SUPPLEMENTARY INFORMATION

Archetypal transcriptional blocks underpin yeast gene regulation in response to changes in growth conditions

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Supplementary Figures in this file

Other files containing supporting information

S1 File. General description of data and clustering results.

S2 File. Matrix containing the log-fold changes for each experiment.

S3 File. Matrix containing the Pearson correlations between experiments.

S4 File. Matrix containing the Pearson correlations between RNAs.

S5 File. Alternative PSR clusters.

S6 File. In-detail description of PSRs analysed in the paper.

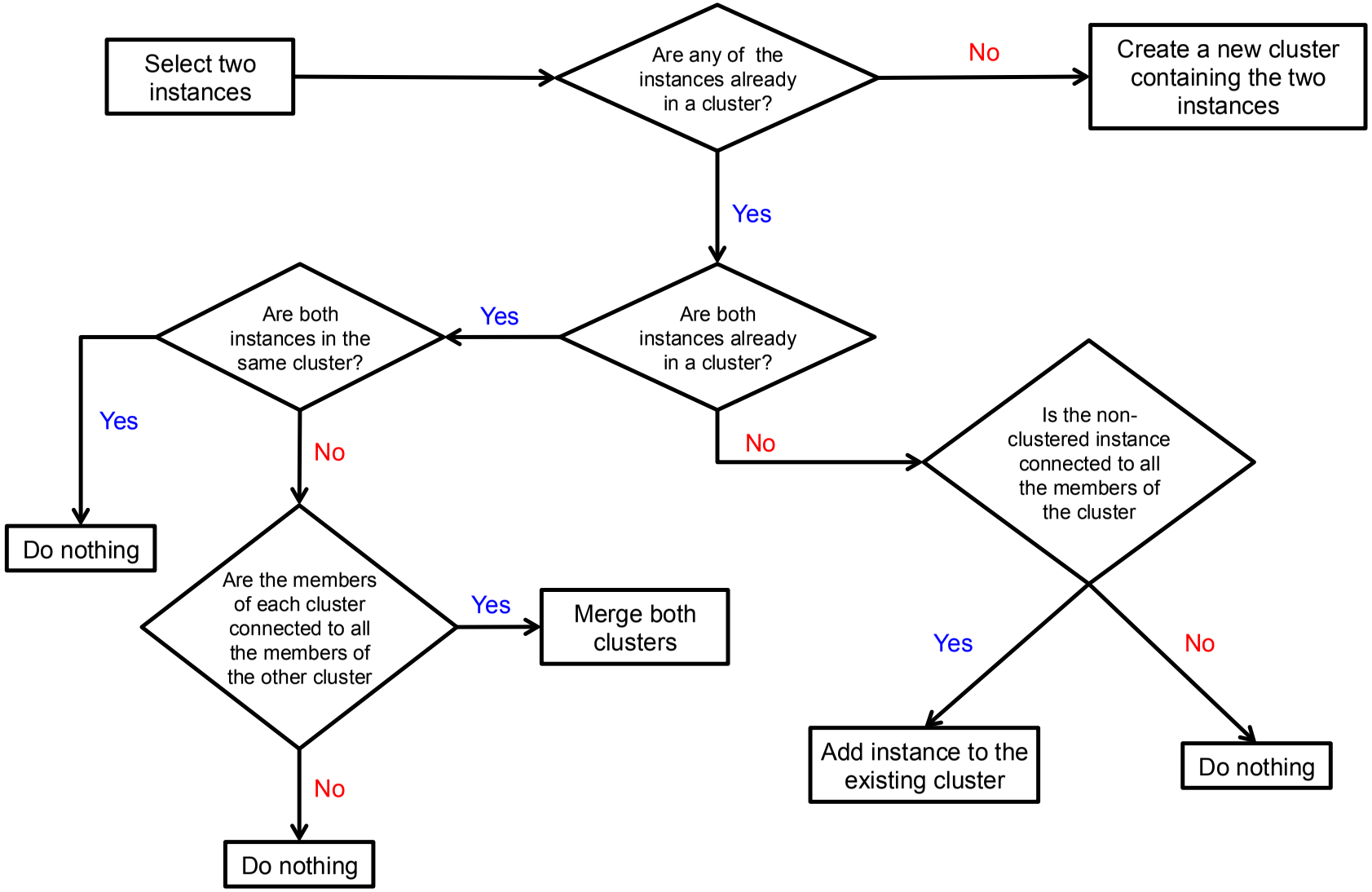
S7 File. Composition of PSR subsets analysed in the paper.

S8 File. Biological processes associated with subsets of PSRs.

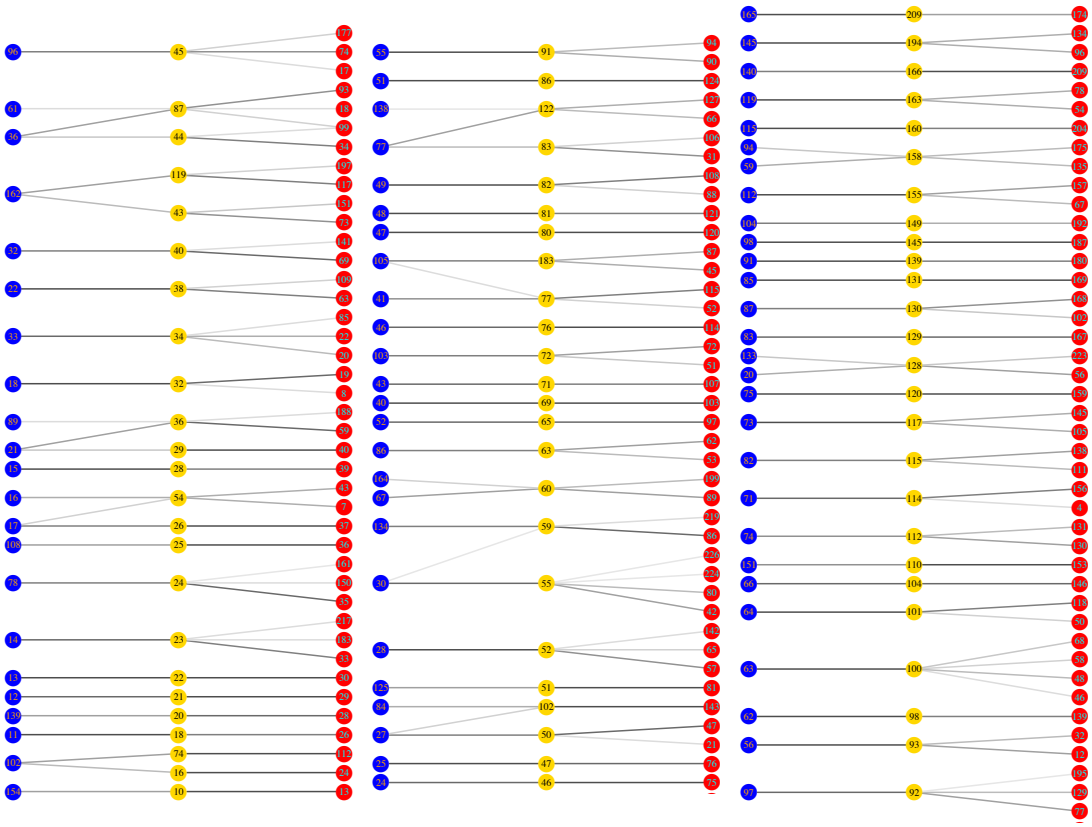
S9 File. Composition of BTRs analysed in the paper.

S10 File. Biological processes associated with BTRs.

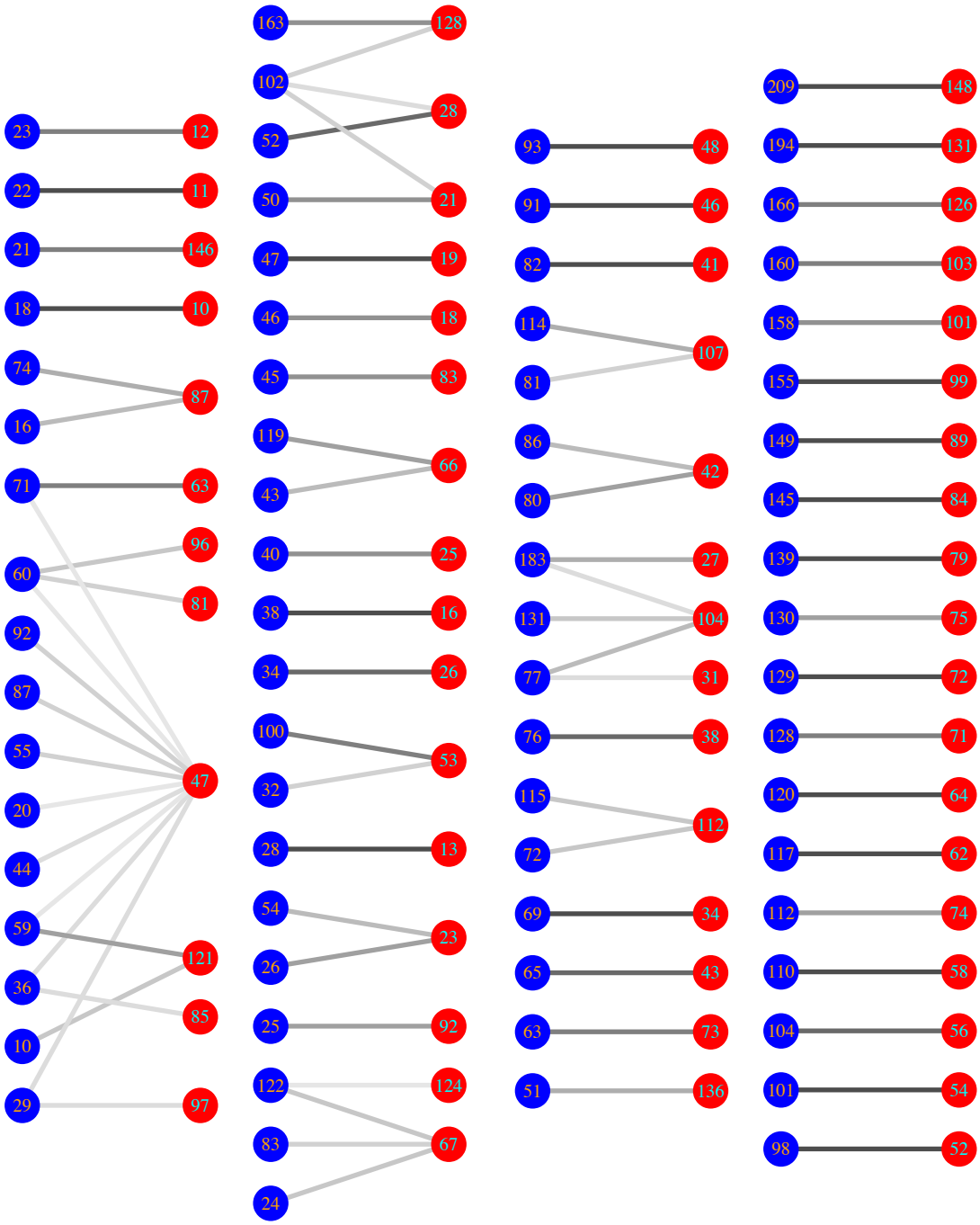
S11 File. edgeR results for NGS-based transcriptomic analyses.


Select two instances
Are any of the instances already in a cluster?
No
Create a new cluster containing the two instances
Yes
Are both instances already in a cluster?
Yes
Are both instances in the same cluster?
Yes
Do nothing
No
Are the members of each cluster connected to all the members of the other cluster
Yes
Merge both clusters
No
Do nothing
No
Is the non-clustered instance connected to all the members of the cluster
Yes
Add instance to the existing cluster
No
Do nothing

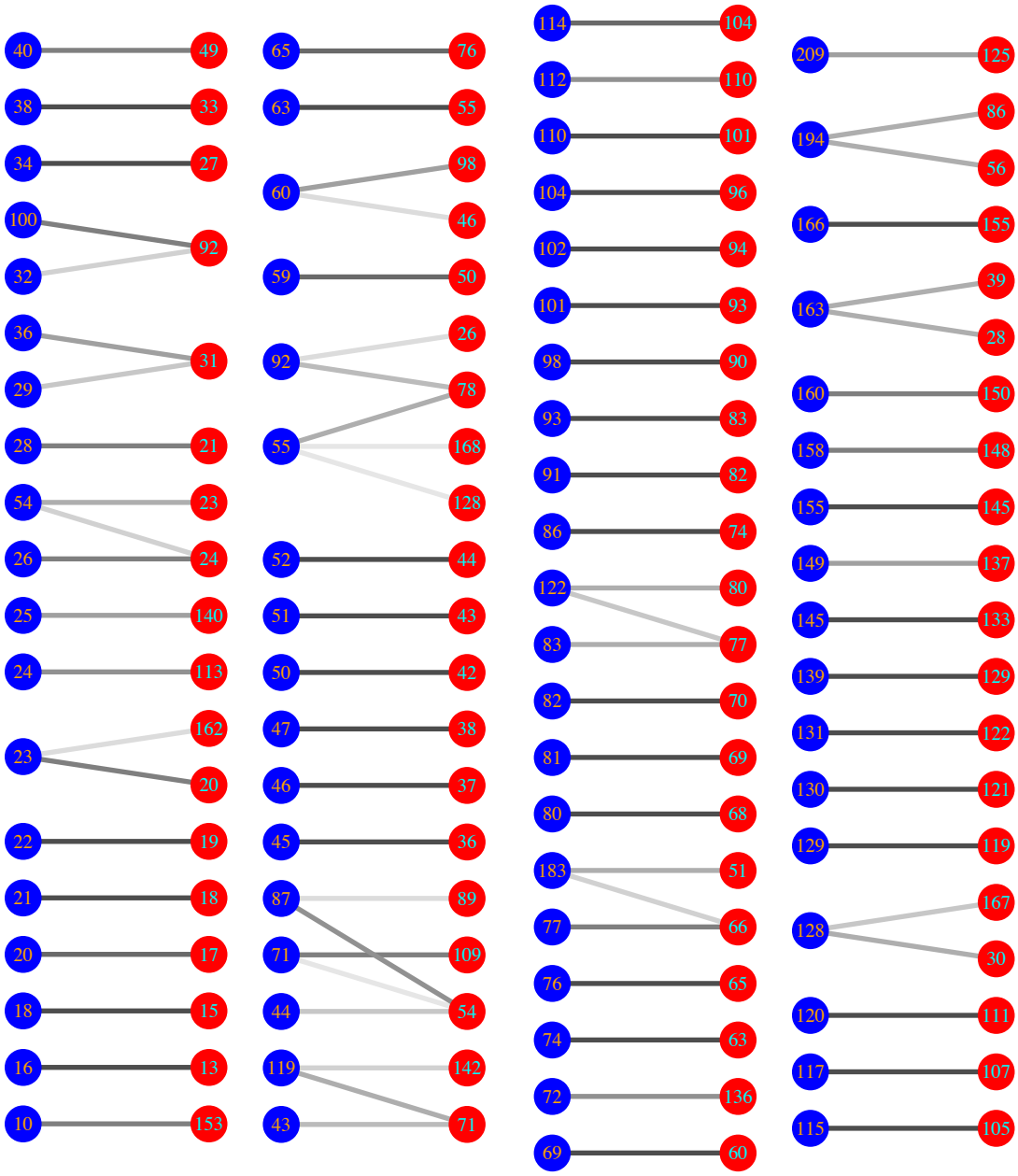
S1 Fig. Decision tree in the assignment of instances to new or existing clusters.



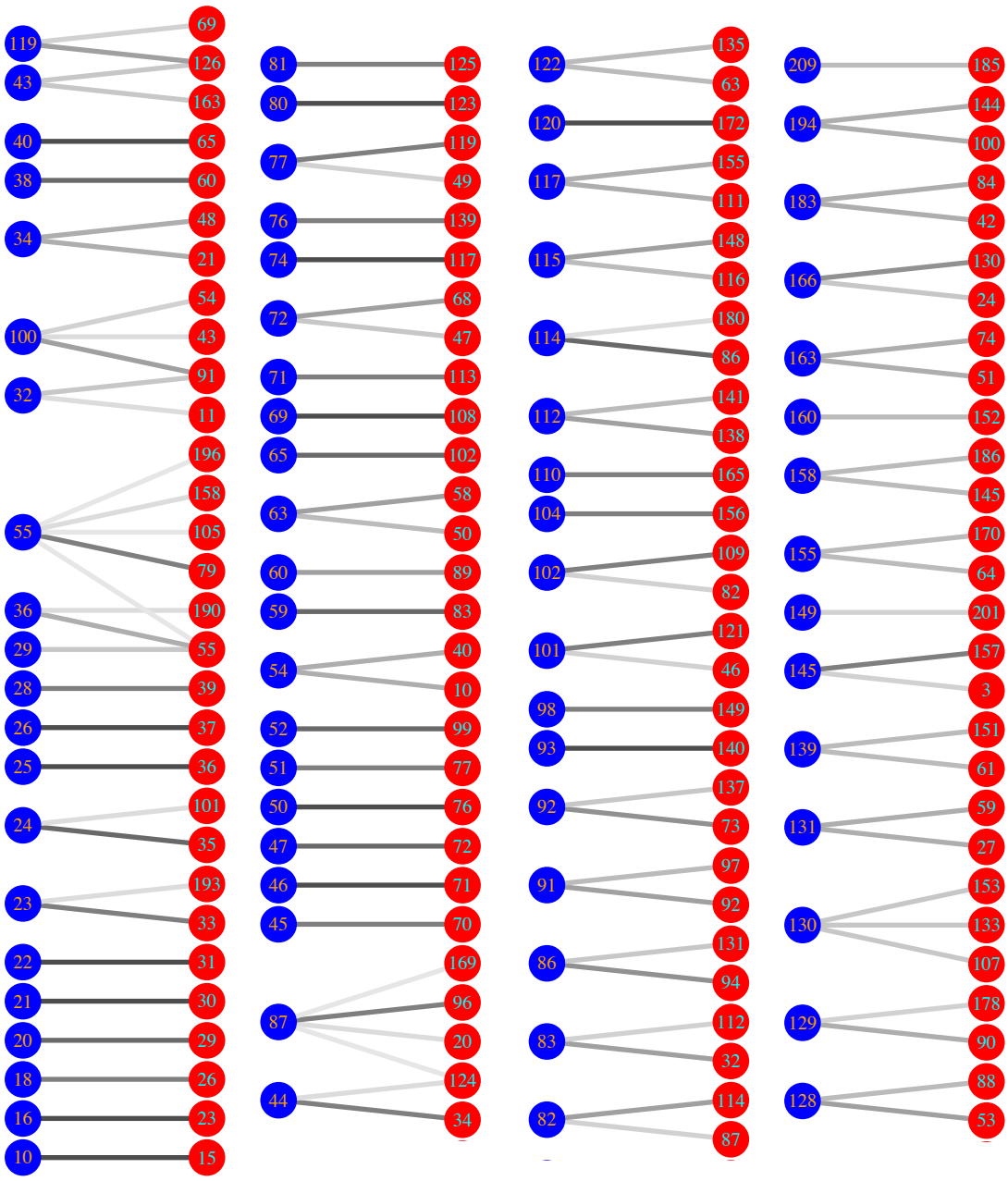
S2 Fig. Relationship between clusters if changing the correlation threshold. 0.4, in blue; 0.5, in yellow; 0.6 in red. The darkness of the lines represent the similarity of the clusters (Jaccard Index).



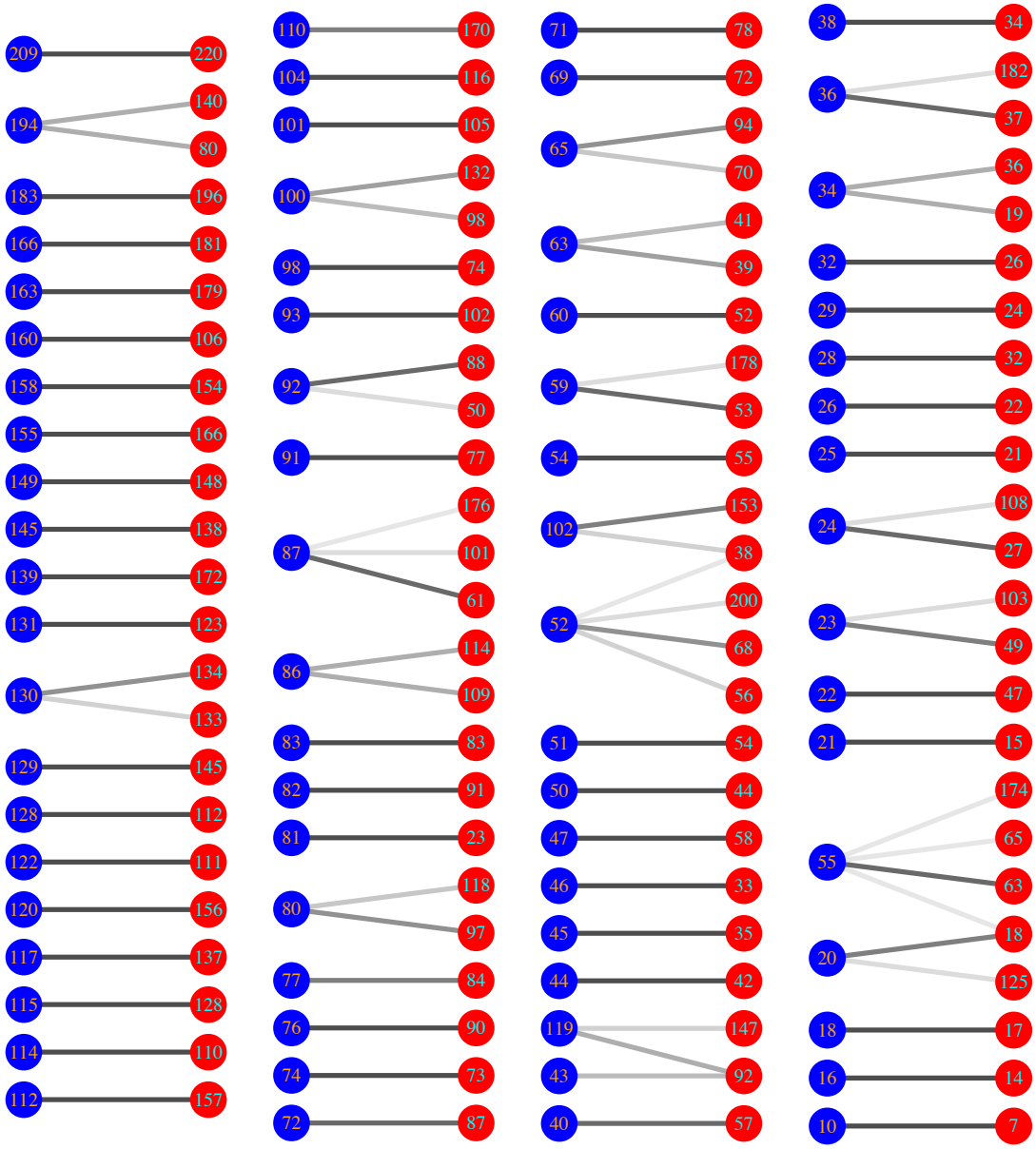
S3 Fig. Relationship between clusters if changing the linkage method. In red, the method described in the main text. In blue, clusters generated when requiring that new members do not decrease the mean of correlations beyond a particular threshold: 0.5 in this example. The darkness of the lines represent the similarity of the clusters (Jaccard Index).



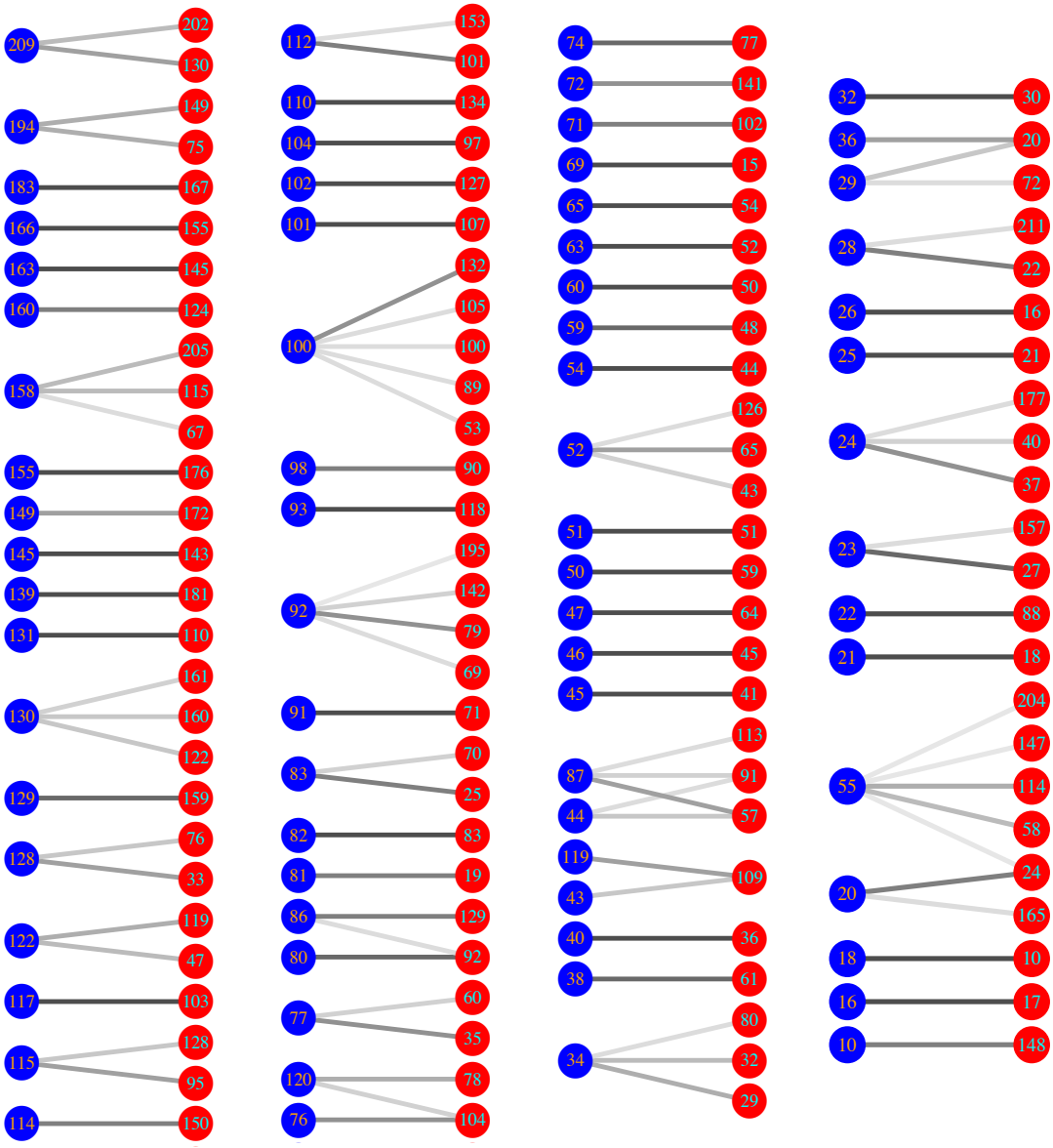
S4 Fig. Relationship between clusters if changing the linkage method. In red, the method described in the main text. In blue, clusters generated when requiring that new members do not decrease the mean of correlations beyond a particular threshold: 0.6 in this example. The darkness of the lines represent the similarity of the clusters (Jaccard Index).



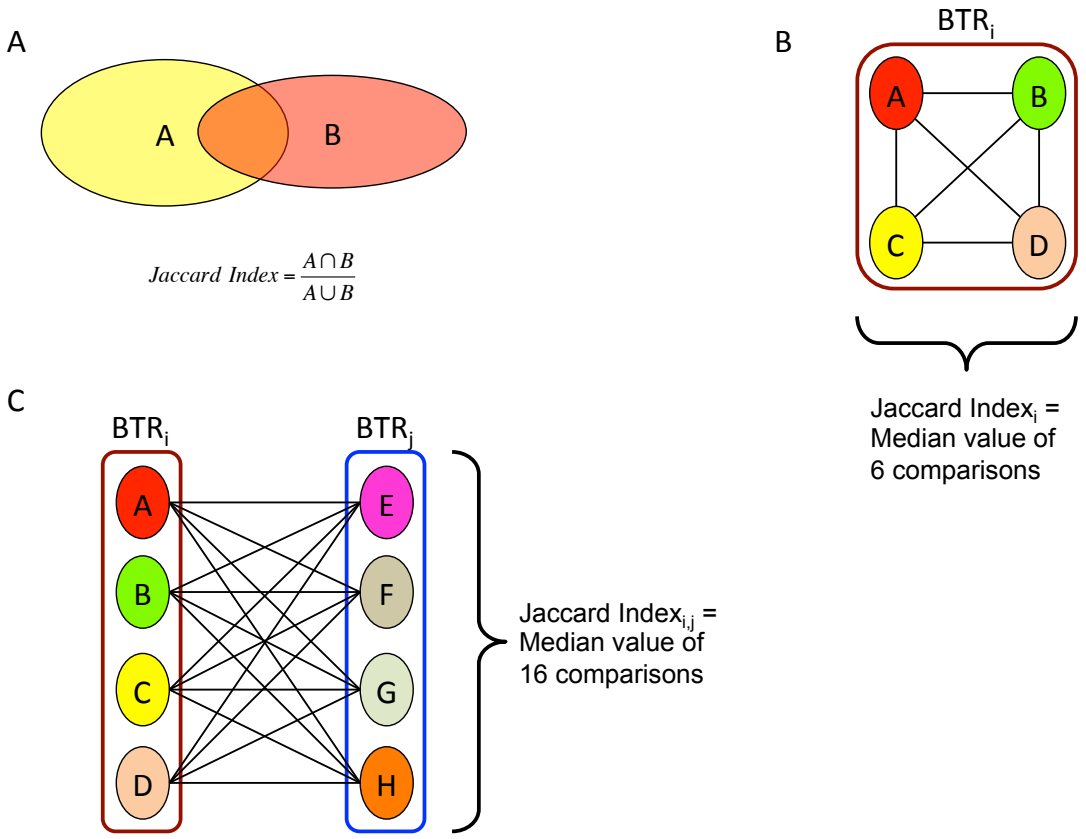
S5 Fig. Relationship between clusters if changing the linkage method. In red, the method described in the main text. In blue, clusters generated when requiring that new members do not decrease the mean of correlations beyond a particular threshold: 0.7 in this example. The darkness of the lines represent the similarity of the clusters (Jaccard Index).



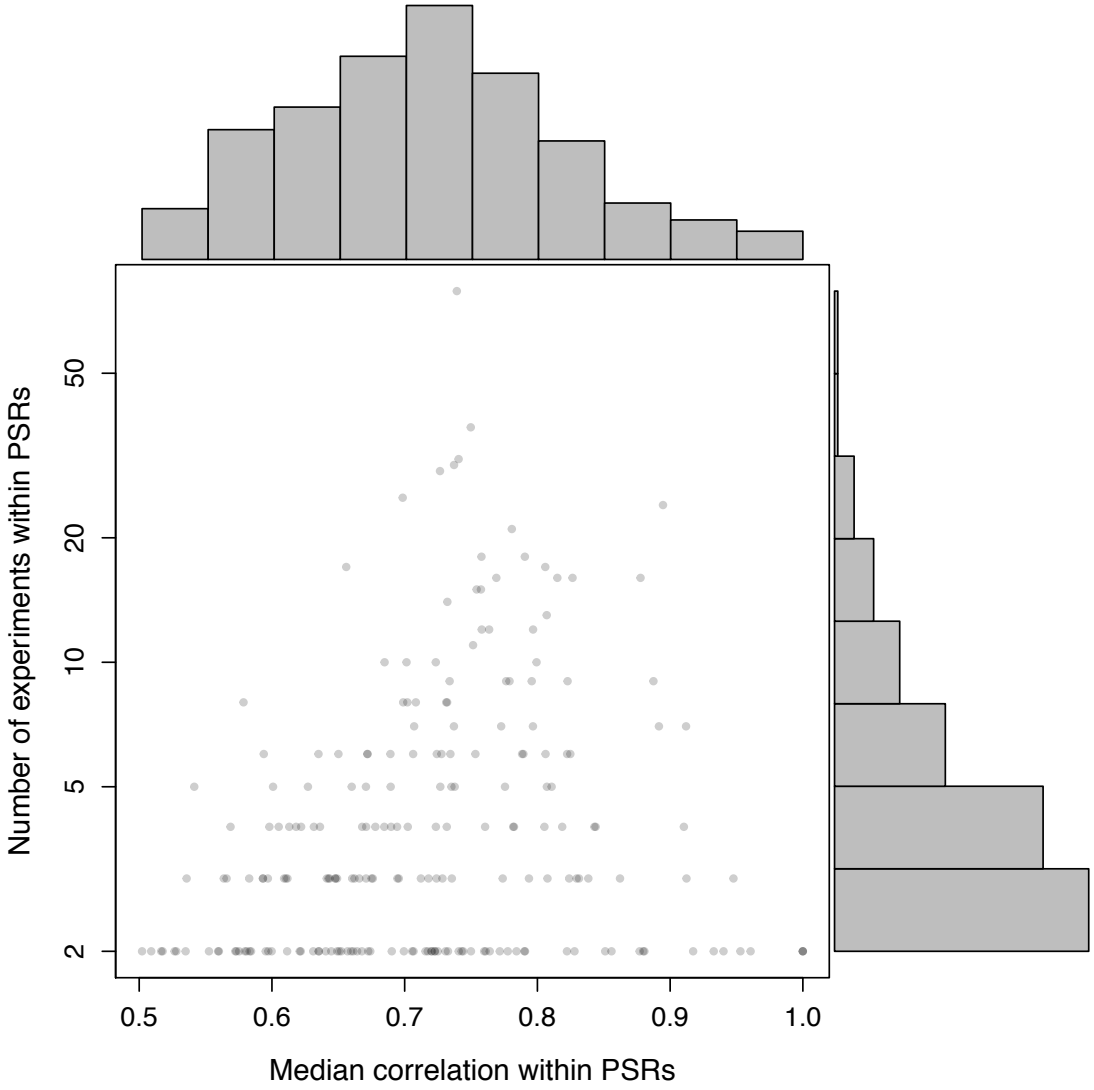
S6 Fig. Relationship between clusters if applying normalization techniques to the downloaded data. In red, the method described in the main text. In blue, clusters generated normalizing data with a Rank-based quantile normalization approach prior to the correlation calculation. The darkness of the lines show how similar are the clusters (Jaccard Index).



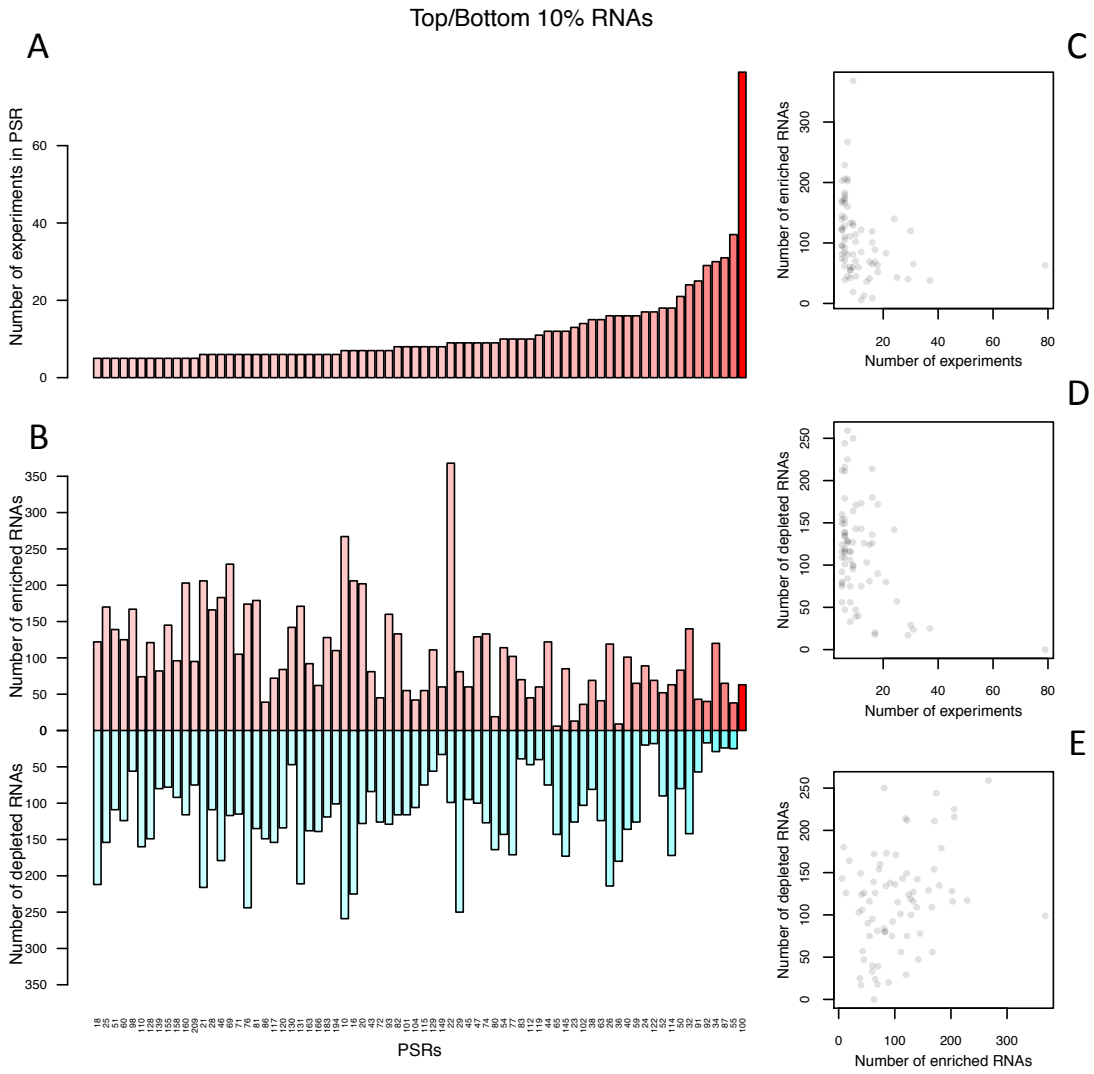
S7 Fig. Relationship between clusters if applying normalization techniques to the downloaded data. In red, the method described in the main text. In blue, clusters generated normalizing data with a Spline-based quantile normalization approach prior to the correlation calculation. The darkness of the lines show how similar are the clusters (Jaccard Index).



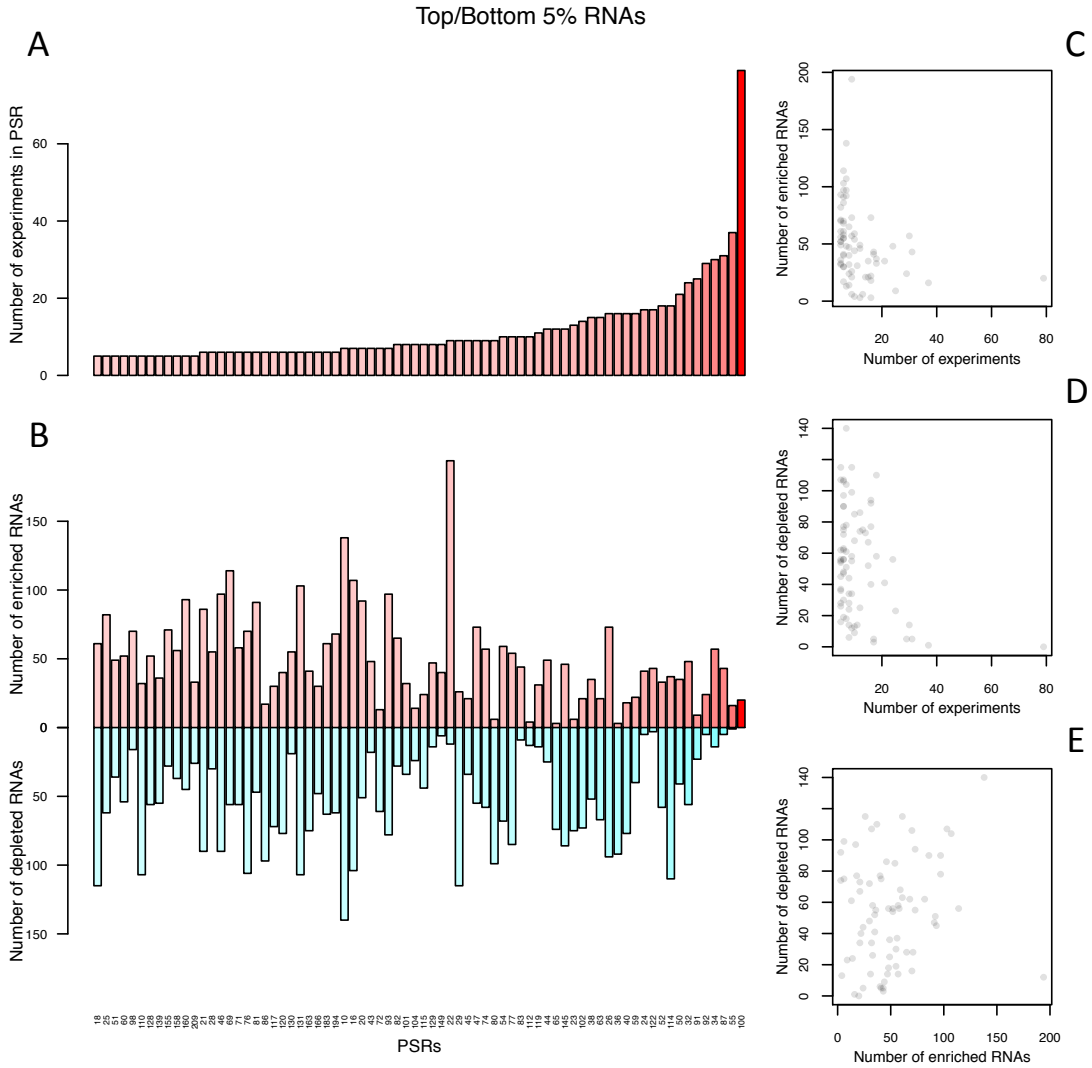
S8 Fig. Analysis of common transcription regulation within and between BTRs. A. Diagram showing the calculation of the Jaccard Index between two sets. B. Analysis of common TFs within a BTR containing 4 RNAs: the black lines represent the pairwise comparisons between the different sets of TFs (one for each RNA). C. Analysis of common TFs between two BTRs: the black lines represent all the pairwise comparisons between sets in different BTRs.



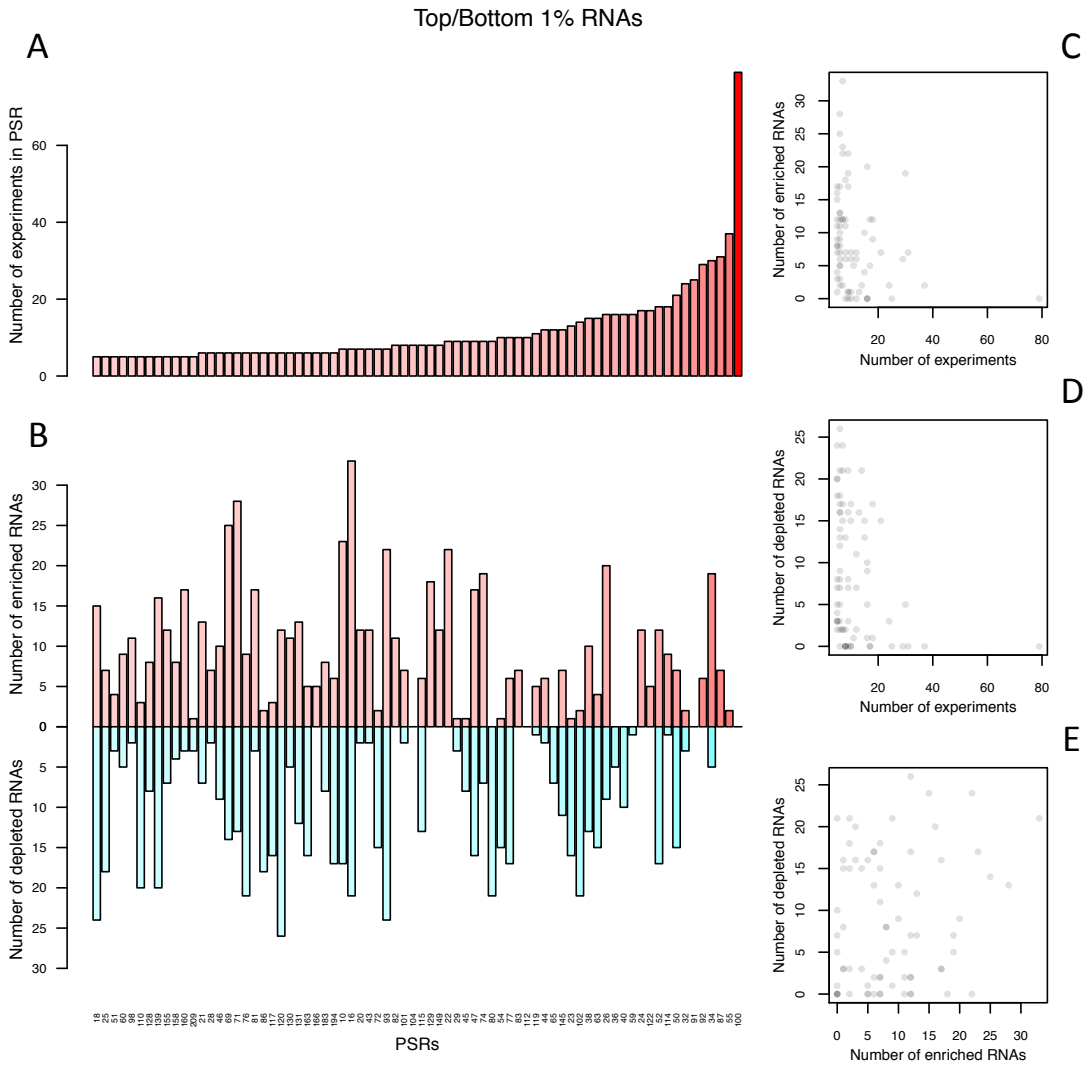
S9 Fig. Characterization of PSRs. Scatterplot shows the distribution of PSRs based on their within-group similarity (median of pairwise correlations within a PSR), and number of experiments within. Intensity of grey dots represents the number of overlapping points: the darker, the greater the number. Top and side histograms show the overall distribution of PSRs according to each variable.



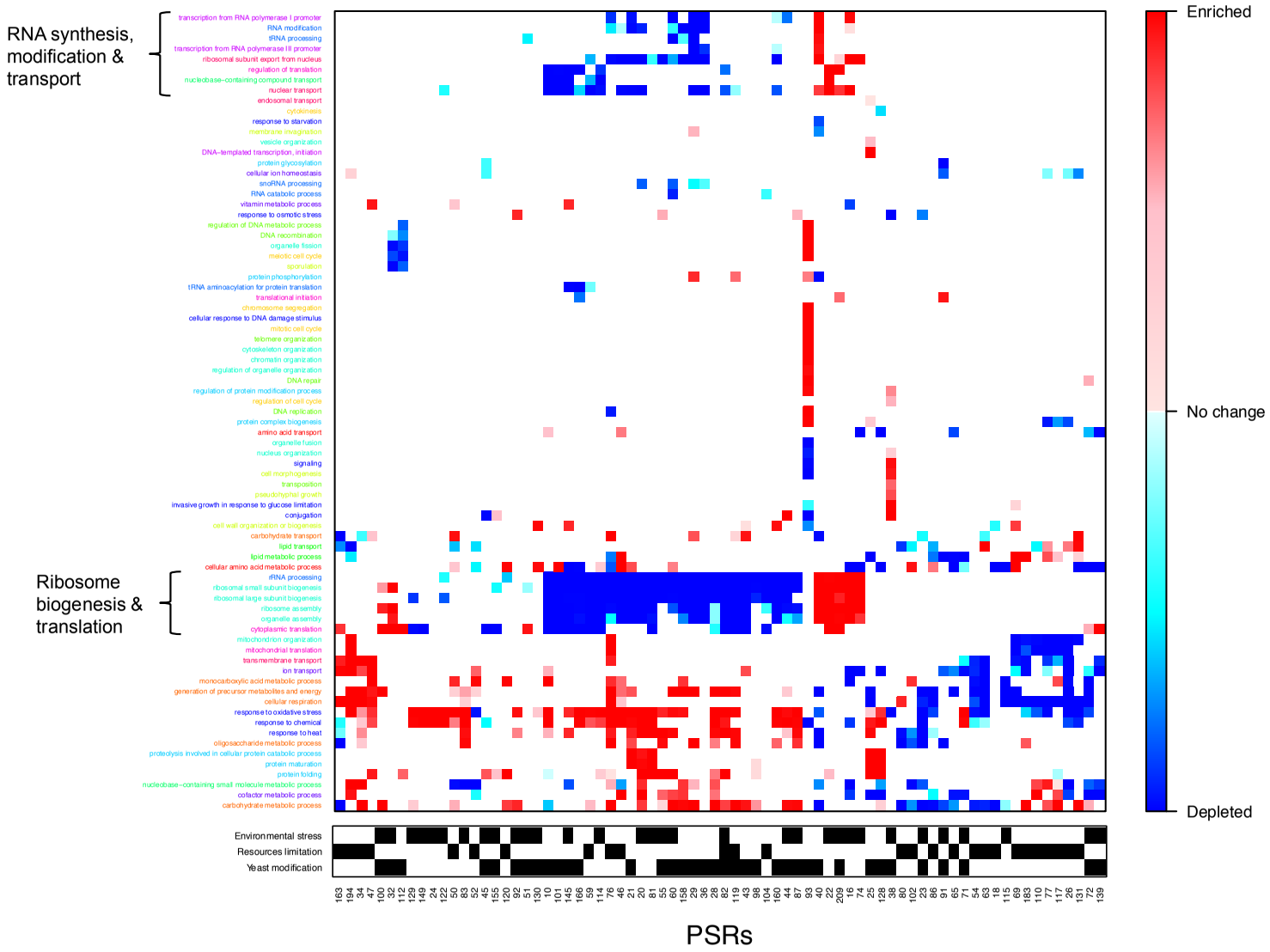
S10 Fig. Response consistency within PSRs (top/bottom 10% RNAs). A. Number of experiments within each PSR, sorted in increasing order. B. Number of consistently depleted and enriched RNAs within each PSR, ordered as in A. C-E. Relationship between number of experiments within PSR, number of enriched transcripts within PSR and number of depleted transcripts within PSR.



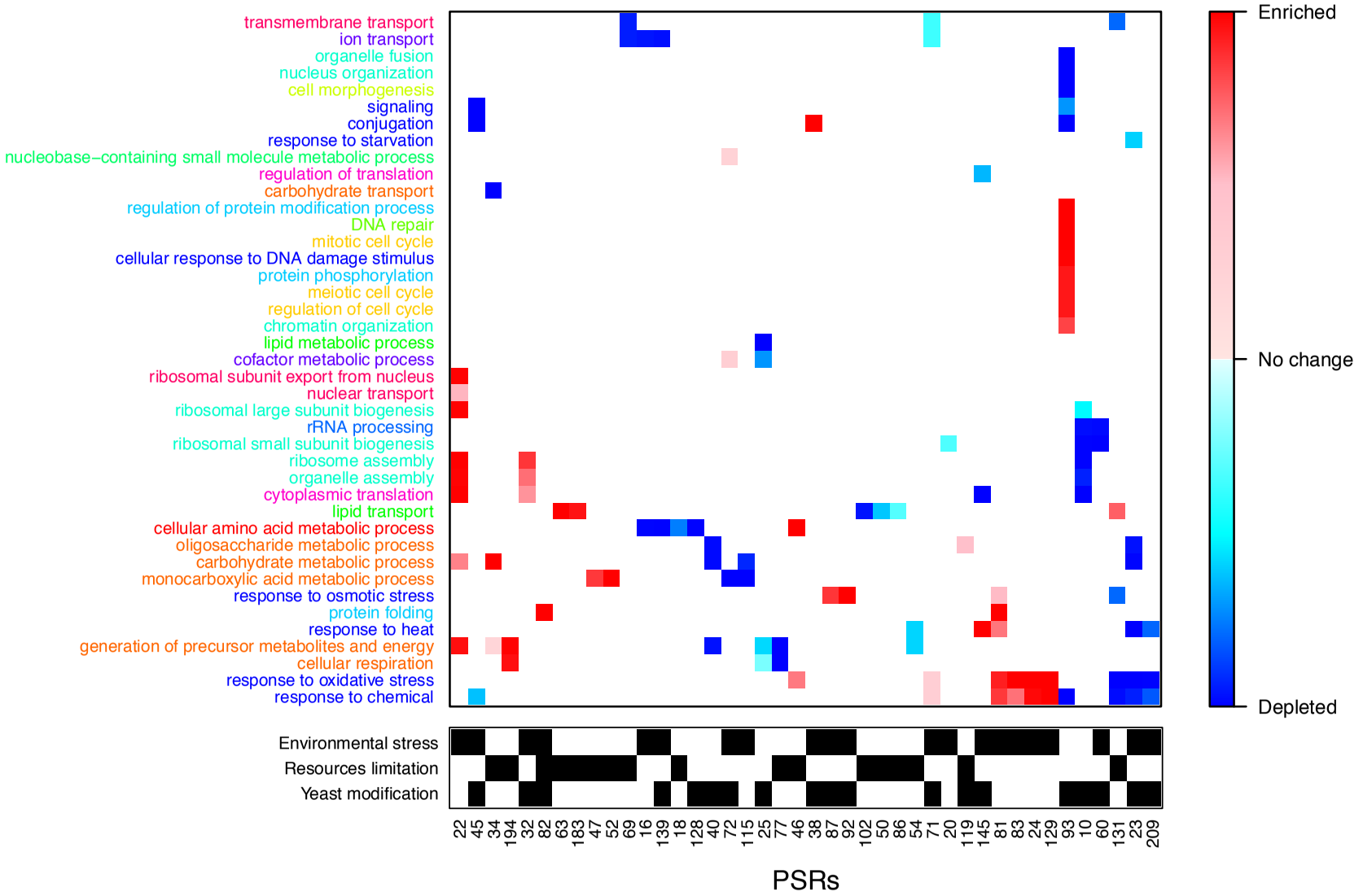
S11 Fig. Response consistency within PSRs (top/ bottom 5% RNAs). A. Number of experiments within each PSR, sorted in increasing order. B. Number of consistently depleted and enriched RNAs within each PSR, ordered as in A. C-E. Relationship between number of experiments within PSR, number of enriched transcripts within PSR and number of depleted transcripts within PSR.



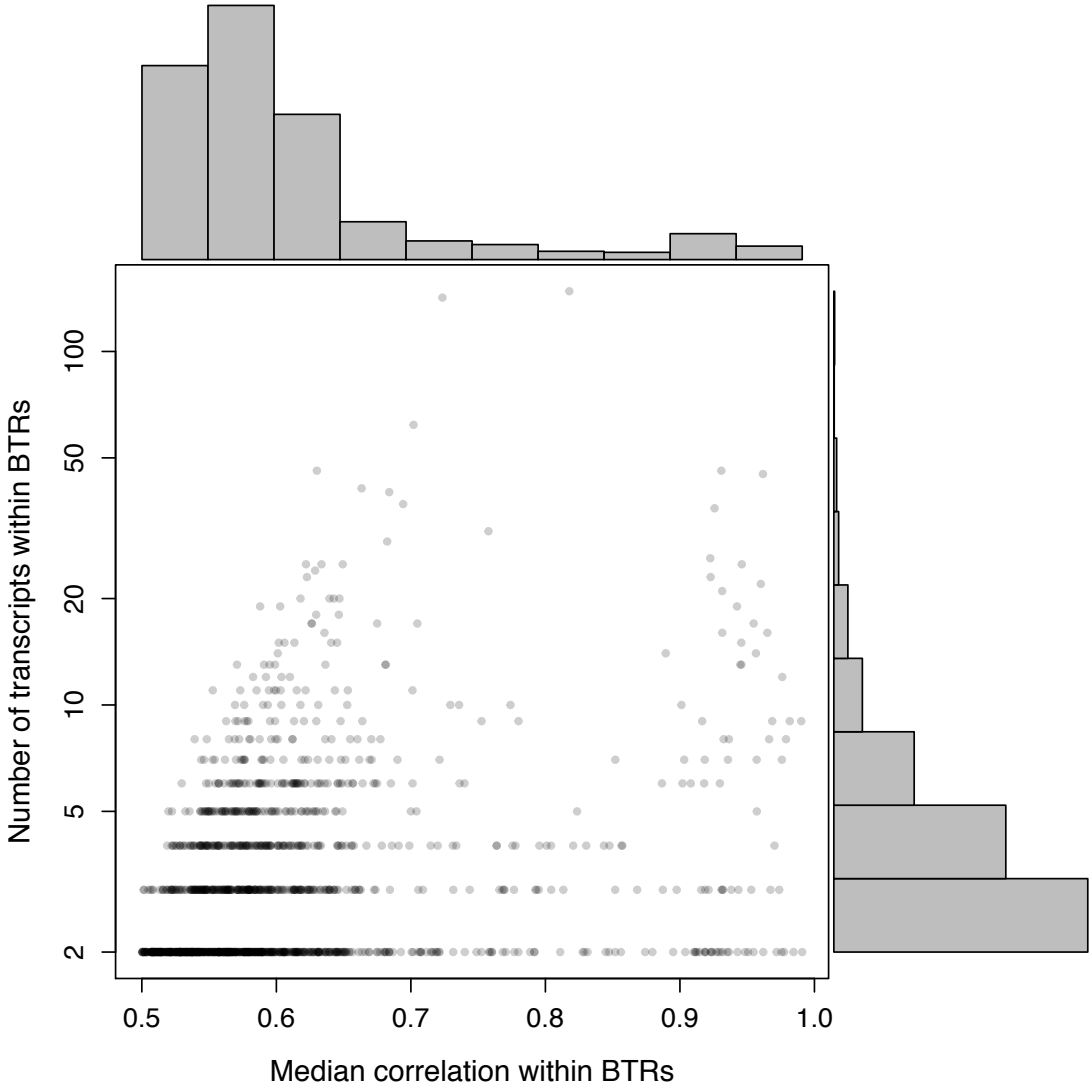
S12 Fig. Response consistency within PSRs (top/ bottom 1% RNAs). A. Number of experiments within each PSR, sorted in increasing order. B. Number of consistently depleted and enriched RNAs within each PSR, ordered as in A. C-E. Relationship between number of experiments within PSR, number of enriched transcripts within PSR and number of depleted transcripts within PSR.


RNA synthesis, modification & transport
Ribosome biogenesis & translation
transcription from RNA polymerase I promoter
RNA modification
tRNA processing
transcription from RNA polymerase III promoter
ribosomal subunit export from nucleus
regulation of translation
nucleobase−containing compound transport
nuclear transport
endosomal transport
cytokinesis
response to starvation
membrane invagination
vesicle organization
DNA−templated transcription, initiation
protein glycosylation
cellular ion homeostasis
snoRNA processing
RNA catabolic process
vitamin metabolic process
response to osmotic stress
regulation of DNA metabolic process
DNA recombination
organelle fission
meiotic cell cycle
sporulation
protein phosphorylation
tRNA aminoacylation for protein translation
translational initiation
chromosome segregation
cellular response to DNA damage stimulus
mitotic cell cycle
telomere organization
cytoskeleton organization
chromatin organization
regulation of organelle organization
DNA repair
regulation of protein modification process
regulation of cell cycle
DNA replication
protein complex biogenesis
amino acid transport
organelle fusion
nucleus organization
signaling
cell morphogenesis
transposition
pseudohyphal growth
invasive growth in response to glucose limitation
conjugation
cell wall organization or biogenesis
carbohydrate transport
lipid transport
lipid metabolic process
cellular amino acid metabolic process
rRNA processing
ribosomal small subunit biogenesis
ribosomal large subunit biogenesis
ribosome assembly
organelle assembly
cytoplasmic translation
mitochondrion organization
mitochondrial translation
transmembrane transport
ion transport
monocarboxylic acid metabolic process
generation of precursor metabolites and energy
cellular respiration
response to oxidative stress
response to chemical
response to heat
oligosaccharide metabolic process
proteolysis involved in cellular protein catabolic process
protein maturation
protein folding
nucleobase−containing small molecule metabolic process
cofactor metabolic process
carbohydrate metabolic process
Environmental stress
Resources limitation
Yeast modification
163 194 34 47 100 32 112 129 149 24 122 50 83 52 45 155 120 92 51 130 10 101 145 166 59 114 76 46 21 20 81 55 60 158 29 36 28 82 119 43 98 104 160 44 87 93 42 22 209 16 74 25 128 38 80 102 23 86 91 65 71 54 63 18 115 69 183 110 177 117 26 131 72 139
PSRs
Enriched
No change
Depleted

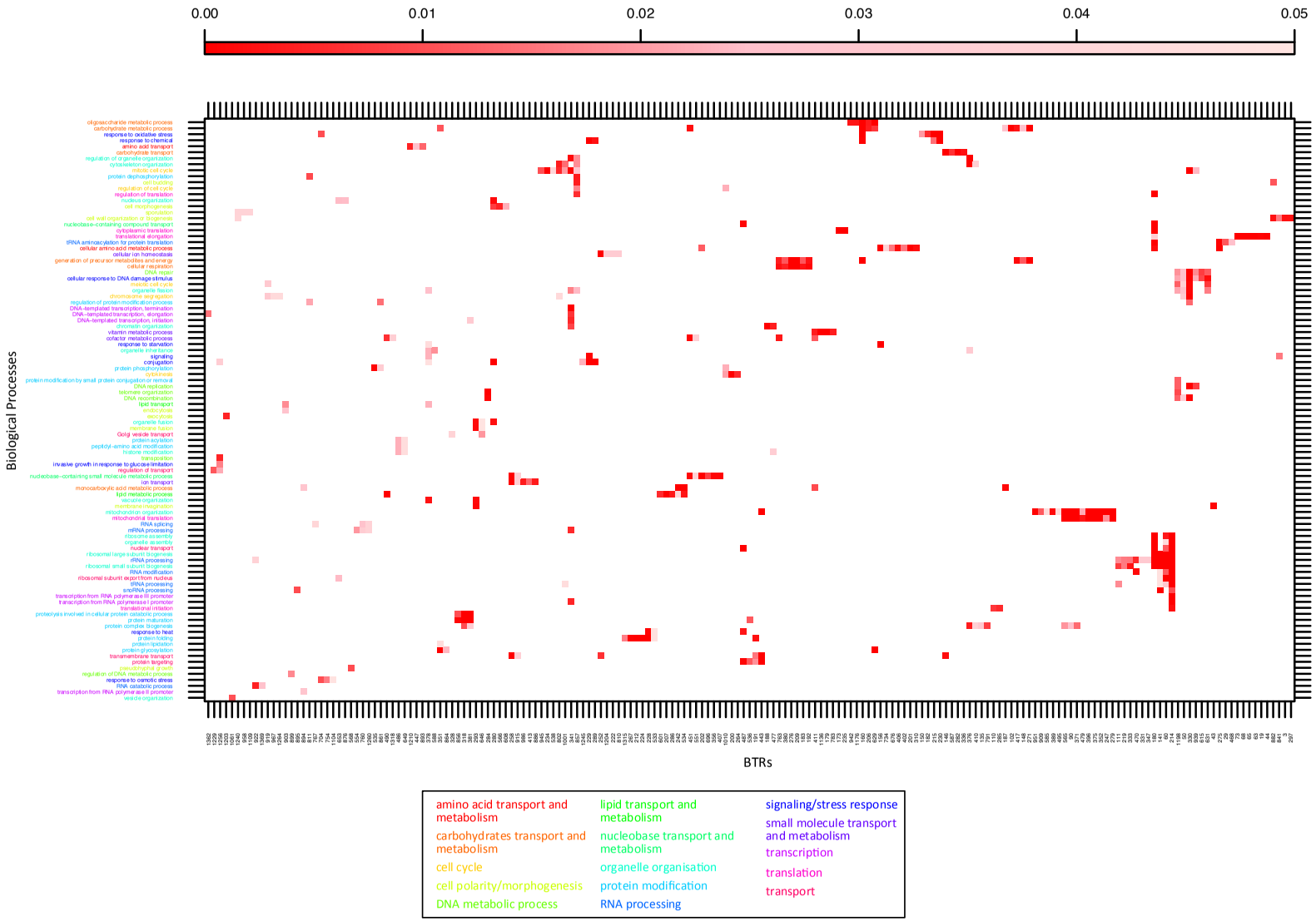
S13 Fig. Biological processes affected by consistent stress response (top/ bottom 10% RNAs). GO Slim terms overrepresented in the set of 10% most-enriched transcripts (red) or the set of 10% most-depleted transcripts (blue). All colouring as in **Fig 3**. The black squares describe the type of stresses the PSRs suffered. The order of both PSRs and biological processes depends on the hierarchical clustering of Euclidean distances calculated along the columns and rows respectively.


transmembrane transport
ion transport
organelle fusion
nucleus organization
cell morphogenesis
signaling
conjugation
response to starvation
nucleobase−containing small molecule metabolic process
regulation of translation
carbohydrate transport
regulation of protein modification process
DNA repair
mitotic cell cycle
cellular response to DNA damage stimulus
protein phosphorylation
meiotic cell cycle
regulation of cell cycle
chromatin organization
lipid metabolic process
cofactor metabolic process
ribosomal subunit export from nucleus
nuclear transport
ribosomal large subunit biogenesis
rRNA processing
ribosomal small subunit biogenesis
ribosome assembly
organelle assembly
cytoplasmic translation
lipid transport
cellular amino acid metabolic process
oligosaccharide metabolic process
carbohydrate metabolic process
monocarboxylic acid metabolic process
response to osmotic stress
protein folding
response to heat
generation of precursor metabolites and energy
cellular respiration
response to oxidative stress
response to chemical
Enriched
No change
Depleted
Environmental stress
Resources limitation
Yeast modification
22 45 34 194 32 82 63 183 47 52 69 16 139 18 128 40 72 115 25 77 46 38 87 92 102 50 86 54 71 20 119 145 81 83 24 129 93 10 60 131 23 209
PSRs

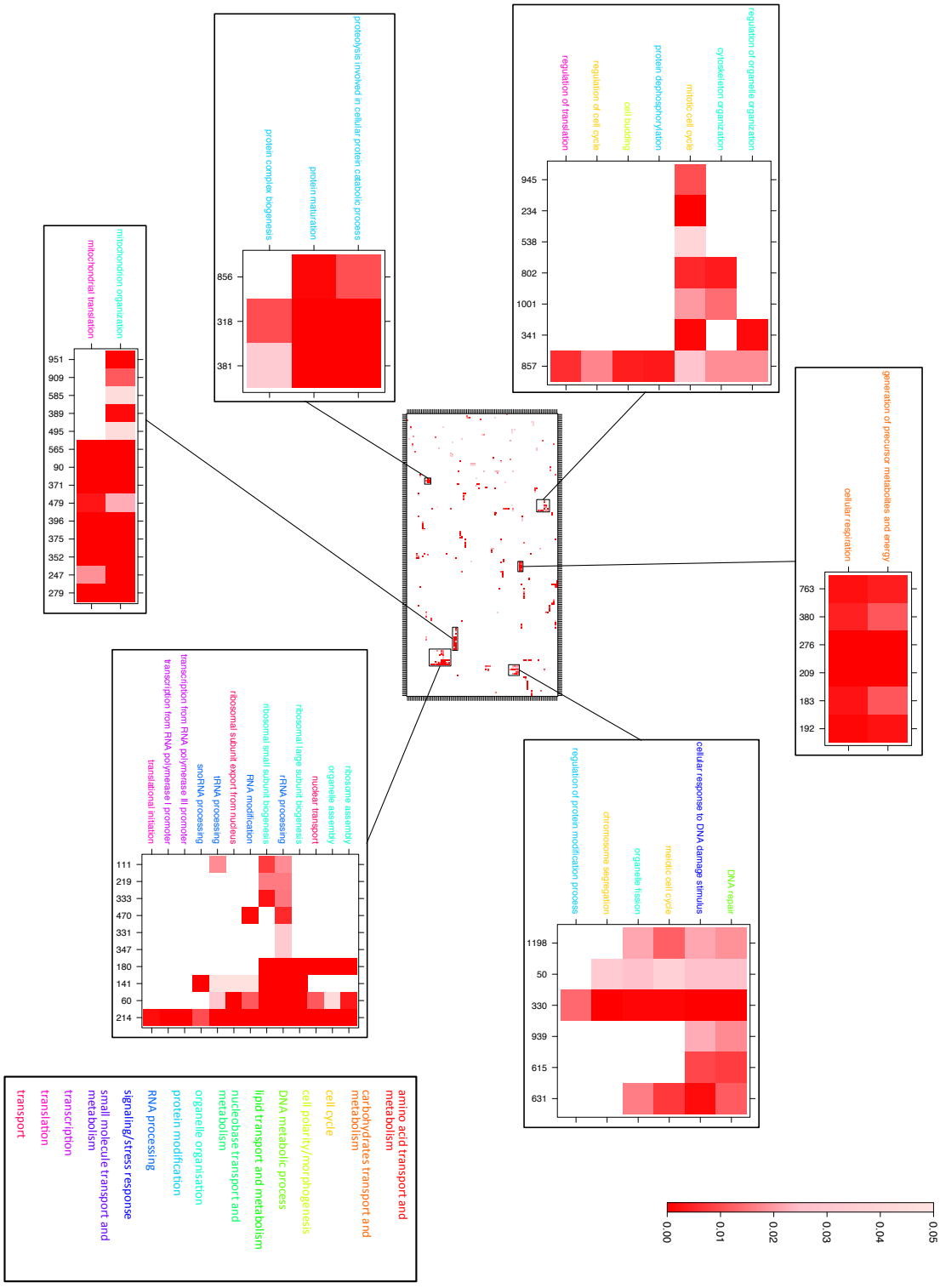
S14 Fig. Biological processes affected by consistent stress response (top/ bottom 1% RNAs). GO Slim terms overrepresented in the set of 1% most-enriched transcripts (red) or the set of 1% most-depleted transcripts (blue). All colouring as in **Fig 3**. The black squares describe the type of stresses the PSRs suffered. The order of both PSRs and biological processes depends on the hierarchical clustering of Euclidean distances calculated along the columns and rows respectively.



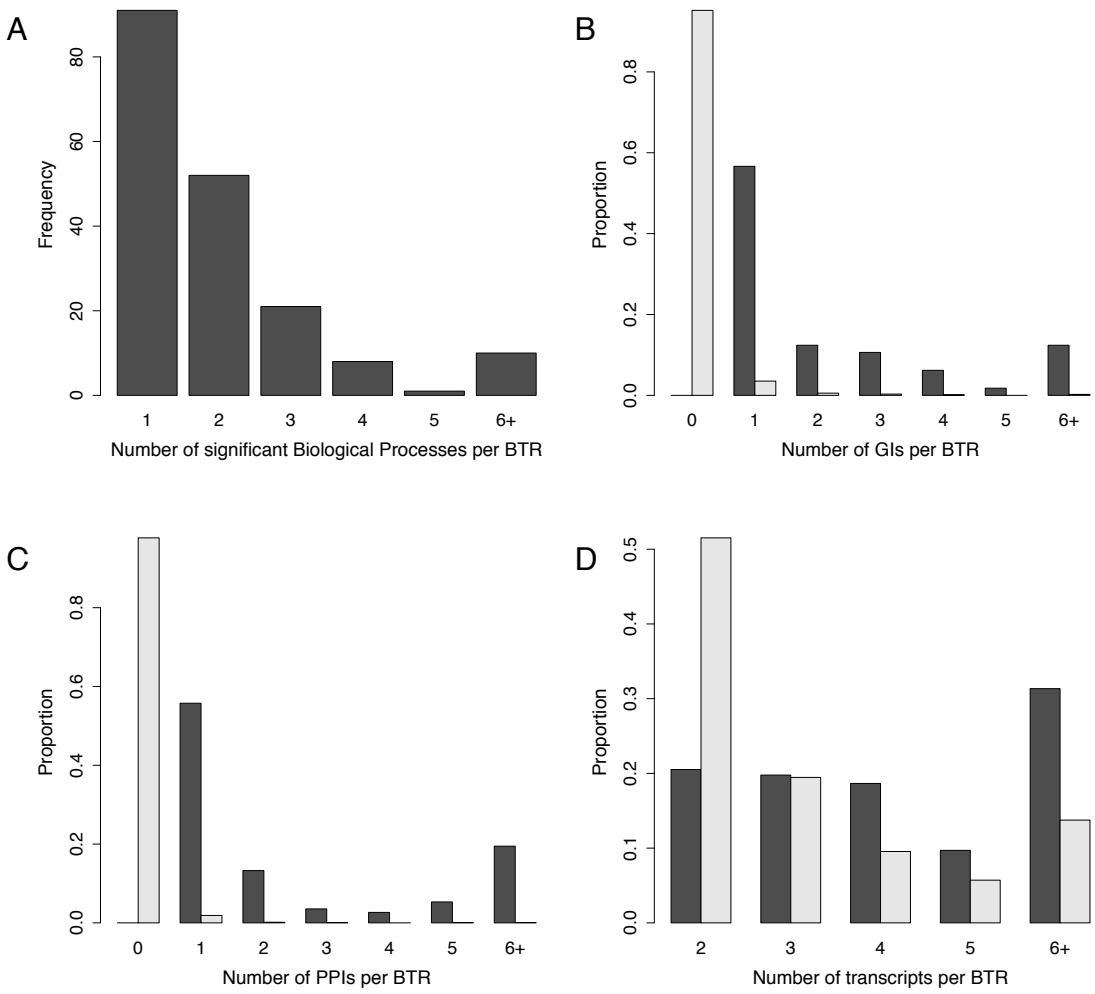
S15 Fig. Characterization of BTRs. Scatterplot shows the distribution of BTRs based on their within-group similarity (median of pairwise correlations within a BTR), and number of transcripts within. Intensity of grey dots represents the number of overlapping points: the darker, the greater the number. Top and side histograms show the overall distribution of BTRs according to each variable.


0.00
0.01
0.02
0.03
0.04
0.05
Biological Processes
BTRs
amino acid transport and metabolism
carbohydrates transport and metabolism
cell cycle
cell polarity/morphogenesis
DNA metabolic process
lipid transport and metabolism
nucleobase transport and metabolism
organelle organisation
protein modification
RNA processing
signaling/stress response
small molecule transport and metabolism
transcription
translation
transport

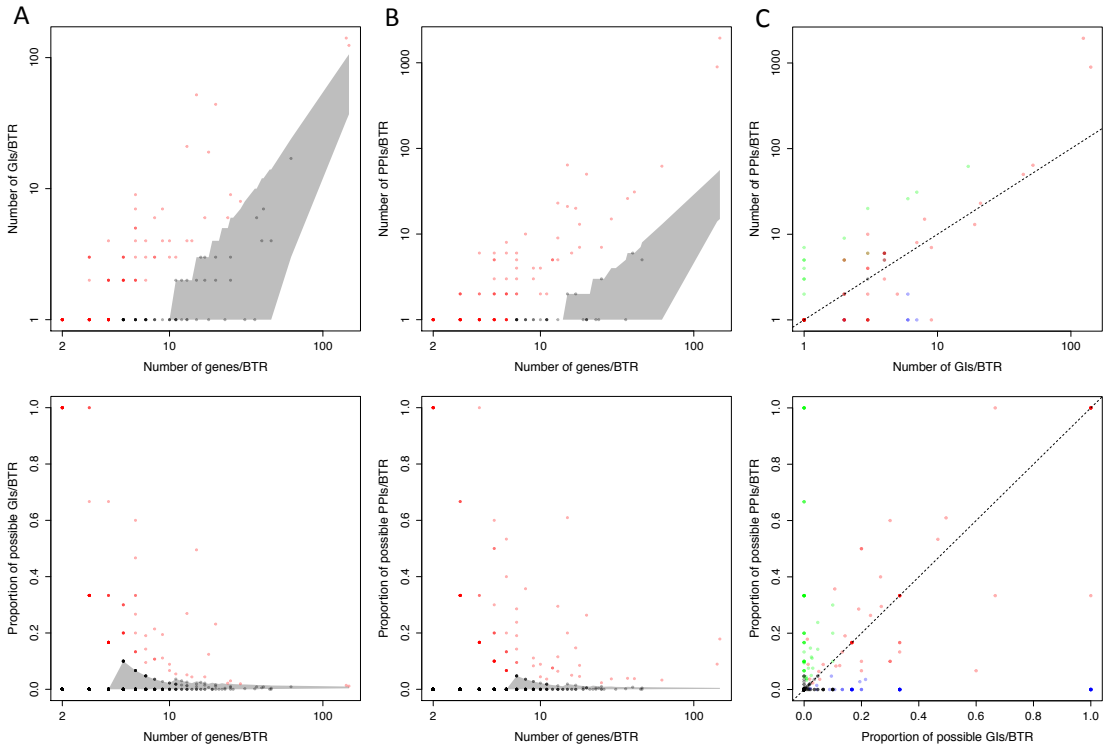
S16 Fig. Biological processes overrepresented within BTRs (whole heatmap). Red intensity represents the FDR value. Terms are grouped in 15 categories, and their name coloured accordingly. Zoomed in version of some areas of the heatmap in **S13 Fig**.


regulation of organelle organization
cytoskeleton organization
mitotic cell cycle
protein dephosphorylation
cell budding
regulation of cell cycle
regulation of translation
945
234
538
802
1001
341
857
proteolysis involved in cellular protein catabolic process
protein maturation
protein complex biogenesis
856
318
381
mitochondrion organization
mitochondrial translation
951
909
585
389
495
565
90
371
479
396
375
352
247
279
generation of precursor metabolites and energy
cellular respiration
763
380
276
209
183
192
ribosome assembly
organelle assembly
nuclear transport
rRNA processing
ribosomal large subunit biogenesis
ribosomal small subunit biogenesis
RNA modification
ribosomal subunit export from nucleus
tRNA processing
snoRNA processing
transcription from RNA polymerase III promoter
transcription from RNA polymerase I promoter
translational initiation
111
219
333
470
331
347
180
141
60
214
cellular response to DNA damage stimulus
DNA repair
meiotic cell cycle
organelle fission
chromosome segregation
regulation of protein modification process
1198
50
330
939
615
631
amino acid transport and metabolism
carbohydrates transport and metabolism
cell cycle
cell polarity/morphogenesis
DNA metabolic process
lipid transport and metabolism
nucleobase transport and metabolism
organelle organisation
protein modification
RNA processing
signaling/stress response
small molecule transport and metabolism
transcription
translation
transport
0.00
0.01
0.02
0.03
0.04
0.05

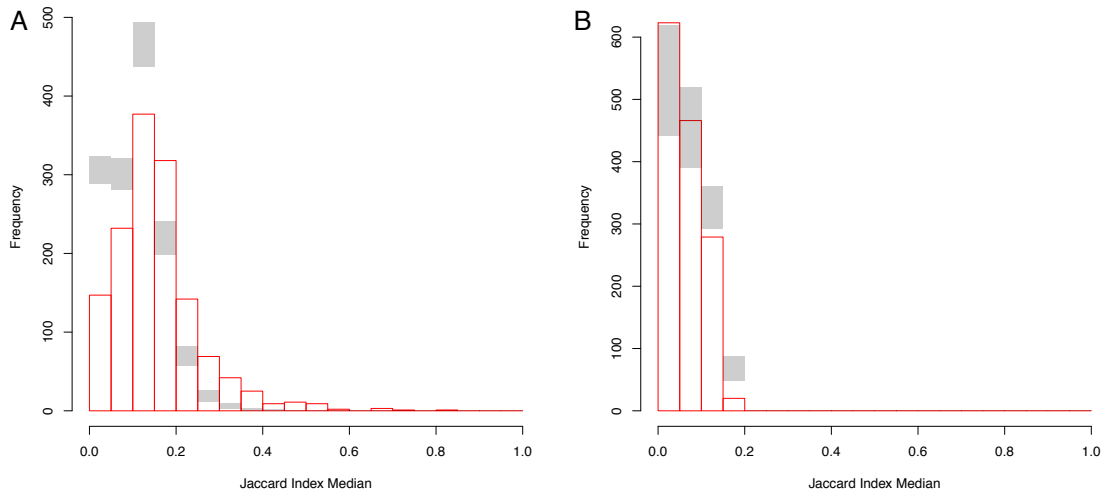
S17 Fig. Biological processes overrepresented within BTRs (zoomed in). Details of BTRs participating in similar biological processes. Red intensity represents the FDR value. Terms are grouped in 15 categories, and their name coloured accordingly.



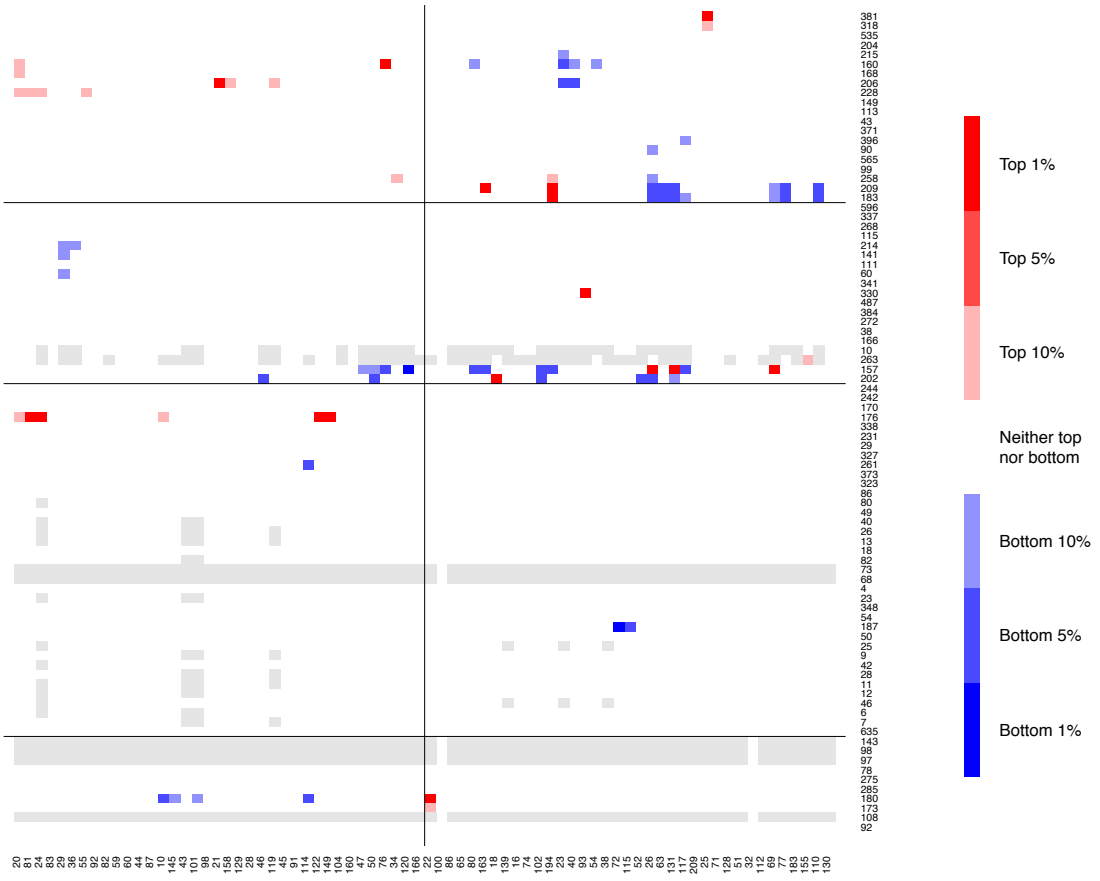
S18 Fig. Functional similarity within BTRs. A Number of GO Slim Biological Processes that are significantly enriched within each BTR. B. Number of significant (dark grey) and non- significant (light grey) genetic interactions within BTR. C. Number of significant (dark grey) and non-significant (light grey) protein-protein interactions within BTR. D. Number of transcripts per BTR for BTRs having a significant enrichment in A-C (dark grey) or not having any enrichment in A-C (light grey).



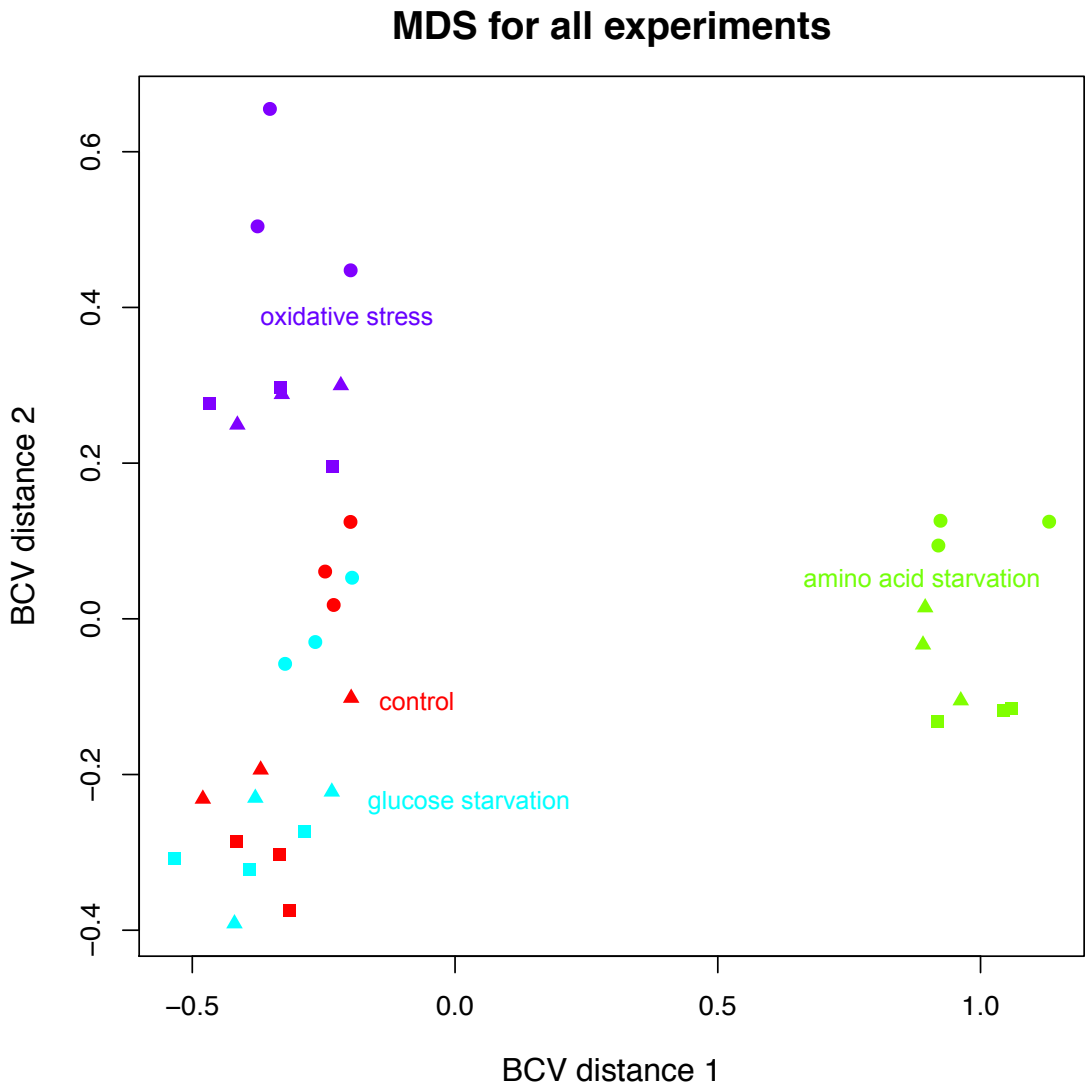
S19 Fig. Significance of interactions within BTRs. Number of (and proportion of all possible) genetic (A) and physical (B) interactions per BTR compared to the size of BTR. Significant cases are shown in red. Random expectation was calculated through a resampling process, and is shown as a grey shade (90% confidence intervals for the expectation). C. Number of (and proportion of all possible) physical and genetic interactions within BTRs. BTRs may have a significant overrepresentation of physical (green), genetic (blue) or both interactions (red). BTRs with no overrepresentation are shown in grey. Significance was established as p-value < 0.05. The intensity of the colour is proportional to the number of cases represented by a single point.



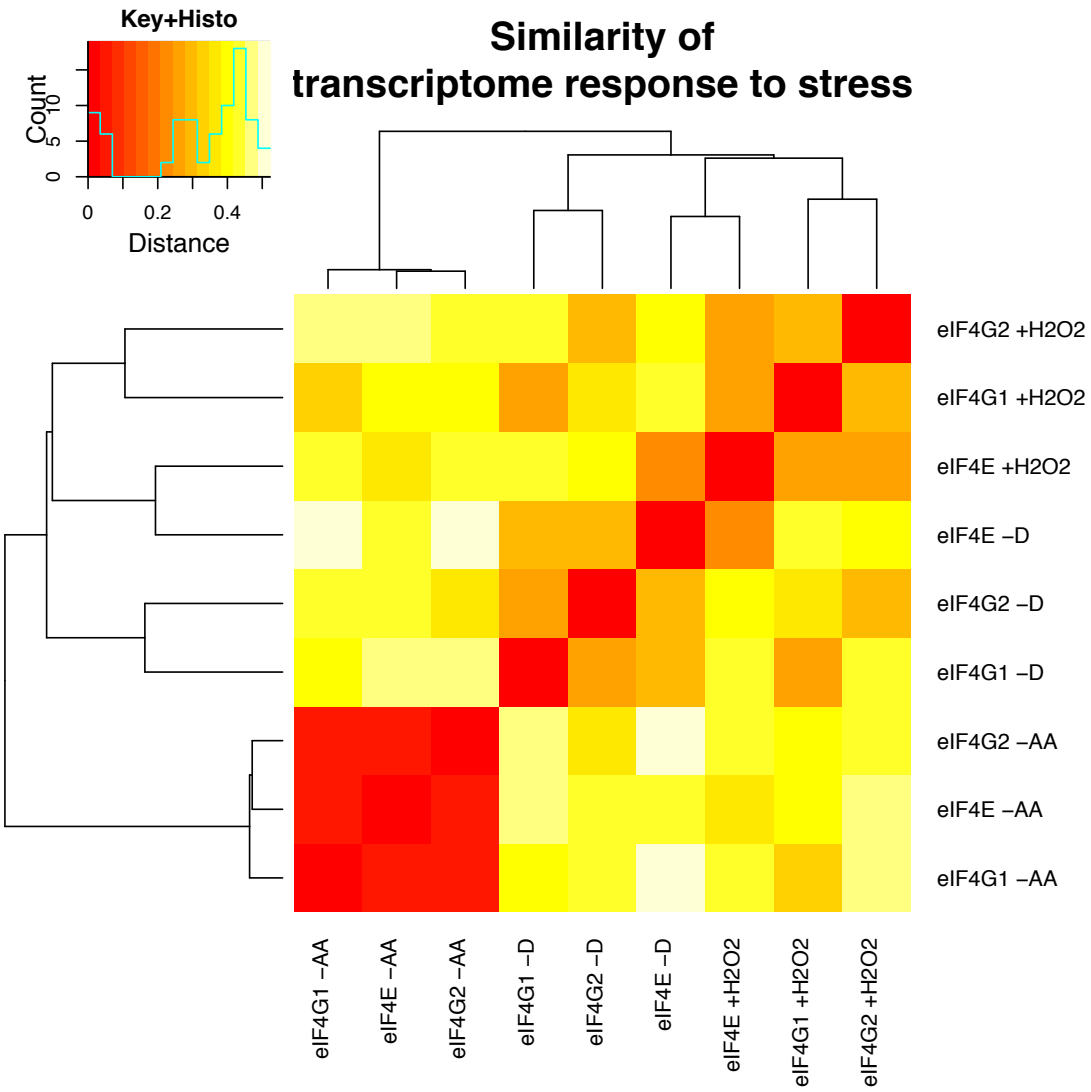
S20 Fig. Regulation of transcription within and between BTRs. Histograms show the distribution of overlapping sets of transcription factors involved in regulating the expression of transcripts measured as the median of Jaccard Indices (number of TFs controlling the expression of both genes/number of TFs controlling the expression of either of the genes). The grey shades show the expected tip of the histogram bars calculated using resampling. A. Within BTRs. B. Between BTRs.



S21 Fig. BTRs suffering extreme expression changes. Heatmap shows if more than half of the members of a specific BTR are in one of the subsets of great changes of a particular PSR. Red shows membership of the subsets of induced RNAs, whereas blue shows membership of the subsets of repressed RNAs. The brighter the colour, the more extreme the percentile. PSRs and BTRs are ordered as they are in **Fig 8**: PSRs in columns, BTRs in rows. Grey squares show when there was no data available. Black lines divide the heatmap in the different global responses and response layers shown in **Fig 8**.

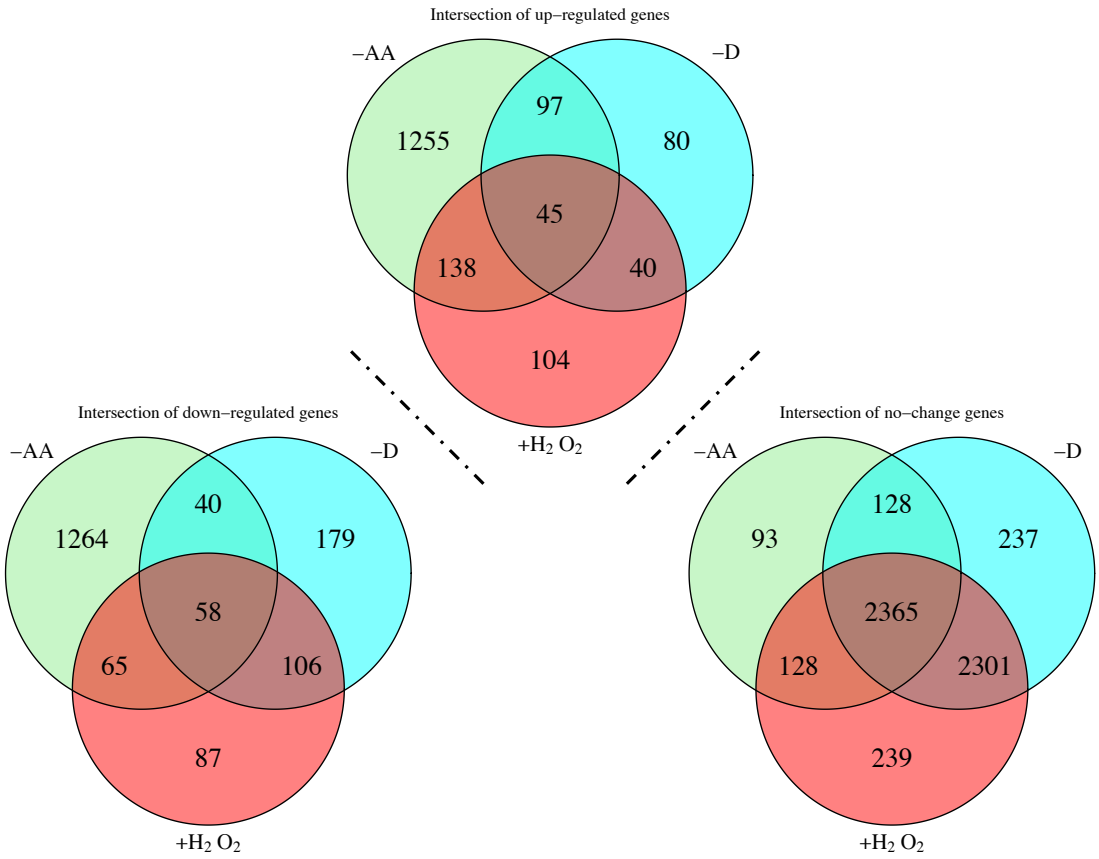


S22 Fig. Multi-dimensional scaling of transcriptomes from yeast grown under different stress conditions. Control (red); amino acid starvation (green); glucose starvation (blue); and, oxidative stress (purple). The point shapes represent the tags used in the experiment: eIF4E (squares); eIF4G1 (triangles); and, eIF4G2 (circles). It demonstrates that transcriptomes cluster because of stress instead of tag.

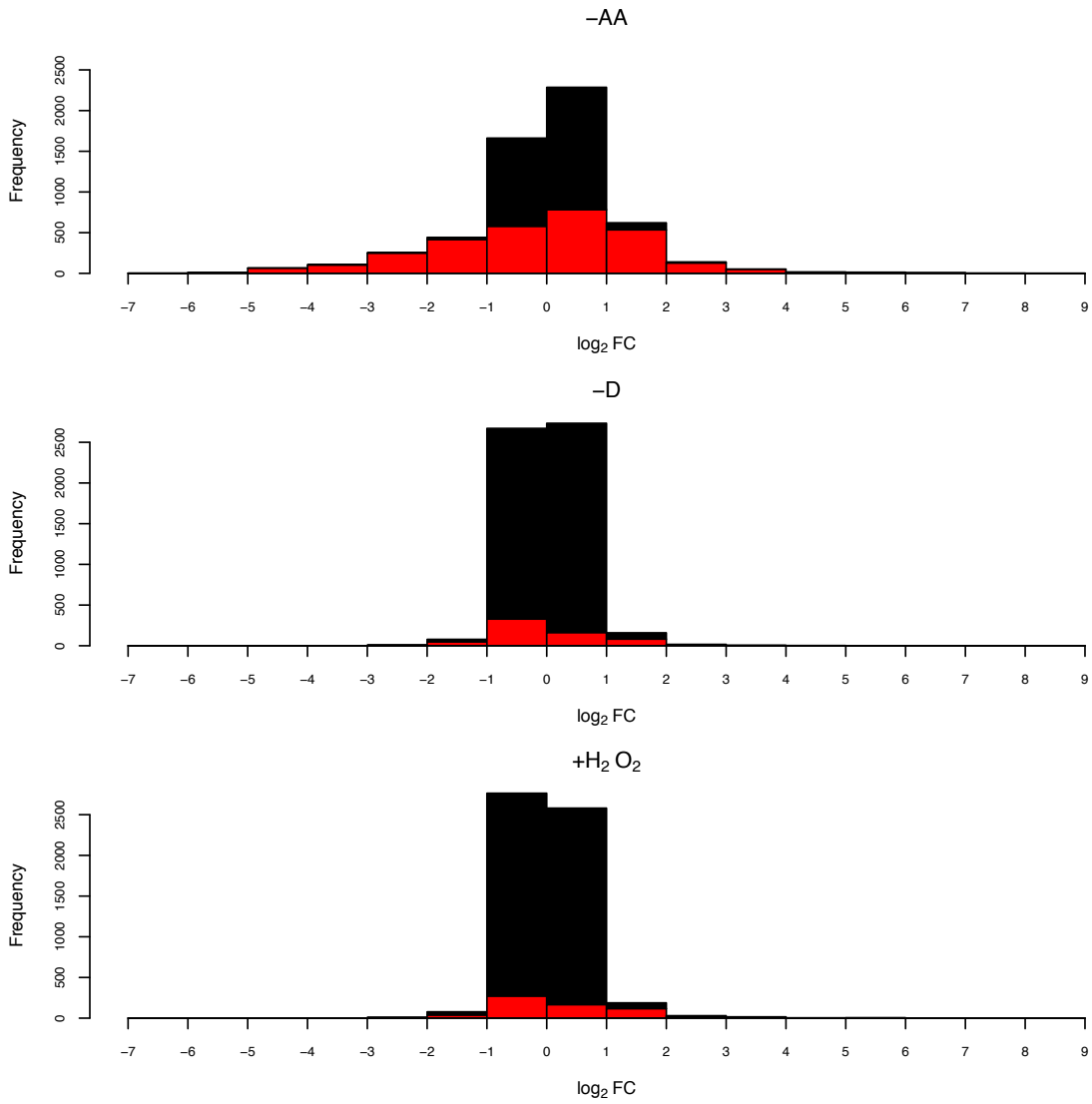


S23 Fig. Similarity of transcriptional response to stress (stress vs. control).

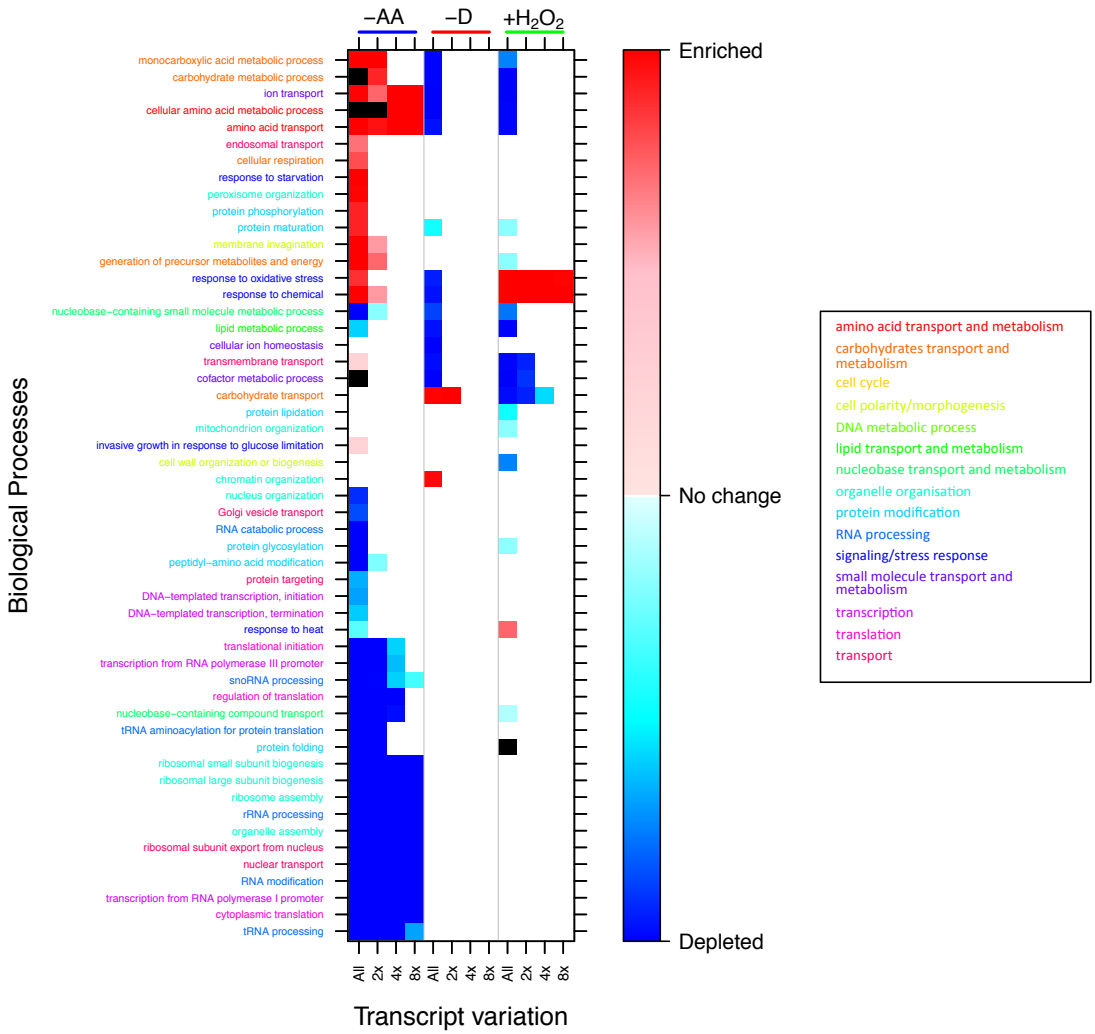
It demonstrates that stress responses cluster because of stress instead of tag.



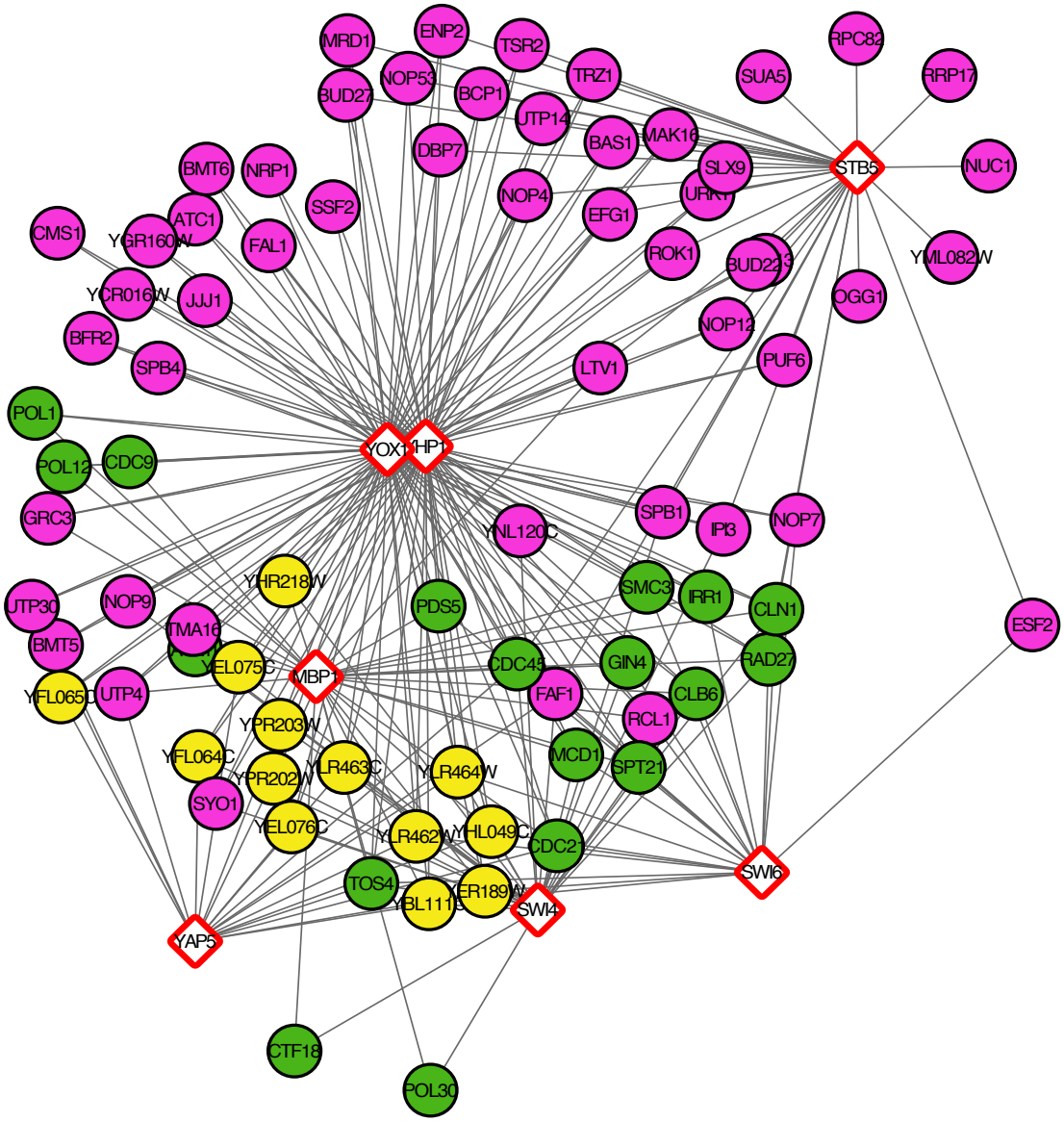
S24 Fig. Common stress responses. Overlapping sets of up-regulated genes (A), down- regulated genes (B), and genes with no statistical change (C) following 3 different stresses: amino acid starvation, glucose starvation, and oxidative stress. Statistical significance set at FDR 1%.



S25 Fig. Magnitude of transcriptional stress-response. Histograms show the distribution of $\log_2$ fold-changes. Significant differentially-expressed transcripts are shown in red, the rest are shown in black.



S26 Fig. Biological processes affected by stress response. GO Slim terms are that are overrepresented in the set significantly-enriched transcripts (red), the set of significantly-depleted transcripts (blue), or in both sets (black). Terms are grouped in 15 categories, and their name coloured accordingly.



S27 Fig. Use of BTRs for functional annotation. Network of transcription factors associated with BTRs 60 (pink), 263 (yellow), and 330 (green); transcription factors shown as diamonds.