for selected QTL within Bayesian credible intervals. Because many traits we examined involved the contribution of alleles from both the RM and BY parents, allele replacement was carried out in the segregants rather than BY or RM. ORFs within the boundaries of each QTL were PCR amplified from both BY and RM and fused to 5' and 3' fragments of *Kluyveromyces lactis* URA3 in a second PCR reaction. After purification these fusion products were co-transformed into recipient segregants. Loss of the URA3 marker was selected for on 5-FOA and allele replacement was confirmed by sequencing. For each gene within a QTL, this procedure was carried out in three segregants with RM and three segregants with BY genotype, each in triplicate. Candidate genes were confirmed by comparing the phenotypes of segregants with RM vs. BY allele replacements. Similar trends were seen across all equivalently allele-replaced strains. To control for the mutagenic effects of transformation, mock replacements (RM for RM and BY for BY) were performed; none of these produced a relevant phenotype.

### **References:**

1. R. B. Brem, G. Yvert, R. Clinton, L. Kruglyak, Genetic dissection of transcriptional regulation in budding yeast. *Science* **296**, 752 (2002).
2. Y. Hu *et al.*, Approaching a complete repository of sequence-verified protein-encoding clones for *Saccharomyces cerevisiae*. *Genome Res* **17**, 536 (2007).
3. K. W. Broman, H. Wu, S. Sen, G. A. Churchill, R/qtl: QTL mapping in experimental crosses. *Bioinformatics* **19**, 889 (2003).
4. M. Yoshida, M. Kijima, M. Akita, T. Beppu, Potent and specific inhibition of mammalian histone deacetylase both in vivo and in vitro by trichostatin A. *J Biol Chem* **265**, 17174 (1990).
5. L. Dong, C. W. Xu, Carbohydrates induce mono-ubiquitination of H2B in yeast. *J Biol Chem* **279**, 1577 (2004).
6. G. Liti *et al.*, Population genomics of domestic and wild yeasts. *Nature* **458**, 337 (2009).
7. J. Schacherer, J. A. Shapiro, D. M. Ruderfer, L. Kruglyak, Comprehensive polymorphism survey elucidates population structure of *Saccharomyces cerevisiae*. *Nature* **458**, 342 (2009).
8. N. Erdeniz, U. H. Mortensen, R. Rothstein, Cloning-free PCR-based allele replacement methods. *Genome Res* **7**, 1174 (1997).

## Supplementary Table and Figure Legends:

Table S1 – *S. cerevisiae* strains used in this study.

Table S2 – Growth conditions used to examine phenotypes of *S. cerevisiae* strains.

Conditions were chosen based on values previously used in the literature to perturb growth or specific biological processes in *S. cerevisiae*. In some cases the concentrations may seem idiosyncratic. However, these were used because they were simple dilutions of a saturated stock solution or because they were employed at those concentrations in other studies.

Table S3 – Correlations between phenotypic changes produced across wild *S. cerevisiae* isolates when inhibiting Hsp90 with Rad (5  $\mu$ M) or GdA (5  $\mu$ M). Color indicates concordance in phenotype. For approximately 90% of conditions, changes in growth were in the same direction for both inhibitors in each strain. In ~10% of conditions a strains showed no effect for one inhibitor but did show an effect for the other. This was almost certainly because (for experimental expediency) we used 5  $\mu$ M concentrations of each inhibitor on each strain, rather than titrating to achieve exactly the same fraction of the MIC. Supporting this explanation, in all of the conditions we examined, we only very rarely observed an instance where the two inhibitors produced opposite effects in the same strain. Furthermore, a common mechanism of action of Rad and GdA, proceeding via Hsp90 inhibition, has been extensively documented in the literature, most recently using proteome-wide techniques in HeLa cells (1).

Table S4 – Quantitative trait loci identified in this study in the absence of Hsp90 inhibition. Permutation of the position strains occupied in plates did not affect the outcome. Growth in each indicated condition was mapped. Where appropriate, growth in DMSO was used as an additive covariate to eliminate any effects of carrier solvent.

Table S5 –Quantitative trait loci that contribute to Hsp90-contingent transitions in phenotype. The difference in OD<sub>600</sub> between growth with and without Rad was mapped (difference) as was growth for each condition with Rad (with rad). In some cases, perhaps because Hsp90-contingent traits often had a complex genetic basis, either method revealed Hsp90-dependent variation that the other did not. However, significant contribution of each QTL in this table to variation in phenotype was confirmed by a non-parametric Wilcoxon rank test.

Fig. S1 – Experimental schema

Fig. S2 – Immunoblot of Hsp104 to assess the effect of radicicol (Rad) treatment on induction of the heat shock response. A) BY and RM cells were grown with increasing concentrations of Rad to an OD<sub>600</sub> of 0.8, harvested, and lysed using Y-PER-S yeast protein extraction reagent (Thermo). Protein concentration was determined by BCA protein assay (Thermo). Samples (40 µg total protein) were separated on 12% SDS-PAGE prior to wet-transfer to nitrocellulose membrane and subsequent immunoblot with anti-Hsp104 and anti-PGK1, used as a loading control. B) Hsp104 immunoblot in

BYxRM progeny (numbered as in Fig. 1, bottom) in selective conditions containing 5  $\mu$ M Rad indicates that this treatment does not produce a heat shock response even in those selective conditions.

Fig. S3 – Growth changes elicited by reducing the Hsp90 buffer in progeny from the BYxRM cross across all segregants and conditions used in this study. Calculations and scale bar as in Fig. 1A.

Fig. S4 – Distribution of QTL identified in this study separated by chromosome. A) Histogram of all QTL from linkage analysis in conditions alone. B) Histogram of QTL from linkage analysis in conditions with reduced Hsp90 buffer. C) Histogram of QTL from linkage analysis of difference in phenotype elicited by reducing the Hsp90 buffer.

Fig. S5 – Schematic of allele replacement strategy employed, described in detail by Erdeniz *et al.* (2). Briefly, the allele to be swapped was amplified from BY or RM genomic DNA and, in two subsequent PCR reactions, fused to overlapping 5' and 3' portions of *K. lactis* URA3. These two constructs were simultaneously used to transform recipient segregants, and integration was selected for by growth on SD-URA media. Release of the URA3 marker was then selected for by growth on 5-FOA and allele replacement was confirmed by sequencing.

Fig. S6 – Representative effects of reducing the Hsp90 reservoir on additional Pdr8-dependent phenotypes in two of six allele replacement strains. Conditions are as



described in Table S2. Growth is normalized to BY allele replacement strain in each condition (set as 100%). Error bars represent standard deviations from three independent biological replicates.

1. M. Muroi *et al.*, Application of proteomic profiling based on 2D-DIGE for classification of compounds according to the mechanism of action. *Chem Biol* **17**, 460.
2. N. Erdeniz, U. H. Mortensen, R. Rothstein, Cloning-free PCR-based allele replacement methods. *Genome Res* **7**, 1174 (1997).

Table S1. *S. cerevisiae* strains used in this study. Sample origin abbreviations are: (ARSC) Agricultural Research Service Culture Collection; (NCYC) National Collection of Yeast Cultures

<b>Strain</b>	<b>Category</b>	<b>Source</b>	<b>Sample Origin</b>	<b>Ploid</b>	<b>MAT</b>
Y12	Beer	Fermentation	Leonid Kruglyak	n	a
YJM326	Clinical	Clinical	Leonid Kruglyak	n	a
YJM421	Clinical	Clinical	Leonid Kruglyak	n	a
YJM428	Clinical	Clinical	Leonid Kruglyak	n	a
YJM436	Clinical	Clinical	Leonid Kruglyak	n	a
YJM653	Clinical	Clinical	Leonid Kruglyak	n	a
I14	Wine	Wine	Leonid Kruglyak	n	a
T73	Wine	Wine	Leonid Kruglyak	n	a
WE372	Wine	Wine	Leonid Kruglyak	n	a
Abbey Ale	Beer	brewing	White Labs	2n	homothallic
Belgian Ale	Beer	brewing	White Labs	2n	homothallic
Budvar Lager	Beer	Czech republic brewery	Wyeast	2n	homothallic
English Ale	Beer	brewing	White Labs	2n	homothallic
Forbidden Fruit Ale	Beer	brewing	Wyeast	2n	homothallic
Irish Ale	Beer	brewing	White Labs	2n	homothallic
Northwest Ale	Beer	brewing	Wyeast	2n	homothallic
Trappist Ale	Beer	brewing	White Labs	2n	homothallic
Urquell Pilsner	Beer	brewing	Wyeast	2n	homothallic
Y-7327	Beer	Tibetan beer starter	ARSC	2n	homothallic
Y-10988	Clinical	patient	ARSC	2n	homothallic
Y-12659	Clinical	Human	feces	2n	homothallic
Y27788	Clinical	US, Baltimore	Clinical	2n	homothallic
Y-27806	Clinical	patient	ARSC	2n	homothallic
Y-492	Clinical	patient	ARSC	2n	homothallic
Y-502	Clinical	patient	ARSC	2n	homothallic
Y-12657	Fruit	olive	ARSC	2n	homothallic
Y-139	Fruit	grape	ARSC	2n	homothallic
Y-1537	Fruit	grapes	ARSC	2n	homothallic
Y2209	Fruit	California	leaves from Lepidopterus	2n	homothallic
Y-35	Fruit	Ilex aquifolium	ARSC	2n	homothallic
Y-382	Fruit	grain	ARSC	2n	homothallic
Y-5511	Fruit	coconut	ARSC	2n	homothallic
Y-7568	Fruit	papaya	ARSC	2n	homothallic
YB-210	Fruit	banana	ARSC	2n	homothallic
YB-3121	Fruit	mimosa	ARSC	2n	homothallic
YB-399	Fruit	cherries	ARSC	2n	homothallic
YB-4081	Fruit	guava	ARSC	2n	homothallic
YB-4082	Fruit	papaya	ARSC	2n	homothallic
YB-432	Fruit	pineapple	ARSC	2n	homothallic
OP1	Soil	Occoneechee Park, VA	Dietzmann, Dietrich	2n	homothallic

OP2	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP3	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP4	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP6	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP7	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP8	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
OP9	Soil	Occonechee Park, VA	Dietzmann, Dietrich	2n	homothallic
SM1	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
SM12	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
SM17	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
SM2	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
SM66	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
SM69	Soil	Stone Mountain, GA	Dietzmann, Dietrich	2n	homothallic
ATCC 26249	Wine	Australia wine research inst. #729	Wine	2n	homothallic
Y-12625	Wine	Spain	Wine	2n	homothallic
Y-12649	Wine	Italy	wine/grape juice	2n	homothallic
Y-162	Wine	ATCC 2398	port wine	2n	homothallic
Y2034	Wine	Wine	California	2n	homothallic
Y-2411	Wine	Turkey	Vineyard	2n	homothallic
Y-266	Wine	Wine	Burgundy wine	2n	homothallic
Y-269	Wine	Wine	Tokay	2n	homothallic
Y-584	Wine	Wine	Moselle wine	2n	homothallic
Y-645	Wine	Wine	Sauternes	2n	homothallic
Y-7115	Wine	Wine	Chablis wine starter	2n	homothallic
Y-865	Wine	Wine	Bordeaux	2n	homothallic
NCYC 3264	Unknown	Unknown	NCYC/SGRP	n/2n	homothallic
NCYC 3265	Soil	USA	NCYC/SGRP	n/2n	homothallic
NCYC 3266	Wine	France	NCYC/SGRP	n/2n	homothallic
NCYC 3284	Oak	Pennsylvania, USA	NCYC/SGRP	n/2n	homothallic
NCYC 3290	Bili wine	West Africa	NCYC/SGRP	n/2n	homothallic
NCYC 3311	Soil	Finland	NCYC/SGRP	n/2n	homothallic
NCYC 3312	soil	Netherland	NCYC/SGRP	n/2n	homothallic
NCYC 3313	White Tecc	Ethiopia	NCYC/SGRP	n/2n	homothallic
NCYC 3314	Barrel fermentation	Napa Valley, USA	NCYC/SGRP	n/2n	homothallic
NCYC 3315	Oak	Pennsylvania, USA	NCYC/SGRP	n/2n	homothallic
NCYC 3318	Wine	Chile	NCYC/SGRP	n/2n	homothallic

NCYC 3319	Wine	Chile	NCYC/SGRP	n/2n	homothallic
NCYC 3445	Palm wine strain	Africa	NCYC/SGRP	n/2n	homothallic
NCYC 3447	Grapes	Australia	NCYC/SGRP	n/2n	homothallic
NCYC 3448	Fruit	Bahamas	NCYC/SGRP	n/2n	homothallic
NCYC 3449	Cladode	Hawaii	NCYC/SGRP	n/2n	homothallic
NCYC 3451	Beer spoilage strain	Ireland	NCYC/SGRP	n/2n	homothallic
NCYC 3452	Shochu Sake strain	Japan	NCYC/SGRP	n/2n	homothallic
NCYC 3453	Baker strain	Netherland	NCYC/SGRP	n/2n	homothallic
NCYC 3454	Baker strain	Singapore	NCYC/SGRP	n/2n	homothallic
NCYC 3455	Clinical isolate	RVI, Newcaslte UK	NCYC/SGRP	n/2n	homothallic
NCYC 3456	Clinical isolate	RVI, Newcaslte UK	NCYC/SGRP	n/2n	homothallic
NCYC 3457	Clinical isolate	RVI, Newcaslte UK	NCYC/SGRP	n/2n	homothallic
NCYC 3458	Clinical isolate	Bergamo, Italy	NCYC/SGRP	n/2n	homothallic
NCYC 3460	Ragi	Japan	NCYC/SGRP	n/2n	homothallic
NCYC 3461	Nectar	Malaysia	NCYC/SGRP	n/2n	homothallic
NCYC 3462	Nectar,	Malaysia	NCYC/SGRP	n/2n	homothallic
NCYC 3466	Rotting fig	California, USA	NCYC/SGRP	n/2n	homothallic
NCYC 3467	Unknown	Unknown	NCYC/SGRP	n/2n	homothallic
NCYC 3468	Trigona, Bertam palm	Malaysia	NCYC/SGRP	n/2n	homothallic
NCYC 3469	Fermenting fruit juice	Netherland	NCYC/SGRP	n/2n	homothallic
NCYC 3470	Wine	Sauternes, Franxe	NCYC/SGRP	n/2n	homothallic
NCYC 3471	Clinical isolate	Bergamo, Italy	NCYC/SGRP	n/2n	homothallic
NCYC 3472	Clinical isolate	Bergamo, Italy	NCYC/SGRP	n/2n	homothallic
NCYC 3486	Ginger beer	West Africa	NCYC/SGRP	n/2n	homothallic
NCYC 3487	Baker strain	Australia	NCYC/SGRP	n/2n	homothallic
RM11-1a	Vineyard isolate	-	Leonid Kruglyak	n	MAT $\alpha$
BY4716	Rotting fig	Laboratory strain	Leonid Kruglyak	n	MAT $\alpha$
1_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
1_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
1_5_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
2_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
2_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
2_4_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
2_5_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
2_6_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
3_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
3_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
3_4_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
3_5_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
4_1_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
4_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
4_4_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
5_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
5_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$



14_5_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
14_6_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
14_7_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
15_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
15_3_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
15_5_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
16_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
17_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
17_4_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
17_5_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
18_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
18_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
18_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
18_4_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
18_6_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
19_1_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
19_2_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
19_3_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
19_4_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
19_5_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
20_1_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
20_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
20_3_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
20_4_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
21_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
21_4_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
21_5_c	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
22_2_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
22_3_a	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
22_4_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
22_5_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$
23_3_d	-	BY x RM segregant	Leonid Kruglyak	n	MAT $\alpha$

Table S2. Conditions used in this study. Treatment was in rich medium (YPD) unless otherwise noted.

<u>Condition</u>	<u>Presumed biological effect(s) and/or compound class</u>	<u>Concentration</u>	<u>Units</u>
1-dodecanol	Antifungal; quorum sensing	110	μM
2,2'-bipyridyl	Metal chelation	100	μM
2-phenylethanol	Quorum sensing	500	μM
4-nitroquinoline-1-oxide	DNA damage	2	μM
Acetic acid	pH stress	50	μM
Acid	pH stress	pH 5	
Alpha factor	Mating pheromone	10	μM
Amphotericin B	Antifungal	0.5	μM
Anisomycin	Protein synthesis inhibition	40	μM
Anisomycin	Protein synthesis inhibition	3	μM
Base	pH stress	pH 9	
Batho-phenanthroline disulfonic acid disodium salt	Metal chelation	50	μM
Benomyl	Microtubule depolymerization	15	μM
Butyric acid	Histone modification	10	mM
Cadmium chloride	Toxic metal ion	8	μM
Caffeine	Purine analog; pleotropic effects	2	mM
Calcofluor white	Antifungal; binds chitin	60	μg/mL
Camptothecin	DNA Topoisomerase I inhibitor	30	mg/mL
CDNB	Oxidative stress; glutathione-S-transferase inhibitor	5	mM
Cerulenin	Antifungal; inhibits fatty acid biosynthesis	2	μM
Cetylpyridinium chloride	Antiseptic; membrane stress	1	μM
Chlorhexidine	Antiseptic; membrane stress	3	μM
Chloroquine	Iron deprivation; other diverse mechanisms	200	mg/mL
Chlorpromazine	Antiseptic; membrane stress	15	μM
Ciclopiroxolamine	Antifungal; binds trivalent metals	1	μg/mL
Clotrimazole	Azole antifungal	0.5	μM
Cobalt chloride	Heavy metal	1.0	mM
CuSO <sub>4</sub>	Heavy metal; oxidative stress	2.0	mg/mL
Cyclosporin A	Cyclophilin inhibition	100	μg/mL
Deoxycholate	Membrane stress	1	mM
Dicumarol	Metabolic perturbation	1	mM
Doxorubicin	DNA intercalation	20	μM
Doxycycline hyclate	Tetracycline antibiotic	1.0	mM
Estradiol	Hormone	2.5	mM
Ethanol	Alcohol stress	5	%
Ethanolamine	Reactive amine	2	mM
Ferric chloride	Heavy metal; oxidative stress	2.5	mM
Ferulic acid	Antioxidant	10	mM
Fluconazole	Azole antifungal	16	μg/mL

Flufenamic acid	Non-steroidal anti-inflammatory	1	mM
Glitoxin	Natural product; diverse reported toxicity mechanisms	1	µg/mL
Guanidine HCl	Hsp104 inhibition; denaturant	5	mM
H <sub>2</sub> O <sub>2</sub>	Oxidative stress	0.015	%
H <sub>2</sub> O <sub>2</sub>	Oxidative stress	0.03	%
Hydroxyurea	Replication stress via ribonucleotide reductase inhibition	25	mM
Hygromycin	Antifungal	0.5	µM
Ibuprofen sodium salt	Non-specific cyclooxygenase inhibition; unknown mechanism of toxicity in yeast	50	µM
Iodoacetate	Alkylation	1.5	mg/mL
Latrunculin B	Actin filament disruption	12.5	µM
Lithium chloride	Osmotic stress	200	mM
Lidocaine	Sodium channel inhibition; unknown mechanism of toxicity in yeast	50	mg/mL
Lovastatin	HMG-CoA reductase inhibition	80	µM
Magnesium chloride	Osmotic stress	150	mM
Manganese chloride	Diverse mechanisms	10	mM
Mastoparan	Peptide toxin; interference with G-protein function	10	µM
Menadione	Oxidative Stress	30	µM
MG132	Proteasome inhibition	50	µM
Micophenolic acid	DNA damaging agent	5	µg/mL
Mitomycin C	DNA damaging agent	1	mM
MMS	DNA damaging agent/ general alkylating agent	0.002	%
Neomycin	Aminoglycoside	100	µM
Nickel chloride	Heavy metal; histone modification	2.5	mM
Nicotinic acid	Metabolite	5	mM
Novobiocin	DNA gyrase inhibition	1	mM
Oleandomycin	Protein synthesis inhibitor	0.5	mM
Oxolinic Acid	DNA gyrase inhibition	50	µM
PABA	Metabolite	1	mM
Paraquat	Oxidative stress	2	mM
Paromomycin	Aminoglycoside antibiotic	500	µM
Pentachlorophenol	Herbicide; unknown toxic mechanism in yeast	31.7	µM
Progesterone	Steroid hormone	250	µM
Promethazine	H1 receptor agonist; unknown toxic mechanism in yeast	20	µM
Propiconazole	Azole antifungal	16	µg/mL
Putrescine	Diverse mechanisms	50	mM
Quercetin	Antioxidant	4	µM
Quinidine	Ion channel blocker	4	mM
Rapamycin	TOR inhibition	0.5	µM
Rapamycin	TOR inhibition	5	µM
Reserpine	Monoamine transport inhibition;	100	µM



	unknown toxic mechanism in yeast		
Resveratrol	Diverse mechanisms	10	μM
Rotenone	Oxidative stress	250	μM
Sodium chloride	Osmotic stress	0.5	M
Sodium metaborate	Pesticide; unknown toxic mechanisms in yeast	100	mM
Sodium orthovanadate	Orthophosphate competitor	1	mM
Sodium thiosulfate	Diverse proposed mechanisms	1	mM
Staurosporine	Kinase inhibition	4	μg/mL
tert-Butyl hydroperoxide	Oxidative stress	1	mM
Trichostatin A	Antifungal; histone deacetylase inhibitor	20	μM
Trifluoperazine	Calmodulin inhibitor	5	μM
Trifluoperazine	Calmodulin inhibitor	25	μM
Trimethoprim	Dihydrofolate reductase inhibition	100	mg/L
Tunicamycin	Inhibits glycosylation; induces unfolded protein response	0.3	μM
UV-irradiation	DNA damage	20	J/m <sup>2</sup>
UV-irradiation	DNA damage	70	J/m <sup>2</sup>
Wortmannin	Kinase inhibition	3.5	μg/mL
YP Galactose	Alternative carbon source	2	%
YP Glycerol	Alternative carbon source	2	%
YP Maltose	Alternative carbon source	2	%
YP Raffinose	Alternative carbon source	2	%
Zinc chloride	Diverse mechanisms; interference with metal homeostasis	5	mM

Table S3: Correlation in phenotypes elicited by pharmacological Hsp90 inhibition with Rad and GdA

Strain	Rad (5 uM)	GdA (5 uM)
Irish Ale	R	R
Northwest Ale	R	R
Y-502	R	R
Y-35	R	R
Y-5511	R	R
Y-7568	R	R
WE372	R	R
Y12	R	R
Y2034	R	R
Y-266	R	R
Y-645	R	R
Trappist Ale	R	NC
Y-2411	R	NC
Y-584	R	NC
Abbey Ale	S	S
English Ale	S	S
Forbidden Fruit Ale	S	S
Urquell Pilsner	S	S
Y-865	S	S
Y-12659	S	S
Y-27788	S	S
YJM421	S	S
YJM428	S	S
Y-139	S	S
Y-1527	S	S
OP7	S	S
T73	S	S
Y-12659	S	S
Y-269	S	S
Y-865	S	S
ATCC 26249	S	R
Belgian Ale	NC	NC
Y-7327	NC	NC
Y-27806	NC	NC
Y-492	NC	NC
YJM653	NC	NC
Y-12657	NC	NC
YB-3121	NC	NC
YB-399	NC	NC
YB-4081	NC	NC
YB-432	NC	NC
YB-2209	NC	NC
OP1	NC	NC
OP2	NC	NC

OP3	NC	NC
OP4	NC	NC
OP6	NC	NC
OP8	NC	NC
SM2	NC	NC
SM66	NC	NC
SM69	NC	NC
Y-12625	NC	NC
Y-12649	NC	NC
Y-162	NC	NC
YJM436	NC	R
I14	NC	R
OP9	NC	R
SM1	NC	R
Y-10988	NC	S
YJM326	NC	S
Y-382	NC	S
YB-210	NC	S
YB-4082	NC	S

Growth in maltose. Increased growth (R) highlighted yellow; decreased growth (S) highlighted blue; no change (NC) highlighted green.

Only examples of changed phenotypes shown below:

Strain	Rad (5 uM)	GdA (5 uM)
Y-27788	R	R
Y-27806	R	R
Y-584	R	R
Y-645	R	R
Y-2411	R	NC
Y-266	NC	R
Y-10988	S	S
Y-269	S	S
SM2	S	NC

Growth in novobiocin. Increased growth (R); decreased growth (S); no change (NC).

Strain	Rad (5 uM)	GdA (5 uM)
Y-2209	R	R
Y-2411	NC	R
Belgian Ale	S	S
Irish Ale	S	S
Trappist Ale	S	S
Y-7327	S	S
YJM421	S	S
T73	S	S
Y-162	S	S
SM69	S	NC

WE372	NC	S
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Growth in rapamycin. Increased growth (R); decreased growth (S); no change (NC).

Strain	Rad (5 uM)	GdA (5 uM)
Belgian Ale	R	R
Y-492	R	R
Y-502	R	R
YB-210	R	R
YB-3121	R	R
Y-645	R	NC
OP1	NC	R
Y-10988	S	S
Y-27788	S	S
Y-584	S	S

Growth in nickel chloride. Increased growth (R); decreased growth (S); no change (NC).

Condition	Time	Status	Marker	Chr	Position (cM)	LOD
1-dodecanol	66	alone	NBR031C	2	208.1	3.6
		alone	YEL021W	5	79.2	11.2
2,2'-bipyridyl	40	alone	NBR031C	2	208.1	6.7
		alone	YEL021W	5	79.2	10.6
		alone	YHL047C	8	0.0	3.9
2-phenylethanol	66	alone	NBR031C	2	208.1	4.5
		alone	YEL021W	5	79.2	14.6
4-NQO	18	alone	gEL02	5	78.5	7.1
	64	alone	YGR088W	7	282.2	7.7
Acetic Acid	40	alone	NBR031C	2	208.1	5.5
		alone	YEL021W	5	79.2	12.4
Acid	18	alone	YPL158C	16	79.8	3.8
	112	alone	YBR230C	2	255.3	5.0
		alone	YDL228C	4	8.8	5.3
Alpha factor	44	alone	YCR041W	3	89.7	9.5
Anisomycin	18	alone	gEL02	5	78.5	6.3
Base	40	alone	gEL02	5	78.5	13.1
Bathophenanthroline sodium salt	40	alone	NBR031C	2	208.1	4.4
		alone	YEL021W	5	79.2	12.9
Benomyl	40	alone	NBR031C	2	208.1	4.0
		alone	YEL021W	5	79.2	14.2
Butyric acid	40	alone	NBR031C	2	208.1	6.1
		alone	YEL021W	5	79.2	9.3
	112	alone	NBR031C	2	208.1	6.1
		alone	YEL021W	5	79.2	9.3
Cadmium chloride	112	alone	YBR283C	2	293.9	6.4
Caffeine	40	alone	NBR031C	2	208.1	4.3
		alone	YEL021W	5	79.2	10.4
Calclofluor white	16	alone	YBR154C	2	218.5	6.7
		alone	gEL02	5	78.5	6.2
	42	alone	gBL05	2	90.7	8.1
		64	alone	gBL05	2	90.7
Camptothecin	40	alone	NBR031C	2	208.1	4.6
		alone	YEL021W	5	79.2	11.8
Cerulenin	18	alone	gEL02	5	78.5	4.4
Cetylpyridinium chloride	40	alone	YLR258W	12	321.2	6.5
	64	alone	YCL026C	3	47.7	4.6
	112	alone	NGR056C	7	314.0	7.2
Chlorhexidine	64	alone	YBR119W	2	192.3	4.3
Chlorpromazine	64	alone	YCR100C	3	169.0	6.4
		alone	YOL073C	15	72.3	7.3
Ciclopiroxolamine	40	alone	NBR031C	2	208.1	5.3
		alone	YEL021W	5	79.2	13.8
Copper Sulfate	18	alone	gEL02	5	78.5	4.8
	112	alone	YCL065W	3	0.0	5.3
		alone	YHR050W	8	71.0	6.8
		alone	YGR088W	7	282.2	5.6
Cyclosporin A	18	alone	gEL02	5	78.5	6.3

		alone	YGL068W	7	166.5	3.8
		alone	YLR257W	12	321.2	4.4
	64	alone	YLR257W	12	321.2	6.8
		alone	NMR032C	13	210.0	3.5
	110	alone	YAL048C	1	9.3	4.8
		alone	gLR07	12	312.4	5.0
Deoxycholate	40	alone	YHL047C	8	0.0	5.6
		alone	YKL025C	11	150.4	4.5
		alone	YLR265C	12	317.7	4.0
		alone	YML098W	13	26.4	3.8
		alone	YPL021W	16	163.9	4.1
DMSO (0.1%)	110	alone	YCL065W	3	0.0	4.3
		alone	YJL196C	10	21.9	4.1
	112	alone	YEL021W	5	79.2	15.2
	138	alone	YEL021W	5	79.2	9.2
	38	alone	NBR031C	2	208.1	5.1
		alone	RPR1	5	79.2	14.0
		alone	YMR216C	13	307.2	4.9
	40	alone	NBR031C	2	208.1	5.1
		alone	YEL021W	5	79.2	13.8
	42	alone	YEL021W	5	79.2	6.7
	64	alone	YDR192C	4	383.8	3.7
		alone	RPR1	5	79.2	15.3
	66	alone	YEL021W	5	79.2	10.9
	88	alone	YBR154C	2	218.5	5.6
		alone	RPR1	5	79.2	15.5
Doxorubicin	18	alone	gEL02	5	78.5	5.9
	44	alone	YCR100C	3	169.0	7.0
		alone	NGR056C	7	314.0	5.8
		alone	YLL052C	12	11.8	5.8
		alone	NNL035W	14	200.8	8.0
	64	alone	YCR100C	3	169.0	5.9
		alone	NGR056C	7	314.0	5.6
		alone	YLL009C	12	57.6	5.4
		alone	NNL035W	14	200.8	7.3
Doxycycline hyclate	40	alone	YEL021W	5	79.2	4.0
Ethanol	18	alone	gEL02	5	78.5	7.3
Ethanolamine	40	alone	NBR034W	2	208.1	4.9
		alone	RPR1	5	79.2	10.7
Ferric chloride	40	alone	YEL021W	5	79.2	10.7
Ferulic acid	40	alone	NBR031C	2	208.1	5.5
		alone	YEL021W	5	79.2	10.8
		alone	YHL047C	8	0.0	4.3
Fluconazole	16	alone	NBR035W	2	219.3	4.3
		alone	gEL02	5	78.5	5.4
	42	alone	YAR035W	1	126.0	4.8
	64	alone	YAR029W	1	119.8	4.5
Flufenamic acid	40	alone	NBR031C	2	208.1	6.1
		alone	YEL021W	5	79.2	7.5

Gliotoxin	18	alone	gEL02	5	78.5	5.2
	64	alone	NNL035W	14	200.8	5.1
Guanidine HCl	18	alone	gEL02	5	78.5	7.3
	64	alone	YLR258W	12	321.2	4.5
	110	alone	YLR258W	12	321.2	5.4
Hydrogen peroxide (0.03%)	112	alone	gEL02	5	78.5	3.8
Hydrogen peroxide 0.015%	20	alone	NBR035W	2	219.3	4.1
	20	alone	gEL02	5	78.5	7.7
	38	alone	YDR192C	4	383.8	6.1
	64	alone	RPR1	5	78.5	10.2
	88	alone	gAL02	1	64.3	4.5
	88	alone	RPR1	5	78.5	7.5
	110	alone	gAL02	1	64.3	4.5
	110	alone	RPR1	5	78.5	7.5
Hydroxyurea	40	alone	YBR136W	2	204.7	4.8
	40	alone	YEL021W	5	79.2	6.9
Ibuprofen	40	alone	NBR031C	2	208.1	5.4
	40	alone	YEL021W	5	79.2	11.4
Iodoacetate	18	alone	gEL02	5	78.5	7.4
	40	alone	YML120C	13	0.8	3.8
	112	alone	YBR140C	2	213.2	3.6
	112	alone	gEL02	5	78.5	9.3
Latrunculin B LiCl	18	alone	gEL02	5	78.5	8.4
	40	alone	YDR015C	4	205.6	3.7
	40	alone	gEL02	5	78.5	5.9
Lovastatin	112	alone	YDR038C	4	232.6	9.5
	40	alone	NBR031C	2	208.1	5.3
	40	alone	YEL021W	5	79.2	12.1
Magnesium chloride	42	alone	YEL021W	5	79.2	12.4
Mastoparan	64	alone	NGR056C	7	314.0	7.1
	110	alone	YBR154C	2	218.5	5.6
Menadione	46	alone	YCL026C	3	47.7	4.5
Micophenolic acid	42	alone	NBR031C	2	208.1	4.0
	42	alone	YEL021W	5	79.2	9.6
	42	alone	NBR031C	2	208.1	4.1
MMS	42	alone	YEL021W	5	79.2	11.2
	42	alone	NBR031C	2	208.1	5.1
	42	alone	YEL021W	5	79.2	10.9
Neomycin	42	alone	NBR031C	2	208.1	5.1
	42	alone	YEL021W	5	79.2	10.9
	42	alone	YHL047C	8	0.0	4.0
Nickel chloride	42	alone	gBR09_3	2	228.5	3.8
Nicotinic acid	42	alone	NBR031C	2	208.1	4.2
	42	alone	YEL021W	5	79.2	13.3
	42	alone	YEL021W	5	79.2	13.3
Novobiocin	66	alone	YBR142W	2	203.5	4.7
	66	alone	YEL021W	5	79.2	4.2
Oleandomycin	42	alone	NBR031C	2	208.1	4.4
	42	alone	YEL021W	5	79.2	11.0
	42	alone	YEL021W	5	79.2	11.0
Oxolinic Acid	110	alone	YBR154C	2	218.5	6.9
	110	alone	YGR068C	7	270.1	5.6
	64	alone	YCL065W	3	0.0	5.4

	64	alone	YDR192C	4	383.8	4.8
	64	alone	NGR056C	7	314.0	4.4
PABA	42	alone	YEL021W	5	79.2	12.5
Paraquat	66	alone	YLR235C	12	275.8	3.8
Paromomycin	42	alone	NBR031C	2	208.1	4.7
		alone	YEL021W	5	79.2	9.3
Pentachlorophenol	18	alone	gEL02	5	78.5	5.5
	64	alone	YEL065W	5	21.3	4.9
		alone	NGR056C	7	314.0	4.6
Pentachlorophenol	110	alone	gEL02	5	78.5	5.5
Progesterone	42	alone	NBR031C	2	208.1	3.7
		alone	YEL021W	5	79.2	9.5
Promethazine	18	alone	NBR035W	2	219.3	5.2
	112	alone	YGR068C	7	270.1	5.7
		alone	YKR044W	11	217.7	4.5
		alone	YNL278W	14	61.0	4.9
		alone	YOR216C	15	309.3	5.0
Propiconazole	18	alone	gEL02	5	78.5	7.1
	44	alone	YDR192C	4	383.8	4.4
		alone	RPR	5	78.5	7.4
Propiconazole	64	alone	RPR1	5	78.5	5.8
	110	alone	RPR1	5	78.5	5.5
Putrescine	40	alone	NBR031C	2	208.1	4.8
		alone	YEL021W	5	79.2	14.1
Rapamycin	20	alone	NBR035W	2	219.3	3.9
		alone	gEL02	5	78.5	8.1
	64	alone	gAL02	1	64.3	4.6
		alone	gEL02	5	78.5	4.7
	88	alone	YNL074C	14	213.0	9.1
	110	alone	YCL022C	3	60.8	3.7
		alone	YNL074C	14	213.0	9.1
		alone	YMR260C	13	331.1	8.0
Reserpine	42	alone	gEL02	5	78.5	5.2
Resveratrol	18	alone	YAR042W	1	126.0	7.6
	44	alone	NAR005C	1	133.0	10.3
	64	alone	YAR042W	1	126.0	9.9
	110	alone	gEL02	5	78.5	8.6
Sodium chloride	18	alone	YOL088C	15	49.7	4.5
	44	alone	YOL088C	15	49.7	3.7
	64	alone	YAR035W	1	126.0	4.5
	110	alone	YOL093W	15	48.8	4.5
		alone	gEL02	5	78.5	4.5
Sodium metaborate	18	alone	NBR031C	2	208.1	4.5
Sodium orthovanadate	42	alone	YEL021W	5	79.2	11.2
		alone	RPR1	5	79.2	15.2
Sodium thiosulfate	66	alone	gEL02	5	78.5	4.4
Staurosporine	18	alone	YAR035W	1	126.0	9.1
	44	alone	YAR035W	1	126.0	10.9
	64	alone	YAR035W	1	126.0	6.5



	110	alone	gLR07	12	312.4	4.5
		alone	gEL02	5	78.5	7.4
tert-butyl Hydroperoxide	18	alone	gEL02	5	78.5	9.0
	64	alone	gEL02	5	78.5	6.2
Trichostatin A	18	alone	gLR07	12	312.4	3.6
	64	alone	YCL022C	3	60.8	3.5
Trifluoperazine (0.5 uM)	64	alone	YNL066W	14	220.0	3.5
Trifluoperazine (5 uM)	20	alone	gEL02	5	78.5	13.0
	64	alone	gEL02	5	78.5	6.4
	88	alone	gEL02	5	78.5	6.4
	110	alone	NBR031C	2	208.1	4.8
Trimethoprim	66	alone	RPR1	5	79.2	14.3
		alone	gEL02	5	78.5	5.0
Tunicamycin	18	alone	NNL035W	14	200.8	4.0
	44	alone	YAR028W	1	119.8	4.5
	64	alone	YCL065W	3	0.0	3.8
		alone	YAR027W	1	119.8	4.0
	110	alone	gEL02	5	78.5	6.2
		alone	YJR033C	10	221.4	3.7
		alone	YEL021W	5	79.2	11.9
UV-irradiation (20 J/m <sup>2</sup> )	18	alone	gEL02	5	78.5	5.4
		alone	YAR028W	1	119.8	4.9
Wortmannin	44	alone	YAR035W	1	126.0	5.5
	64	alone	YLR257W	12	321.2	5.0
		alone	YBR138C	2	198.7	4.0
	42	alone	NEL011C	5	79.2	6.0
YP galactose		alone	NBR031C	2	208.1	8.1
	138	alone	YKR066C	11	224.5	5.2
YP glycerol	66	alone	YKL025C	11	150.4	4.0
YP maltose	66	alone	YEL021W	5	79.2	6.5
YP raffinose	42	alone	RPR1	5	79.2	15.5
YPD	64	alone	YEL021W	5	79.2	11.3
	66	alone	RPR1	5	79.2	15.5
	88	alone	YEL021W	5	79.2	14.7
	112	alone	YEL021W	5	79.2	11.6
	138	alone	YCL025C	3	49.5	4.4
	138	alone	YLR317W	12	328.3	3.9
Zinc chloride		alone	NNL035W	14	178.9	3.7

Condition	Time	Condition mapped	Marker	Chr	Position (cM)	LOD	
4-NQO	110	difference	YGL134W	7	118.4	3.9	
	44	difference	YGL160W	7	94.4	4.6	
Acetic Acid	40	difference	gMR12	13	425.9	4.3	
		difference	NBR031C	2	208.1	6.6	
		difference	YKL174C	11	60.4	3.8	
Acid	18	difference	NPR020W	16	282.6	3.8	
		difference	YBL080C	2	25.2	7.5	
Alpha factor	44	difference	YDL143W	4	109.4	5.6	
		difference	NKR006C	11	197.2	6.6	
		difference	NNL035W	14	200.8	6.1	
		difference	YCL065W	3	0.0	4.0	
Anisomycin	18	difference	YKL174C	11	60.4	3.8	
		difference	NPR020W	16	282.6	3.6	
		difference	RPR1	5	78.5	3.9	
Base	112	difference					
Bathophenanthroline sodium salt	40	difference	YKL025C	11	150.4	7.6	
		difference	YPR196W	16	381.6	3.6	
Benomyl	40	difference	YKL025C	11	150.4	4.7	
Camptothecin	40	difference	NBR031C	2	208.1	7.8	
		difference	YHL047C	8	0.0	4.1	
CDNB	40	difference	YML120C	13	0.0	6.1	
Cerulein	18	difference	NBR035W	2	219.3	6.2	
		difference	gEL02	5	78.5	4.7	
Cetylpyridinium chloride	112	difference	YGL024W	7	211.7	5.2	
		difference	YML056C	13	59.0	5.9	
Chlorhexidine	20	difference	gBR07_2	2	208.3	4.8	
Clotrimazole	64	difference	YLR261C	12	322.9	3.7	
		difference	YLR258W	12	321.2	6.8	
Copper Sulfate	112	difference	YCL065W	3	0.0	3.8	
		difference	YGR088W	7	282.2	3.8	
Cyclosporin A	44	difference	YFR053C	6	164.6	3.5	
		difference	YIL030C	9	147.5	3.6	
		difference	YLR140W	12	210.5	3.5	
		difference	YLR257W	12	321.2	6.6	
Deoxycholate	40	difference	YBR119W	2	182.9	3.5	
		difference	YLR265C	12	317.7	4.2	
Doxorubicin	112	difference	YBR119W	2	182.9	3.5	
		64	difference	YCR100C	3	169.0	7.9
		difference	YDR192C	4	383.8	4.4	
Ethanol	18	difference	NNL035W	14	200.8	7.0	
		difference	YNR044W	14	296.9	4.9	
		difference	NBR034W	2	208.1	5.5	
Ferric chloride	40	difference	YKL025C	11	150.4	3.6	
		difference	gNL07_2	14	198.8	3.9	
Ferulic acid	40	difference	YAR053W	1	136.3	3.8	
Fluconazole	42	difference	YER144C	5	235.5	5.7	
		64	difference	YAR042W	1	126.0	3.8
		110	difference	YLR214W	12	270.3	5.0
Gliotoxin	18	difference	NBR035W	2	219.3	4.5	

	44	difference	YLR258W	12	321.2	5.1
	64	difference	YLR258W	12	321.2	5.3
	110	difference	YLR258W	12	321.2	6.0
Hydrogen peroxide (0.03%)	18	difference	YBR154C	2	218.5	5.1
Hydroxyurea	40	difference	YBR136W	2	204.7	4.4
Latrunculin B	18	difference	YCL065W	3	0.0	4.3
		difference	YGR088W	7	282.2	4.5
LiCl	40	difference	YDR290W	4	449.4	3.6
		difference	YGL035C	7	195.9	5.0
		difference	NKL002C	11	159.5	4.8
Lovastatin	40	difference	YBR161W	2	214.1	4.3
		difference	YKL025C	11	150.4	6.0
Mastoparan	18	difference	NBR035W	2	219.3	3.5
	64	difference	YBR147W	2	216.9	3.8
	110	difference	YKL073W	11	133.1	4.8
Menadione	46	difference	YGL068W	7	166.5	7.8
		difference	NJR009W	10	216.9	6.3
		difference	YLR140W	12	210.5	4.8
Menadione	64	difference	YGL068W	7	166.5	3.5
Micophenolic acid	42	difference	YKL025C	11	150.4	14.2
MMS	42	difference	NBR034W	2	208.1	3.7
Neomycin	42	difference	YHL047C	8	0.0	4.2
Nickel chloride	42	difference	YHL047C	8	0.0	5.4
Novobiocin	42	difference	YBR147W	2	206.2	4.7
	66	difference	YBR147W	2	206.2	4.1
Paromomycin	42	difference	NBR031C	2	208.1	4.0
Pentachlorophenol	18	difference	YBR161W	2	224.4	3.6
Propiconazole	44	difference	NNL035W	14	200.8	4.5
		difference	YOR127W	15	237.4	3.8
	110	difference	YDR192C	4	383.8	3.7
Rapamycin	64	difference	YNL074C	14	213.0	9.4
		difference	YCL018W	3	56.6	5.5
Resveratrol	44	difference	YLR257W	12	321.2	4.9
	110	difference	YAL010C	1	101.8	3.6
Sodium chloride	110	difference	YOL089C	15	48.8	4.4
Sodium metaborate	44	difference	YAR035W	1	126.0	3.7
	64	difference	YAR035W	1	126.0	3.6
Sodium orthovanadate	42	difference	YHL047C	8	0.0	3.6
Staurosporine	18	difference	YBR154C	2	218.5	4.7
		difference	gEL02	5	78.5	3.7
	44	difference	YLR258W	12	321.2	4.8
	64	difference	YAR035W	1	126.0	4.6
	110	difference	YAR035W	1	126.0	3.6
Trifluoperazine (0.5 uM)	64	difference	YCL022C	3	60.8	3.7
Trifluoperazine (5 uM)	20	difference	YEL028W	5	67.6	3.7
	64	difference	YDR192C	4	383.8	5.6
		difference	gER06	5	272.5	4.6
		difference	YGL035C	7	195.9	6.0
		difference	NKL002C	11	159.5	5.9

Trimethoprim	66	difference	YBR147W	2	206.2	4.5
Tunicamycin	44	difference	NNL035W	14	200.8	3.8
	64	difference	YCR064C	3	128.5	3.6
		difference	YDR192C	4	383.8	5.9
		difference	YPR146C	16	324.8	4.3
UV-irradiation (20 J/m <sup>2</sup> )	40	difference	YBR136W	2	204.7	3.9
Wortmannin	44	difference	YAR035W	1	126.0	4.7
	64	difference	YAR035W	1	126.0	4.6
		difference	YLR257W	12	321.2	5.7
YP raffinose	66	difference	YKL025C	11	150.4	6.0
Zinc chloride	138	difference	YKL025C	11	150.4	4.4
1-dodecanol	66	with rad	NBR031C	2	208.1	5.1
		with rad	YEL021W	5	79.2	10.0
2,2'-bipyridyl	40	with rad	NEL011C	5	79.2	5.3
2-phenylethanol	66	with rad	NBR031C	2	208.1	5.5
		with rad	YEL021W	5	79.2	12.2
4-NQO	18	with rad	NBR035W	2	219.3	5.3
		with rad	gEL02	5	78.5	8.4
Acetic Acid	40	with rad	NBR031C	2	208.1	4.0
		with rad	YEL021W	5	79.2	12.7
Acid	18	with rad	gEL02	5	78.5	6.2
	40	with rad	NGR056C	7	314.0	4.6
Alpha factor	44	with rad	YCR041W	3	89.7	6.8
Anisomycin	18	with rad	NBR035W	2	219.3	4.8
		with rad	gEL02	5	78.5	7.6
Base	40	with rad	gEL02	5	78.5	11.2
Bathophenanthroline sodium salt	40	with rad	NBR034W	2	208.1	4.0
		with rad	YEL021W	5	79.2	11.6
Benomyl	40	with rad	NBR031C	2	208.1	4.4
		with rad	YEL021W	5	79.2	14.2
Butyric acid	40	with rad	NBR031C	2	208.1	5.6
		with rad	YEL021W	5	79.2	8.1
Butyric acid	112	with rad	NBR031C	2	208.1	5.6
		with rad	YEL021W	5	79.2	8.1
Cadmium chloride	112	with rad	YBR283C	2	293.9	6.8
		with rad	YKL025C	11	150.4	3.7
Caffeine	40	with rad	NBR034W	2	208.1	4.9
		with rad	YEL021W	5	79.2	10.0
Calcofluor white	16	with rad	YBR154C	2	218.5	5.2
		with rad	gEL02	5	78.5	3.6
	42	with rad	YBR005W	2	95.5	6.9
	64	with rad	YBR005W	2	95.5	7.8
Camptothecin	40	with rad	YEL021W	5	79.2	12.4
CDNB	40	with rad	YML121W	13	0.0	16.1
Cerulenin	18	with rad	NBR035W	2	219.3	5.1
		with rad	gEL02	5	78.5	8.6
	64	with rad	YCR100C	3	169.0	8.3
		with rad	YGR278W	7	476.2	3.6
Cetylpyridinium chloride	40	with rad	YLR258W	12	321.2	4.8

	64	with rad	YCL026C	3	47.7	3.8
		with rad	NNL035W	14	200.8	15.8
	112	with rad	YLR258W	12	321.2	3.6
Ciclopiroxolamine	40	with rad	NBR031C	2	208.1	5.4
		with rad	YEL021W	5	79.2	10.7
Clotrimazole	20	with rad	RPR1	5	78.5	3.7
	46	with rad	YLR258W	12	321.2	4.5
	64	with rad	YLR258W	12	321.2	7.9
	88	with rad	YLR258W	12	321.2	7.6
Copper Sulfate	18	with rad	gEL02	5	78.5	6.0
	40	with rad	YBR142W	2	214.8	8.6
	112	with rad	YGL160W	7	94.4	4.2
		with rad	YNR044W	14	296.9	6.1
		with rad	YOR072W	15	189.2	4.1
Cyclosporin A	18	with rad	NBR035W	2	219.3	4.4
		with rad	gEL02	5	78.5	8.2
	44	with rad	YDL097C	4	133.1	3.8
		with rad	YGL068W	7	166.5	3.9
Deoxycholate	40	with rad	YHL047C	8	0.0	4.8
		with rad	YKL025C	11	150.4	5.1
		with rad	YML098W	13	26.4	3.8
	112	with rad	YHL047C	8	0.0	4.8
		with rad	YKL025C	11	150.4	5.1
		with rad	YML098W	13	26.4	3.8
DMSO (0.1%)	112	with rad	YEL021W	5	79.2	15.0
	138	with rad	YEL021W	5	79.2	11.8
	40	with rad	YEL021W	5	79.2	13.4
	42	with rad	YEL021W	5	79.2	7.4
	66	with rad	YEL021W	5	79.2	13.1
Docycycline hyclate	40	with rad	YEL021W	5	79.2	3.8
Doxorubicin	18	with rad	gEL02	5	78.5	5.5
	64	with rad	YDR192C	4	383.8	7.8
		with rad	YGR278W	7	476.2	6.2
		with rad	YLL017W	12	51.8	5.5
		with rad	YMR216C	13	307.2	5.5
Ethanol	18	with rad	NBR035W	2	219.3	5.2
		with rad	gEL02	5	78.5	8.9
	110	with rad	YDR192C	4	383.8	6.0
Ethanolamine	40	with rad	NBR031C	2	208.1	4.4
		with rad	RPR1	5	79.2	9.5
Ferric chloride	40	with rad	NBR031C	2	208.1	6.3
		with rad	YEL021W	5	79.2	9.6
Ferulic acid	40	with rad	NBR031C	2	208.1	4.7
		with rad	YEL021W	5	79.2	12.2
Fluconazole	42	with rad	YER144C	5	235.5	3.5
		with rad	YLR258W	12	321.2	5.2
	64	with rad	YGR051C	7	241.1	4.3
		with rad	YJR033C	10	221.4	4.1
		with rad	YOL043C	15	109.0	4.8

Flufenamic acid	40	with rad	NBR031C	2	208.1	7.6	
		with rad	YEL021W	5	79.2	5.8	
Gliotoxin	18	with rad	gEL02	5	78.5	5.0	
		44	with rad	YEL065W	5	21.3	3.9
			with rad	NGR056C	7	314.0	4.3
			with rad	YLL009C	12	57.6	4.6
			with rad	NNL035W	14	200.8	4.4
Guanidine HCl	18	with rad	NBR035W	2	219.3	5.3	
		with rad	gEL02	5	78.5	8.5	
Hydrogen peroxide (0.03%)	18	with rad	gEL02	5	78.5	4.6	
		40	with rad	YEL065W	5	21.3	4.2
			with rad	NGR056C	7	314.0	4.6
			with rad	NNL035W	14	200.8	7.3
Hydrogen peroxide 0.015%	20	with rad	NBR035W	2	219.3	4.1	
		with rad	RPR1	5	78.5	4.6	
	38	with rad	YDR192C	4	383.8	4.5	
		with rad	RPR1	5	78.5	6.1	
		with rad	YGL134W	7	118.4	4.3	
	64	with rad	YAL028W	1	64.3	5.1	
		with rad	gEL02	5	78.5	6.0	
	88	with rad	YGL134W	7	118.4	4.0	
		with rad	YAL028W	1	64.3	5.6	
		with rad	gEL02	5	78.5	5.9	
		with rad	YGL134W	7	118.4	5.1	
		with rad	YAL028W	1	64.3	5.6	
	110	with rad	gEL02	5	78.5	5.9	
with rad		YGL134W	7	118.4	5.1		
with rad		NBR031C	2	208.1	3.6		
40		with rad	YEL021W	5	79.2	7.9	
		with rad	YHL047C	8	0.0	3.6	
Iodoacetate	18	with rad	NBR031C	2	208.1	5.3	
		with rad	YEL021W	5	79.2	11.8	
Ibuprofen	40	with rad	gEL02	5	78.5	8.9	
		with rad	YML120C	13	0.8	3.7	
		with rad	gEL02	5	78.5	4.3	
Latrunculin B	18	with rad	NBR035W	2	219.3	4.8	
		with rad	gEL02	5	78.5	9.3	
LiCl	110	with rad	YER150W	5	249.5	4.3	
		with rad	gEL02	5	78.5	5.0	
		with rad	YGL035C	7	195.9	3.6	
Lovastatin	40	with rad	YDR038C	4	232.6	9.7	
		with rad	YEL021W	5	79.2	12.0	
Magnesium chloride	42	with rad	YEL021W	5	79.2	11.3	
		with rad	gEL02	5	78.5	3.7	
Mastoparan	18	with rad	gEL02	5	78.5	3.7	
		with rad	YDR192C	4	383.8	4.2	
	44	with rad	YGL024W	7	211.7	4.2	
		with rad	NBR035W	2	219.3	7.4	
		with rad	NDL012C	4	173.2	5.5	
64	with rad	YOL073C	15	72.3	5.5		

		with rad	YPL144W	16	88.4	5.5
	110	with rad	YDR192C	4	383.8	6.4
Menadione	46	with rad	YLL052C	12	11.8	5.8
Micophenolic acid	42	with rad	NBR031C	2	208.1	4.6
		with rad	YEL021W	5	79.2	11.7
MMS	42	with rad	YEL021W	5	79.2	9.4
Neomycin	42	with rad	NBR031C	2	208.1	4.4
		with rad	YEL021W	5	79.2	11.9
Nickel chloride	42	with rad	YBR198C	2	220.8	3.8
		with rad	YML120C	13	0.0	3.6
Nicotinic acid	42	with rad	YEL021W	5	79.2	12.7
Novobiocin	42	with rad	YEL021W	5	79.2	5.6
	66	with rad	YEL021W	5	79.2	4.6
Oleandomycin	42	with rad	YEL021W	5	79.2	12.4
PABA	42	with rad	YEL021W	5	79.2	13.2
Paraquat	66	with rad	NBR031C	2	208.1	8.8
		with rad	YEL021W	5	79.2	5.8
		with rad	YHL047C	8	0.0	6.0
Paromomycin	42	with rad	YEL021W	5	79.2	10.8
Pentachlorophenol	18	with rad	NBR035W	2	219.3	6.2
		with rad	gEL02	5	78.5	6.9
	44	with rad	YCR100C	3	169.0	5.1
		with rad	YDR192C	4	383.8	5.8
	64	with rad	YCR100C	3	169.0	6.0
		with rad	gEL02	5	78.5	7.1
		with rad	NGR056C	7	314.0	5.9
		with rad	YLL003W	12	63.6	5.3
	110	with rad	YDR192C	4	383.8	5.1
		with rad	gEL02	5	78.5	8.6
		with rad	YGR278W	7	476.2	4.6
Progesterone	42	with rad	YEL021W	5	79.2	10.0
Propiconazole	18	with rad	NBR035W	2	219.3	3.9
		with rad	gEL02	5	78.5	9.1
	44	with rad	YDR192C	4	383.8	6.0
		with rad	gEL02	5	78.5	6.1
		with rad	YGR278W	7	476.2	5.3
	64	with rad	gEL02	5	78.5	6.4
	110	with rad	YDR192C	4	383.8	3.6
		with rad	RPR1	5	78.5	5.7
Putrescine	40	with rad	NBR031C	2	208.1	4.5
		with rad	YEL021W	5	79.2	13.1
Rapamycin	20	with rad	NBR035W	2	219.3	4.3
		with rad	RPR1	5	78.5	4.4
	38	with rad	YDR192C	4	383.8	4.8
		with rad	gEL02	5	78.5	4.6
	64	with rad	YCL018W	3	56.6	5.5
		with rad	YNL074C	14	213.0	8.1
	88	with rad	YNL074C	14	213.0	10.0
	110	with rad	YNL074C	14	213.0	8.3

Reserpine	42	with rad	YMR260C	13	331.1	8.5
			YPL021W	16	163.9	4.4
Resveratrol	18	with rad	gEL02	5	78.5	7.5
	44	with rad	YAR035W	1	126.0	5.9
	64	with rad	YAR035W	1	126.0	5.5
	110	with rad	YAR035W	1	126.0	4.2
Sodium chloride	18	with rad	NBR035W	2	219.3	4.4
			gEL02	5	78.5	8.9
	44	with rad	NAR004W	1	131.3	3.6
			YOL088C	15	49.7	7.4
	64	with rad	YAR035W	1	126.0	4.5
			YGL024W	7	211.7	3.6
			YIL139C	9	40.7	4.1
			YLR257W	12	321.2	4.2
	110	with rad	NAR004W	1	131.3	4.4
	Sodium metaborate	18	with rad	NBR035W	2	219.3
			gEL02	5	78.5	8.0
Sodium orthovanadate	42	with rad	NBR031C	2	208.1	4.8
			YEL021W	5	79.2	11.3
Sodium thiosulfate	66	with rad	NBR031C	2	208.1	4.1
			RPR1	5	79.2	12.7
Staurosporine	18	with rad	NBR035W	2	219.3	4.5
			gEL02	5	78.5	9.0
	44	with rad	YAR035W	1	126.0	5.2
			YGL068W	7	166.5	4.0
			YLR257W	12	321.2	4.6
	110	with rad	YDR192C	4	383.8	5.6
			YGR278W	7	476.2	4.9
tert-butyl Hydroperoxide	4	with rad	NAR004W	1	131.3	5.6
			gEL02	5	78.5	6.6
	18	with rad	NBR035W	2	219.3	4.9
			gEL02	5	78.5	10.1
	64	with rad	RPR1	5	78.5	4.9
tert-butyl Hydroperoxide	110	with rad	YEL039C	5	59.9	5.6
Trichostatin A	18	with rad	NBR035W	2	219.3	4.1
			gEL02	5	78.5	9.6
	44	with rad	YGL068W	7	166.5	4.4
			YLR258W	12	321.2	5.2
Trifluoperazine (0.5 uM)	20	with rad	YNL074C	14	213.0	4.3
Trifluoperazine (5 uM)	20	with rad	YNL066W	14	220.0	4.6
	38	with rad	YDR192C	4	383.8	6.0
			RPR1	5	78.5	8.2
	64	with rad	YDR192C	4	383.8	3.6
			RPR1	5	78.5	7.4
	88	with rad	YDR192C	4	383.8	4.0
			RPR1	5	78.5	7.6
	110	with rad	YDR192C	4	383.8	4.0
		RPR1	5	78.5	7.6	
Trimethoprim	66	with rad	YEL021W	5	79.2	11.9



Tunicamycin	18	with rad	NBR035W	2	219.3	5.1
		with rad	gEL02	5	78.5	5.3
	44	with rad	YDR192C	4	383.8	5.0
UV-irradiation (20 J/m <sup>2</sup> )		with rad	YGR278W	7	476.2	4.2
	42	with rad	YBR136W	2	204.7	4.8
		with rad	YEL021W	5	79.2	12.1
Wortmannin	18	with rad	NBR035W	2	219.3	4.3
		with rad	gEL02	5	78.5	7.3
	44	with rad	YCL065W	3	0.0	4.2
YP galactose		with rad	YDR192C	4	383.8	4.2
	42	with rad	NEL011C	5	79.2	6.8
	YP glycerol	138	with rad	NBR031C	2	208.1
YPD	42	with rad	YEL021W	5	79.2	12.2
	64	with rad	RPR1	5	79.2	15.5
	66	with rad	YEL021W	5	79.2	14.3
	88	with rad	RPR1	5	79.2	15.7
	112	with rad	YEL021W	5	79.2	14.4
Zinc chloride	138	with rad	YEL021W	5	79.2	12.7
	138	with rad	YHL047C	8	0.0	4.4
		with rad	NNL035W	14	178.9	3.6

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Figure S1

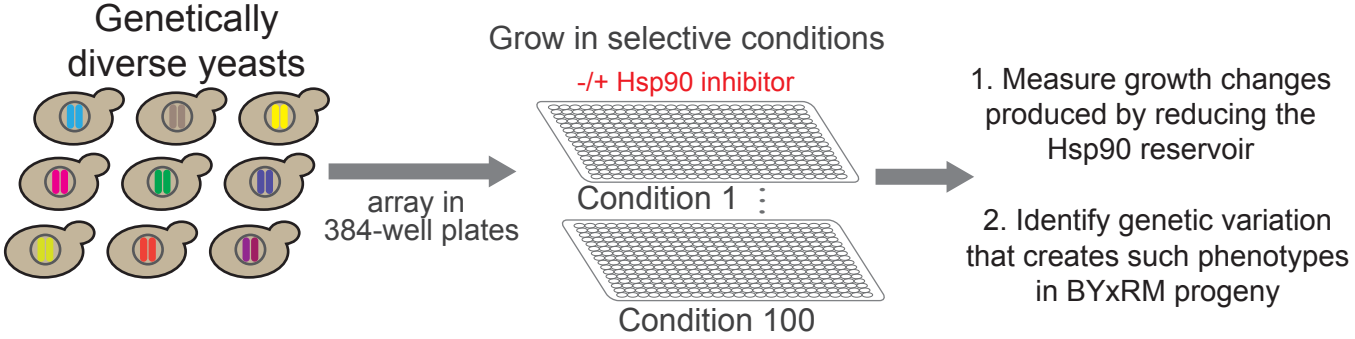


Figure S2

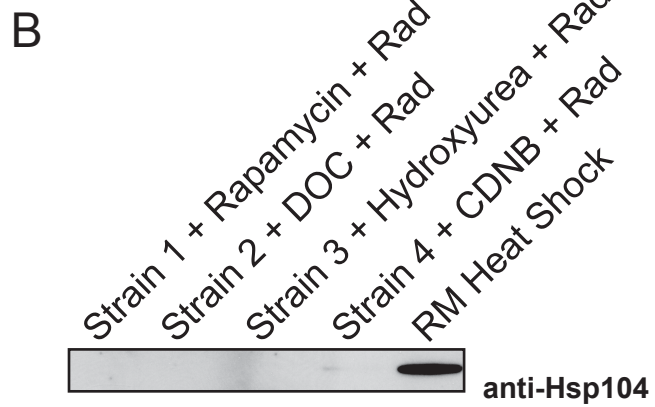
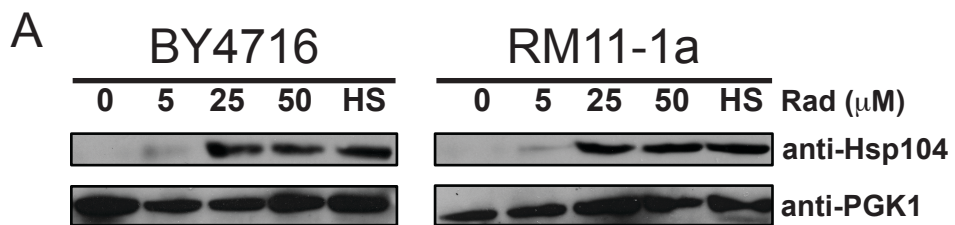


Figure S3

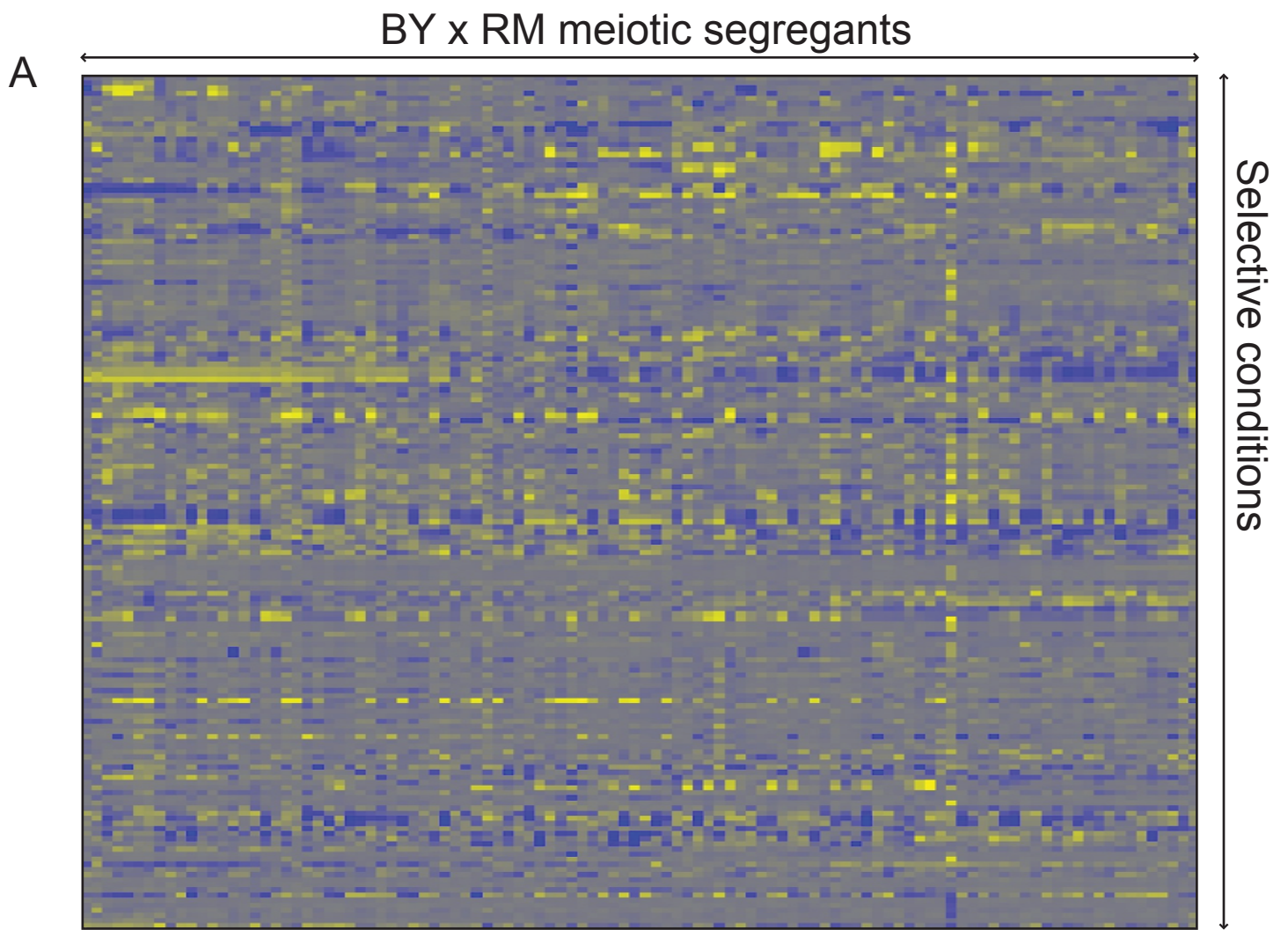


Figure S4

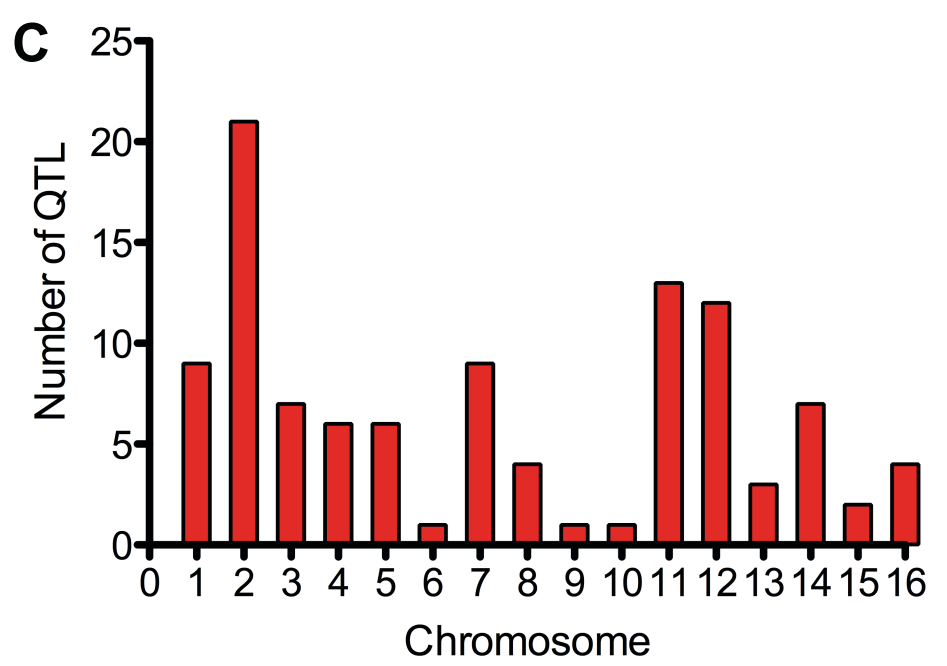
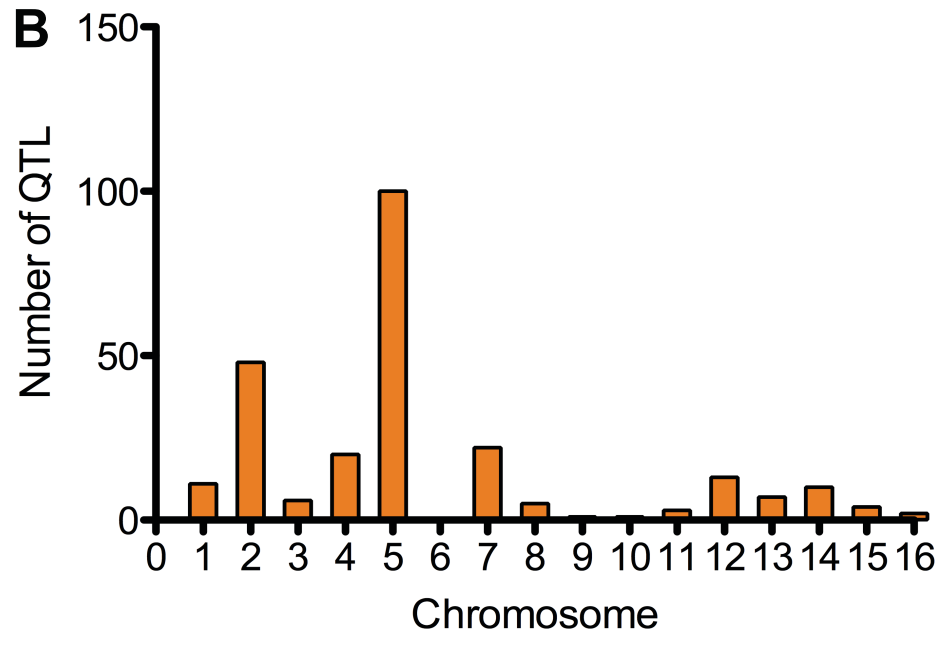
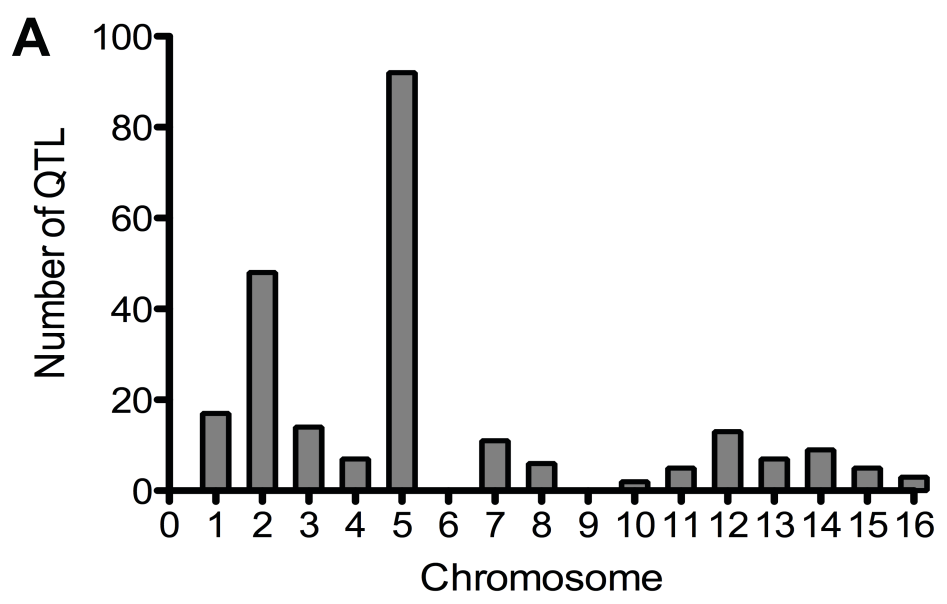
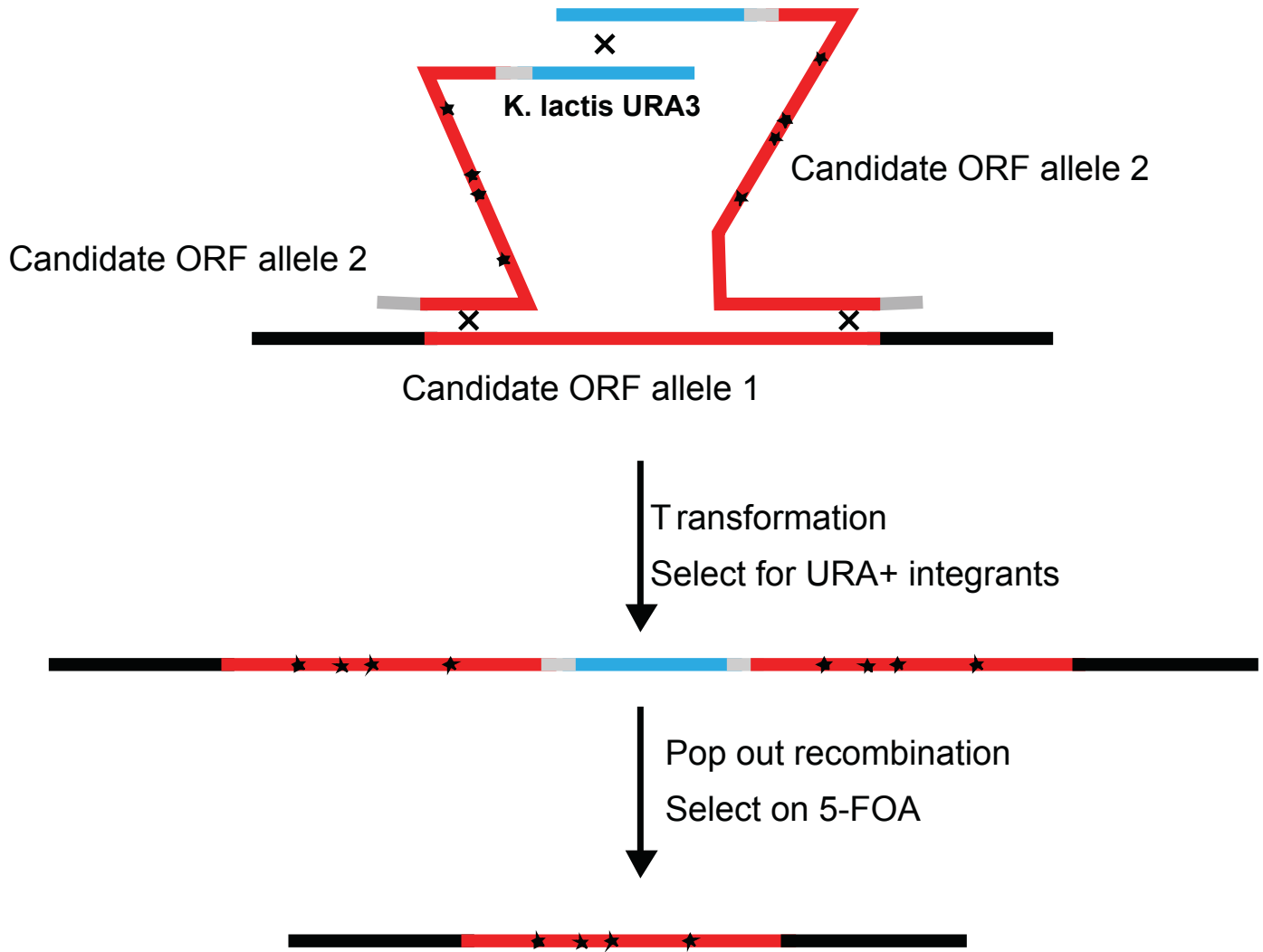


Figure S5



Adapted from Erdeniz et al. (1997)

Figure S6

