

SUPPLEMENTARY LEGENDS

Supplementary Table S1: The orthology between yeast and human genes from InParanoid7 (Ostlund et al. 2010) has been listed in this table. The information is arranged in 4 columns: Yeast ORF, Yeast common, Human Ensembl ID, Human common. In case of where there are more than one paralog in an organism, all the genes are listed in the cell in a space delimited fashion.

Supplementary Table S2: This table contains significant genetic interactions for rpt1-1, a temperature sensitive allele of RPT1. The table has 6 columns: 1. Query systematic name (ORF) 2. Query standard name (Common name) 3. Array systematic name (ORF) 4. Array standard name (Common name) 5. Epsilon score (only those which are > 0.08 or < -0.08) 6. p-value (only significant ones: $pval < 0.05$).

Supplementary Table S3: This table contains information of all significant yeast synthetic sick or lethal interactions (Costanzo et al. 2010) between genes that are conserved in human based on InParanoid7 (Ostlund et al. 2010). The information is arranged in following order: Yeast gene names 1. ORF A 2. ORF B 3. Common name A 4. Common name B 5. Epsilon interaction score e (only $e < -0.08$ and associate p-value < 0.05 are reported) 6. Are genes in the interaction conserved in human? - Conserved or blank 7. Is any one of the genes in the interaction a cancer gene? - Cancer related or blank Human gene names (if both the genes in the interaction are conserved. In case of one-to-many or many-to-many orthology all human paralogs are listed.) 8. Ensembl ID A 9. Ensembl ID B 10. Common A 11. Common B.

Supplementary Table S4: This table contains filtered set of interactions between conserved genes that satisfy the following prioritization criteria: (i) $\epsilon < -0.2$ or $\epsilon < -0.08$ for both AB-BA interaction in cases where both have been screened. (see Methods - Processing yeast genetic interaction data) (ii) Only 1-1 orthologs are considered. The information is arranged the same order as Supplementary Table S3.

Supplementary Figure S1: Genetic interaction test results for all interactions tested for this study.

Each box contains the growth rate for single and double knock-downs for genes in the interaction we tested. Further, the double knockdown prediction from single knock-downs is also a bar in the plot. Statistically significant differences are indicated with 1, 2 or 3 asterisks: more asterisks refer to more significant synthetic sick/lethal interaction, as explained in the legend shown in panel. The red and green color of the asterisks refer to negative and positive genetic interactions respectively. The number of days the IMR90 fibroblast cells were grown in the presence of the shRNAs is indicated in each plot.