**Supplemental Figure 1. Over- and underrepresentation of phenotype genes in Gene Ontology categories**

Proportions of lethal, non-lethal, and undocumented genes present in (A) biological processes, (B) molecular functions, or (C) cellular component categories. Only categories that have significantly over- or under-represented numbers of lethal genes relative to non-lethal genes are shown based on adjusted p-values of Fisher exact tests where *, **, and *** indicate $\alpha = 0.05$, 0.01, and 0.001, respectively. Categories in which lethal genes are underrepresented are indicated by a cyan background.
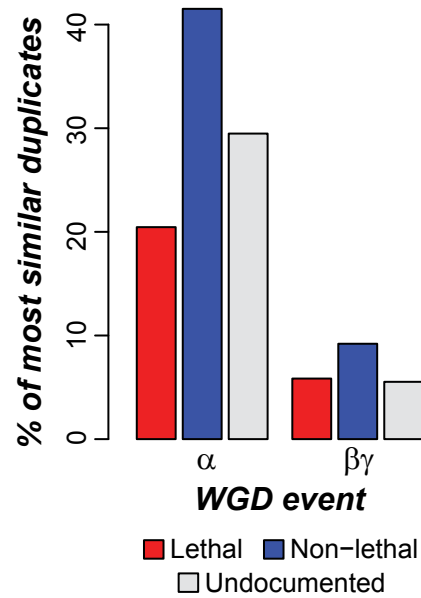
Supplemental Figure 2. Proportions of most similar paralogs produced in whole genome duplication events.

Proportion of lethal, non-lethal, and undocumented genes with close paralogs (most similar by BLASTP e-value) generated in the α or βγ WGD events.
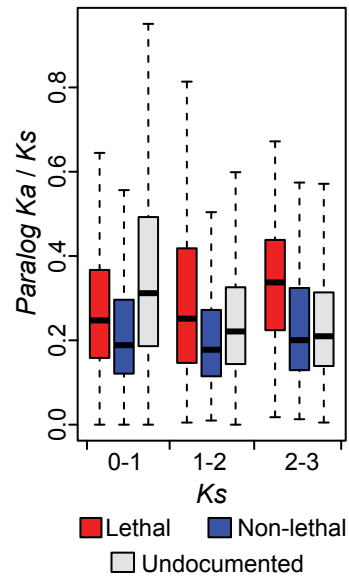
Supplemental Figure 3. Evolutionary rates between paralogs.

Box plots of *Ka*/*Ks* values between paralogous pairs of lethal, non-lethal, or undocumented genes. Gene pairs are non-exclusive with regard to phenotype category. Distributions of ratios are shown as they relate to the rate of synonymous substitutions (*Ks*) between a gene pair, where low *Ks* values indicate recent duplicates and high *Ks* values indicate older duplicates.
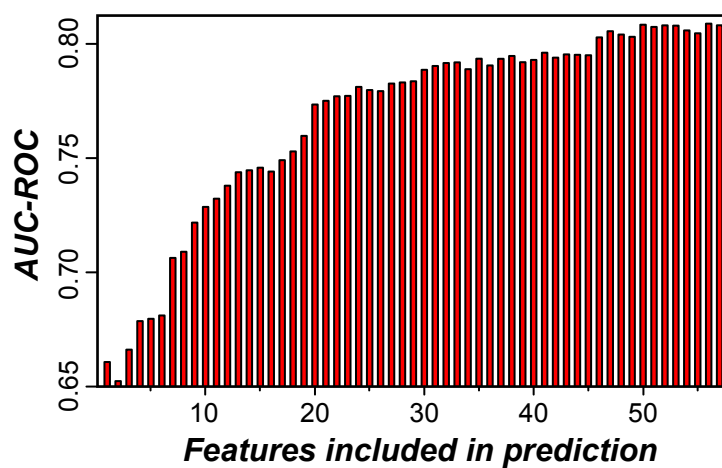
Supplemental Figure 4. Performance of essential gene predictions with increasing numbers of features.

AUC-ROCs of 57 Random Forest models using 1 to 57 features detailed in Table 1. Features were included in the order of highest-to-lowest absolute SVM weight.

1   **Supplemental Table 1. Sign, absolute weight, and rank of Support Vector Machine weights**

2   **for *A. thaliana* and *S. cerevisiae* features.**

Feature	Atha sign[1]	Atha weight[1]	Atha rank	Scer sign[1]	Scer weight[1]	Scer rank	Signs agree
Coexpression module size	+	0.9823	1	+	0.3662	20	yes
Core eukaryotic gene	+	0.5404	7	+	0.8895	6	yes
Expression variation	-	0.0321	35	-	0.2745	22	yes
Gene network interaction	+	0.5766	6	+	0.6367	12	yes
GOslim C Extracellular region	-	0.1828	27	-	0.7235	11	yes
GOslim C Mitochondrion	+	0.6244	4	-	0.0727	35	no
GOslim C Nucleolus	+	0.195	26	+	0.9202	5	yes
GOslim C Nucleoplasm	+	0.3	14	+	0.3767	19	yes
GOslim C Nucleus	-	0.1953	25	+	0.7825	9	no
GOslim C Plasma membrane	-	0.1315	30	+	0.3406	21	no
GOslim F Kinase activity	-	0.2966	15	+	0.2674	23	no
GOslim F Lipid binding	-	0.2	23	+	0.2107	27	no
GOslim F Nucleotide binding	+	0.0539	34	+	0.592	14	yes
GOslim F Protein binding	-	0.1619	28	+	0.1586	32	no
GOslim F Sequence-specific DNA binding transcription factor activity	-	0.2509	17	-	0.6155	13	yes
GOslim F Signal transducer activity	-	0.2	24	+	0.7657	10	no
GOslim P Cell communication	-	0.3	13	-	0.2115	26	yes
GOslim P Cell cycle	+	0.2808	16	+	0.8246	8	yes
GOslim P Cell death	-	0.1305	31	-	0.1006	34	yes
GOslim P Cellular component organization	+	0.2337	18	+	0.5538	15	yes
GOslim P Metabolic process	+	0.0777	33	-	0.1736	30	no
GOslim P Nucleobase-containing compound metabolic process	+	0.135	29	+	0.1748	29	yes
GOslim P Regulation of gene expression, epigenetic	-	0.2252	21	-	0.9479	4	yes
GOslim P Reproduction	+	0.4421	9	-	1.2043	2	no
GOslim P Response to abiotic stimulus	-	0.3578	11	-	1.1569	3	yes
GOslim P Response to biotic stimulus	-	0.3827	10	+	0.5	16	no
GOslim P Response to endogenous stimulus	-	0.1054	32	+	0.5	17	no
GOslim P Signal transduction	-	0.2259	20	-	0.2613	24	yes
GOslim P Translation	+	0.4995	8	-	0.1618	31	no
Median expression	+	0.3273	12	+	1.4755	1	yes
Number of protein domains	+	0.0296	36	-	0.1034	33	no
Paralog Ka/Ks	+	0.6081	5	+	0.8728	7	yes
Paralog Ks	-	0.2172	22	+	0.4232	18	no
Percent ID	-	0.9598	2	-	0.2095	28	yes
Protein length	+	0.227	19	-	0.0232	36	no
Single copy	+	0.8883	3	+	0.2251	25	yes

3

4   1. Sign and absolute weight of features given by Support Vector Machine analysis. Sign indicates the relationship between a

5   feature a lethality (a positive weight is related to phenotype lethality while a negative weight is related to non-lethality) and

6   weight indicates the importance of a feature to essential gene predictions, where a higher weight indicates greater importance.

1