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Supporting Online Material for

The Chemical Genomic Portrait of Yeast: Uncovering a Phenotype for All Genes

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This PDF file includes:

Materials and Methods
SOM Text
Figs. S1 to S11
Tables S1 to S3
References

Supporting Online Material

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Contents: **Page**

1. Materials and Methods 2

1.1 Experimental protocols 2

Fitness assay and growth measurement by TAG3 arrays 2
Deletion pools 2
Strain batches 2
Control conditions 2
Experimental conditions and explanation of experiment names 4
Replicates, varying concentrations, and varying time-points of collection 5

1.2 Microarray analysis 5

Normalization of array intensities 5
Background intensity and poor tags 5
Sensitivity scoring 5
Sensitivity scoring method 1: log ratio (fold change) 6
Sensitivity scoring method 2: z-scores and p-values 6
Automated experiment analysis scripts. 6

1.3 Measuring significance 7

Measuring errors. 7
Empirical p-values and false discovery rates (FDR) 7
Choosing significance cutoffs 8

1.4 Genes exhibiting at least one significant phenotype 9

Measuring significant genes using theoretical FDR 9
Measuring significant genes using FDR of the control set 10
Measuring significant genes using Bonferroni correction 11
Measuring significant genes using repeated experiments 11
Excluding "noisy" experiments 12

2. Supporting text 12

Multi-drug resistance genes inferred from multi-drug sensitive strains 12
Strains exhibiting a phenotype in rich media 12
Resistant strains 13
Number of strains inhibited in each experiment 13
Erroneous deletion strains, including homozygous PDR5 13
Suspicious strains and batches 13
Overlapping genes ("off-by-one error") 13

3. Supporting figures 15

4. Supporting tables 27

5. Supporting references 38

1. Materials and Methods

1.1 Experimental protocols

Fitness assay and growth measurement by TAG3 arrays

The deletion collections have been described (*1*). Each gene deletion cassette has four oligonucleotide barcodes, or "tags": an "uptag" and a "downtag" on the sense strand, and complementary tags on the antisense strand. The abundance of these tags, measured using a microarray (or "array"), provides a measure of growth of the corresponding deletion strains. One array is used per experiment (control or treatment).

The protocol for pooled, competitive growth of the deletion strains, genomic DNA purification and PCR, and tag hybridization follows Ref. (*2*). Arrays were washed using a custom-built washing station. The array type for all experiments was TAG3 (Affymetrix GenFlex Tag Array, Part No. 510389). A detailed protocol is available in Ref. (*3*), though it describes the next-generation TAG4 arrays and analysis.

Arrays were scanned using one of two scanners (denoted in each experiment's name, described further below): the older model Agilent GeneArray G2500A Scanner, or the newer model Affymetrix GeneChip Scanner 3000.

Deletion pools

Pools of deletion mutants were constructed as described in Ref (*1*). We used five pools over the course of this study, named according to date:

het_04_01_02 (heterozygous, constructed in April 2001)
het_09_02
het_06_03
hom_05_01
hom_09_02

Each experiment name (in the downloadable data at http://chemogenomics.stanford.edu, and described further below) contains the pool that was used.

Strain batches

Each deletion strain is associated with a batch, or collection of strains that were made together, in the same location (see http://yeastdeletion.stanford.edu for more information). Batches are denoted by chrX_Y, where X is the chromosome and Y is an index. For example, "YAL002W:chr1_1" represents the deletion strain for the gene *YAL002W*, where the batch name is chr1_1. All strains associated with batch chr1_1 were made by a single laboratory or group. The gene names in our downloadable data include the strain-batch number.

The number of strains exceeds the number of genes because some gene deletions were constructed more than once, in different batches. Most of the re-constructed strains were done so because of a problem with the original deletion; a few were re-constructed to add an additional tag.

Control conditions

Each treatment array was compared to an associated control set of no-drug arrays that matched (a) the deletion pool used in the experiment, (b) the number of growth generations of the experiment (*2*), and (c) the scanner for the experiment (one of two scanners). These

combinations yielded 34 control sets, each composed of between 3 and 48 control arrays. The control conditions are listed in the table below and downloadable at http://chemogenomics.stanford.edu/.

The fields in the table below are

set ID number for the control set

pool The name of the deletion collection pool tested.
Uses the form het/hom_MM_YY
E.g. hom_05_01 is the homozygous pool that was created in May 2001.

scanner One of two scanner models (named "affymetrix" or "agilent") used to measure intensities on the TAG arrays. The model of "affymetrix" is "Affymetrix GeneChip Scanner 3000". The model of "agilent" is "Agilent GeneArray G2500A Scanner." The Affymetrix model is more recent.

generations The number of generations for which the pool was grown in drug.
A negative sign preceding the number indicates that the pool was taken directly from the freezer, thawed, diluted and grown in the condition.
Absence of a negative sign indicates that the pool was thawed, inoculated into YPD and grown overnight until log phase (OD600= 2.0)(~10 generations of recovery) before drug addition.
E.g., 5gen indicates that the pool was grown overnight and then grown for 5 generations in the condition.
-5gen indicates that the pool was taken directly from the freezer and grown for 5 generations in the condition.
See also Ref (*2*).

num controls The number of control arrays that were performed for the given parameters (pool, scanner, and generation time). This defines the sample size for the statistical significance analysis.
The number of controls in each set are shown in the following table:

set	pool	scanner	generations	num controls
5	het_04_01_2	agilent	15	6
6	het_04_01_2	agilent	20	48
7	het_04_01_2	agilent	5	17
9	het_06_03	affymetrix	20	33
10	het_06_03	agilent	20	3
12	het_09_02	agilent	-5	6
13	het_09_02	agilent	0	7
14	het_09_02	agilent	10	6
15	het_09_02	agilent	20	13
16	het_09_02	agilent	5	6
21	hom_05_01	agilent	15	11
22	hom_05_01	agilent	20	26
23	hom_05_01	agilent	5	17
24	hom_09_02	affymetrix	-10	4
25	hom_09_02	affymetrix	-5	19
26	hom_09_02	affymetrix	0	3
27	hom_09_02	affymetrix	10	3
28	hom_09_02	affymetrix	20	35
29	hom_09_02	affymetrix	5	4
31	hom_09_02	agilent	-5	5
32	hom_09_02	agilent	0	8
33	hom_09_02	agilent	10	6
34	hom_09_02	agilent	5	6

Experimental conditions and explanation of experiment names

The data presented here were collected from May 2001 through August 2005. Prior to executing a full genome-wide screen, all the compounds/conditions were" pre-screened" against wild-type yeast, and those compounds/treatments that produced a measurable 10-15% inhibition of wildtype growth (IC-15) were chosen for further full-genome screening. The complete list of experiments and resulting data are available at http://chemogenomics.stanford.edu.

The format of the experiment names in the downloadable data is

filename:cond1:conc1:unit1:cond2:conc2:unit2:generations:pool:scanner

The fields are:

filename Unique identifier of the array, and the name of the corresponding .cel intensity file.
Uses the form YY_MM_DD_XX, where YY is the year, MM is the month, DD is the day, and XX is the sample number.
E.g., 01_05_31_04 is 2001 May 31 Sample 4.

cond1 Name of the condition tested (drug name or other condition).
E.g., 37C is 37 degrees Celsius;
E.g., methotrexate is the drug methotrexate.

conc1 The concentration at which the drug was tested, if applicable.

unit1 The units of concentration, if applicable.
E.g., conc1 of 5 and unit1 of uM is 5 uM.

cond2 As cond1, but for the second (double-drug) condition, if applicable.

conc2 As conc1, but the second (double-drug) condition, if applicable.

unit2 As unit1, but the second (double-drug) condition, if applicable.

generations The number of generations for which the pool was grown in drug.
A negative sign preceding the number indicates that the pool was taken directly from the freezer, thawed, diluted and grown in the condition.
Absence of a negative sign indicates that the pool was thawed, inoculated into YPD and grown overnight until log phase (OD600= 2.0)(~10 generations of recovery) before drug addition.
E.g., 5gen indicates that the pool was grown overnight and then grown for 5 generations in the condition.
-5gen indicates that the pool was taken directly from the freezer and grown for 5 generations in the condition.
See also Ref (*2*).

pool The name of the deletion collection pool tested.
Uses the form het/hom_MM_YY
E.g. hom_05_01 is the homozygous pool that was created in May 2001.

scanner One of two scanners (named "affymetrix" or "agilent") used to measure intensities on the TAG arrays. The model of "affymetrix" is "Affymetrix GeneChip Scanner 3000". The model of "agilent" is "Agilent GeneArray G2500A Scanner.

Replicates, varying concentrations, and varying time-points of collection

Certain conditions were tested in replicate (number of replicates ranged from 1 to 14), with a median replicate correlation of 0.72 (Fig. S6). Certain compounds were also tested at varying concentrations and varying time-point of collection. Excluding replicates and variations, the heterozygous set comprises 354 unique conditions, and the homozygous set comprises 178 unique conditions.

1.2 Microarray analysis

Briefly, to determine a gene deletion strain's sensitivity to a particular treatment, we compare its growth in the treatment relative to that in control (no-drug) experiments. We do this by reading the intensity measures of each tag from the control and treatment microarrays, normalizing, filtering, and comparing the abundance of the tag between treatment and control to calculate statistically significant differences in strain growth.

Normalization of array intensities

Output of the Affymetrix scanner is an intensity value for each tag on the array. Arrays must be normalized to have the same mean intensity, to allow comparisons between arrays. For this we used "mean normalization," dividing the intensity of each tag by the mean intensity of the array. To make this normalization more accurate, we separated the tags into four groups (uptag sense, uptag antisense, downtag sense, and downtag antisense) and divided each tag's intensity by the mean of the appropriate group, instead of the mean of the entire array. This procedure accounts for the separate PCR amplification of uptags and downtags, as well as any other tag-group-specific intensity trends. We scaled the mean intensity of each array to be 1500.

Background intensity and poor tags

We calculated the mean intensity for 3600 unused tags (i.e., those tags that are not assigned to any deletion strain and therefore should not show any signal), and defined this as the mean "background intensity" for the control array. Any other tag whose intensity was less than two standard deviations greater than this mean background was defined as below background, and therefore designated a "poor" tag. In other words,

$$\text{Background cutoff} = \mu^{c}_{unused} + 2\sigma^{c}_{unused},$$

where μ^{c}_{unused} is the mean of the unused tags on the control array c, and σ^{c}_{unused} is their standard deviation. For a given control set, any tag that was below background in at least three-quarters of the control experiments was considered unusable and excluded from further analysis.

Sensitivity scoring

We compared each tag's normalized intensity in the treatment to the same tag's intensity in the control (no-drug) set of arrays that matched the treatment's pool, scanner, and collection time-point. Each control set contained between 3 and 48 arrays, as described above. We used two types of scores in comparing treatment to controls.

Sensitivity scoring method 1: log ratio (fold change)

For analyses where significance calling was not necessary (in clustering, for example), we used the simple $\log_2$ ratio of the mean control intensity vs. the treatment intensity to calculate the fitness defect (FD):

$$\text{log-ratio}_{\text{FD}} = \log_2(\mu_i^c / x_i^t),$$

where μ_i^c is the mean intensity of tag *i* across multiple control conditions and x_i^t is the intensity of tag *i* in the treatment. We averaged the log-ratios of the up- and downtags to yield one log-ratio for each gene.

If more than half of the four tags for a strain had been defined as unusable in the controls (as described above), we could not calculate a fitness defect, and the scores for these cases are null. In some cases, improved tags were designed for these strains over the course of the study, so strains that were not measurable in earlier pools became measurable in later pools.

We found empirically that the log-ratio performed better than z-scores or p-values (below) for clustering and other correlation-based analyses (Fig. 3).

Sensitivity scoring method 2: z-scores and p-values

In order to call significant sensitivity (e.g., for Figs. 1 and 2), we need to calculate a p-value. The p-value here is the probability of obtaining a result at the observed sensitivity (or greater), given that there is no sensitivity. The methods employed by the expression microarray community to generate p-values usually involve a t-test, or variants of it. We followed a similar approach.

We defined a fitness defect (FD) z-score (also known as standard score or normal score):

$$z_{\text{FD}} = \frac{\mu_i^c - x_i^t}{\sigma_i^c},$$

where μ_i^c and x_i^t are as defined above, and σ_i^c is the standard deviation of tag *i* in the control conditions. We calculated a fitness defect p-value from this z-score using the t-distribution with *n*-1 degrees of freedom, where *n* is the number of control arrays. We generated a p-value for every gene-experiment test in this manner.

There are other methods for generating p-values from this type of data, such as using a t-statistic instead of a z-score, or comparing the test statistic to something other than the t-distribution, such as a normal distribution. We tested these, and chose the method above, by comparison to the empirical p-value, described further below.

Automated experiment analysis scripts.

Three perl scripts are used to parse the CEL data from the Affymetrix scanners, perform normalization, and assign fitness defect scores. The first script, "raw_file_data.pl" maps the raw intensity data in each input CEL file to their associated strain-tags. A second script, "normalize_data.pl" takes the output produced by the first script and normalizes it so that the data for each experiment has a mean intensity of 1500. The last script, "fitness_profile.pl", calculates both fitness defect log ratios and significance values for a given set of control and

treatment experiments using the normalized data produced by the second script. All scripts are available on the supplementary website.

1.3 Measuring significance

Measuring errors.

We use the following table in discussing the following sections.

	# Declared non-significant	# Declared significant	Total
# True null hypotheses (In this study, true non-sensitive tests)	**U**	**V**	m_0
# Non-true null hypotheses (In this study, true sensitive tests)	**T**	**S**	$m - m_0$
Total	m - R	**R**	m

R is a random variable that we can observe, and U, V, T, and S are random variables that we cannot observe (*4*). We represent observations of R, U, V, T, and S as *r, u, v, t,* and *s*, respectively.

Empirical p-values and false discovery rates (FDR)

We used our large control set to calculate empirical p-values at each theoretical p-value measure. An empirical p-value $\hat{p}$ (*5*) is commonly defined as

$$\hat{p} = r/m,$$

where m is the number of samples and r (an observation of R) is the number of these samples whose significance scores exceed a given threshold, given that all hypotheses are null (i.e., all observed significance calls are false; r is equal to v.) This is essentially the proportion of false positives out of all tests.

We directly estimated the number of false positives, at varying significance cutoffs, in the following manner. We scored each control array as if it were a mock treatment experiment, comparing to the remaining controls in the set (i.e., leave-one-out), calculating z-scores and p-values in a manner analogous to that of the treatment analysis above:

$$z_{FD} = \frac{\mu_i^{c-c'} - x_i^{c'}}{\sigma_i^{c-c'}},$$

where here $x_i^{c'}$ is the intensity of tag i in the left-out control array c' being scored as a treatment, $\mu_i^{c-c'}$ is the intensity of tag i across the control conditions (excluding $x_i^{c'}$), and $\sigma_i^{c-c'}$ is the standard deviation of tag i in the control conditions (excluding $x_i^{c'}$). P-values are again

calculated from this score using the *t*-distribution, with *n-1* degrees of freedom, where *n* is the number of control samples (between 2 and 47 per leave-one-out control set).

Empirical p-value. We calculated the fraction of tests that were (false) positive in the controls at varying thresholds, for an *empirical p-value* (P_{emp}) at each sensitivity score cutoff. (See below table and Fig. S7A.) For example, in the 148 homozygous control arrays, there are m = 4769 strains x 148 arrays = 705,812 total tests. At theoretical $p < 0.01$, there are r = 6362 positive tests in the control dataset, all of which are false. Using the formula $\hat{p} = r/m$ = 6392 / 705,812 = .009. This empirical p-value is very close to the theoretical value of 0.01.

Other theoretical p-value thresholds and their corresponding empirical p-values:

Homozygous experiments				
	Theoretical p-value threshold			
	0.01	**0.001**	**1.0E-04**	**1.0E-05**
FP Total falsely significant tests in 148 control arrays (out of 4769 x 148 = 705,812 tests)	6362	1411	484	225
P_{emp} Empirical p-value (FP / 705,812 tests)	0.0090	0.0020	0.0007	0.0003

Theoretical p-value matches empirical p-value. In general, we found the empirical p-value to be very close to the theoretical p-value calculated from the z-score and t-distribution as described above (Fig. S7B). (Differences between the theoretical and empirical p-values were due to a few very "noisy" outlier arrays, i.e., rare arrays that have a large number of falsely sensitive strains.) For this reason, we used the z-scores and t-distribution p-values to calculate significance.

Empirical false discovery rate (FDR). At $p < 0.01$, each control array has a median of v = 26 (false) positive strains. In contrast, a treatment array contains a median of r = 230 positives. This yields an empirical false discovery rate per array (FDR_{emp} per array) of around 26/230 = 11%, or FDR = 0.11, which is fairly low. At more stringent thresholds, the FDR falls to zero (presumably at the expense of true positives):

Homozygous experiments				
	Theoretical p-value threshold			
	0.01	**0.001**	**1.0E-04**	**1.0E-05**
v_{array} Median sensitive genes per control array	26	3	0	0
r_{array} Median sensitive genes per treatment array	230	99	50.5	30.5
FDR_{emp} per array = v_{array} / r_{array} Empirical false discovery rate (FDR) of genes per array	0.1130	0.0303	0	0

Choosing significance cutoffs

As a starting point for general use of these data, we suggest a p-value cutoff of $p < .01$. At that stringency, less than 1% of the tests in the control arrays were called positive, and the false discovery rate was ~0.1 (10% of significant genes per treatment are false). However, to estimate the number of strains that exhibited any significant phenotype in this study, we must control for multiple hypothesis testing not only across genes, but also across experiments. This is described further in the next section.

1.4 Genes exhibiting at least one significant phenotype

If only 26 strains are falsely sensitive in each experiment (as would occur at a within-experiment p-value of .01, or an FDR of .1), then after 418 experiments, there would be V = 418 x 26 = 10,868 false significance calls, or about two false significance calls per gene, on average. Thus, most of the genome would falsely show a phenotype in at least one condition at $p < 0.01$.

This is a problem of multiple hypothesis testing, not only within a single experiment, as is usually the issue in microarrays, but also across several hundred experiments. Methods for controlling multiple hypothesis testing include controlling the family-wise error rate (FWER) using Bonferroni correction, and more recent methods controlling the false discovery rate (FDR). We briefly discuss both in the context of our dataset, though we focus on FDR.

Measuring significant genes using theoretical FDR

Using the table of error variables above, the FDR Q_e is defined as (*4*)

$$Q_e = E(Q) = E(V / R),$$

or the number of tests called falsely significant (V) out of all tests called significant (R). A conservative method of estimating FDR was proposed by Benjamini and Hochberg (*4*). The method orders p-values and finds the largest *i* for which the following is true:

$$P_{(i)} \leq \frac{i}{m} q^*,$$

where *m* is the total number of tests and q^* is a selected FDR level, such as 0.1.

FDR for multiple genes within one experiment. First we consider only a single experiment, where *m* is the number of strains on an array (5984 for heterozygous, 4769 for homozygous). A Benjamini-Hochberg FDR threshold of 0.1 per treatment experiment generally corresponded to a p-value cutoff between 0.01 and 0.0001, depending on the experiment. Using FDR < 0.1, we found that 4707 genes are sensitive in at least one homozygous treatment, and 5182 are sensitive in at least one heterozygous treatment. These phenotypes combined with the 888 strains showing a phenotype in rich media (*6*) yields a total of 5856 genes showing a phenotype (out of 5984 strains in the collection), or 98% of the genome.

We can also use the empirical FDRs described above; these yield similar results.

FDR for multiple genes and multiple experiments. Alternatively, we set *m* to be the number of total tests that performed: *m* = 6000 genes x 1000 treatment experiments = 6,000,000 tests. To apply this approach, we ordered the ~6,000,000 p-values from all of the tests (heterozygous and homozygous) and found the largest *i* for which the above inequality was true. We again used q^* = 0.1, meaning 10% of all of the resulting positive tests are presumably false. 206,000 tests met the inequality, corresponding to a p-value of 0.003. At $p < 0.003$, 4663 genes are sensitive in at least one homozygous treatment, and 5122 are sensitive in at least one heterozygous treatment. These phenotypes combined with the 888 strains showing a phenotype in rich media (*6*) yields a total of 5870 genes showing a phenotype (out of 5984 strains in the collection), or 98% of the genome.

However, an FDR of 0.1 across all gene-experiment tests is not stringent enough for this analysis, for the following reason. Of 200,000 positive tests, 10%, or 20,000 will be false. This is an average of 20,000/6,000 = 3 false hits per gene; thus, the entire genome would likely show a phenotype by chance.

*FDR controlling the number of genes sensitive in **any** experiment.* Instead, we want to control the FDR of the number of genes showing a phenotype in *any* condition. Suppose we desire this FDR to be less than 0.1; in other words, we desire that less than 10% of the genes showing a phenotype in any condition will be false (i.e., not have any true phenotype). If we control the number of total false positive tests to be, say, 600 rather than the 20,000 above, then we will falsely call significance for a maximum of 600 genes (or fewer, if multiple false tests belong to the same gene). An FDR of 0.006 returns 95,000 positive tests, of which 95,000 x 0.006 = 570 are expected to be false. This FDR corresponds to a p-value of 1e-5. At $p < 1e-5$, 4175 genes are sensitive in at least one homozygous treatment, and 4226 are sensitive in at least one heterozygous treatment. These phenotypes combined with the 888 strains showing a phenotype in rich media (*6*) yields a total of 5834 genes showing a phenotype (out of 5984 strains in the collection), or 97% of the genome.

Measuring significant genes using FDR of the control set

We utilized our large control set in an alternative approach for counting the number of genes truly exhibiting any phenotype. Intuitively, we want to know how many strains are sensitive in the treatment experiments but not in the control experiments. Specifically, how many strains are sensitive in significantly more treatment experiments than control experiments? As an example, if we see a strain falsely sensitive in two control arrays, but we also see it sensitive in 30 treatment arrays, it is likely to fit the definition of sensitive in at least one condition. As another example, a gene that is sensitive in one control array and also sensitive in one treatment array should not be counted as truly exhibiting a phenotype.

Using the control leave-one-out analysis described above, we generated a sensitivity matrix of 4769 homozygous deletion strains x 148 homozygous control arrays, and a second sensitivity matrix of 5984 heterozygous deletion strains x 145 heterozygous control arrays. We counted the number of arrays, k, out of the total control arrays (148 or 145) that inhibited, or "perturbed" each strain. We generated a distribution for k analogous to Fig. 2a for these control arrays (Figs. S2, S3). However, the 148- and 145-array control sets were smaller than the 418- and 726-array treatment sets, so we could not compare k, the number of perturbing experiments, between control and treatment sets. Thus, we needed to simulate control sets that matched the number of treatment arrays (Fig. S8).

The distribution of k in the controls was well described by a binomial distribution (Figs. S2, S3), where each control is an independent event, described by parameters n and p. n is the number of control arrays (148 or 145), and p is set to

$$p = k_u / n_c$$

where k_u is the mean number of perturbing experiments for a gene in the control set, and n_c is the number of control arrays (148 or 145).

We scaled this binomial distribution of k by keeping p as above, but setting n to match the number of treatment arrays (418 or 726). This serves as our simulated, expanded set of control arrays. Using this expanded control set whose size matched the treatment set, we then defined a significance threshold for k (binomial $p < 0.05$), above which a significant number of strains are k-perturbed, or perturbed in at least k experiments. For example, at a sensitivity threshold of 0.01, the threshold for k is 7 experiments. Only 414 strains are 7-perturbed (sensitive in at least 7 experiments) in the simulated control set, and 4115 strains are 7-perturbed in the treatment set (Figs. S2, S8), for an FDR of ~0.1.

In total, we found approximately 4000 homozygous strains were truly perturbed for p-value thresholds ranging between 0.1 and 1e-6. At p-value thresholds less stringent than 0.1, fewer than 4000 strains were called truly perturbed because there were many false positives in the

controls, forcing k to be large and therefore miss many true positives (Fig. S2). At p-value thresholds more stringent than 1e-6, many true positives were discarded due to the excessive stringency, also resulting in fewer than 4000 strains perturbed. Thus, there was an optimal set of p-values that all returned the number of true positive perturbed homozygous strains to be approximately 4000.

To generate concrete numbers for the main text, we used a threshold of p < 1e-5 for homozygotes because its FDR was close to 0.1, and it had the added benefit of simplicity: its k cutoff was 1 (Fig. S2) (as opposed to other p-values that had similar FDRs but $k > 1$). We also noted that the p-value threshold of 1e-5 was the same as that calculated by the Benjamini-Hochberg FDR method controlling false genes sensitive in any treatment (described above).

For the heterozygous experiments, the p-value threshold that limited the FDR to ~ 0.1 was 1e-6 (Fig. S3).

Gene-specific distributions. We also performed a gene-specific analysis, where we fit a binomial distribution for each individual gene g, where here p is the fraction of control arrays in which gene g is perturbed:

$$p = k_g / n_c$$

where k_g is the mean number of false positives for a gene in the control set, and n_c is the number of control experiments. This accounts for gene-specific effects. However, the end results are very similar to the general fits: between 3800 and 4300 strains are perturbed, depending on the threshold, and p < 1e-5 was again found to control the FDR of false genes to be near 0.1 (Figs. S2, S3).

Estimating FDR by data permutation. A popular alternative method of estimating FDR is permutation of the treatment and control data, especially Significance Analysis of Microarrays (SAM) (*7*) and related algorithms. SAM requires replicates, and few of our treatment experiments contained true replicates, so we were unable to apply SAM directly. (However, many conditions were tested at varying time-points of collections, and varying compound concentrations, which could potentially be considered replicates for the purposes of SAM, though concentration-specific or time-specific genes could be lost). Our approach using the control arrays, is akin to permutation methods, though it compares only to the control experiments, not the control and treatment experiments combined.

Measuring significant genes using Bonferroni correction

The Bonferroni method is recognized as overly stringent (*4*), so we note its results only for completeness. If the number of multiple tests is m = 6000 strains, the new significance level for an experiment is 0.01 / 6000 = 1e-6, yielding 95% of the genome exhibiting a phenotype. If the number of tests m is 6000 strains x 1000 experiments, the new significance threshold is 0.01 / (6000 x 1000) = 1e-9, yielding 82% of the genome exhibiting a phenotypes.

Measuring significant genes using repeated experiments

We also counted the number of perturbed genes using the subset of conditions having at least two repeated experiments, including true replicates, varying concentrations, and varying time-points of collection. Because not all treatments had repeats, this set contains fewer experiments than the full set. Additionally, some true positive genes may be missed if they only appear under one concentration or time-point. Nonetheless, we call a strain "replicate-perturbed" if it is

significantly sensitive in at least two repeated experiments. At p < 1e-5, this yielded 2104 strains replicate-perturbed as heterozygotes, and 2147 replicate-perturbed as homozygotes. These phenotypes combined with the 888 strains showing a phenotype in rich media (*6*) yields a total of 4316 genes showing a phenotype (out of 5984 strains in the collection), or 72% of the genome. While this set probably has very few false positives, it is probably also lacking many true positives, since any experiments without repeats were excluded, and the p-value threshold of 1e-5 is likely overly conservative here.

Excluding "noisy" experiments

We also tested the number of strains exhibiting any phenotype if we excluded experiments that inhibited a large number of strains (e.g., the experiments that inhibited more than 5-10% of strains, Fig. S11). This did not greatly impact the results, as most genes were sensitive in multiple other experiments.

2. Supporting text

Multi-drug resistance genes inferred from multi-drug sensitive strains

To measure multi-drug resistance genes, we restricted our analysis to small molecule experiments, excluding conditions of environmental change, such as amino acid dropout. See Table S1 for a list of environmental vs. small molecule conditions.

We define "multi" as > 20% of unique small molecule treatments, at a p-value threshold of p < 0.01. There are 145 unique *small molecule* treatments against the homozygous collection and 348 against the homozygous collection. Thus we classify genes as MDR if they are sensitive in at least 30 unique small molecules as homozygotes, or 70 unique small molecules as heterozygotes.

We considered those small molecules that induce sensitivity in homozygous MDR gene deletion strains (Table S3), and analyzed two common molecular descriptors: molecular weight and partition coefficient (or lipophilicity, as defined by XLogP) (Fig. S9). Compounds frequently inhibiting MDR gene strains are significantly larger than other compound(Mann-Whitney p = 0.006). The distribution for lipophilicity was markedly bimodal, with one population being lipophilic and the other being hydrophilic, suggesting two underlying mechanisms for resistance; these could potentially reflect transporter structure preferences (*8*).

Strains exhibiting a phenotype in rich media

Of those 888 strains previously observed as exhibiting a phenotype in rich media (Fig. 1B) (*6*) ("slow growers"), ~600 also showed a growth defect in condition(s) in this study, and ~300 strains did not. These ~900 slow-growers are often annotated "ribosomal," and we hypothesized that the corresponding genes are rate-limiting for growth in rich media. That could potentially make it more difficult to detect sensitivity, for the following reason. When the competitive pool is slowed overall by the addition of drug stress, the deficit of the slow-growing strains may be relatively less severe, giving them more "room" and more time to grow, and as a result their relative abundance increases (compared to the other strains). Thus, they may look less sensitive. It is possible that the ~300 slow-grower strains that did not show sensitivity in this study may have actually been sensitive, but were not detected as such.

Resistant strains

Analogous to the counts of sensitivities described in the main text, we counted the number of conditions in which each strain was resistant (Fig. S10). Many of those strains that appear frequently-resistant in both heterozygous and homozygous treatments are the slow-growing, primarily ribosomal strains mentioned above (*6*). We consider it unlikely that these strains are truly resistant. To test the traditional definition of resistance (i.e., that the strain grows better in drug than in control media), an individual growth confirmation is recommended. We have not systematically analyzed our data to define truly resistant strains.

Number of strains inhibited in each experiment

We counted the number of strains inhibited in each experiment, at $p < 1e\text{-}5$. Most experiments inhibited less than 5% of genes (Fig. S11). The median number of strains inhibited was 9 strains for heterozygous experiments and 30.5 strain for homozygous experiments.

Erroneous deletion strains, including homozygous PDR5

We identified strains that, upon PCR confirmation experiments, did not have the correct gene deleted. These were reported to the yeast deletion consortium for correction in YKOv.2. Unfortunately, one of the strains in this set was the homozygous deletion strain of *PDR5*, the known multidrug resistance efflux transporter. The heterozygote was correct, however, and this strain was identified as MDR as a heterozygote; we thus think it likely to have been found MDR as a homozygote, but because we had no real *PDR5* strain, we were not able to evaluate it.

Suspicious strains and batches

In the heterozygous cluster analysis, we noted a few abnormally strong clusters whose genes were functionally unrelated but the strains in each cluster originated from a common deletion collection generation batch. We believe this is due to unrelated artifacts, e.g. a secondary site mutation in the parent strain used to make each batch. This could lead to deletion strains sharing some secondary genotype. The most obvious batches showing this effect were

chr00_1
chr3_1
chr00_5
chr13_4
chr12_4
chr13_1b
chr4_4
chr13_5
chr13_2
chr7_5

647 strains belonged to these suspicious batches, and we exclude these strains from most analyses.

The homozygous strains did not show this pattern.

Overlapping genes ("off-by-one error")

We occasionally found that strains were highly correlated (and thus clustered together) in co-fitness if their physical genome locations were overlapping. One explanation for this phenomenon is that deleting one ORF completely leads to deletion of part of a neighboring ORF (or regulatory element), as a result the neighbor ORF's phenotype is similar and both show similar fitness profiles. A similar observation has been reported elsewhere (*9*).

3. Supporting figures

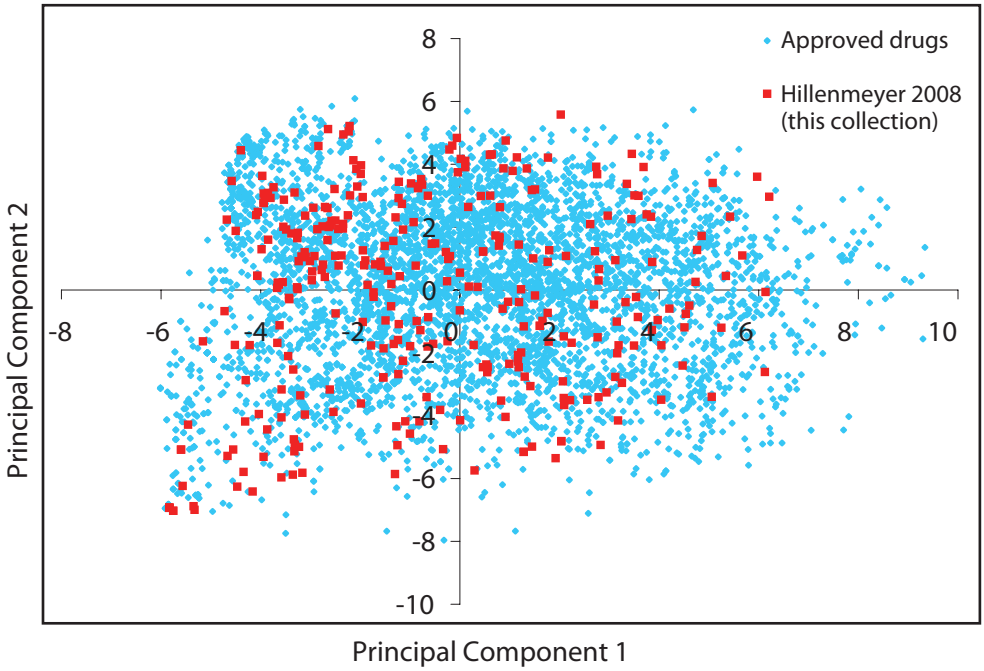


Figure S1. Compound library diversity.

We compared our collection of compounds (see Table S2 for chemical structures) to a set of 5000 approved drugs defined in the Pipeline Pilot software (Accelrys, Inc.). We represented each compound as its MDL 166-bit public keys, or substructures (Durant et al., 2001). We performed principal components analysis (PCA) on the keys and plotted the first two principal components for each compound. Each point on the plot represents a compound. Each axis (principal component) is a linear combination of the substructure keys (which can be considered an "eigen-key") that maximizes the variance.

Intuitively, we do this because substructure keys may be correlated, and if we want to visualize the libraries in only two-dimensions, where each dimension is a substructure key, then we want to use the most informative substructure keys possible. PCA chooses not an actual substructure key, but a linear combination of keys that explains the most of the variance across compounds.

Our collection of compounds shows diversity that is qualitatively comparable to the approved drug set. Many of our tested compounds are actually WHO/FDA approved compounds, which may explain some of the overlap. Interestingly, there seem to be areas of chemical space that are not accessed by either set, given the shape of the distribution on the left side of the plot.

Note that we also tested many non-drug environmental stresses, which do not have chemical structures and cannot be included in this type of diversity analysis.

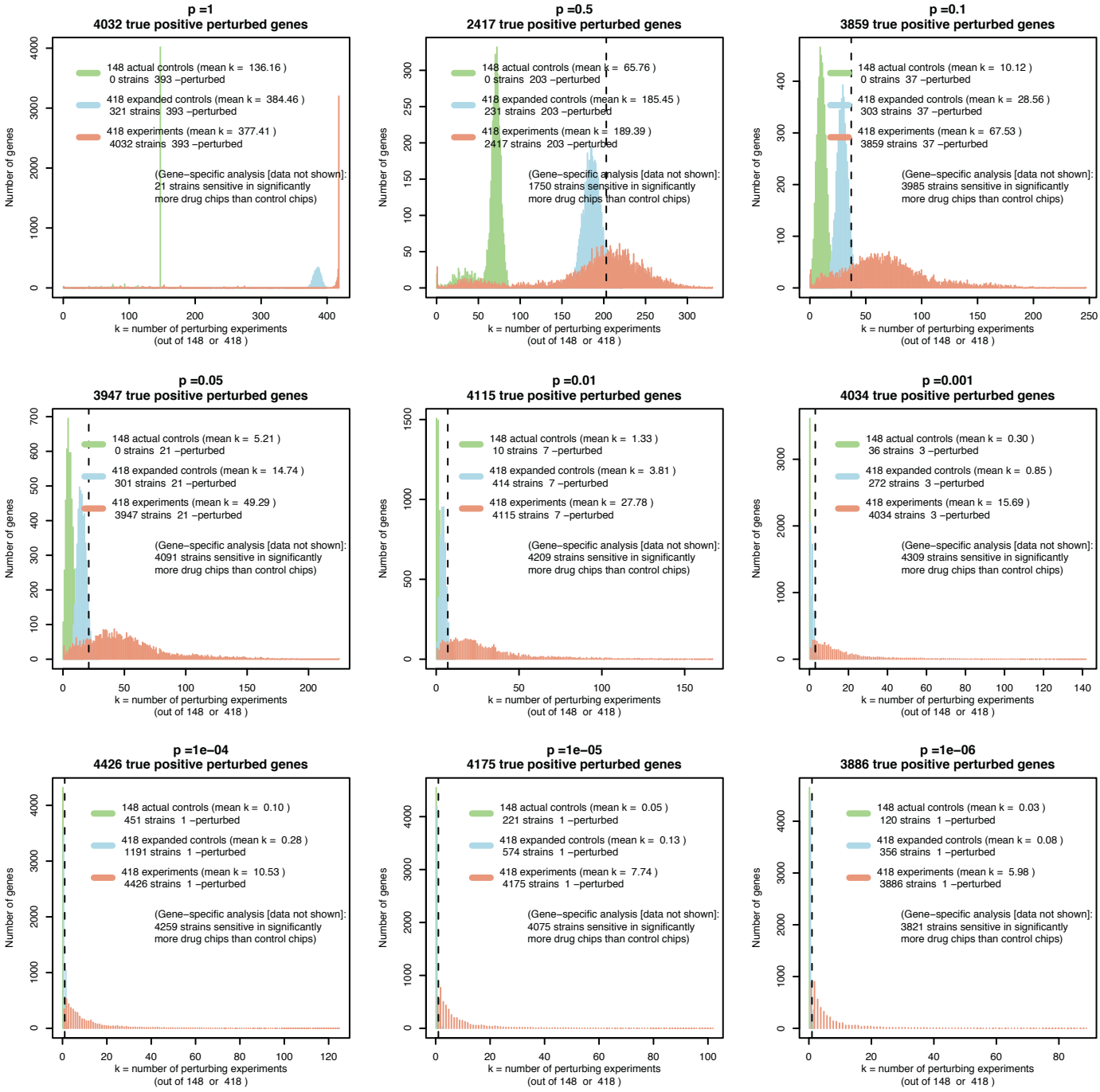


Figure S2. Measuring the number of strains significantly perturbed as homozygotes.

Each panel represents a p-value threshold, where strains in an experiment below the threshold are called significantly sensitive, or perturbed. Each panel is analogous to Fig. 2A. The x-axis, k, represents the number of experiments perturbing each strain. The y-axis represents the number of genes that are perturbed by that number of experiments. The actual control distribution for 148 control chips is shown in green. This distribution is well-described by a binomial distribution, which was used to generate a size-matched null distribution of 418 control chips (blue distribution), by setting *p* to the mean fraction of control chips perturbing each gene, and *n* to the number of experiment chips (peach distribution). The dashed line represents the significant k where the binomial $p < 0.05$, meaning that less than 5% of strains are k-perturbed above that k in the control chips (blue distribution).

We performed a similar gene-specific analysis, where we fit a binomial distribution for each individual gene g, where here p is the fraction of control chips in which gene g is perturbed. This accounts for gene-specific effects, however, the results are very similar to the general fits, suggesting that gene-specific effects do not play a major role.

Approximately 3900-4400 strains are perturbed in this study, depending on the significance threshold. For further analysis, we used p<1e-5, because it limits the perturbations in the control set to about 10% of strains (574), and because of the simplicity of using k = 1.

Note that some of these strains were already perturbed in rich media (Deutschbauer 2005), but not all. When we include those genes and the essential genes, 93% of the genome is perturbed (5438 out of 5860 possible homozygous deletion strains).

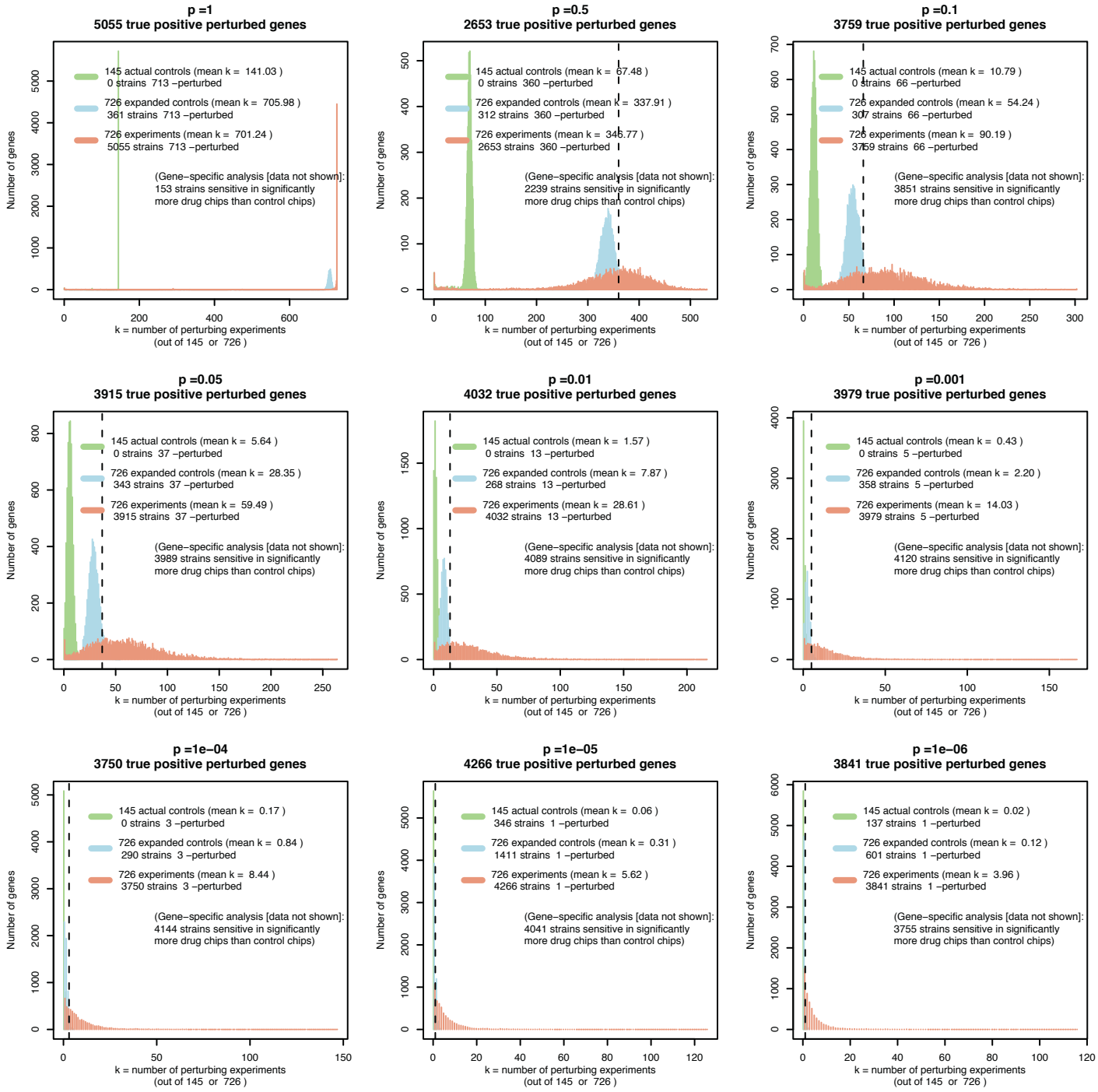


Figure S3. Measuring the number of strains significantly perturbed as heterozygotes. (As Figure S2, but heterozygous.)

Note that we we exclude the 647 strains from suspect batches (see Supporting Text).

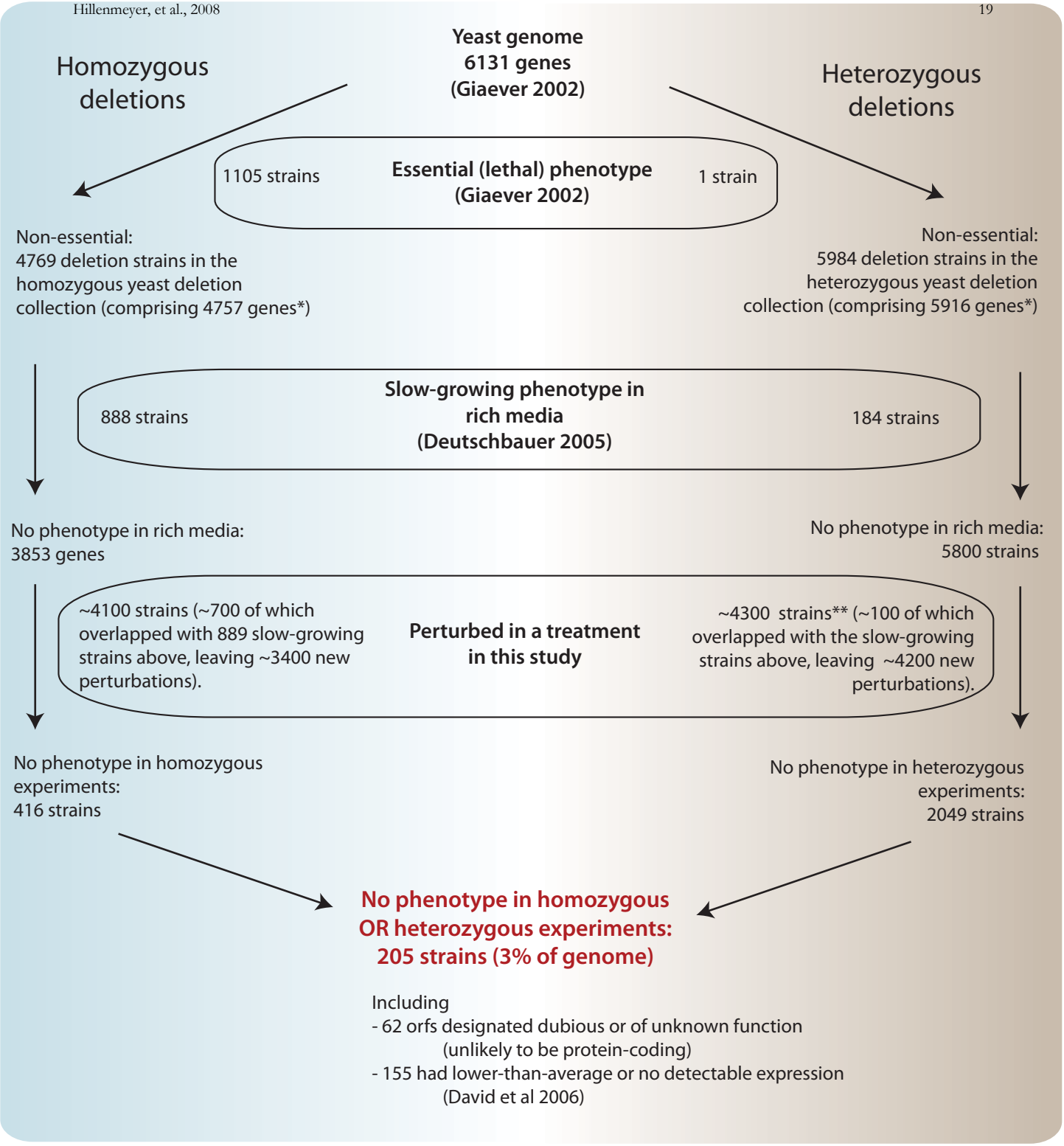


Figure S4. A phenotype for all genes. The left side of the flow chart tracks the phenotypes of homozygous deletion strains; the right side, heterozygous deletion strains.

* Not all gene deletion strains could be constructed (Giaever 2002). Additionally, some deletions were constructed more than once, over time, causing the number of strains to exceed the number of genes. Most of the re-constructed strains were done so because of a problem with the original deletion; a few were re-constructed to add an additional tag.

** 647 heterozygous strains were excluded from this analysis because they are from suspicious batches. See Supplement for details. Numbers are approximate because the analysis was performed at varying p-value thresholds (with similar results).

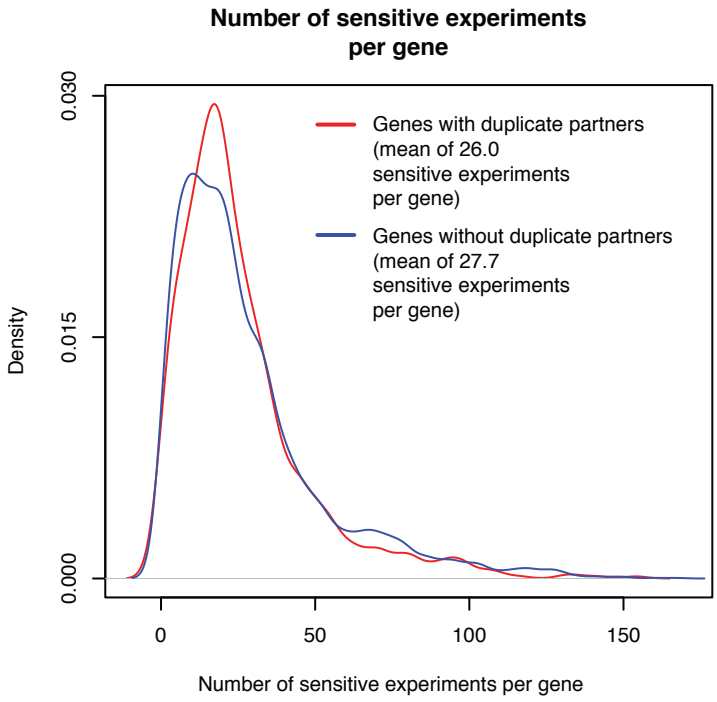


Figure S5. Duplicated genes. Deletion strains of genes having duplicated partners are not sensitive in significantly fewer experiments than genes without duplicates, as might have been predicted by the redundancy hypothesis (Gu et al, 2003, Deutscher et al., 2006, Papp et al., 2004).

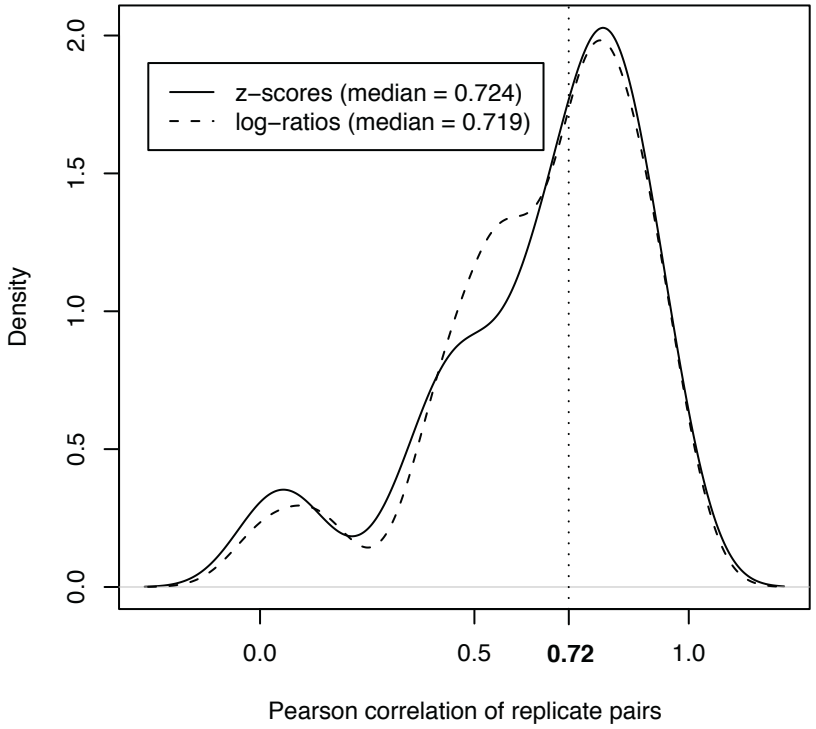
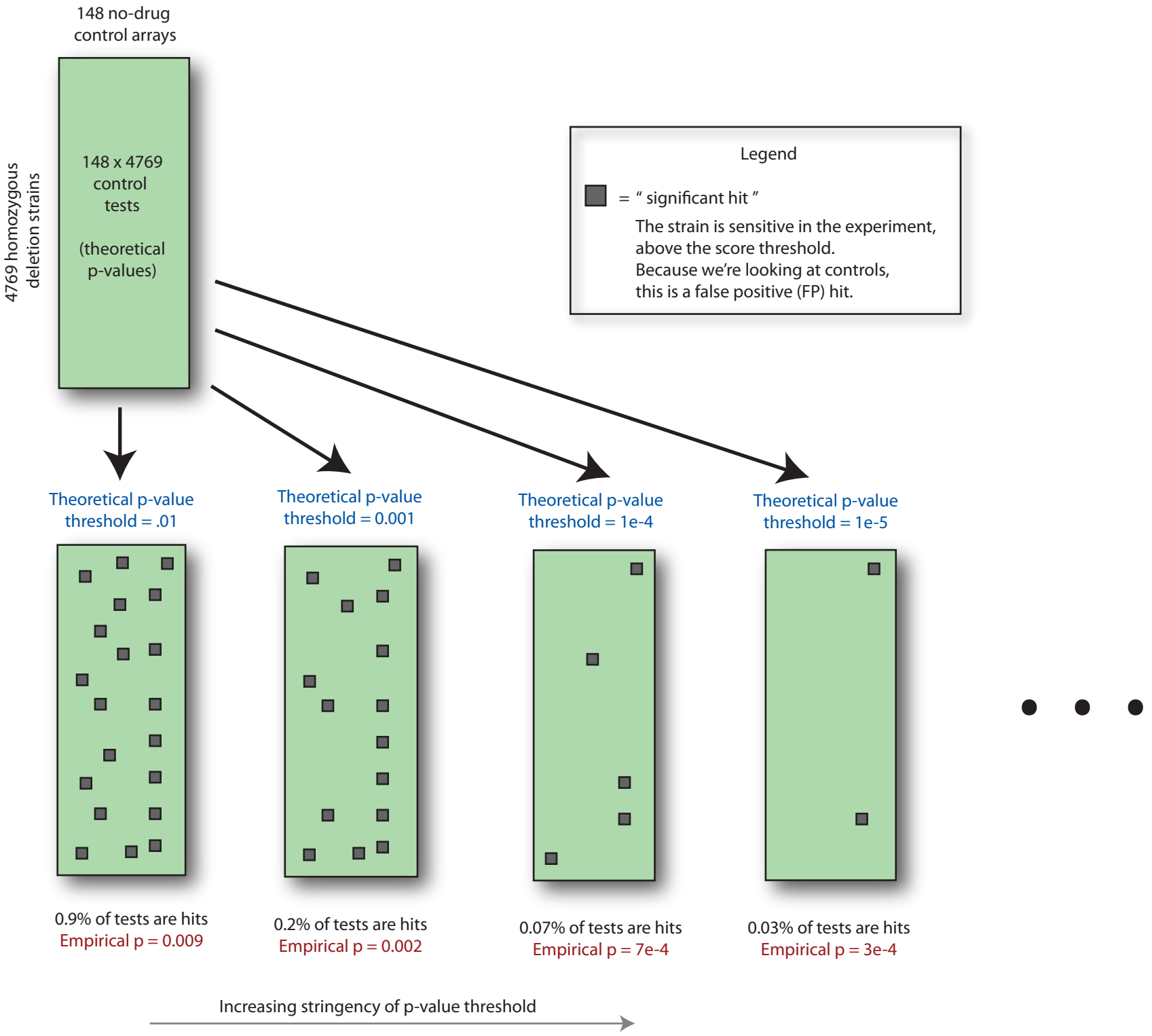


Figure S6. Distribution of correlations for pairs of replicates. The median is 0.72. The bimodal distribution suggests that a small subset of replicates that were not correct.

a. False positive significant hits in homozygous control arrays



b. Comparing theoretical p-values to empirical p-values

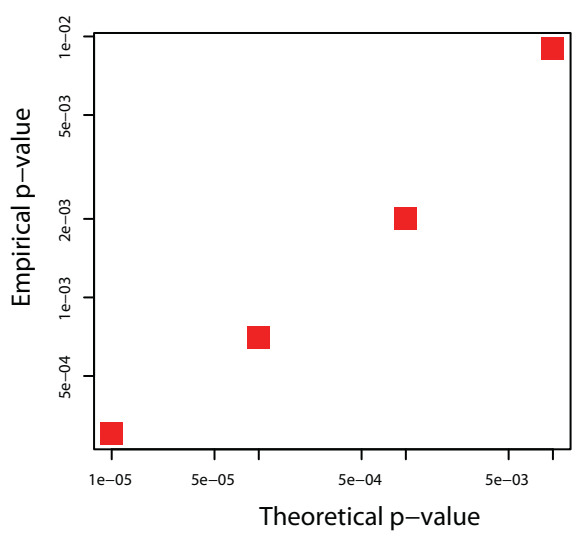


Figure S7. Calculating empirical p-values from theoretical p-values.

a. False positive significant hits in homozygous control arrays. First we calculate p-value for each gene-experiment test in the no-drug control experiments (i.e., for each cell in the green 148 x 4769 matrix). We do this by considering each control experiment to be a mock treatment experiment, comparing to the remining controls in the set (excluding the one being considered), and generating a z-score and p-value in exactly the same way that we generate a z-score and p-value for the treatment experiments. After this is done, we have p-values for the matrix of control experiments. We then count the number of significant hits at varying p-value thresholds. At less stringent thresholds, more false hits are observed. At more stringent thresholds, fewer false hits are observed. The theoretical p-value is shown above each filtered matrix, and the empirical p-value is shown below.

b. Comparing theoretical p-values to empirical p-values (log scale). We found fairly good agreement between theoretical p-values and empirical p-values calculated from the control arrays shown in (a).

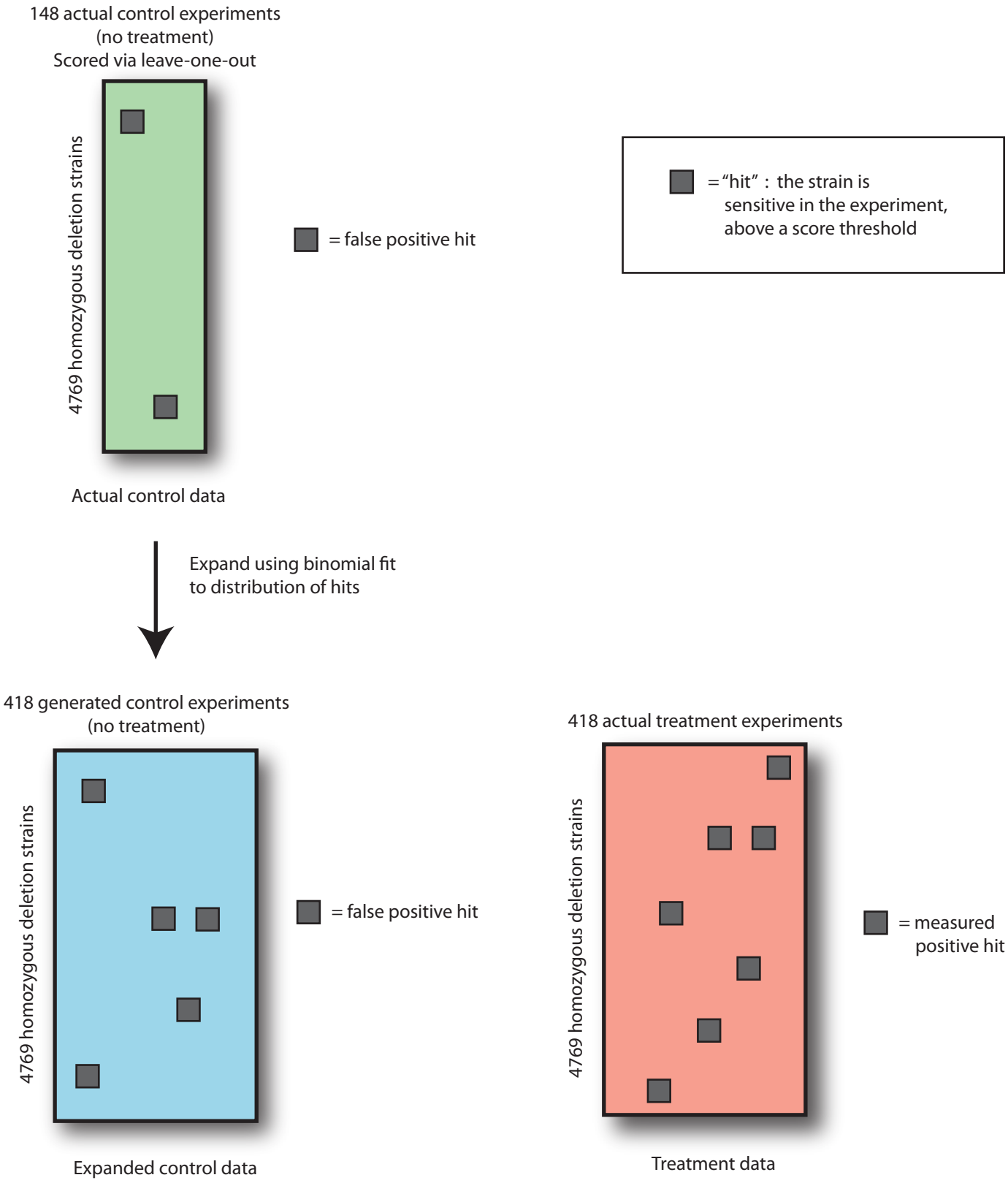


Figure S8. Calculating the empirical p-value and False Discovery Rate (FDR), using an expanded control set.

First we considered the148 homozygous control experiments (green matrix) that were scored as described in Fig. S7 and Materials and Methods. We expanded this into a set of 418 simulated controls (blue matrix) by fitting a binomial distribution to the number of experiments perturbing each gene deletion strain (Fig. S2). Finally, we compared the treatments (peach matrix) to the size-matched controls (blue), both of which had 418 experiments, and asked how many experiments perturbed each strain in the treatments, and in the controls. From this comparison, we can compute an FDR as the number of strains perturbed in the controls, divided by the number of strains perturbed in the treatments.

(The colors of these matrices match those used in Fig. S2.)

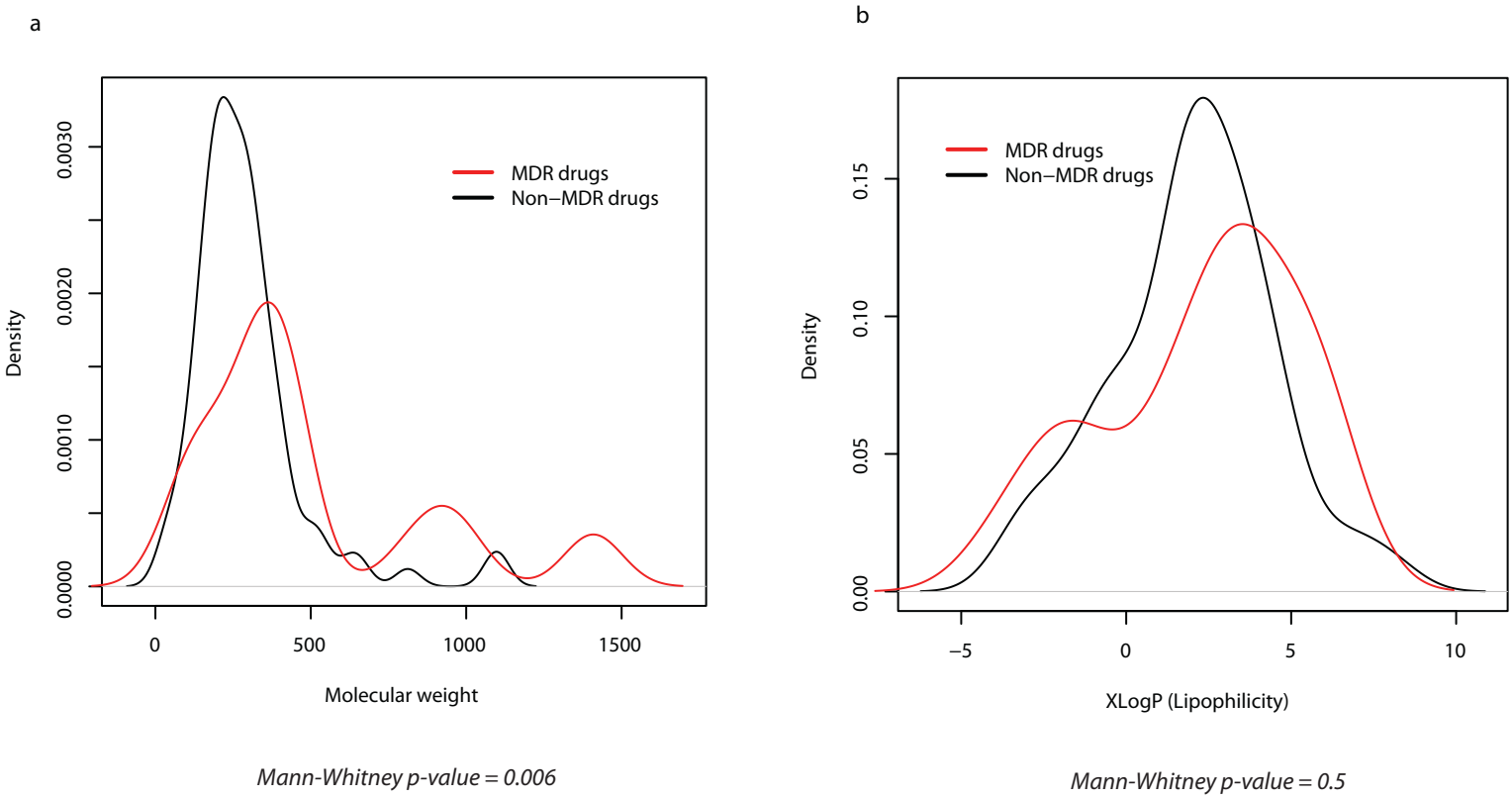


Figure S9. Distributions of molecular weight and XLogP of compounds inhibiting MDR gene deletion strains.

a. The distributions of molecular weights for MDR drugs (red) and non-MDR drugs (black). MDR drugs are significantly heavier than non-MDR drugs.

b. The distributions of XLogP values for MDR drugs (red) and non-MDR drugs (black) followed a bimodal distribution, suggesting that there may be two types of compounds that inhibit MDR gene deletion strains.

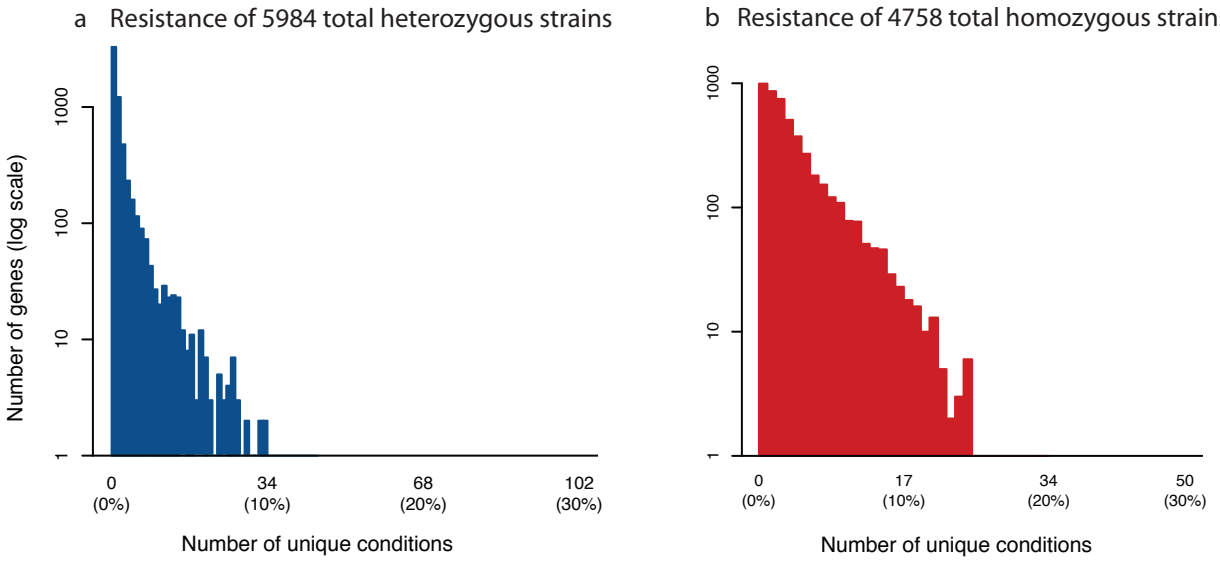


Figure S10. Number of conditions causing resistance.

The number of (a) heterogyzous and (b) homozygous deletion strains resistant in the given number/percent of conditions.

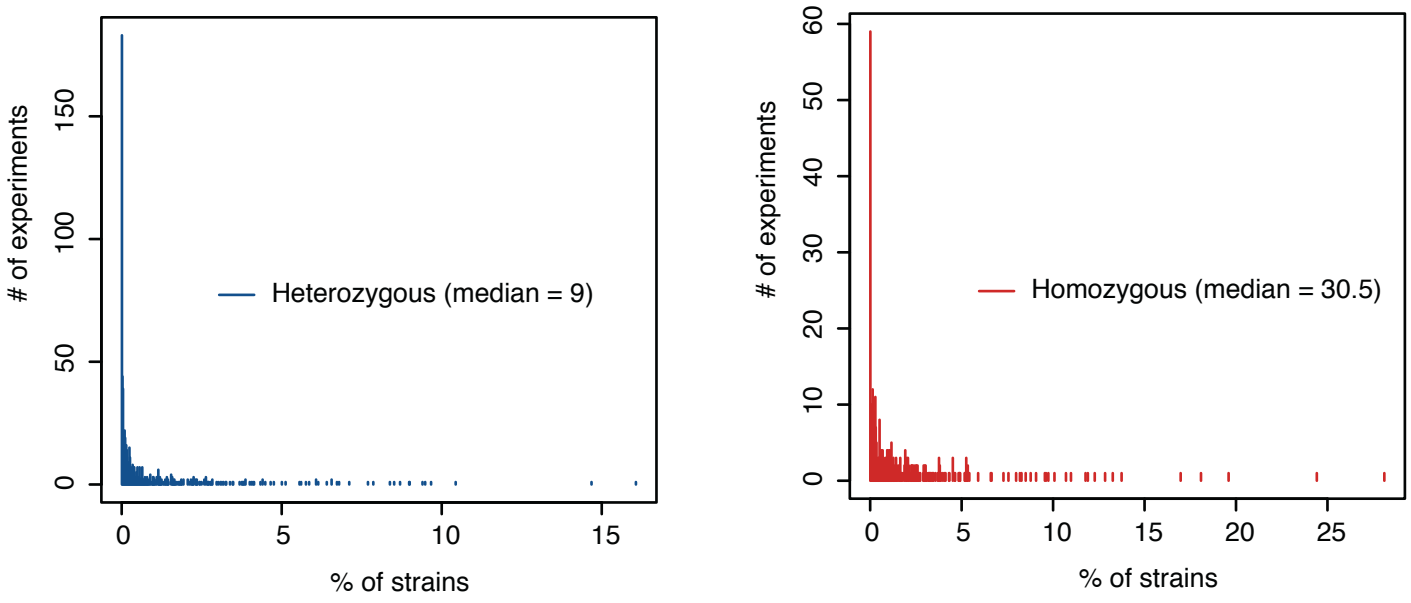


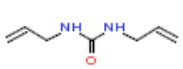
Figure S11. Percent of genes inhibited per experiment, at p < 1e-5. The x-axis is the percent of gene deletion strains inhibited, and the y-axis is the number of experiments inhibiting that number of deletion strains. Few experiments inhibit more than 5% of strains, but there are a few noisy experiments that inhibit many strains.

4. Supporting tables

	Category	Conditions
Environmental stress	amino acid dropout	adenine dropout, arginine dropout, isoleucine dropout, lysine dropout, threonine dropout, tryptophan dropout, tyrosine dropout
	high pH	pH7.5, pH8
	media change	YP glycerol, minimal media, sorbitol, synthetic complete
	radiation	no drug irradiated
	temperature change	20 degrees C, 23 degrees C, 25 degrees C, 37 degrees C
	vitamin dropout	PABA drop-out, biotin partial drop-out, calcium pantothenate partial drop-out, folic acid drop-out, inositol drop-out, niacin drop-out, pyridoxine HCl partial drop-out, thiamine HCl drop-out, vitamin drop-out control media
Small molecules	alkylating	4NQO, BCNU, MMS, angelicin, angelicin irradiated, busulfan, carmustine, chlorambucil, mechlorethamine, melphalan, mitomycin c, psoralen, psoralen irradiated, semustine, streptozotocin, thio-tepa, thiotepa, trichlormethine
	anesthetic	droperidol, dyclonine, oxethazine
	antibacterial	acriflavinium hydrochloride, aklavin hydrochloride, ansamitocin, bithionol, borrelidin, bostrycoidin, calvatic acid, cinerubin, clofoctol, dianemycin, hygromycin, meclocycline sulfosalicylate, merbromin, metampicillin, nitromide, paromomycin sulfate, piromidic acid, rutilantin,
	antifungal	5-fluorocytosine, amphotericin B, aureobasidin A, berberine chloride, caspofungin, chloroacetoxyquinoline, ciclopirox olamine, clotrimazole, cloxyquin, econazole, econazole nitrate, exalamide, fenpropimorph, fluconazole, hexetidine, itraconazole, ketoconazole, lipoxamycin, miconazole, nocodazole, nystatin, pyrithione zinc, sulconazole nitrate, terbinafine, thiabendazole,
	antihelminthic	carbendazine, fenbendazole, mebendazole
	antihistamine	ethaverine hydrochloride, meclizine hydrochloride, pimethixene maleate, promethazine hydrochloride, trimeprazine tartrate
	antihypertensive	fendiline hydrochloride, nicardipine hydrochloride, nitrendipine, phenoxybenzamine hydrochloride, prazosin hydrochloride, protoveratrine B, reserpine
	antiinflammatory	RIL1 (Biomol), aminophenazone, beclomethasone dipropionate, bufexamac, curcumin, dichlofenac sodium, diflunisal, embelin, fenbufen, fenoprofen, flufenamic acid, glafenine, mefenamic acid, niflumic acid, parthenolide, piperine, sodium meclofenamate, suxibuzone, tolfenamic acid
	antimalarial	lapachol, pyrimethamine, quinacrine hydrochloride, tetrandrine
	antimetabolite	5-fluorouracil, bleomycin, cytarabine, methotrexate
	antineoplastic	1,3-diallylurea, 5-fluorouridine, aclacinomycin A, aminopterin, amsacrine, bouvardin, bruceantin, carboplatin, cisplatin, daunorubicin, doxorubicin, formestane, idarubicin, indirubin, methoxsalen, mitotane, mitoxanthrone, mitoxanthrone hydrochloride, motuporamine, nimustine, oxaliplatin, paclitaxel, podophyllotoxin, solasodine, teniposide
	antioxidant	allyl disulfide, allyl sulfide, ethoxyquin, ferulic acid, potassium disulfite, resveratrol
	antiparkinson	L-dopa, benztropine, bromocriptine mesylate
	antiviral	brefeldin A, distamycin A, filipin, floxuridine, helenine, papuamide B, tunicamycin, usnic acid,
	chelating	4-isopropyltropolone, dimercaptopropanol, phenanthroline monohydrochloride, thujaplicin alpha
	cytoskeleton inhibitor	benomyl, citrinin, colchicine, latrunculin, monastrol, rhizoxin, wiskostatin
	diuretic	spironolactone, triamterene
	double drug	5-fluorocytosine and amphotericin B, 5-fluorocytosine and fluconazole, 5-fluorocytosine and itraconazole, 5-fluorocytosine and ketoconazole, 5-fluorouracil and leucovorin, 5-fluorouracil and methotrexate, LiCl and fk506, NaCl and fk506, amphotericin B and fluconazole, amphotericin B and itraconazole, methotrexate and leucovorin, pH7.5 and fk506
	enzyme inhibitor	RO 106-9920 (Calbio), caracemide, dicumarol, lawsone, mycophenolic acid, perillic acid, proadifen hydrochloride, sirtinol, splitomicin, telomerase inhibitor ix (Biomol), trichostatin A
	flavanoid	biochanin A, chrysin, dihydroxyflavone, ipriflavone, naringenin, nerol, osajin, phloretin, quercetin, xanthohumol
	hormone	bathophenanthroline disulfonate, bisphenol, estradiol, estradiol acetate, estradiol diacetate, estradiol propionate, estrone acetate, hexestrol, methoxyvone, progesterone
	immunosuppressant	FK506, lefunamide, myriocin, rapamycin
	insecticide	benzyl benzoate, dieldrin, phenothrin
	ionic	CdCl2, CoCl2, CuSO4, FeCl4, HgCl2, LiCl, MnCl2, NaCl, NaF, ZnCl2, sodium arsenite
	kinase inhibitor	AG 1387 (Biomol), AG 1478 (Biomol), AG 957 (Biomol), DNA protein kinase inhibitor, PP2, bay 11-7082, damnacanthal, emodin, staurosporine, terreic acid, tyrphostin, wortmannin
	laxative	bisacodyl, danthron, phenolphthalein
	lipid modifying	atorvastatin, benfluorex hydrochloride, fenofibrate, lovastatin, probucol, ursodiol
	nucleic acid synthesis inhibitor	aphidicolin glycinate, camptothecin, coralyne, hydroxyurea, juglone, nalidixic acid, novobiocin,
	other	1,7-octadiene, 1,8-nonadiene, 4,6-dichloroindole-2-carboxylic acid, 2-cyanoethyl acrylate, BCS, CID 144303, CID 403818, CID 604586, CID 621889, CID 622648, CID 630688, CID 632839, CID 652287, CID 678146, CID 683517, CID 688028, CID 693573, CID 693632, CID 697443, DMAEC, DMSO 1%, DMSO 2%, DMSO 4%, chemical diversity labs 14a, chemical diversity labs 14f, chemical diversity labs 1c10, chemical diversity labs 218, chemical diversity labs 232, chemical diversity labs 246, chemical diversity labs 275, chemical diversity labs 3f2, chemical diversity labs 41, chemical diversity labs 6842, chloroxine, citropten, cyclamin, dimethylellipticinium, gossypol, mecysteine hydrochloride, mitomycin c, nsc95397, parkinson-
	oxidative stress	H2O2, K2Cr2O7, MPP+, nitric oxide, paraquat, rotenone
	phosphatase inhibitor	PP1, calyculin A, cantharidin, cantharidin analog, cantharidin disodium, endothall, norcantharidin, phosphatase inhibitor, ptp2
	protein synthesis inhibitor	anisomycin, bromhexine hydrochloride, cycloheximide, neomycin sulfate, streptovitacin, zaluzanin
	psychoactive	adenophostin A, alverine citrate, amitriptyline hydrochloride, amoxepine, caffeine, chlorzoxazone, clozapine, domperidone, drofenine hydrochloride, flunarizine hydrochloride, haloperidol, metergoline, paroxetine hydrochloride, pimpinellin, piperidolate hydrochloride, promazine hydrochloride, propiomazine maleate, trifluoperazine dihydrochloride
	reagent	acetic acid, alizarin, aminacrine, azobenzene, benzaldehyde, fusarubin
	vitamin	PABA, leucovorin, menadione epoxide, vitamin K3

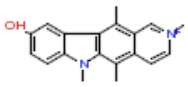
Table S1. Experiments performed. Categories are divided into environmental stress (top) and small molecules (bottom). Category names are on the left, and conditions within each category are on the right. Small molecule categories are based on pharmacological action and indication for use.

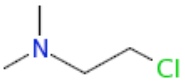
Table S2. 316 compounds tested in this study for which the chemical structures were available. Not included are non-compound experiments such as environmental stresses and compounds for which the chemical structure was not known or unavailable.

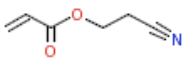

1,3-diallylurea

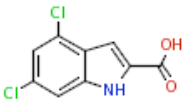

1,7-octadiene

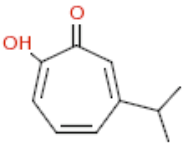

1,8-nonadiene


2,6-Dmhe


2-Dimethylaminoethyl chloride


2-cyanoethyl acrylate


4,6-dichloroindole-2-carboxylic acid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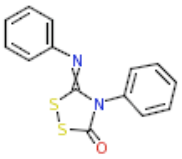
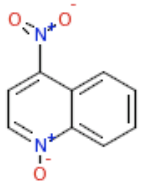
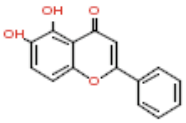

403818 nci


4nqo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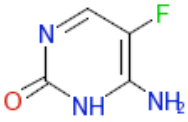
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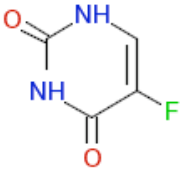
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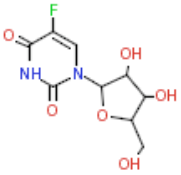
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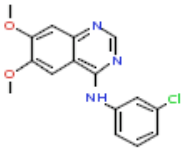
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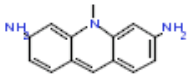
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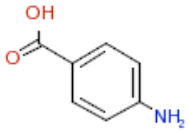
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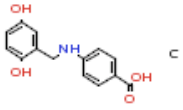
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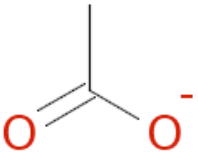
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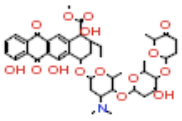
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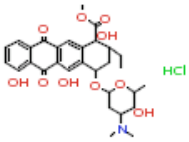
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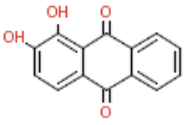
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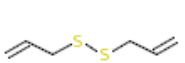
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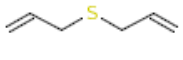
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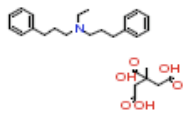
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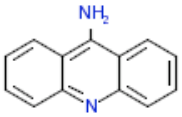
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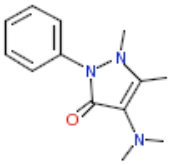
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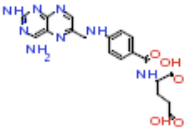
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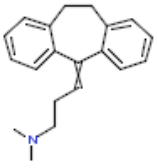
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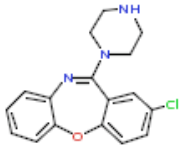
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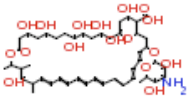
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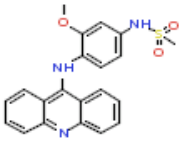
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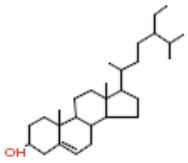
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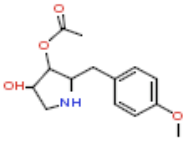
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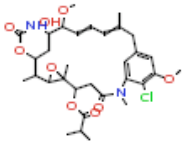
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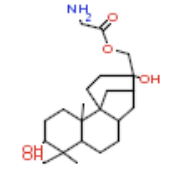
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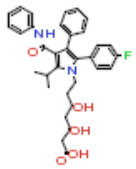
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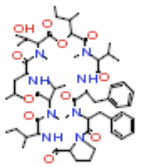
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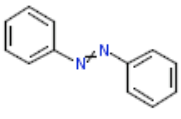
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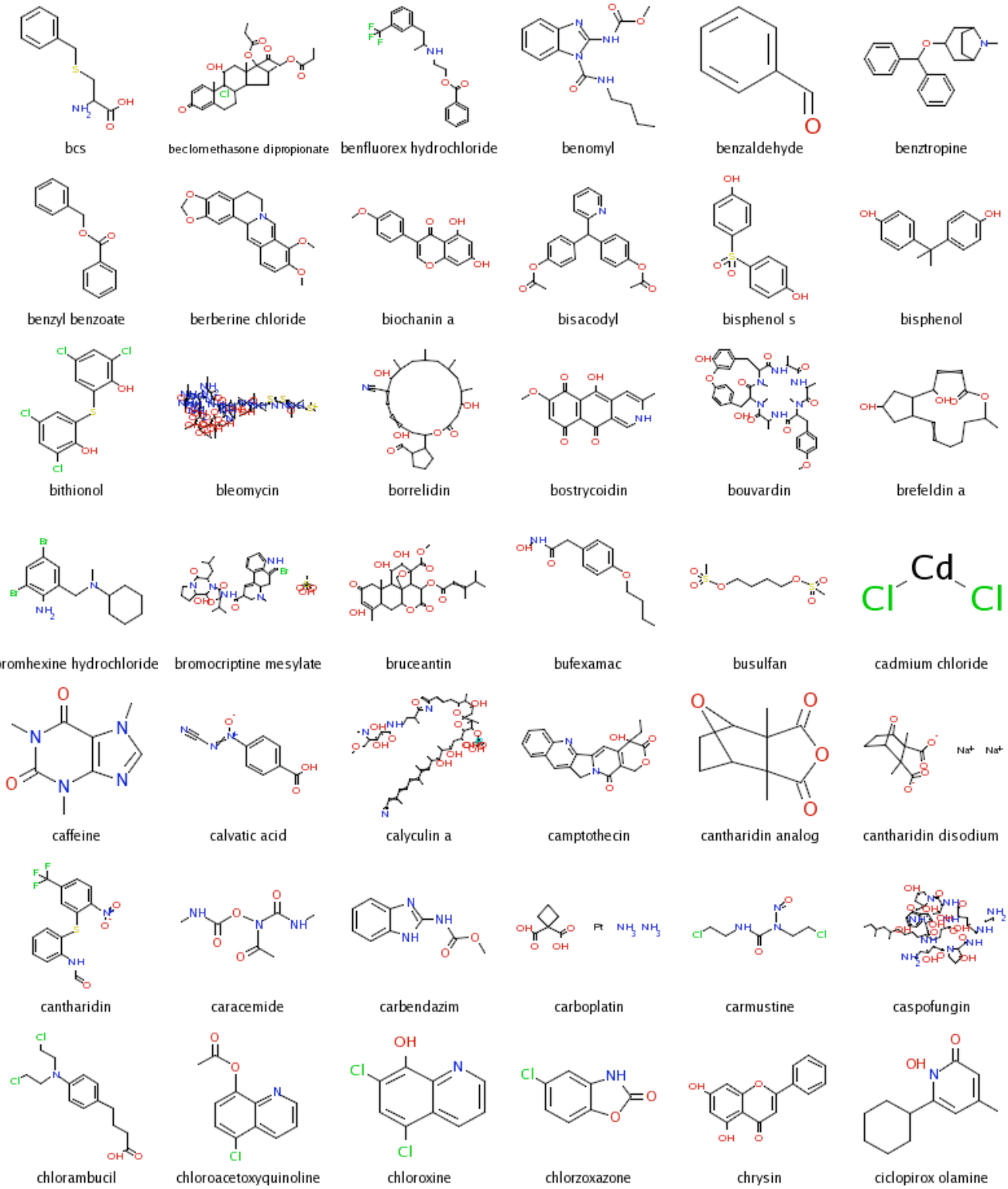

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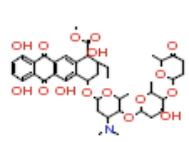
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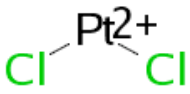
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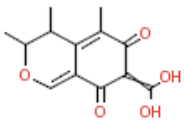
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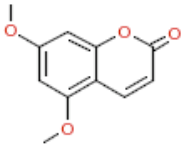
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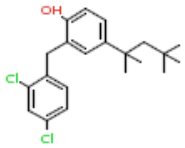
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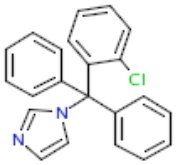
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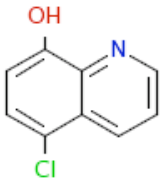
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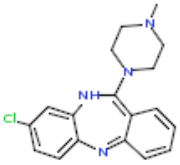
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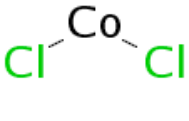
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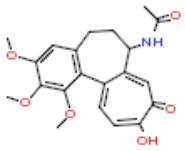
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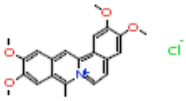
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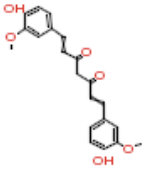
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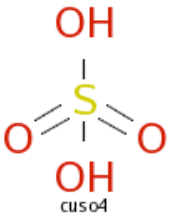
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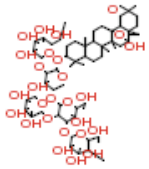
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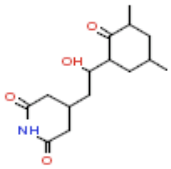
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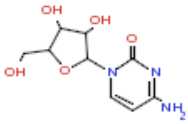
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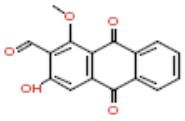
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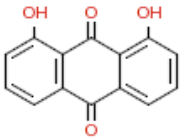
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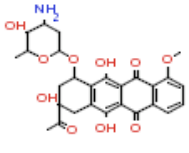
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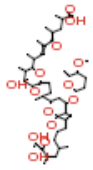
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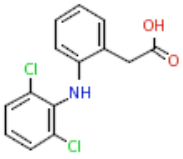
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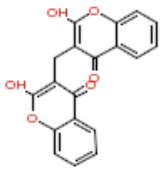
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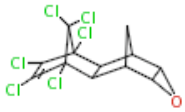
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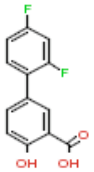
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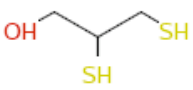
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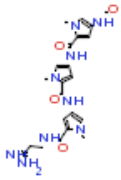
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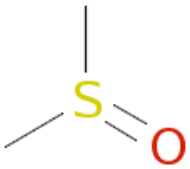
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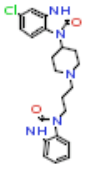
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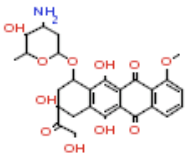
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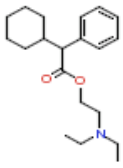
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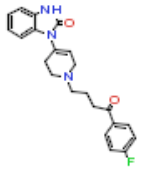
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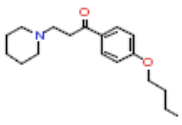
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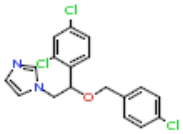
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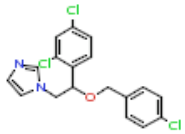
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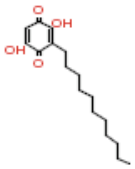
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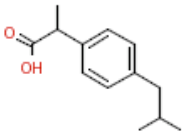
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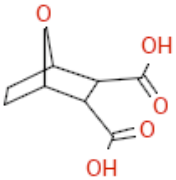
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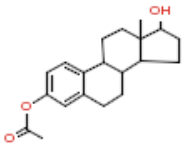
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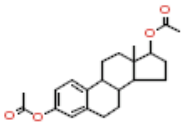
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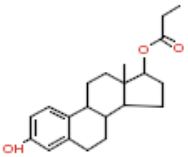
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estradiol

estrone acetate

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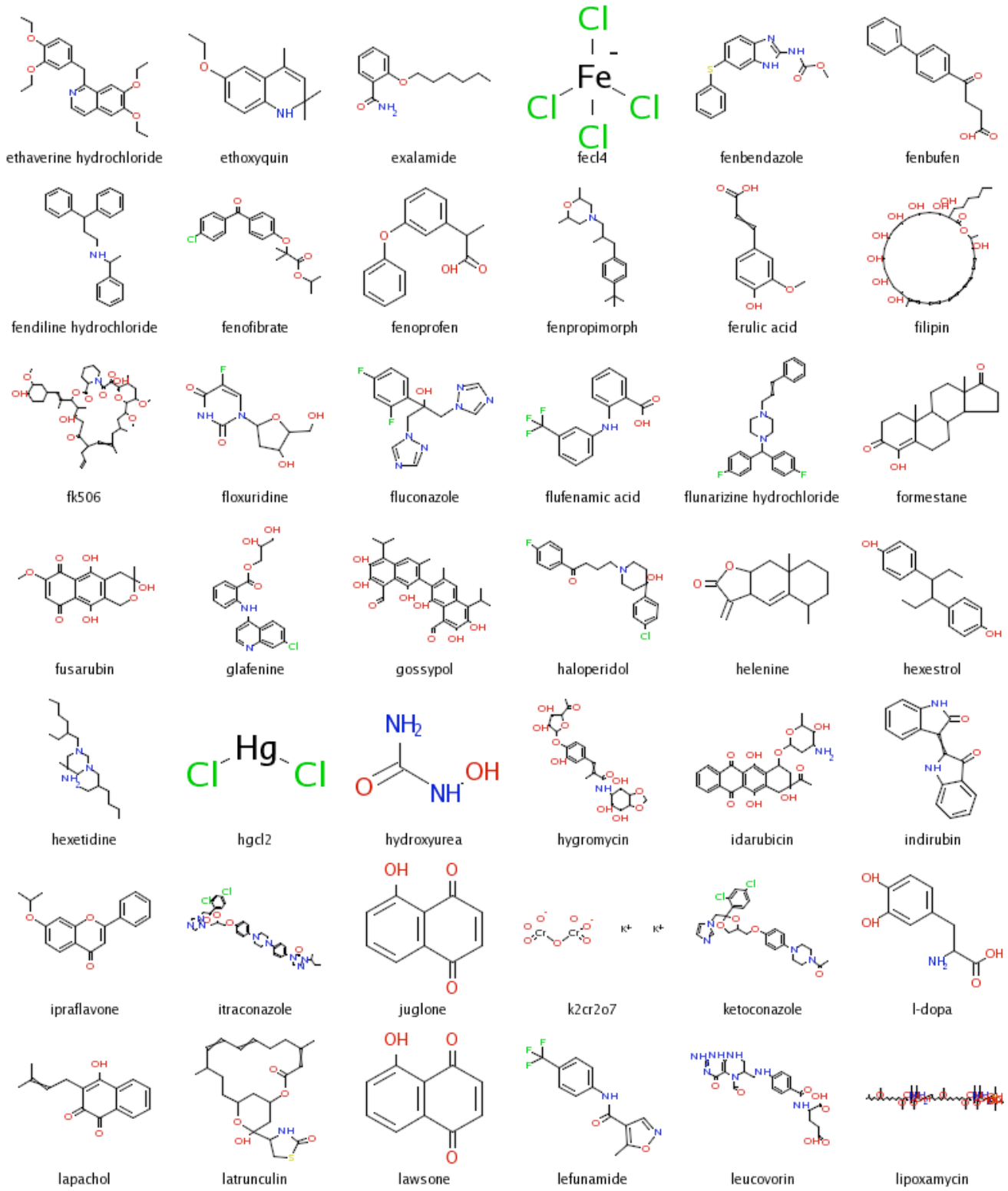

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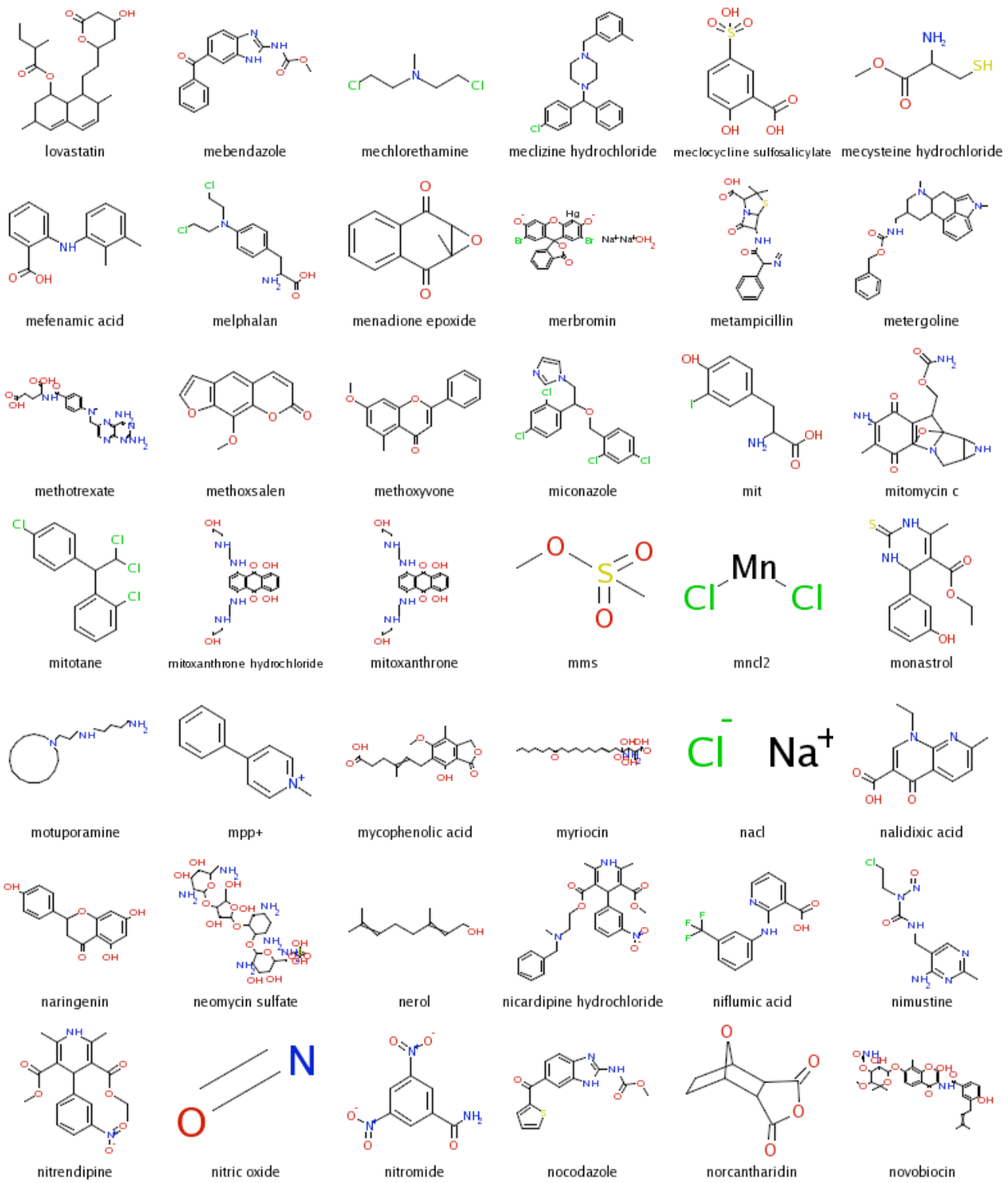

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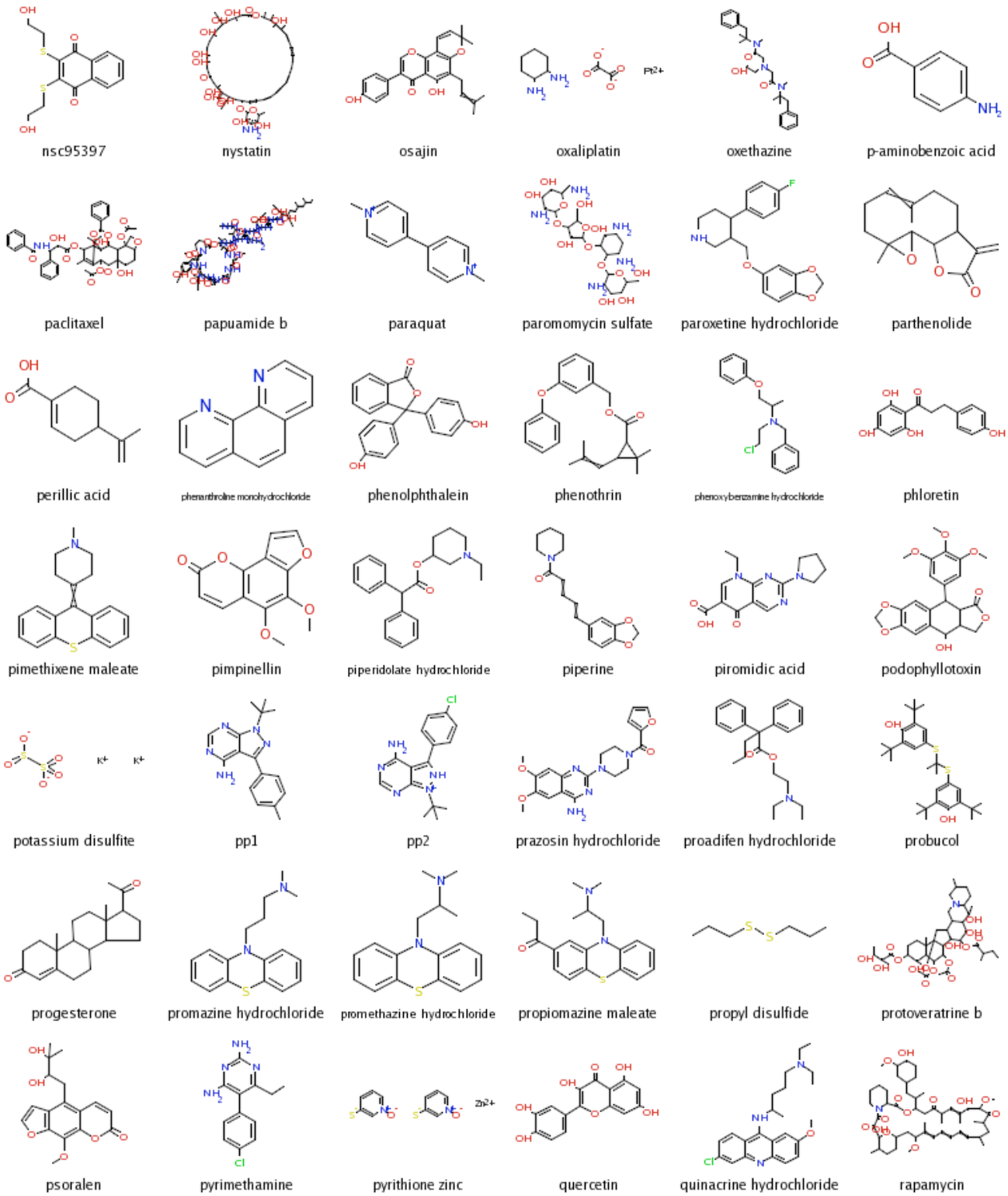

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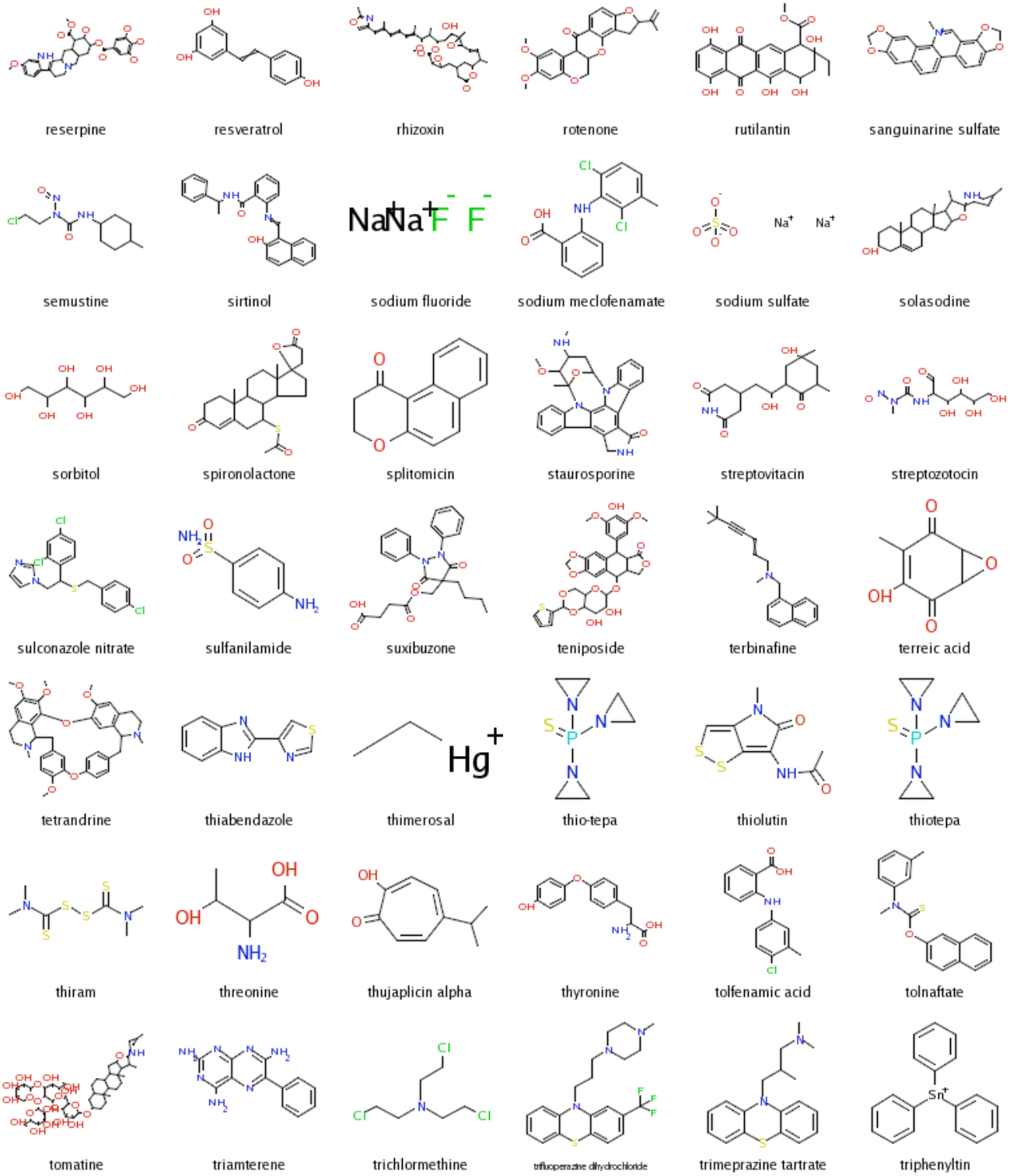

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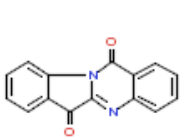

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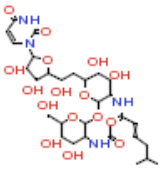

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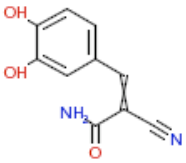

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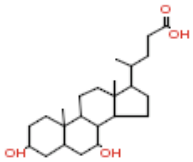

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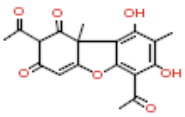

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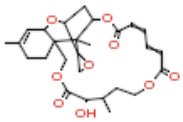

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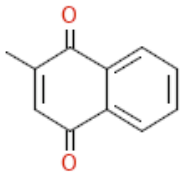

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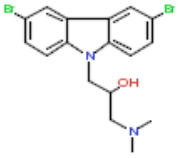

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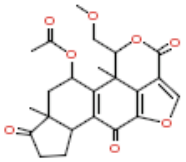

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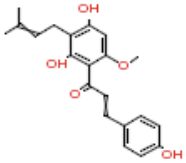

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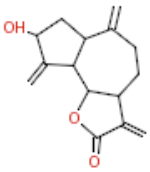

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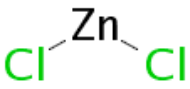

zncl2

Condition	Number of MDR strains inhibited	Molecular weight	XLogP (partition coefficient, or hydrophobicity)
rapamycin	252	914.172	5.773
wiskostatin	225	426.146	3.985
mitomycin c	212	334.327	-2.347
LiCl, fk506	204	na	na
fk506, NaCl	180	na	na
latrunculin	174	421.551	3.228
ZnCl2	171	136.295	na
methotrexate	163	454.44	-1.433
hydroxyurea	162	76.0547	-1.432
LiCl	162	na	na
fk506	160	804.018	3.534
synthetic minimal media	159	na	na
MnCl2	156	na	na
allyl disulfide	152	146.276	3.176
oxaliplatin	152	397.286	na
nocodazole	151	301.322	2.654
complete minimal media	150	na	na
nystatin	149	926.095	0.585
cadium chloride	149	na	na
calyculin a	145	1009.17	1.913
NaCl	144	na	na
bleomycin	143	1415.56	na
pH8	143	na	na
papuamide b	140	1402.59	-3.706
cisplatin	131	300.045	na
paraquat	131	408.449	na
pH7.5	130	na	na
synthetic complete	125	na	na
CoCl2	124	98.9155	1.477
miconazole	121	416.127	6.02
lovastatin	117	404.54	4
CuSO4	116	161.625	na
minimal media	115	na	na
ptp2	115	na	na
clotrimazole	114	344.837	5.98
NaAsO2	111	na	na
HgCl2	105	271.495	na
1,7-octadiene	102	na	na

Table S3. Compounds inhibiting gene deletion strains defined as MDR. Conditions that inhibited the greatest number of homozygous MDR strains, along with their molecular weight and XLogP, a measure of hydrophobicity.

5. Supporting references

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