Supplementary Files:

Supplementary File 1: Excel file containing the transcriptional profiling data.

Supplementary File 2: Archived .zip folder containing the .gmx .gmt and .chip files necessary for the execution of GSEA from C. albicans genome data. See http://www.broadinstitute.org/cancer/software/gsea/wiki/index.php/Data_formats for details on these file formats. Because of issues with the Enrichment Map plug-in systematic gene numbers do not contain the “orf19.” prefix.

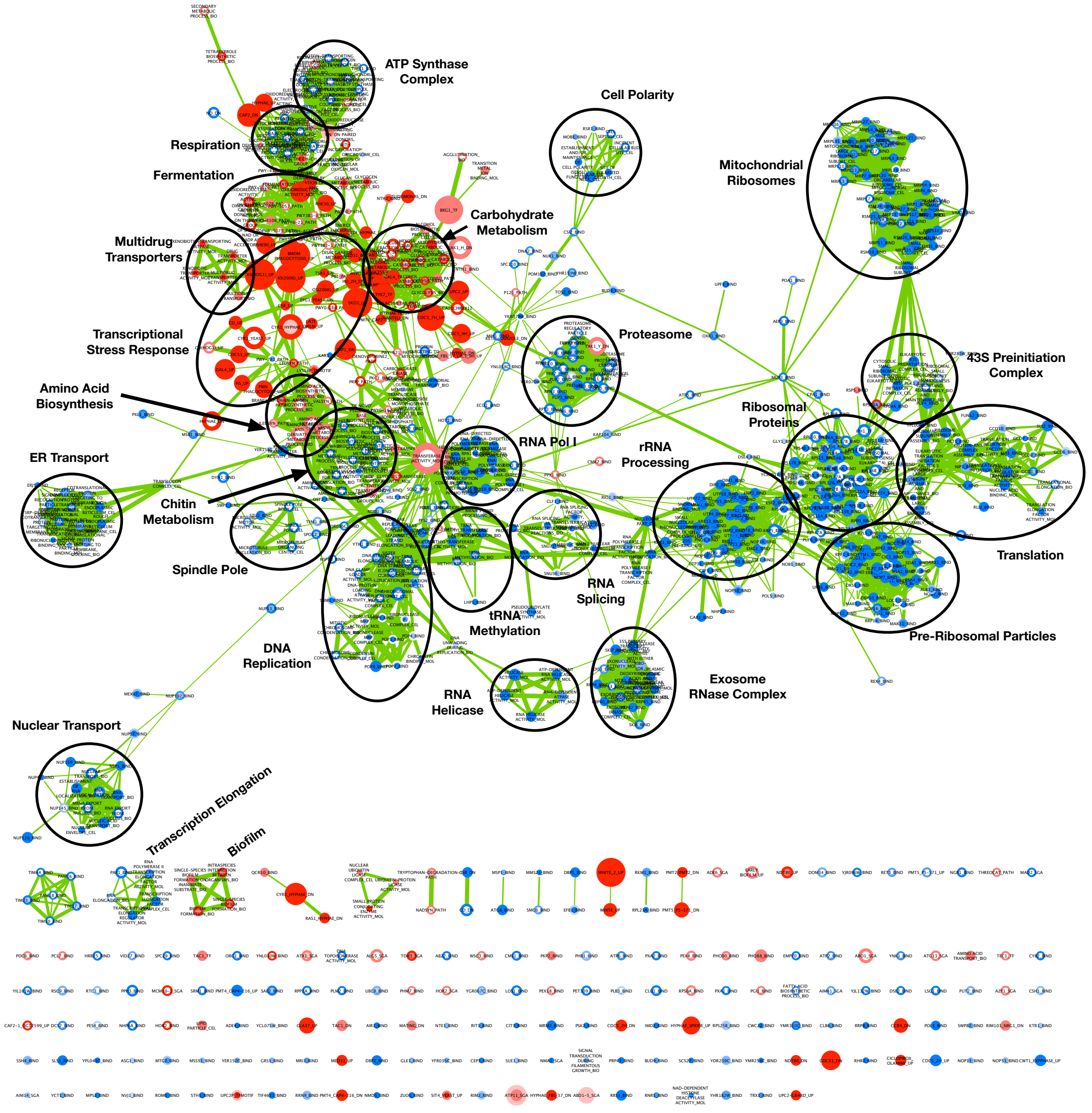
Supplementary File 3: Archived .zip folder containing Cytoscape Session Files (.cys) for Supplementary Figure 1, Figure 7 and Supplementary Figure 6.

Supplementary File 4: Excel file containing significantly-modulated transcripts at each time point during hypoxia adaptation

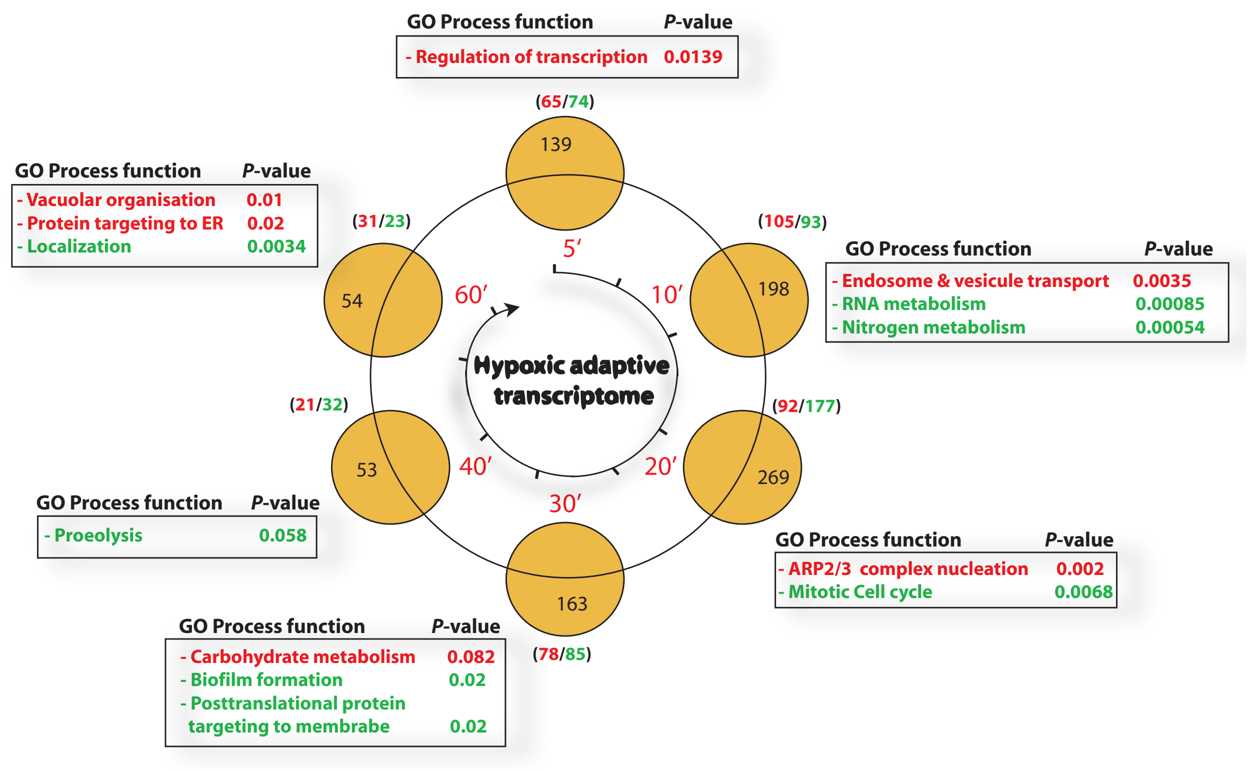
Supplementary File 5: Excel file whose worksheets contain the input files used in the Network Components Analysis as well as the resulting output files.

Supplementary File 6: Quicktime .mov file illustrating the temporal changes in transcript abundance, in the context of a simplified transcription factor network, during the 1st hour of hypoxia in wild type cells.

Supplementary File 7: Quicktime .mov file illustrating the temporal changes in transcript rate changes, in the context of a simplified transcription factor network, during the 1st hour of hypoxia in wild type cells.

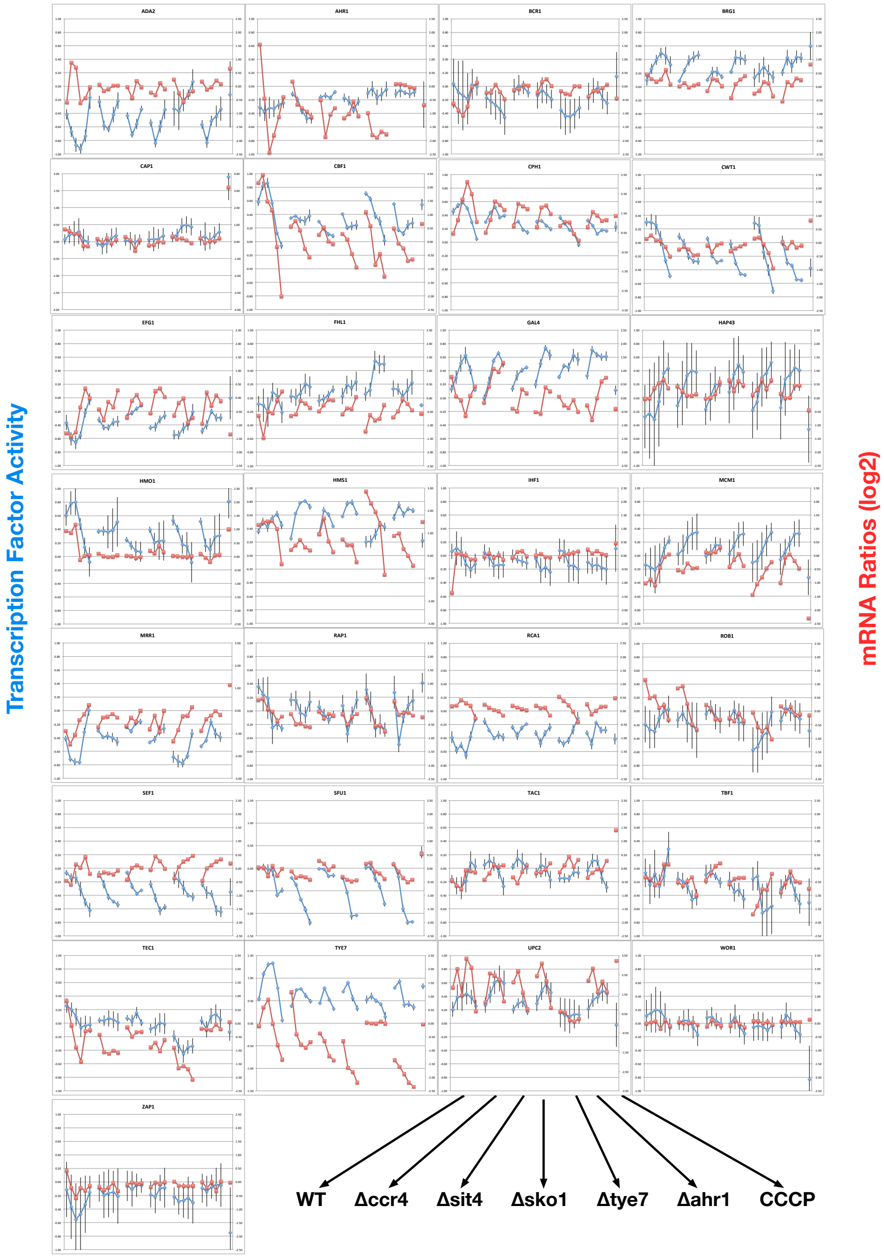


Supplementary Figure 1: Enrichment Map of the early hypoxic response at 5 and 30 min. Enrichment Map combining the GSEA results from the hypoxic profiles in wild type cells after 5 (inside of nodes) or 30 minutes (outer edge of nodes). Red nodes represents upregulated gene sets while downregulated gene sets are colored in blue. If a gene set was not significantly modulated at either the 5 or 30 min time point, its inside or outer edge remains white. The Enrichment Map plug-in was then used to cluster gene sets according to the overlap between their member genes, resulting in larger functional subclusters. For better visualization and to allow selection or specific subclusters readers are invited to use the Cytoscape file which has has been included in Supplementary File 3.



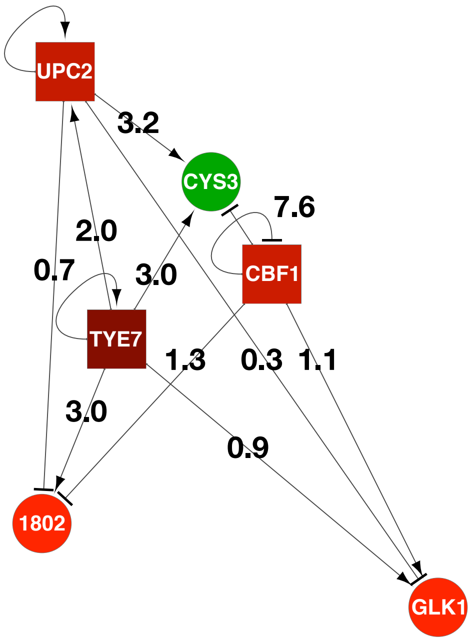
Supplementary Figure 2: Graphical representation of the number of specific transcripts and significant GO categories at each time point during hypoxia

Venn diagrams were built between each time point and the total of genes remaining in the others. Numbers in the outer circle are genes considered time point-specific. Numbers in red and in green represent, respectively, upregulated and repressed transcripts throughout the time course. Similarly, GO annotation symbolized in red and in green represent functional categories enriched in up- and downregulated genes, respectively.



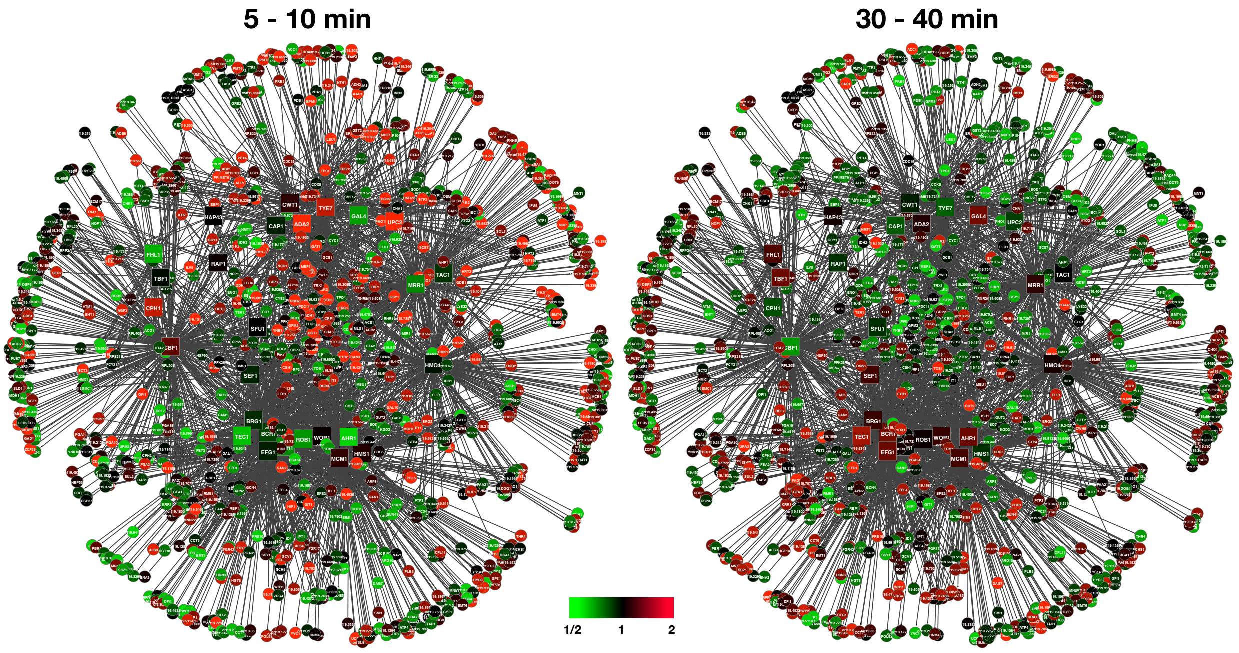
Supplementary Figure 3: Estimated Transcription Factor Activity values for all 29 modelled TFs.

Promoter occupancy data of 29 *C. albicans* TF was combined with transcriptional profiles from 3155 TF targets in a Network Component Analysis to produce estimates of Transcription Factor Activities (TFA) during the early hypoxic responses in 6 *C. albicans* strains or following treatment of wild type cells with CCCP. Changes in TFA values are indicated by the blue line while the red lines show changes in the TF gene transcript levels. Error bars represent the Standard Deviation of the calculated TFAs from 50 runs of the NCA algorithm.



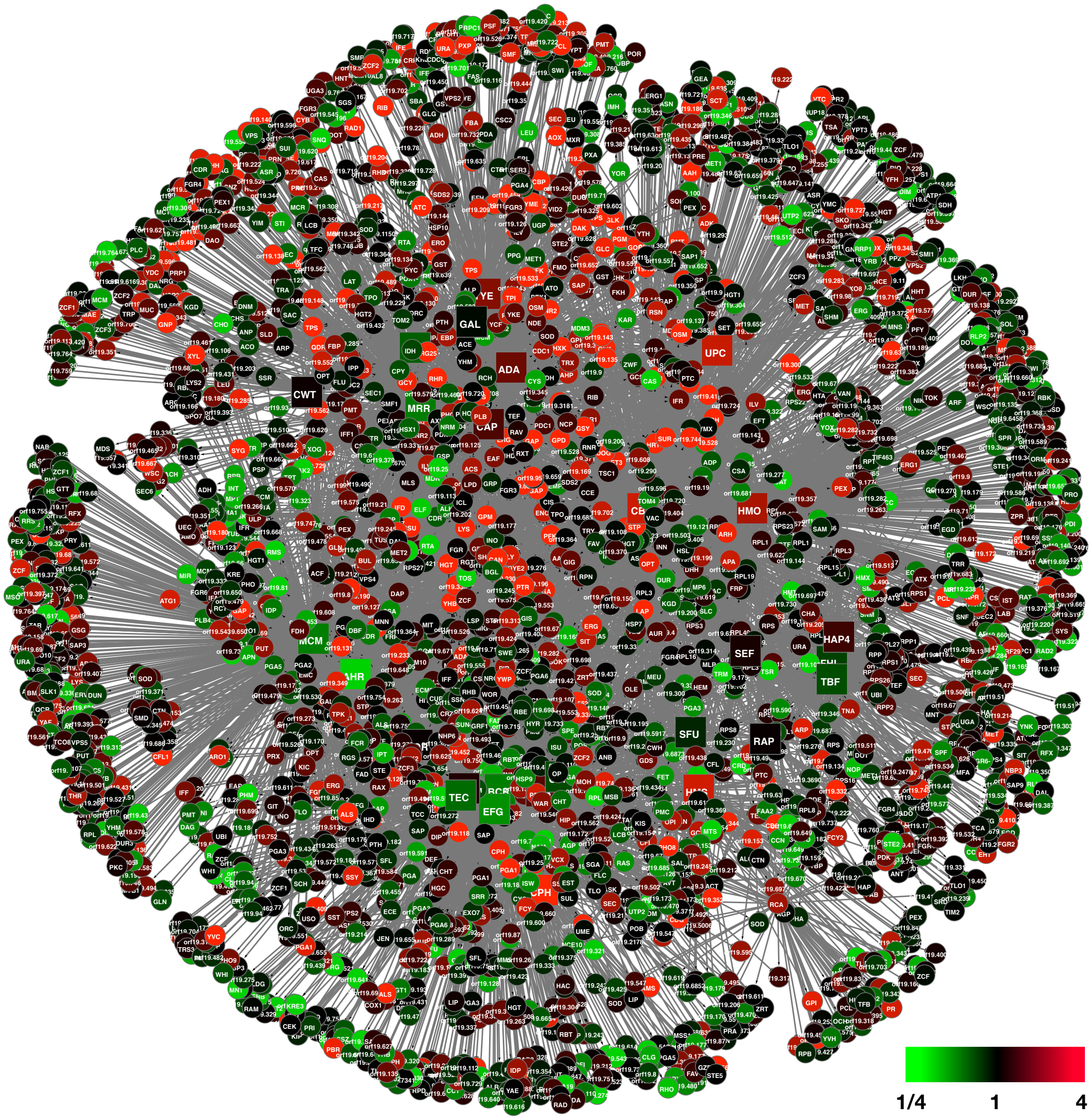
Supplementary Figure 4: Effect of the calculated Connectivity Strength values on the TF network layout.

The layout of this 6 node TF network was produced with the same edge-weighted spring embedded algorithm as the larger networks in Figure 6 and Supplementary Figure 5. Numbers represent the Connectivity Strength values calculated in the NCA model that represent the influence of a TF on its gene target. Stronger CS values are modeled as stronger springs which result in a reduction in edge length between a TF and its target.

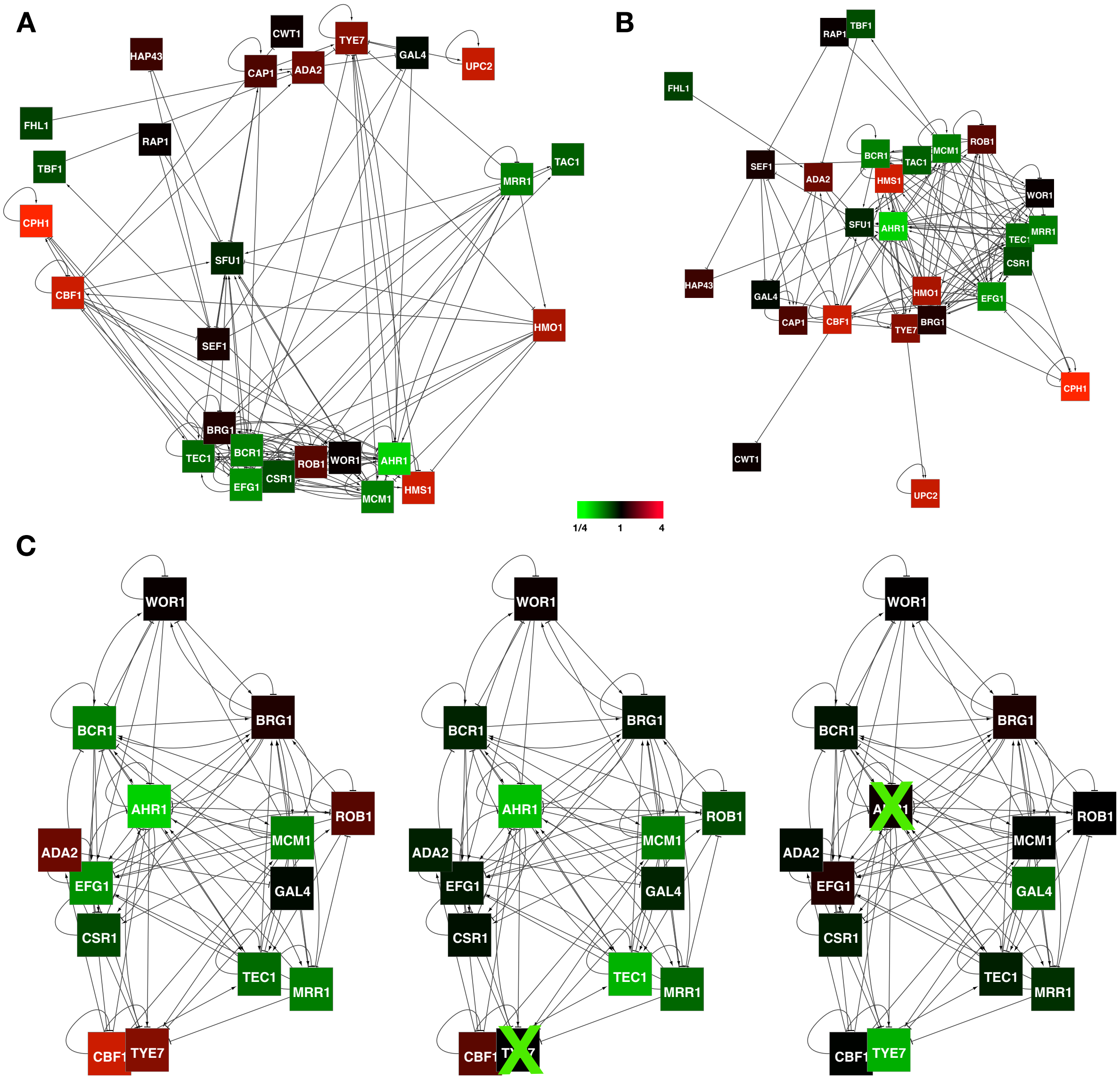


Supplementary Figure 5: Visualization of transcript rate changes in the context of TF networks

Nodes from the same TF network as in Figure 6 were colored according to the rates of change in transcript abundance between the 5-10 min and the 30-40 min time points. Temporal changes of the rates of transcript abundance are also available as a Quicktime video in Supplementary File 7.



Supplementary Figure 6: Transcription factor network of from all TF gene targets. Cytoscape was used to construct a transcription factor network of 3140 nodes and 7331 edges representing the interactions between 28 TFs (square nodes) and 3112 gene targets (round nodes). This network also integrates NCA modeling data whereby the spring strength between a TF and its gene target is influenced by its Connectivity Strength (See Supplementary Figure 4). Nodes are colored red or green according to their change in transcript abundance after 20 min of hypoxic response in wild type cells.



WT 20 min

Δtye7 30 min

Δahr1 30 min

Supplementary Figure 7: Interactions between TFs and TF gene promoters.
(A) Network of TF nodes in the same position as in the network in Figure 6. **(B)** Independent layout of TFs and TFs gene targets in the absence of non-TF genes. In both figures the nodes are colored according to the change in transcript abundance after 20 min of hypoxia in wild type cells. **(C)** Network of TFs with a 1st or 2nd generation interaction with the TYE7 or AHR1 gene promoters. Nodes are colored according to transcript levels changes in the conditions indicated below.