# IDENTIFICATION OF KEY TRANSCRIPTION FACTORS IN GLUCOSE SENSING PATHWAY IN *SACCHAROMYCES CEREVISIAE*

by

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# IDENTIFICATION OF KEY TRANSCRIPTION FACTORS IN GLUCOSE SENSING PATHWAY IN *SACCHAROMYCES CEREVISIAE*

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# ABSTRACT

## IDENTIFICATION OF KEY TRANSCRIPTION FACTORS IN GLUCOSE SENSING PATHWAY IN *SACCHAROMYCES CEREVISIAE*

In this study, a genome-scale transcriptional regulatory network (TRN) in *S. cerevisiae* was constructed and integrated with the transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae* to identify key transcription factors (transcription factors around which a considerable collective change in the expression of the genes occur in response to environmental and genetic perturbations). Identification of key transcription factors demonstrates the regulatory mechanisms invoked in the cell and potential biomarkers, without *a priori* requirement of change in the transcription level of the transcription factors. Biologically meaningful key transcription factors identified with this approach shed light on the transcriptional regulatory mechanism controlling the glucose signaling in *S. cerevisiae*. For example, key transcription factors identified in *ΔSNF1* reveal the predicted role of Snf1p kinase, highlighting the effectiveness of the approach used and a large genome-scale TRN. In this study, after the key transcription factors were identified, the perturbation-responsive subnetworks were constructed by interconnecting key transcription factors and their differentially expressed target genes responsive to the same perturbation. Based on whether the key transcription factors have their differential expression changed significantly, it was investigated if the transcription factors are regulated mainly transcriptionally or mainly post-transcriptionally.

# ÖZET

## *SACCHAROMYCES CEREVISIAE’DA* GLİKOZ ALGILAMA YOLİZİNDEKİ ANAHTAR YAZILIM ETMENLERİNİN BELİRLENMESİ

Glikoz, *Saccharomyces cerevisiae*’da en çok tercih edilen karbon kaynağıdır. Bu çalışmada, *S. cerevisiae*’da genom ölçekli bir yazılım düzenleyici ağ oluşturulmuş ve bu ağ *S. cerevisiae*’nın glikoz algılama yolizi mutantlarının literatürde mevcut olan gen ekspresyonu verisi ile bütünleştirilerek anahtar yazılım etmenleri (etraflarındaki gen ekspresyonunda, çevresel ve genetik pertürbasyonlara tepki olarak önemli toplu bir değişim meydana gelen yazılım etmenleri) belirlenmiştir. Anahtar yazılım etmenlerinin belirlenmesi, hücrede başlatılan düzenleyici mekanizmaları ve olası biyolojik göstergeleri, yazılım etmenlerinin yazılım düzeylerinde değişim gözlenmese de gösterir. Kullanılan yaklaşımla belirlenmiş biyolojik olarak anlamlı anahtar yazılım etmenleri *S. cerevisiae*’nın glikoz algılamasını kontrol eden yazılım düzenleyici mekanizmaya ışık tutmuştur. Örneğin, *ΔSNF1*’da belirlenen anahtar yazılım etmenleri, kullanılan yaklaşımın ve geniş genom ölçekli bir yazılım düzenleyici ağın verimliliğini vurgulayarak, Snf1p’in öngörülen rolünü açığa çıkarmıştır. Bu çalışmada, anahtar yazılım etmenleri belirlendikten sonra, anahtar yazılım etmenleri ile onların aynı değişimlere istatistiksel olarak anlamlı yanıt veren hedef genleri birbirlerine bağlanarak, değişimlere yanıt veren altağlar da oluşturulmuştur. Anahtar yazılım etmenlerinin, değişimlere istatistiksel olarak anlamlı yanıt verip vermediklerine dayanarak, yazılım etmenlerinin başlıca yazılım sırasında mı yoksa başlıca yazılım sonrası mı düzenlendikleri araştırılmıştır.

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| | |
|---|---|
| $<C>$ | Average clustering coefficient of the network |
| $<k>$ | Average degree of the network |
| $b$ | Betweenness centrality |
| $C$ | Clustering coefficient |
| $f$ | Frequency |
| $k$ | Degree |
| $l$ | Number of interactions |
| $N$ | Number of nodes |
| $n$ | Cumulative distribution |
| P | Probability |
| $p$ | $p$-value |
| $Z$ | $Z$-score |

| | |
|---|---|
| $\gamma$ | Power law exponent |
| $\Gamma(m, i, n)$ | Number of the shortest paths between nodes $N_m$ and $N_n$, passing through $N_i$ |
| $\Gamma(m, n)$ | Total number of paths between nodes $N_m$ and $N_n$ |
| $\mu$ | Mean |
| $\sigma$ | Standard deviation |

| | |
|---|---|
| AER | Aerobic |
| AKG | α-ketoglutarate |
| AMP | Adenosine monophosphate |
| ANA | Anaerobic |
| ATP | Adenosine-5'-triphosphate |
| cAMP | Cyclic adenosine monophosphate |
| Clim | Carbon limitation regime |
| DNA | Deoxyribonucleic acid |
| FC | Fold change |
| GDP | Guanosine diphosphate |

| | |
|---|---|
| Gln | Glutamine |
| Glu | Glutamate |
| GO | The Gene Ontology |
| GPCR | G protein-coupled receptors |
| GTP | Guanosine-5'-triphosphate |
| GWLA | Genome-wide location analysis |
| MIPS | Munich Information Center for Protein Sequences |
| mRNA | Messenger ribonucleic acid |
| ORF | Open reading frame |
| PKA | Protein kinase A |
| PKB | Protein kinase B |
| PRS | Perturbation-responsive subnetwork |
| rDNA | Ribosomal deoxyribonucleic acid |
| RNA | Ribonucleic acid |
| *S. cerevisiae* | *Saccharomyces cerevisiae* |
| SF | Scale-free |
| SGD | *Saccharomyces* Genome Database |
| TF | Transcription factor |
| TOR | Target Of Rapamycin |
| TRN | Transcriptional regulatory network |
| tRNA | Transfer ribonucleic acid |
| YEASTRACT | Yeast Search for Transcriptional Regulators And Consensus Tracking |

# 1. INTRODUCTION

## 1.1. Glucose Sensing and Signaling in *Saccharomyces cerevisiae*

Glucose is the preferred carbon and energy source for most cells and can act as a "growth hormone" to regulate several aspects of cell growth, metabolism, and development. Defects in glucose sensing, signaling, and metabolism cause severe and prevalent metabolic disorders in mammals known as diabetes (Özcan and Johnston, 1999).

Glucose is metabolized through glycolysis to pyruvate (Figure 1.1). In the presence of oxygen, most organisms convert pyruvate to carbon dioxide and water via the tricarboxylic acid cycle, generating 36 ATPs. Only when oxygen becomes limiting do most cells resort to fermentation, because it yields only two ATPs per molecule of glucose. *Saccharomyces cerevisiae* is one of the few organisms that prefer to ferment glucose, even when oxygen is abundant. The tendency of *S. cerevisiae* to carry out aerobic fermentation is called the 'Crabtree effect' (Johnston and Kim, 2005).

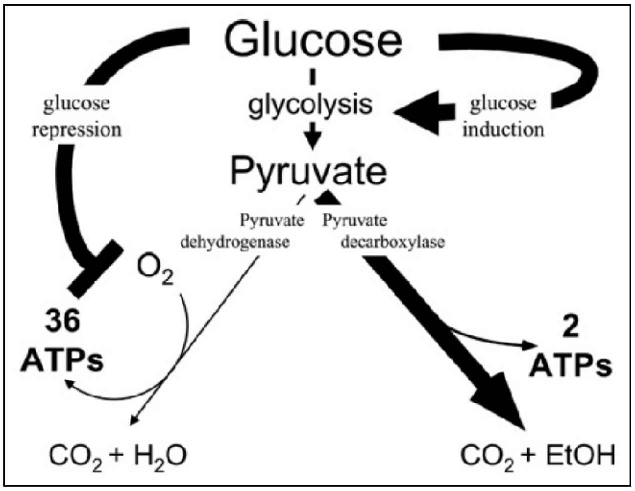

Figure 1.1. Simplified scheme of the glucose metabolism in yeast (Johnston and Kim, 2005)

Glucose, the most preferred carbon source of the budding yeast *S. cerevisiae*, elicits broad changes in the yeast cell that uses the sugar efficiently and exclusively. These changes include regulation of gene expression at the transcriptional, post-transcriptional, translational and post-translational levels (Kaniak *et al.,* 2004). However, the main effect of glucose takes place at the transcriptional level (Gancedo, 1998). For these adaptations to occur, the cell must sense glucose and transmit a signal to the appropriate targets.

Glucose induction and glucose repression are the two major constituents of glucose signaling. In glucose induction pathway, glucose has to be sensed so that glucose transporters can be transcribed and translated to transport glucose inside the cell. Glucose repression pathway becomes active after the glucose has been transported inside the cell and phosphorylated (Raghevendran *et al*., 2005). Although these two pathways show different characteristics, they are shown to be connected to each other by a regulatory network in *S. cerevisiae* (Kaniak *et al.,* 2004).

Zaman *et al.* have identified the glucose-mediated transcriptional response through the contribution of five distinct but interconnected pathways (Figure 1.2): Ras/PKA, Gpr1p/Gpa2p and Sch9p, playing significant roles in the early steps in signal transduction, and Snf1p, Rgt2p/Snf3p, members of the glucose repression and glucose induction pathways, respectively. Moreover, the heme-activated transcriptional regulators Hap1p and the Hap2p/3p/4p/5p complex regulate a significant fraction of the genes repressed independently of PKA (Santangelo, 2006; Zaman *et al.*, 2009).

### 1.1.1. Early Steps in Signal Transduction

The Ras/PKA pathway (Figure 1.3) is activated immediately in the presence of glucose; it responds to changes in glucose concentration and initiates the signaling processes that lead to cellular growth and division. Ras is a guanine nucleotide-binding protein which is inactive in the GDP-bound state and active when GTP is bound. The polypeptides encoded by the two RAS genes in *S. cerevisiae*, Ras1p and Ras2p, are about 70 per cent identical overall. In its GTP-bound state Ras activates adenylate cyclase (Cyr1p). Glucose addition to cells increases the level of GTP-bound Ras, yielding an increase in intracellular cAMP production by adenylate cyclase, to block the inhibitory effect of the *BCY1*-encoded regulatory subunit on the catalytic subunits of PKA, encoded redundantly by *TPK1*, *TPK2*, and *TPK3*. The PKA catalytic subunits phosphorylate a variety of proteins involved in metabolism and transcription.

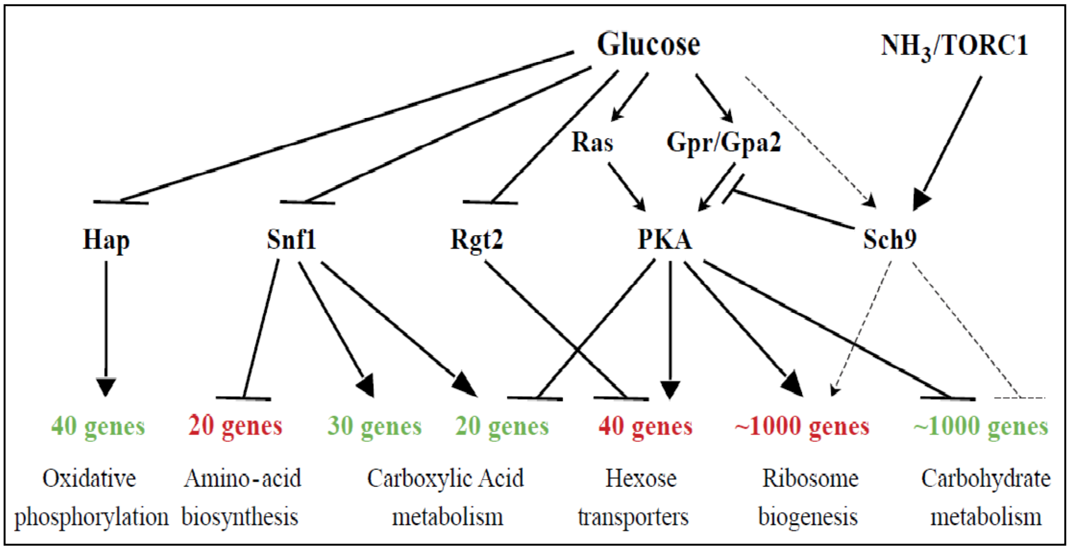

Figure 1.2. Diagram of the regulatory wiring connecting the addition of glucose to the transcriptional responses of the cell (Zaman *et al.*, 2009)

Gpr1p and Gpa2p represent a glucose sensing pathway that function in a similar manner to Ras to activate PKA. The GPCR-like seven-transmembrane protein located on the yeast cell surface, Gpr1p, stimulates the adenylate cyclase in response to glucose through its associated GTP-binding protein, Gpa2p (Santangelo, 2006; Zaman *et al.*, 2009).

Sch9p, an AGC family kinase, is the closest yeast homolog to the mammalian pro-survival Akt/PKB (a component of the mammalian insulin response pathway) as well as to the TOR regulated S6 kinase. *SCH9* overexpression suppresses lethality caused by the loss of PKA signaling (Toda *et al.*, 1988). It is still unknown whether the ability of Sch9p to compensate mutations in the Ras/PKA pathway reflects a convergence of Sch9p and PKA activities from different signaling paths or a direct participation of Sch9p in glucose signaling (Santangelo, 2006). Zaman *et al.* suggested that Sch9p does not contribute significantly to glucose signaling as does PKA but provides a parallel pathway to PKA for glucose-mediated transcriptional changes. They have also proposed a potential cross-talk between the TOR and Gpa2p/PKA pathways by which diminished TOR signaling enhances the signaling response through the PKA pathway (Zaman *et al.*, 2009).

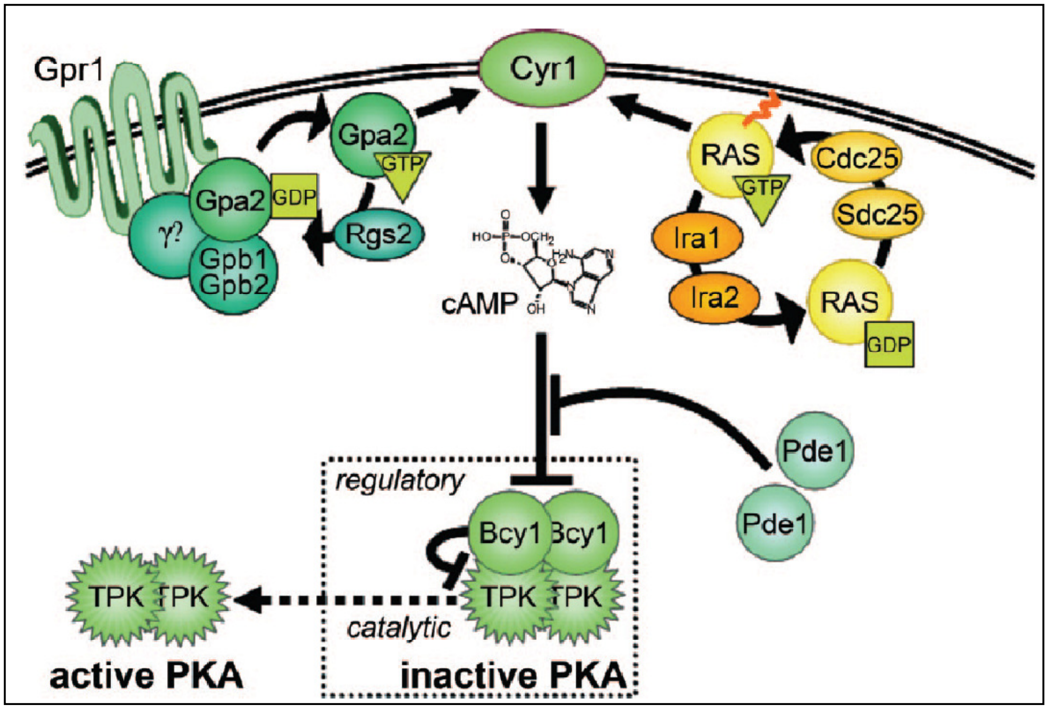

Figure 1.3. Cytoplasmic events in PKA signaling (Santangelo, 2006)

PKA and Snf1p cooperate in the regulation of many processes such as carboxylic acid metabolism, β-oxidation of fatty acids, stress response and filamentous growth; however they are activated by glucose excess or depletion, respectively (Figure 1.4). On the other hand, PKA and Tor1p are both active in response to the nutritional stimuli (glucose and nitrogen) thus function in parallel, to promote the growth (Zhang *et al.*, 2010).

### 1.1.2. Glucose Induction Pathway in *Saccharomyces cerevisiae*

The glucose induction (Figure 1.5) is initiated by two yeast membrane glucose sensors Snf3p and Rgt2p with very long cytoplasmic tails that sense low and high concentrations of glucose, respectively. When glucose binds to sensors, the sensors undergo a conformational change that activates the membrane-bound casein kinase, Yck1p. Two proteins, Mth1p and Std1p, which interact with the cytoplasmic tails in glucose grown cells, are phosphorylated by Yck1p. Phosphorylated Mth1p and Std1p are ubiquitinated by the protein Grr1p. Ubiquitinated proteins are recognized by the proteasomal machinery and degraded. All the above-mentioned protein-protein interactions occur in the cytoplasm, resulting in a signal being sent to the nucleus, where the transcription factor Rgt1p becomes hyperphosphorylated. Once Rgt1p becomes hyperphosphorylated, it is believed that an unknown protein activates the transcription of the glucose-transporter-encoding *HXT* genes. In the absence of glucose, the proteins Mth1p and Std1p move to the nucleus, where they interact with the active Rgt1p protein and repress the transcription of *HXT* genes (Raghevendran *et al.*, 2005). Rgt1p activity is further influenced by the Snf1p and PKA pathways, and components of the Rgt system are subject to various positive and negative feedback loops (Kaniak *et al.*, 2004; Zaman *et al.*, 2009).

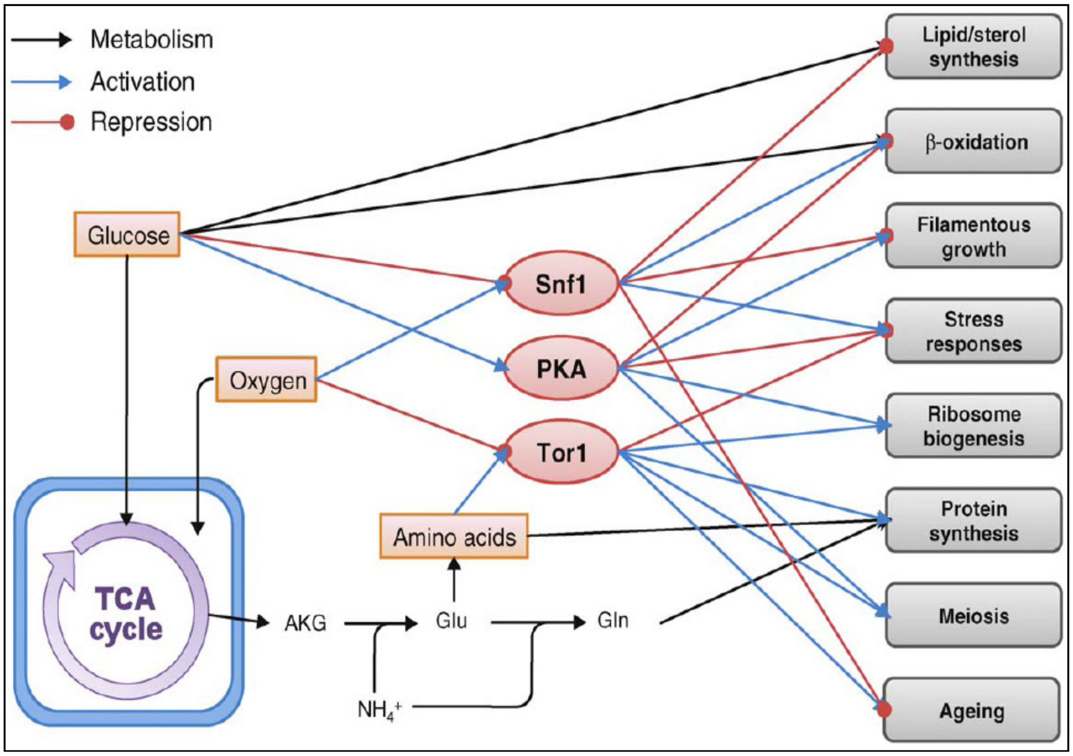

Figure 1.4. Interactions between Snf1p, Tor1p and PKA pathways in yeast (Zhang *et al.*, 2010)

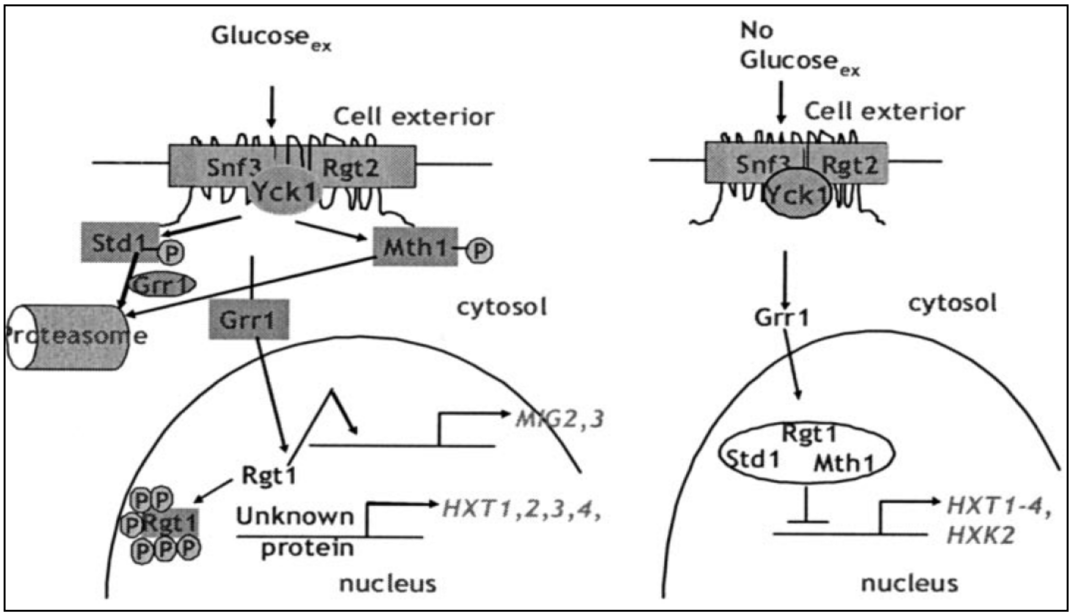

Figure 1.5. Glucose induction pathway in *S. cerevisiae* (Raghevendran *et al.*, 2005)

### 1.1.3. Glucose Repression Pathway in *Saccharomyces cerevisiae*

In the presence of glucose, inactive Mig1p (a DNA-binding protein with Zinc finger domain) gets dephosphorylated by the Glc7p phosphatase via its regulatory subunit Reg1p. It is believed that the metabolic enzyme, hexokinase 2 (Hxk2p, it phosphorylates glucose in glycolysis) positively regulates this step either directly or indirectly. Active Mig1p (unphosphorylated) interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes. *MIG1* expression is regulated by Mig2p. Snf1p, the yeast homolog of mammalian AMP-activated protein kinase, gets activated by three upstream kinases when the glucose becomes depleted, and activates genes that are repressed in glucose-containing media but are derepressed and needed for growth in the presence of nonfermentable carbon sources, such as glycerol and ethanol (Figure 1.6). Snf1p complex is a heterotrimer, composed of a catalytic α-subunit (Snf1p), a regulatory γ-subunit (Snf4p), and a scaffolding β-subunit (one of Sip1p, Sip2p or Gal83p). Active Snf1p enables the transcription of many genes responsible for oxidative growth through activation of the transcriptional activators Cat8p and Adr1p and inactivation of the Mig1p transcriptional repressor (Raghevendran *et al.*, 2005). In the presence of glucose, the Reg1p/Glc7p protein phosphatase 1 complex dephosphorylates and inactivates Snf1p (Sanz *et al.*, 2000).

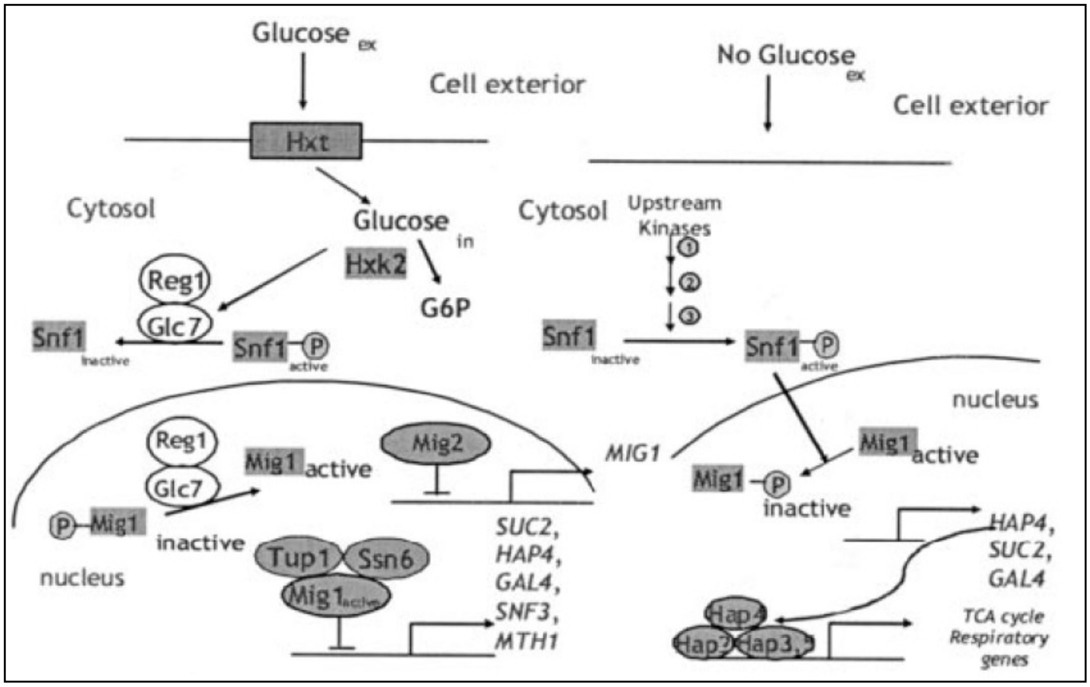

Figure 1.6. Glucose repression pathway in *S. cerevisiae* (Raghevendran *et al.*, 2005)

## 1.2. Transcriptional Regulatory Networks

Gene expression is a carefully regulated and controlled process. Under a given condition or in a particular cell type, only a fraction of the genes are expressed. There is a complex transcriptional regulatory network (TRN) that controls which genes are expressed in response to various environmental and developmental signals (Palsson, 2006).

Transcription factors (TFs) determine which genes in a cell will be transcribed by recognizing and binding to short stretches of double-helical DNA of defined sequence. TFs may act as transcriptional activators or transcriptional repressors (Alberts *et al.*, 1994). The basic functional element of a TRN is the promoter region of a gene or operon that contains the regulatory binding sites for the relevant TFs regulating the expression of a particular gene. The locations and orientations of these binding sites, as well as the affinity of the TFs to particular variants of the site, determine the expression levels of a gene in response to changes in the active TF concentrations inside the cell. In the light of the information given above, the TRN is defined by which TF binds to which promoters and what the integrated effect of all these TFs is on the expression of all the genes (Ptashne and Gann, 2002).

There are three types of intracellular biochemical reaction networks: metabolic, transcriptional regulatory and signaling networks. The ultimate goal of systems biology is to integrate all of these three to generate whole-cell models of microbes and other organisms. The major advantage of TRN reconstruction over other types of network reconstructions is the availability of high-throughput experimental data, such as genome-wide mRNA expression and genome-wide location analysis (GWLA), that is directly relevant to the TRN structure (Herrgard *et al.*, 2004).

For TRNs the number of TFs cannot be simply used to predict the complexity of the network, owing to the fact that TFs can have multiple target genes and can often act in synergistic combinations (Herrgard *et al.*, 2004). However, the fraction of TF encoding genes tends to be higher in organisms that encounter a wider range of environmental conditions during their lifespans (Cases *et al.*, 2003). This indicates that a number of TFs can only achieve a certain level of complexity. Well-studied organisms can be used to assess this complexity of TRNs in terms of the number of components, TFs and target genes, and regulatory interactions. For instance, in *S. cerevisiae*, a well studied model organism, the documented TFs (185) and their target genes (6297) are involved in 42609 interactions (YEASTRACT, taken on April 27th, 2009) (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008). There are two other yeast TRNs available in literature. The study of Lee *et al.*, 2002 (updated at December 5, 2003) contains 4323 regulatory interactions between 106 TFs and 2343 target genes (p-value $< 0.001$) (Lee *et al.*, 2002). The data on the yeast regulatory network constructed by Luscombe *et al.* consists of 7074 interactions between 142 TFs and 3420 target genes (Luscombe *et al.*, 2004).

### 1.2.1. Scale Free Networks

It is supposed that biological networks have a scale-free (SF) network structure instead of random network structure. Biological interaction networks are defined as sets of $N$ nodes ($N_i$, $i = 1, \ldots, N$) linked together with interactions represented by $l$. The number of links of a node is defined as the degree ($k_i$) of a node and $<k>$ is the average degree of the network. In random networks each pair of nodes are connected with a probability that follows a Poisson distribution ($P(k) \sim e^{-k}$) peaking strongly at $<k>$ and decaying exponentially for higher $k$ values than $<k>$. SF networks are extremely heterogeneous where a few highly connected nodes are dominant by which rest of the less connected nodes are linked to network. Comparison between random networks and SF networks is illustrated in Figure 1.7. The degree distribution of a SF network follows power law, i.e. $f(k)=Ak^{-\gamma}$, with $2< \gamma <3$, where $f(k)$ is the frequency of the nodes with a degree of $k$ and $A$ is a constant. $\gamma_c$, the power law exponent of cumulative degree distribution, $n(k)$, and $\gamma$ are related by:

$$\gamma = 1-\gamma_c \tag{1.1}$$

SF networks also exhibit power law correlations in clustering and betweenness vs. degree plots (Jeong *et al.,* 2000; Rodriguez-Caso *et al.*, 2005).

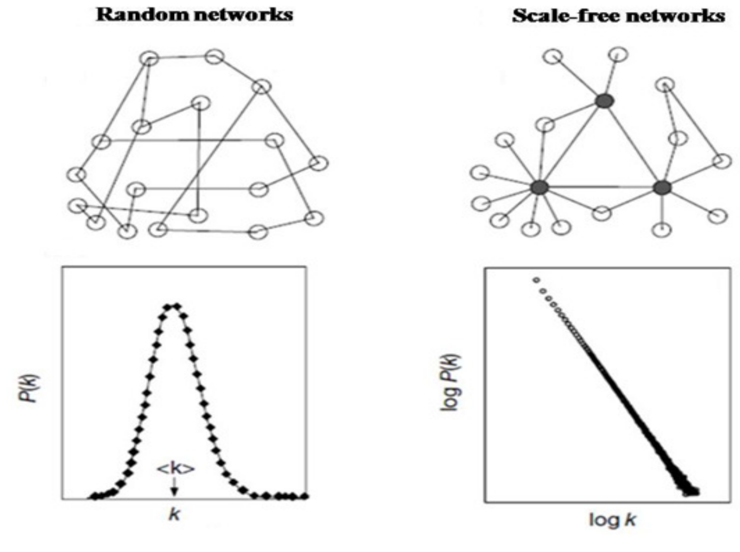

Figure 1.7. Representative structures of random and scale-free networks (Jeong *et al.,* 2000)

A SF network includes a small number of highly connected nodes (hubs) and a large number of poorly connected nodes (non-hubs) (He and Zhang, 2006). Hub nodes are generally distinguished by their degree but there is no consensus on how many interactions a hub node should have. In the study of Hsing *et al.*, the hub selection criterion was based on the position of a sharp turn on an accumulative degree distribution plot, whereas Hwang *et al.* accepted the nodes having half of the maximum degree of the network as hubs (Hsing *et al.*, 2008; Hwang *et al.*, 2008). Betweenness measures the centrality of the nodes in networks and most of the shortest paths in a network go through the nodes with high betweenness. Hence, these nodes become the central nodes controlling the communication among other nodes in the network. In addition, Goh *et al.* have found that the betweenness of a node is correlated to its degree (Goh *et al.*, 2003; Yu *et al.*, 2007).

## 1.3. Key Transcription Factors and Reporter Features

The study of Luscombe *et al.* on the dynamics of the TRNs revealed that over half of the active interactions between TFs and their target genes are completely replaced by new ones when conditions are changed (Luscombe *et al.*, 2004). This result highlights the importance of the dynamics of a network, considering that significant changes occur in a network between two different conditions.

In previous studies, TRNs were studied by analyzing transcriptome data, assuming that there may be an all-to-all interaction among the studied genes, which leads to the identification of several false positives (Pe’er *et al.*, 2001; Segal *et al.*, 2003). However, the topology of TRN itself affects the regulatory response of the network following a perturbation. Integrating known biological interactions in the analysis of transcriptome data reduces the degrees of freedom in data analysis.

Many TFs do not respond at transcriptional level per se, but through post-translational regulation. Key TFs are TFs around which most significant transcriptional changes occur in response to environmental and genetic perturbations, where there is substantial regulation either to maintain homeostasis (i.e., a constant level of the expression of target genes) or adjust the expression levels of the target genes to another level required for proper functioning of the TRN (Patil and Nielsen, 2005). Identification of key TFs demonstrates a considerable collective change in the expression of the genes regulated by them when passing from one condition to another, the regulatory mechanisms invoked in the cell and potential biomarkers, following a perturbation, without *a priori* requirement of change in the transcription level of the TFs.

Patil and Nielsen developed and implemented an algorithm for successful identification of reporter metabolites (metabolites around which the most significant transcriptional changes occur) in yeast by the integration of the genome-scale metabolic network with transcriptome data (Patil and Nielsen, 2005). Reporter metabolites algorithm has been generalized and extended to the reporter features algorithm in order to include reporter gene ontologies, reporter TFs, reporter proteins and reporter complexes (Oliveira *et al.*, 2008). Reporter features algorithm has recently been used in many studies regarding yeast. Usaite *et al.* applied the algorithm to identify reporter TFs and regulatory proteins whose target genes were most significantly affected and responded as a group to genetic disruptions of the Snf1p complex (Usaite *et al.*, 2009). Mo *et al.* have analyzed the intracellular flux distributions using reporter features algorithm to identify the dominant metabolic features that were collectively perturbed (Mo *et al.*, 2009). In a study of Cimini *et al.*, key proteins involved in the cellular response to *SDH3* deletion were identified (Cimini *et al.*, 2009). The change in the activity of TFs can be positive or negative, however reporter features algorithm does not specify the direction of the change but only the significancy of the change.

## 1.4. The Aim of this Thesis

The aim of this thesis is to acquire a more detailed and comprehensive understanding of the transcriptional regulatory mechanism controlling the glucose signaling in yeast *S. cerevisiae* through the reconstruction of a genome-scale TRN in *S. cerevisiae* and analyzing its topology, and by integrating it with transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae,* to identify the key TFs with the use of reporter features algorithm by Oliveira *et al.* (Oliveira *et al.*, 2008).

# 2. METHODS

## 2.1. Construction of the Transcriptional Regulatory Network

A genome-scale TRN in baker's yeast *S. cerevisiae* was constructed by assembling regulatory interactions from different data sources (Lee *et al.*, 2002; Luscombe *et al.*, 2004; YEASTRACT (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008)).

The documented regulations between all TFs and genes described in YEASTRACT, a freely accessible database available at http://www.yeastract.com/ and updated at April 27, 2009, include 42609 interactions between 185 TFs and 6297 target genes (Teixeira *et al.*, 2006; Monteiro *et al.*, 2008).

The publicly available datasets on the regulatory network of *S. cerevisiae* were downloaded from the supporting websites of the original publications of Lee *et al.*, 2002 updated at December 5, 2003 and Luscombe *et al.*, 2004 (Lee *et al.*, 2002; Luscombe *et al.*, 2004).

The regulatory interaction dataset of Lee *et al.* scores the interactions in terms of significance with $p$-value cut-offs of 0.001 or 0.005. The stricter option of 0.001 was selected and 4323 regulatory interactions were achieved with a $p$-value less than 0.001 between 106 TFs and 2343 target genes (Lee *et al.*, 2002). The data on the yeast regulatory network treated by Luscombe *et al.* consist of 7074 interactions between 142 TFs and 3420 target genes (Luscombe *et al.*, 2004).

If an interaction was present in any of the above three datasets, it was included to the TRN being constructed. The regulatory interactions, which were represented as two columns, are between TFs and non-TF target genes or between two TFs.

## 2.2. Topological Study of the Transcriptional Regulatory Network

The network was visualized using the program Cytoscape v2.6.3, a general purpose open source bioinformatics software capable of visualizing biomolecular interaction networks (Shannon *et al.*, 2003).

The degree distribution, betweenness centrality and clustering coefficient, which provide global information about the network, were obtained by using Networkx Module programming in Python v2.6.2, after self-interactions were excluded.

The clustering coefficient ($C_i$) of a node $N_i$ is the number of neighboring of $l_\mathrm{i}$ links between nodes divided by the total number allowed by its degree, $k_i$ ($k_i$ –1),which shows the interconnection of the neighbors. The clustering coefficient of the whole network is,

$$<C>=\frac{1}{N}\sum_{i=1}^{N}\frac{2l_i}{k_i(k_i-1)} \tag{2.1}$$

The number of short paths connecting each pair of nodes that contain the node $N_i$ is indicated as betweenness centrality ($b_i$) for a node $N_i$. It is defined as,

$$b_i=\sum_{m\neq n}\frac{\Gamma(m,\ i,\ n)}{\Gamma(m,\ n)} \tag{2.2}$$

where $\Gamma(m,\ i,\ n)$ is the number of the shortest paths between nodes $N_m$ and $N_n$, passing through $N_i$, whereas $\Gamma(m,\ n)$ is the total number of paths between those two nodes. The ratio $\Gamma\ (m,\ i,\ n)\ /\ \Gamma\ (m,\ n)$ shows the significance of the node $N_i$ in connecting $N_m$ and $N_n$ (Rodriguez-Caso *et al.*, 2005).

In order to analyze if the constructed TRN exhibits SF distribution, 1000 random networks were generated by assigning the same number of interactions among the same number of nodes as in the TRN. Degree and betweenness measures were taken as the basis for hub identification. Every node in the network was ranked according to its degree and betweenness, and the nodes at the intersection of the top 20 highest degree and top 20 highest betweenness nodes were selected as the hub nodes. The significant shared Gene Ontology (GO) biological process terms ($p$-value<0.01) associated with the selected hubs were found from the *Saccharomyces* Genome Database (SGD). Biological process refers to a biological objective that the gene or its product contributes (The Gene Ontology Consortium, 2000).

### 2.3. Identification of Key Transcription Factors

Differential gene expression data, in which two strains or two conditions were compared with multiple measurements for each strain, were used in the present study. For genetic perturbations the *ΔSNF1*, *ΔSNF4*, *ΔSNF1ΔSNF4*, *ΔMIG1*, *ΔMIG2*, *ΔMIG3*, *ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* mutants were compared with wild type strain and for environmental perturbation transcriptional data obtained under anaerobic and aerobic conditions for carbon limitation regime were used in the framework of this thesis (Tai *et al.*, 2005; Westholm *et al.*, 2008; Usaite *et al.*, 2009).

The following steps were performed in order to identify key TFs responsive to each specific perturbation, after eliminating the nodes of the yeast TRN which were not quantified in the corresponding transcriptome data.

- $p$-value for each gene i in the TRN was calculated by using Student’s t-test and converted into $Z$-score ($Z_{ni}$) using the inverse normal cumulative distribution function ($\theta^{-1}$).

$$Z_{ni} = \theta^{-1}(1-p_i) \qquad (2.3)$$

- Each TF was scored as the average of the $Z$-scores of its k neighboring genes.

$$Z_{TF} = \Sigma\, Z_{ni} / \mathrm{k} \qquad (2.4)$$

- $Z_{TF}$ scores were corrected for the background distribution of $Z$-scores, by subtracting the mean, $\mu_k$, and dividing by the standard deviation, $\sigma_k$, of 1000 sets of k genes randomly selected from the graph. The MATLAB code performing $Z_{\text{corrected,TF}}$ calculations is given in Appendix B.

$$Z_{\text{corrected,TF}} = (Z_{\text{TF}} - \mu_{\text{k}}) / \sigma_{\text{k}} \quad (2.5)$$

- $Z_{\text{corrected,TF}}$ scores were converted back into $p$-values using the normal cumulative distribution function. TFs were ranked according their $Z_{\text{corrected,TF}}$ scores and TFs with a $p$-value less than 0.05 were defined as key TFs.

The GO biological process terms and definitions associated with each key TF and the significant shared GO biological process terms ($p$-value<0.01) associated with the key TFs responsive to each specific perturbation were found from the SGD (The Gene Ontology Consortium, 2000).

### 2.4. Identification of Perturbation-Responsive Subnetworks

Perturbation-responsive subnetworks (PRSs), composed of key TFs and their differentially expressed target genes ($p$-value<0.05) responsive to the same perturbation, were identified. The GO biological process terms significantly associated with the target genes for each PRS ($p$-value<0.01) were found from the SGD (The Gene Ontology Consortium, 2000).

### 2.5. Identification of Regulation of Key Transcription Factors

Regulation of key TFs was evaluated based on whether the TFs have their differential expression changed significantly ($p$-value<0.05). There are two possible cases (Oliveira *et al.*, 2008):

(i) If the key TF is differently expressed, it is mainly transcriptionally governed.
(ii) If the key TF is not differentially expressed, it is mainly post-transcriptionally regulated.

# 3. RESULTS AND DISCUSSION

## 3.1. Topological Study of the Transcriptional Regulatory Network

The genome-scale transcriptional regulatory network in *S. cerevisiae* which contains 198 TFs and 6158 non-TF target genes was constructed and 44007 interactions between TFs and non-TF target genes or between two TFs were identified (Table A.4). An overview of the network produced in Cytoscape is displayed in Figure 3.1, where the network of interest was represented by 6356 nodes and 44007 edges.

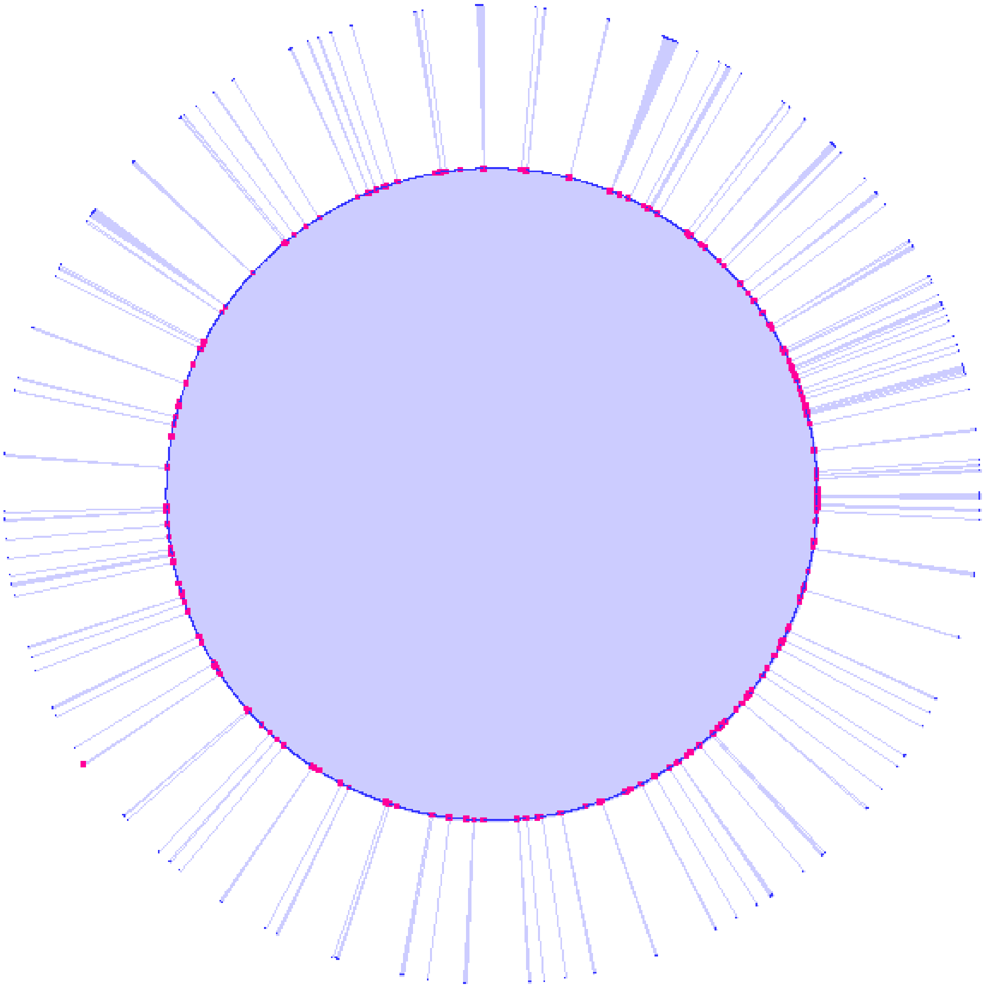

Figure 3.1. Representation of the reconstructed transcriptional regulatory network (pink and blue nodes represent TFs and non-TF target genes, respectively)

When self-interactions were excluded, the number of interactions between 6356 nodes reduced to 43922. Complete list of topological properties, i.e. degree (*k*), clustering coefficient (*C*) and betweenness (*b*), of individual nodes is given in Table A.1. The degree of the nodes of the TRN ranges from 1 to 2188, whereas for 1000 random networks the maximum degree was calculated to be 35. The average degree $<k>$, average clustering coefficient $<C>$ and average betweenness $<b>$ for the complete network were calculated to be 13.82, 0.24 and 10613, respectively. The average clustering coefficient for random networks was calculated to be 0.002 (Table 3.1). The remarkably higher average clustering coefficient than that of random networks implies that the network of interest is scale-free.

Table 3.1. Topological parameters of the yeast transcriptional regulatory network

| **Topological parameters** | **Yeast transcriptional regulatory network** | **Random network** |
|---|---|---|
| $N$ | 6356 | 6356 |
| $l$ | 43922 | 43922 |
| $<k>$ | 13.82 | 13.82 |
| $<C>$ | 0.24 | 0.002 |

The cumulative frequency, $n(k)$, and clustering coefficient, $C(k)$, distributions with respect to degree, $k$, followed power law, indicating that many nodes are linked to few nodes, but only a few of them are linked to many nodes (Figure 3.2 and Figure 3.3). The degree exponent of the network, $\gamma$, was found to be 2.012, which provides additional evidence that the constructed yeast TRN is scale-free and biologically significant. The cumulative frequency of nodes, $n(k)$, and clustering coefficients, $C(k)$, were presented in Table A.2 and Table A.3.

The average betweenness distribution was also well-characterized with power law scaling (Table A.3 and Figure 3.4), indicating that many nodes are located at the periphery and a few nodes at the centre, hence responsible for the communication within network.

### 3.1.1. Hub Nodes

In order to check that identified key TFs in the present study were size independent, hubs were first determined using both degree and betweenness measures as the basis for hub identification. 17 nodes which were at the intersection of the top 20 highest degree and top 20 highest betweenness nodes were considered as hub nodes. (Table 3.2, Table 3.3, Figure 3.5, Figure 3.6)

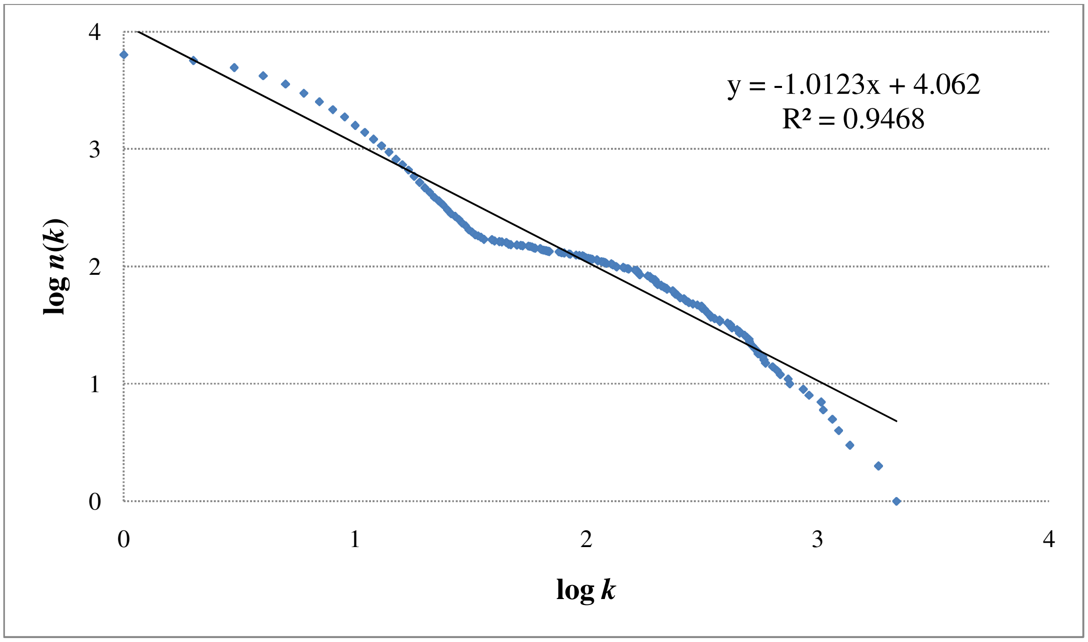

Figure 3.2. Cumulative degree distribution of the nodes of the yeast regulatory network

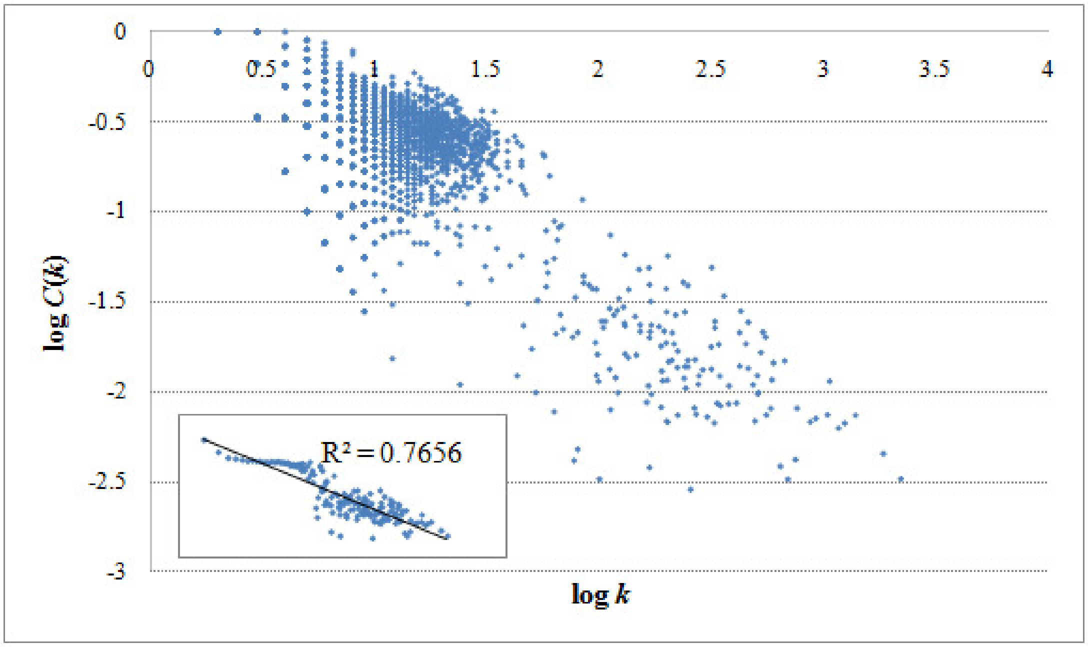

Figure 3.3. The distribution for clustering coefficient (power law fitting is presented in inset)

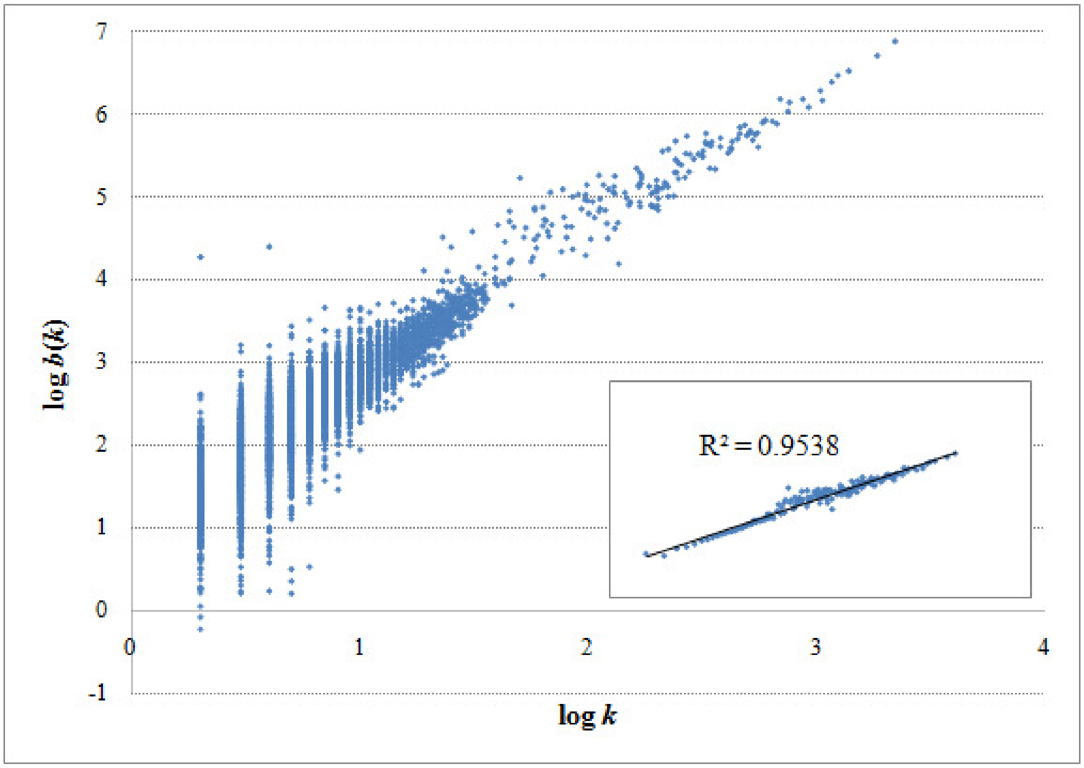

Figure 3.4. The distribution for betweenness (power law fitting is presented in inset)

All selected hubs were TFs. The degree (*k*) of these hub nodes ranges from 534 to 2188 with an average of 926 interactions, whereas the betweenness (*b*) ranges from 643610 to 7721326.

The highest degree and highest betweenness node of the constructed yeast TRN was found to be Sfp1p. Sfp1p is a TF and it has a role in the control of cell size and regulates ribosomal protein gene expression in response to nutrients and stress. The transcriptional control of ribosomal protein genes is crucial to alter the demand for protein biosynthetic capacity (Marion et al., 2004).

The significant shared GO biological process terms (*p*-value<0.01) associated with the selected hubs are listed in Table 3.4. Since all of the selected hubs were TFs, the GO terms with the lowest *p*-values were found to be “regulation of transcription” and “transcription”, as expected. The hubs identified were found to be enriched significantly with very general GO biological process terms, such as “regulation of nitrogen compound metabolic process” and “regulation of macromolecule biosynthetic process”. The appearance of the terms “response to arsenic”, “response to inorganic substance”, “response to stimulus”, “response to chemical stimulus”, “response to heat” and “response to temperature stimulus” strengthens the idea that hubs are vital to control the communication among other nodes in the network in response to a disturbance in cellular homeostasis.

Table 3.2. Top 20 highest degree and top 20 highest betweenness nodes

| ***k*** | **Top 20 highest degree nodes** | | ***b*** | **Top 20 highest betweenness nodes** |
|---|---|---|---|---|
| 2188 | YLR403w | | 7721326 | YLR403w |
| 1829 | YML007w | | 5162138 | YML007w |
| 1375 | YHR084w | | 3379020 | YHR084w |
| 1230 | YNL216w | | 2988666 | YNL216w |
| 1156 | YNL103w | | 2489871 | YNL103w |
| 1055 | YMR016c | | 1949936 | YDL020c |
| 1033 | YDL020c | | 1544447 | YKL112w |
| 916 | YMR037c | | 1540598 | YPR104c |
| 865 | YPR104c | | 1491427 | YMR016c |
| 756 | YGL071w | | 1414625 | YGL071w |
| 744 | YPR199c | | 1230908 | YMR037c |
| 688 | YKL112w | | 1094498 | YPR199c |
| 666 | YGL013c | | 861633 | YER111c |
| 637 | YOL108c | | 839314 | YEL009c |
| 594 | YER111c | | 836047 | YOL108c |
| 585 | YEL009c | | 804470 | YGL073w |
| 577 | YGL073w | | 779413 | YGL013c |
| 552 | YBL005w | | 752603 | YML027w |
| 547 | YBR083w | | 705126 | YOR028c |
| 534 | YKL043w | | 643610 | YLR451w |

Table 3.3. Hub nodes

| **ORF Name** | **Gene Name** | | **ORF Name** | **Gene Name** |
|---|---|---|---|---|
| YLR403w | SFP1 | | YGL071w | AFT1 |
| YML007w | YAP1 | | YPR199c | ARR1 |
| YHR084w | STE12 | | YKL112w | ABF1 |
| YNL216w | RAP1 | | YGL013c | PDR1 |
| YNL103w | MET4 | | YOL108c | INO4 |
| YMR016c | SOK2 | | YER111c | SWI4 |
| YDL020c | RPN4 | | YEL009c | GCN4 |
| YMR037c | MSN2 | | YGL073w | HSF1 |
| YPR104c | FHL1 | | | |

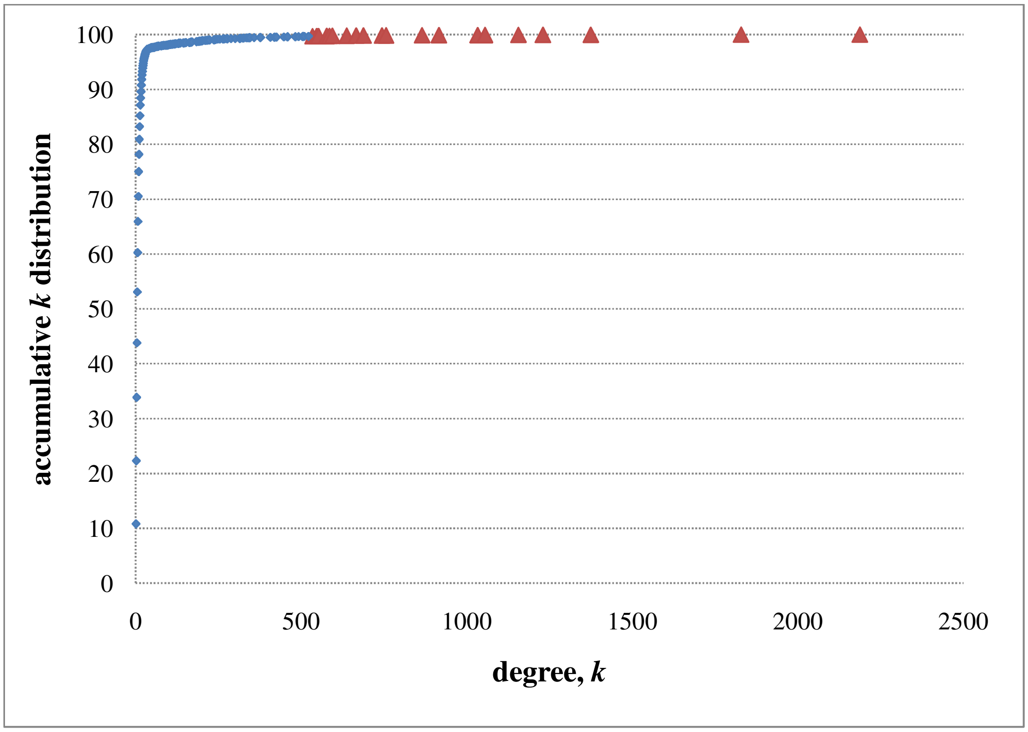

Figure 3.5. Accumulative percent distribution for degree (red triangles represent the hubs)

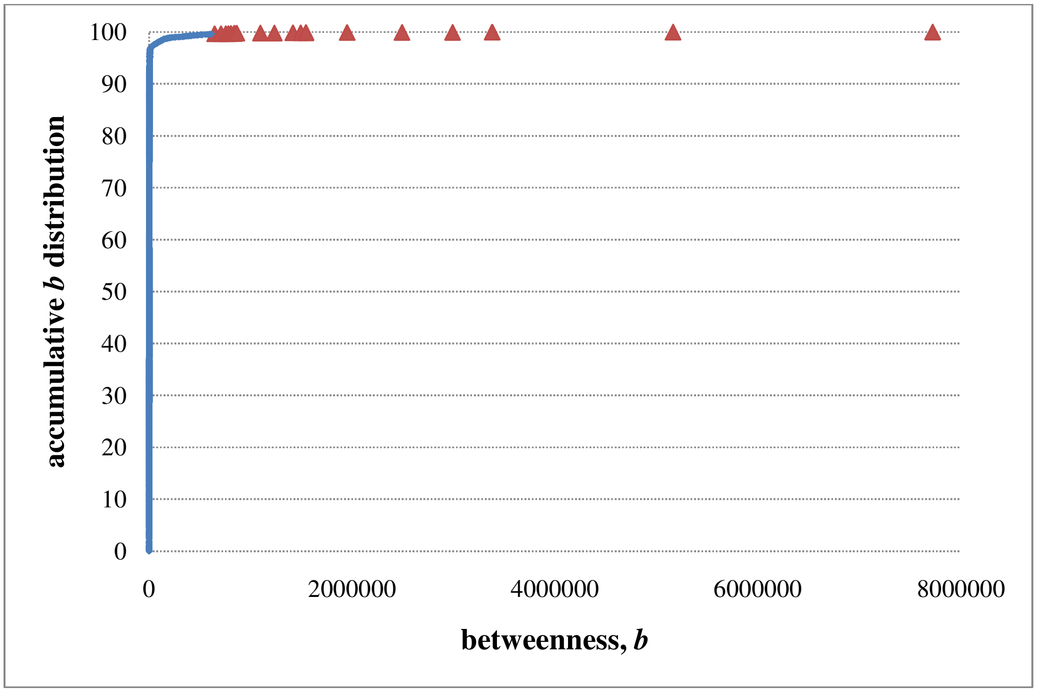

Figure 3.6. Accumulative percent distributions for betweenness (red triangles represent the hubs)

Table 3.4. Significant shared GO biological process terms of hubs

| GO Term | *p*-value | Gene(s) annotated to the term |
|---|---|---|
| regulation of transcription | 9.05E-15 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| transcription | 1.38E-14 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7.97E-14 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of nitrogen compound metabolic process | 8.45E-14 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of gene expression | 1.33E-13 | RPN4,GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of macromolecule biosynthetic process | 1.87E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of transcription, DNA-dependent | 2.94E-13 | GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of cellular biosynthetic process | 3.05E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of biosynthetic process | 3.30E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of RNA metabolic process | 4.52E-13 | GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| transcription, DNA-dependent | 4.90E-13 | GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| RNA biosynthetic process | 5.16E-13 | GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of transcription | 6.38E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of gene expression | 6.84E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| regulation of macromolecule metabolic process | 8.57E-13 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 1.63E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of nitrogen compound metabolic process | 1.63E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| regulation of primary metabolic process | 1.95E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of macromolecule biosynthetic process | 3.24E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| regulation of cellular metabolic process | 3.48E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of cellular biosynthetic process | 4.91E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of biosynthetic process | 4.91E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| regulation of transcription from RNA polymerase II promoter | 5.21E-12 | GCN4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, INO4, FHL1, ARR1 |
| regulation of metabolic process | 6.76E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| biological regulation | 8.43E-12 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, SOK2, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of macromolecule metabolic process | 1.33E-11 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of cellular metabolic process | 2.01E-11 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of metabolic process | 2.34E-11 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of transcription, DNA-dependent | 3.40E-11 | GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |

Table 3.4. Significant shared GO biological process terms of hubs (continued)

| GO Term | *p*-value | Gene(s) annotated to the term |
|---|---|---|
| positive regulation of RNA metabolic process | 5.32E-11 | GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of cellular process | 8.38E-11 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of transcription from RNA polymerase II promoter | 1.04E-10 | GCN4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| positive regulation of biological process | 1.14E-10 | RPN4, GCN4, SWI4, PDR1, AFT1, STE12, ABF1, MET4, INO4, FHL1, ARR1 |
| transcription from RNA polymerase II promoter | 4.71E-10 | GCN4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, INO4, FHL1, ARR1 |
| regulation of cellular process | 7.28E-10 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| regulation of biological process | 1.58E-09 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| nucleic acid metabolic process | 1.39E-08 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| RNA metabolic process | 1.90E-08 | GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| cellular macromolecule biosynthetic process | 3.58E-08 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| macromolecule biosynthetic process | 3.66E-08 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7.78E-08 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| response to arsenic | 3.22E-07 | RPN4, YAP1, MET4, ARR1 |
| gene expression | 4.09E-07 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| cellular nitrogen compound metabolic process | 5.68E-07 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| nitrogen compound metabolic process | 7.13E-07 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| cellular biosynthetic process | 1.53E-06 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| biosynthetic process | 2.17E-06 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, AP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| positive regulation of gene-specific transcription | 0.0001 | GCN4, SWI4, STE12, FHL1 |
| cellular macromolecule metabolic process | 0.00018 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| response to inorganic substance | 0.0002 | RPN4, YAP1, MET4, ARR1 |
| response to stimulus | 0.00022 | RPN4, PDR1, HSF1, STE12, ABF1, YAP1, MSN2, MET4, RAP1, ARR1 |
| macromolecule metabolic process | 0.00025 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| response to chemical stimulus | 0.00049 | RPN4, PDR1, STE12, YAP1, MSN2, MET4, ARR1 |
| regulation of gene-specific transcription | 0.0006 | GCN4, SWI4, STE12, FHL1 |
| response to heat | 0.00259 | HSF1, YAP1, MSN2 |
| negative regulation of transcription from RNA polymerase II promoter | 0.00298 | GCN4, PDR1, ABF1, FHL1 |
| positive regulation of gene-specific transcription from RNA polymerase II promoter | 0.00332 | GCN4, STE12, FHL1 |
| response to temperature stimulus | 0.00373 | HSF1, YAP1, MSN2 |
| primary metabolic process | 0.0054 | RPN4, GCN4, SWI4, PDR1, AFT1, HSF1, STE12, ABF1, SFP1, YAP1, MSN2, MET4, RAP1, INO4, FHL1, ARR1 |
| negative regulation of transcription, DNA-dependent | 0.00654 | GCN4, PDR1, ABF1, RAP1, FHL1 |

Table 3.4. Significant shared GO biological process terms of hubs (continued)

| GO Term | *p*-value | Gene(s) annotated to the term |
|---|---|---|
| negative regulation of RNA metabolic process | 0.00671 | GCN4, PDR1, ABF1, RAP1, FHL1 |
| negative regulation of transcription | 0.0078 | GCN4, PDR1, ABF1, RAP1, FHL1 |
| negative regulation of cellular process | 0.00786 | GCN4, PDR1, HSF1, ABF1, RAP1, FHL1 |
| negative regulation of gene expression | 0.00839 | GCN4, PDR1, ABF1, RAP1, FHL1 |
| negative regulation of biological process | 0.00901 | GCN4, PDR1, HSF1, ABF1, RAP1, FHL1 |

According to the reporter metabolites algorithm, $Z_{TF}$ score of a TF should be calculated as the aggregated $Z$-scores of the neighboring genes of that TF divided by the square root of its degree (Patil and Nielsen, 2005). However, in reporter features algorithm, $Z_{TF}$ score of a TF is defined as the average of the aggregated $Z$-scores of the neighboring genes of that TF, which, as proposed, assures that $Z_{TF}$ score of each TF is size-independent (Oliveira *et al.*, 2008). None of the selected hubs were found to be a key TF as it can be seen in Section 3.2. This result highlights that the $Z_{corrected,TF}$ score of each TF, which depends on the $Z_{TF}$ score, was size-independent (independent of degree) and identified key TFs were not false-positive results because of their possible high degree.

## 3.2. Key Transcription Factors

### 3.2.1. Key TFs Responsive to Deletion of the Genes *SNF1* and *SNF4*

Budding yeast is able to utilize a wide variety of carbons other than glucose; alternative sugars such as galactose, sucrose, maltose, and melbiose as well as nonsugar carbons such as ethanol, lactate, glycerol, acetate, or oleate (Turcotte *et al.*, 2009). When glucose becomes depleted (the AMP:ATP ratio is increased), Snf1p gets activated and enables the transcription of many genes responsible for oxidative growth through activation of the transcriptional activators Cat8p and Adr1p and inactivation of the Mig1p transcriptional repressor (Raghevendran *et al.*, 2005). In addition, Snf1p complex regulates energy homeostasis by switching off ATP-consuming anabolic pathways, switching on ATP-producing catabolic pathways, such as fatty acid oxidation, and participating stress response and filamentous growth (Usaite *et al.*, 2009). Snf1 protein kinase complex is a heterotrimer, composed of a catalytic α-subunit (Snf1p), a regulatory γ-subunit (Snf4p), and a scaffolding β-subunit (one of Sip1p, Sip2p or Gal83p).

In the presence of glucose, the Reg1p/Glc7p protein phosphatase 1 complex dephosphorylates and inactivates Snf1p and active Mig1p (unphosphorylated) represses the transcription of many genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption and gluconeogenesis (Sanz *et al.*, 2000).

Our aim in this part of the study was to test applicability and validity of the use of our larger TRN, consisting of only TFs and their target genes, and the reporter feature algorithm to predict the possible role of Snf1p kinase and compare the results with those which are reported by Usaite *at al.* using the integration of three level omics data (Usaite *et al.*, 2009).

Key TFs responsive to the deletions of *SNF1*, *SNF4* and deletion of both *SNF1* and *SNF4* genes were identified using the triplicate transcriptome data of Usaite *et al.*. In the experiments of Usaite *et al.*, Snf1p complex mutants (the deletion mutants of α and/or γ-subunits of the Snf1p complex, i.e., *ΔSNF1, ΔSNF4* and *ΔSNF1ΔSNF4*) and the wild type strain have been grown in carbon limited media, so that Snf1p complex is expected to be active in the wild type strain (Usaite *et al.*, 2009).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5457, 39522 and 192, respectively. By using reporter features algorithm, 33, 10 and 16 key TFs around which most transcriptional changes occur were identified as a response to deletions of *SNF1*, *SNF4* and deletion of both *SNF1* and *SNF4*, respectively (Table 3.5, Table 3.6 and Table 3.7). Key TFs were ranked from high to low $Z_{\text{corrected,TF}}$ score. $Z_{\text{corrected,TF}}$ scores, *p*-values and degrees for each key TF are represented in Table C.1, Table C.2 and Table C.3.

3.2.1.1. Response to the Deletion of *SNF1*. Thirty three key TFs around which most transcriptional changes occur were identified as a response to deletion of *SNF1* (Table 3.5).

Cat8p, Swi1p and Swi3p were identified to be key TFs as a response to the deletion of *SNF1* specifically. *CAT8* encodes a zinc-finger cluster protein that mediates derepression of a number of genes during the diauxic shift. Snf1p is necessary for the activity of Cat8p, activating Cat8p directly by phosphorylation, as well as inactivating Mig1p, relieving the repression of *CAT8* expression, and allowing the Hap2p/3p/4p/5p complex to positively regulate the expression of *CAT8* (Hedges *et al.*, 1995; Turcotte *et al.*, 2009). Swi1p and Swi3p are subunits of chromatin remodeling complex SWI/SNF and the transcriptional activator Cat8p requires the chromatin remodeling complex SWI/SNF for transcriptional activation (Biddick *et al.*, 2008). Cat8p and Swi1p have also been identified as reporter effectors in *ΔSNF1* in the study of Usaite *et al.* (Usaite *et al.*, 2009). In addition to Swi1p and Swi3p, the algorithm has also identified Hpc2p, Sin3p and Ada2p (Swi8), which are also involved in chromatin remodeling, as key TFs in this case.

The algorithm identified Opi1p as a key TF in *ΔSNF1* mutant. Sin3p is defined in SGD as component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity. Wagner *et al.* have demonstrated that Opi1p interacts with Sin3p affecting a large number of regulatory systems in yeast and higher eukaryotes (Wagner *et al.*, 2001). The synthesis of phospholipids is a major activity throughout cell growth and Zhang *et al.* have suggested that Snf1p activates Opi1p, which represses phospholipid biosynthesis (Sreenivas and Carman, 2003; Zhang *et al.*, 2010). Gis1p, which is reported to be involved in phospholipid metabolic process, was also identified as a key TF in *ΔSNF1*.

Oaf1p and Cst6p were also among the identified key TFs in *SNF1* deletion mutant. Cst6p is involved in the regulation of oleate responsive genes and Oaf1p is an oleate-activated TF, which activates genes involved in β-oxidation of fatty acids, peroxisome organization and biogenesis. This result is consistent with the fact that Snf1p regulates β-oxidation of fatty acids (Usaite *et al.*, 2009). It has been reported that Snf1p is necessary for the activity of Adr1p in this regulation, although it is not known whether Snf1p activates Adr1p directly or indirectly. However, Adr1p was not identified as a key TF in any Snf1p complex mutants in the present study. Gene expression is under combinatorial control and many Adr1p dependent genes are activated by other transcription factors as well. For example, the promoters of genes encoding peroxisomal proteins and the enzymes of β-oxidation bind both Adr1 and the heterodimeric, oleate-responsive transcription factors Oaf1p and Pip2p (Ratnakumar *et al.*, 2009).

Gsm1p, which is involved in the regulation of energy metabolism in yeast, was identified as a key TF in *ΔSNF1*. Gsm1p increases the expression of *HAP4*, which encodes the limiting and activating subunit of the Hap2p/3p/4p/5p complex, and the expression of *GSM1* is increased in nonfermentable carbons by the Hap2p/3p/4p/5p complex, providing a putative autoregulatory loop between *HAP4* and *GSM1* (Turcotte *et al.*, 2009).

Although the expression products of *CAT8* and *GSM1* were identified as key TFs in *ΔSNF1*, which are positively controlled by Hap4p, Hap4p was not present among the identified key TFs.

In *ΔSNF1* mutant, the algorithm also identified Mig3p as a key TF as expected, since Mig3p is known to be regulated by Snf1p kinase, i.e., it is subject to Snf1p dependent phosphorylation and subsequent degradation in the absence of glucose. Westholm *et al.* have found that Mig3p downregulates *SIR2*, which counteracts aging in both yeast and animals, and suggested that this explains accelerated aging in yeast as a result of reduced Snf1p activity (Ashrafi *et al.*, 2000; Westholm *et al.*, 2008).

However, Mig1p and Mig2p did not appear as key TFs in *ΔSNF1*. These results bring about the possibility that there are other proteins similar to Snf1p that might act on Mig1p and also Mig2p. In the absence of glucose, Mig1p, but not Mig2p, is inactivated by the Snf1p protein kinase. The nuclear localization of Mig1p is regulated by glucose, i. e., Snf1p action causes Mig1p to move to the cytoplasm, but Mig2p is located in the nucleus both in the presence and absence of glucose. The existence of a protein (possibly also a protein kinase) that regulates Mig2p activity in response to glucose has been previously suggested by Lutfiyya *et al.* (Lutfiyya *et al.*, 1998).

Imp2’p, which is involved in carbohydrate metabolic processes, was identified as a key TF in *ΔSNF1*. Imp2’p is required for the rapid glucose derepression of the maltose, galactose, raffinose and ethanol utilization pathways (Lodi *et al.*, 1995). Snf1p complex activates genes encoding enzymes of alternative carbon sources consumption (Usaite *et al.*, 2009). Imp2'p has also been identified as a reporter effector in *ΔSNF1* in the study of Usaite *et al.* (Usaite *et al.*, 2009).

Cst6p and Aca1p, which are also involved in utilization of nonoptimal carbon sources, were found to be key TFs in *ΔSNF1*. Garcia-Gimeno and Struhl suggest that Cst6p (Aca2p) and Snf1p possibly act in a common pathway of glucose repression and that Cst6p might be a substrate or transcriptional regulator of Snf1p. The fact that overexpression of Aca1p is found to suppress the inability of Δ*ACA2* mutant strains to grow on nonoptimal carbon sources may be the possible explanation for the considerable collective change in the expression of the genes regulated by Aca1p (Garcia-Gimeno and Struhl, 2000).

Pdc2p, which is involved in the regulation of glucose catabolic process to ethanol and in the regulation of thiamin biosynthetic process, was identified as a key TF indicating the role of Snf1p in the regulation of carbon metabolism. Gis1p, involved in the expression of genes during nutrient limitation, was also identified as a key TF in *ΔSNF1*. Pedruzzi *et al.* have proposed that Gis1p has a role in the RAS/cAMP pathway downstream of Rim15p controlling the transcription of a set of genes, such as *SSA3*, which are essential for long term survival following nutrient limitation (Pedruzzi *et al.*, 2000).

Sfl1p, involved in repression of flocculation-related genes, and activation of stress responsive genes, was found to be a key TF in *ΔSNF1*. It is negatively regulated by cAMP-dependent protein kinase A subunit Tpk2p. This TF is required for normal cell surface assembly in vegetative growth and its null mutation shows pseudohyphal and invasive growth. Dig2p is involved in the invasive growth in response glucose limitation, and overexpression of *BYE1* and *SPS18* genes causes decreased vegetative growth. The identification of Sfl1p, Dig2p, Sps18p and Bye1p as key TFs indicate also a possible role of Snf1p in these processes. The key TFs Hmlalpha1p and Hmra1p are involved in mating-type specific regulation of transcription.

Sfl1p is negatively regulated by cAMP-dependent PKA subunit Tpk2p and Gis1p has a role in the RAS/cAMP pathway. Identification of Sfl1p and Gis1p as key TFs in response to *SNF1* deletion is logical, since PKA and Snf1p are reported to cooperate in the regulation of many processes such as carboxylic acid metabolism, β-oxidation of fatty acids, stress response and filamentous growth (Zhang *et al*., 2010).

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways which is important in the regulation of cell growth in response to nutrients, and Elp6p, which is involved in protein urmylation, were identified as key TFs. Loss of urmylation pathway was reported to cause invasive growth and confers sensitivity to rapamycin due to genetic interactions with TOR pathway (Goehring et al., 2003). These observations indicate that Snf1p may possibly interacting/collaborating with TOR pathway to integrate the information related to nutritional state with energy and redox metabolism. These results agree with the study of Usaite *et al*. where an interactive role of Snf1p and Tor1p has also been suggested (Usaite *et al*., 2009).

Xbp1p, Pdr8p, Hot1p, Cup2p, Rlm1p, Sfl1p and Sut1p, which are involved in the regulation of stress response to different conditions, were identified as key TFs in *ΔSNF1*. These results are in good correlation with the previous observations that Snf1p complex regulates energy homeostasis also by participating stress response (Usaite *et al*., 2009).

To sum up, the algorithm identified key TFs that are involved in chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids, biogenesis, oxidative phosphorylation (energy metabolism), carbohydrate metabolic process, alternative carbon source consumption and stress response, as a response to *SNF1* deletion. These results are totally consistent with the predicted role of Snf1p kinase; such that loss of Snf1p kinase activity during carbon-limited growth affects significantly glucose repression related genes, fatty acid and lipid metabolism (mainly through posttranscriptional regulation), biogenesis, carnitine metabolism, stress response, nitrogen metabolism and energy metabolism (Usaite *et al*., 2009). Key TFs involved in processes, such as oleate response and protein urmylation, that have not previously been implicated as being regulated by Snf1p were also identified. Key TFs Gat4p, Rts2p and Yrm1p probably have roles in one or more of the processes mentioned above.

Table 3.5. Key TFs identified for *ΔSNF1* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Hpc2p<br>(YBR215w) | 3 | Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes<br>• DNA replication-independent nucleosome assembly<br>• regulation of transcription involved in G1/S-phase of mitotic cell cycle<br>• RNA elongation from RNA polymerase II promoter |
| 2 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 3 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |
| 4 | Elp6p<br>(YMR312w) | 7 | Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity<br>• protein urmylation<br>• regulation of transcription from RNA polymerase II promoter<br>• tRNA wobble uridine modification |
| 5 | Pdc2p<br>(YDR081c) | 16 | Transcription factor required for the synthesis of the glycolytic enzyme pyruvate decarboxylase, required for high level expression of both the THI and the PDC genes<br>• glucose catabolic process to ethanol<br>• positive regulation of gene-specific transcription from RNA polymerase II promoter<br>• regulation of thiamin biosynthetic process |
| 6 | Pdr8p<br>(YLR266c) | 24 | Transcription factor; targets include ATP-binding cassette (ABC) transporters, major facilitator superfamily transporters, and other genes involved in the pleiotropic drug resistance (PDR) phenomenon<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to stress |
| 7 | Rds3p<br>(YPR094w) | 8 | Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance<br>• nuclear mRNA splicing, via spliceosome<br>• response to xenobiotic stimulus<br>• spliceosome assembly |
| 8 | Rtg2p<br>(YGL252c) | 9 | Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p<br>• extrachromosomal rDNA circle accumulation involved in replicative cell aging<br>• intracellular signaling pathway<br>• mitochondria-nucleus signaling pathway |

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 9 | Cup2p<br>(YGL166w) | 29 | Copper-binding transcription factor; activates transcription of the metallothionein genes CUP1-1 and CUP1-2 in response to elevated copper concentrations<br>• response to copper ion<br>• transcription initiation from RNA polymerase II promoter |
| 10 | Gis1p<br>(YDR096w) | 187 | JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis<br>• ascospore wall assembly<br>• histone demethylation<br>• phospholipid metabolic process |
| 11 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 12 | Gat4p<br>(YIR013c) | 122 | Protein containing GATA family zinc finger motifs<br>• transcription |
| 13 | Hot1p<br>(YMR172w) | 73 | Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p<br>• hyperosmotic response<br>• regulation of transcription from RNA polymerase II promoter |
| 14 | Yrm1p<br>(YOR172w) | 24 | Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes<br>• drug transmembrane transport<br>• positive regulation of transcription from RNA polymerase II promoter |
| 15 | Xbp1p<br>(YIL101c) | 168 | Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate<br>• response to stress |
| 16 | Dig2p<br>(YDR480w) | 5 | Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription<br>• invasive growth in response to glucose limitation |
| 17 | Cat8p<br>(YMR280c) | 126 | Zinc cluster transcriptional activator necessary for derepression of a variety of genes under non-fermentative growth conditions, active after diauxic shift, binds carbon source responsive elements<br>• positive regulation of gluconeogenesis<br>• positive regulation of transcription from RNA polymerase II promoter |
| 18 | Bye1p<br>(YKL005c) | 24 | Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit<br>• negative regulation of transcription from RNA polymerase II promoter |

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 19 | Opi1p<br>(YHL020c) | 29 | Transcriptional regulator of a variety of genes; phosphorylation by protein kinase A stimulates Opi1p function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance<br>• endoplasmic reticulum unfolded protein response<br>• negative regulation of transcription from RNA polymerase II promoter<br>• phospholipid biosynthetic process<br>• positive regulation of transcription from RNA polymerase II promoter |
| 20 | Imp2'p<br>(YIL154c) | 7 | Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat<br>• cellular carbohydrate metabolic process<br>• DNA repair |
| 21 | Rts2p<br>(YOR077w) | 29 | Basic zinc-finger protein, similar to human and mouse Kin17 proteins which are chromatin-associated proteins involved in UV response and DNA replication<br>• biological process unknown |
| 22 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 23 | Sin3p<br>(YOL004w) | 31 | Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity<br>• chromatin silencing at rDNA<br>• chromatin silencing at silent mating-type cassette<br>• chromatin silencing at telomere<br>• double-strand break repair via nonhomologous end joining<br>• histone deacetylation<br>• negative regulation of transcription from RNA polymerase II promoter<br>• negative regulation of transposition, RNA-mediated<br>• positive regulation of gene-specific transcription from RNA polymerase II promoter<br>• positive regulation of transcription from RNA polymerase II promoter |
| 24 | Gsm1p<br>(YJL103c) | 23 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 25 | Sps18p<br>(YNL204c) | 63 | Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation<br>• sporulation resulting in formation of a cellular spore |
| 26 | Oaf1p<br>(YAL051w) | 248 | Oleate-activated transcription factor, acts alone and as a heterodimer with Pip2p; activates genes involved in beta-oxidation of fatty acids and peroxisome organization and biogenesis<br>• fatty acid metabolic process<br>• negative regulation of transcription<br>• peroxisome organization<br>• positive regulation of transcription |

Table 3.5. Key TFs identified for *ΔSNF1* mutant (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 27 | Sfl1p<br>(YOR140w) | 55 | Transcriptional repressor and activator; involved in repression of flocculation-related genes, and activation of stress responsive genes; negatively regulated by cAMP-dependent protein kinase A subunit Tpk2p<br>• negative regulation of transcription from RNA polymerase II promoter |
| 28 | Aca1p<br>(YER045c) | 29 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources<br>• transcription initiation from RNA polymerase II promoter |
| 29 | Cst6p<br>(YIL036w) | 187 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability<br>• cellular response to oleic acid<br>• DNA metabolic process<br>• transcription initiation from RNA polymerase II promoter |
| 30 | Sut1p<br>(YGL162w) | 84 | Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression<br>• regulation of transcription<br>• regulation of transcription from RNA polymerase II promoter<br>• sterol transport |
| 31 | Rlm1p<br>(YPL089c) | 180 | MADS-box transcription factor, component of the protein kinase C-mediated MAP kinase pathway involved in the maintenance of cell integrity; phosphorylated and activated by the MAP-kinase Slt2p<br>• fungal-type cell wall organization<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to acid<br>• signal transduction |
| 32 | Hmlalpha1p<br>(YCL066w) | 18 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 33 | Hmra1p<br>(YCR097w) | 18 | Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells<br>• regulation of transcription, mating-type specific |

These key TFs identified as a response to deletion of *SNF1* were found to be enriched significantly with very general GO biological process terms, such as “regulation of nitrogen compound metabolic process” (*p*-value=$1.76\text{x}10^{-14}$) and “regulation of macromolecule biosynthetic process” (*p*-value=$5.19\text{x}10^{-14}$) (Table D.1). GO term with the lowest *p*-value was found to be “transcription” (*p*-value=$1.69\text{x}10^{-18}$), as expected.

3.2.1.2. Response to the Deletion of *SNF4*. Ten key TFs around which most transcriptional changes occur were identified as a response to deletion of *SNF4* (Table 3.6).

In *ΔSNF4* mutant, Gal80p, involved in galactose metabolic process, was identified as a key TF. *GAL* genes are repressed directly by Mig1p (Nehlin *et al.*, 1991). Under low glucose condition, Mig1p is expected to be inactivated by Snf1p complex thus *GAL* genes are expected not to be repressed in wild type cells. Interestingly, Mig1p did not appear to be a key TF in *ΔSNF4* as in *ΔSNF1*. However, Mig2p did appear as a key TF in *ΔSNF4* mutant. Instead of Mig1p, Mig2p may repress *GAL80* in *ΔSNF4* mutant. In fact, Mig2p was shown to fine-tune glucose repression by targeting a subset of the Mig1p repressed genes (Westholm *et al.*, 2008). Mig2p has also been identified as a reporter effector in *ΔSNF4* in the study of Usaite *et al.* (Usaite *et al.*, 2009).

Haa1p, involved in adaptation to weak acid stress and in the transcription of *TPO2*, *YRO2*, and other genes putatively encoding membrane stress proteins, and Ndt80p, meiosis-specific transcription factor required for exit from pachytene and for full meiotic recombination, were among the key TFs identified as a response to deletion of *SNF4*.

Six key TFs (highlighted in Table 3.6) identified as a response to *SNF1* deletion were also determined as key TFs in the deletion of *SNF4*.

Table 3.6. Key TFs identified for *ΔSNF4* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Imp2'p<br>(YIL154c) | 7 | Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat<br>• cellular carbohydrate metabolic process<br>• DNA repair |
| 2 | Rds3p<br>(YPR094w) | 8 | Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance<br>• nuclear mRNA splicing, via spliceosome<br>• response to xenobiotic stimulus<br>• spliceosome assembly |
| 3 | Pdr8p<br>(YLR266c) | 24 | Transcription factor; targets include ATP-binding cassette (ABC) transporters, major facilitator superfamily transporters, and other genes involved in the pleiotropic drug resistance (PDR) phenomenon<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to stress |

Table 3.6. Key TFs identified for *ΔSNF4* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 4 | Yrm1p<br>(YOR172w) | 24 | Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes<br>• drug transmembrane transport<br>• positive regulation of transcription from RNA polymerase II promoter |
| 5 | Dig2p<br>(YDR480w) | 5 | Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription<br>• invasive growth in response to glucose limitation |
| 6 | Hmlalpha1p<br>(YCL066w) | 18 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 7 | Mig2p<br>(YGL209w) | 61 | Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 8 | Gal80p<br>(YML051w) | 6 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 9 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 10 | Ndt80p<br>(YHR124w) | 38 | Meiosis-specific transcription factor required for exit from pachytene and for full meiotic recombination; activates middle sporulation genes; competes with Sum1p for binding to promoters containing middle sporulation elements (MSE)<br>• meiosis<br>• transcription |

These key TFs identified as a response to deletion of *SNF4* were found to be enriched significantly with very general GO biological process terms, such as “nucleic acid metabolic process” (*p*-value=0.00036) and “regulation of nitrogen compound metabolic process” (*p*-value=0.00164), as well as with more specific GO biological process terms, such as “response to stimulus” (*p*-value=0.00105) and “response to chemical stimulus” (*p*-value=0.00255) (Table D.2). GO term with the lowest *p*-value was found to be “transcription” (*p*-value=0.00024), as expected.

3.2.1.3. Response to the Deletion of both *SNF1* and *SNF4*. Sixteen key TFs around which most transcriptional changes occur were identified as a response to deletion of both *SNF1* and *SNF4* (Table 3.7).

Cdc39p, Haa1p and War1p were among the key TFs identified for *ΔSNF1ΔSNF4*. Both Haa1p and War1p are involved in response to acid and Cdc39p is implemented in pseudohyphal growth.

Twelve key TFs (highlighted in Table 3.7) identified as a response to *SNF1* deletion were also determined as key TFs in the deletion of both *SNF1* and *SNF4*.

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Cdc39p<br>(YCR093w) | 9 | Component of the CCR4-NOT complex, which has multiple roles in regulating mRNA levels including regulation of transcription and destabilizing mRNAs by deadenylation; basal transcription factor<br>• negative regulation of transcription from RNA polymerase II promoter<br>• nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay<br>• nuclear-transcribed mRNA poly(A) tail shortening<br>• pseudohyphal growth<br>• regulation of cell cycle<br>• regulation of transcription from RNA polymerase II promoter<br>• response to pheromone involved in conjugation with cellular fusion<br>• RNA elongation from RNA polymerase II promoter |
| 2 | Rds3p<br>(YPR094w) | 8 | Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance<br>• nuclear mRNA splicing, via spliceosome<br>• response to xenobiotic stimulus<br>• spliceosome assembly |
| 3 | Rtg2p<br>(YGL252c) | 9 | Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p<br>• extrachromosomal rDNA circle accumulation involved in replicative cell aging<br>• intracellular signaling pathway<br>• mitochondria-nucleus signaling pathway |
| 4 | Lys14p<br>(YDR034c) | 12 | Transcriptional activator involved in regulation of genes of the lysine biosynthesis pathway; requires 2-aminoadipate semialdehyde as co-inducer<br>• lysine biosynthetic process via aminoadipic acid |

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 5 | Hpc2p<br>(YBR215w) | 3 | Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes<br>• DNA replication-independent nucleosome assembly<br>• regulation of transcription involved in G1/S-phase of mitotic cell cycle<br>• RNA elongation from RNA polymerase II promoter |
| 6 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 7 | Sps18p<br>(YNL204c) | 63 | Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation<br>• sporulation resulting in formation of a cellular spore |
| 8 | Gis1p<br>(YDR096w) | 187 | JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis<br>• ascospore wall assembly<br>• histone demethylation<br>• phospholipid metabolic process |
| 9 | Cup2p<br>(YGL166w) | 29 | Copper-binding transcription factor; activates transcription of the metallothionein genes CUP1-1 and CUP1-2 in response to elevated copper concentrations<br>• response to copper ion<br>• transcription initiation from RNA polymerase II promoter |
| 10 | Gat4p<br>(YIR013c) | 122 | Protein containing GATA family zinc finger motifs<br>• transcription |
| 11 | Hot1p<br>(YMR172w) | 73 | Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p<br>• hyperosmotic response<br>• regulation of transcription from RNA polymerase II promoter |
| 12 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 13 | Elp6p<br>(YMR312w) | 7 | Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity<br>• protein urmylation<br>• regulation of transcription from RNA polymerase II promoter<br>• tRNA wobble uridine modification |

Table 3.7. Key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 14 | Cst6p<br>(YIL036w) | 187 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability<br>• cellular response to oleic acid<br>• DNA metabolic process<br>• transcription initiation from RNA polymerase II promoter |
| 15 | Xbp1p<br>(YIL101c) | 168 | Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate<br>• response to stress |
| 16 | War1p<br>(YML076c) | 32 | Homodimeric Zn2Cys6 zinc finger transcription factor; binds to a weak acid response element to induce transcription of PDR12 and FUN34, encoding an acid transporter and a putative ammonia transporter, respectively<br>• response to acid |

These key TFs identified as a response to deletion of both *SNF1* and *SNF4* were found to be enriched significantly with very general GO biological process terms, such as “nucleic acid metabolic process” (*p*-value=0.00398) and “cellular nitrogen compound metabolic process” (*p*-value=0.00538), as well as with a more specific GO biological process term, “response to chemical stimulus” (*p*-value=0.004) (Table D.3). GO term with the lowest *p*-value was found to be “transcription from RNA polymerase II promoter” (*p*-value=$4.13 \times 10^{-6}$), as expected.

3.2.1.4. Comparison of the Responses to Deletions of *SNF1*, *SNF4* and both *SNF1* and *SNF4*. Comparison of the key TFs identified as a response to each deletion is shown in Figure 3.7. The number of key TFs can tell us how much transcriptional response occurs in a cell that was subjected to a specific genetic perturbation. The deletion of *SNF1* possibly is the cause of the largest perturbation at transcriptional response.

Regulator of Drug Sensitivity, Rds3p, is the only key TF that was identified for all three Snf1p complex mutants and was found to be regulated mainly post-transcriptionally (Table 3.14). It is defined in SGD as component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance. Two other TFs, Pdr8p and Yrm1p, were also identified for both *ΔSNF1* and *ΔSNF4* mutants, which regulate genes involved in the pleiotropic drug resistance (PDR) phenomenon and genes involved in multidrug resistance, respectively. Nevertheless, the relationship of Snf1p with drug resistance needs further investigation.

Six key TFs identified for both *ΔSNF1* and *ΔSNF4* mutants are known to be involved in invasive growth in response glucose limitation (Dig2p), carbohydrate metabolic processes (Imp2'p), mating-type specific regulation of transcription (Hmlalpha1p) and stress response (Pdr8p). However, no significant shared GO biological process terms could be associated with them.

No significant shared GO biological process terms could be associated with the two key TFs (Haa1p, involved in response to acid, and Rds3p) identified for both *ΔSNF4* and *ΔSNF1ΔSNF4* mutants either.

As it can be seen in Table D.6, 12 key TFs identified for both *ΔSNF1* and *ΔSNF1ΔSNF4* mutants were found to be enriched significantly with very general GO biological process terms, such as "transcription from RNA polymerase II promoter" (*p*-value=$7.81 \times 10^{-5}$), as expected. These key TFs are involved in several biological processes, i.e., utilization of nonoptimal carbon sources (Cst6p), chromatin remodeling (Ada2p, Hpc2p), stress response (Cup2p, Xbp1p and Hot1p), phospholipid biosynthesis (Gis1p); and Rtg2p and Elp6p collaborate with TOR pathway.

Significant shared GO biological process terms (*p*-value<0.01) of the key TFs identified only for each specific perturbation were also investigated.

Sixteen key TFs identified only for *ΔSNF1* mutant were found to be enriched significantly with very general GO biological process terms, such as "regulation of nitrogen compound metabolic process" (*p*-value= *p*-value=$6.20 \times 10^{-11}$) and "regulation of macromolecule biosynthetic process" (*p*-value=$1.22 \times 10^{-10}$) (Table D.4). GO term with the lowest *p*-value was found to be "regulation of transcription" (*p*-value=$9.10 \times 10^{-12}$), as expected. These key TFs are involved in several biological processes, i.e., utilization of nonoptimal carbon sources (Cat8p, Aca1p), chromatin remodeling (Swi1p, Swi3p and Sin3p), stress response (Sut1p, Sfl1p and Rlm1p), phospholipid biosynthesis (Opi1p), β-oxidation of fatty acids (Oaf1p), energy metabolism (Gsm1p) and regulation of glucose catabolic process to ethanol (Pdc2p).

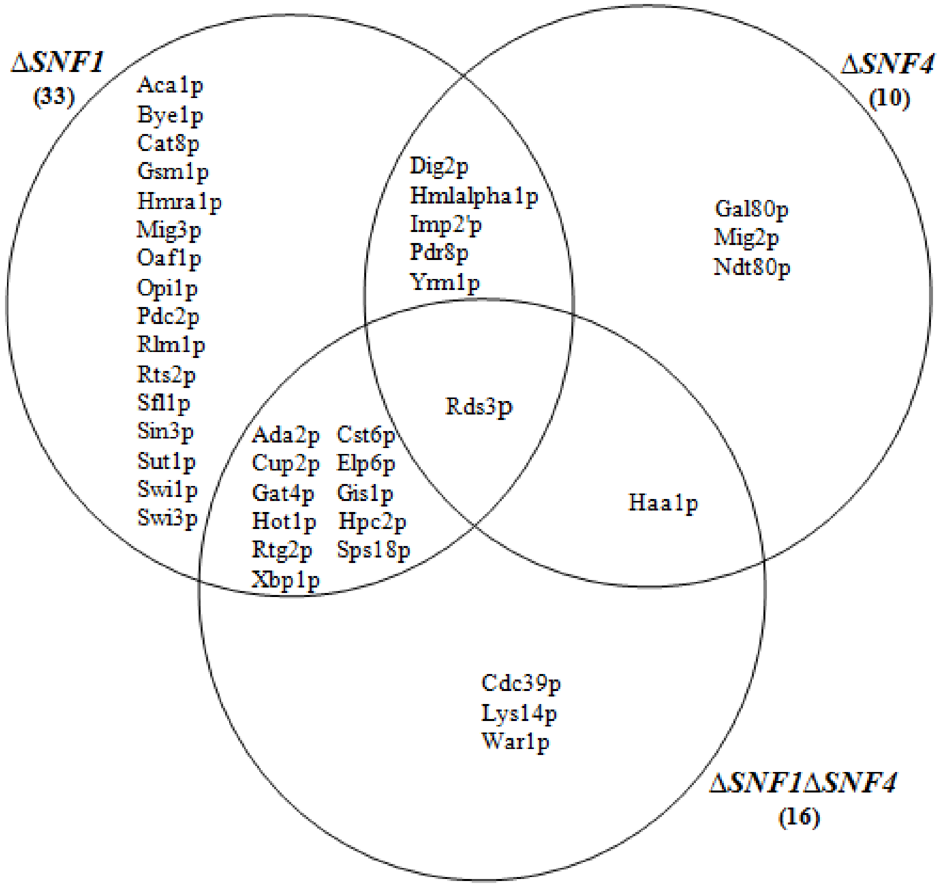

Figure 3.7. Comparison of the key TFs identified for *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants (the number of key TFs for each specific mutant is given in brackets)

The three key TFs identified only for *ΔSNF4* mutant (Gal80p, Mig2p, Ndt80p) were found to be enriched significantly with more specific GO biological process terms, such as “regulation of transcription by carbon catabolites” (*p*-value=0.00052), “cellular response to nutrient” (*p*-value=0.00087) and “response to nutrient” (*p*-value=0.00109) (Table D.5). Reporter metabolites algorithm by Patil and Nielsen has also been performed in the study of Usaite *et al.* to discover metabolic hot spots that significantly respond to the loss of Snf1p kinase activity, and they have found that deleting *SNF4* gene affects mainly only carbon metabolism (Patil and Nielsen, 2005; Usaite *et al.*, 2009). Our results is consistent with their findings, since two of these three key TFs in *ΔSNF4*, Gal80p and Mig2p, are involved in carbon metabolism. In particular, TFs regulating chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids and energy metabolism were not identified for *ΔSNF4* mutant, but for *ΔSNF1* and/or *ΔSNF1ΔSNF4*.

Three TFs (Cdc39p, Lys14p and War1p) were identified only as a response specifically to the deletion of both *SNF1* and *SNF4* genes. However no significant GO biological process terms could be associated with this set. War1p is involved in response to acid and Cdc39p is implemented in pseudohyphal growth.

3.2.1.5. Perturbation-Responsive Subnetworks of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* Mutants. Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes ($p$-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetworks in *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants are given in Table 3.8. The overviews of these subnetworks produced in Cytoscape are displayed in Figure 3.8, Figure 3.9 and Figure 3.10, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in the corresponding mutants with respect to wild type strain are indicated. Key TFs indicated in black in these figures were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.14). GO biological process terms significantly associated with the target genes in each PRS ($p$-value<0.01) were identified and represented in Table 3.9, Table 3.10 and Table 3.11.

Table 3.8. The numbers of TFs, their target genes and interactions for the PRSs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants

| **Mutant** | **Number of Key TFs** | **Number of Target Genes** | **Number of Interactions** |
|---|---|---|---|
| *ΔSNF1* | 33 | 542 | 961 |
| *ΔSNF4* | 10 | 86 | 97 |
| *ΔSNF1ΔSNF4* | 16 | 370 | 587 |

Table 3.9. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| small molecule catabolic process | 42 out of 542 genes, 7.7 per cent | 4.54E-12 |
| monocarboxylic acid metabolic process | 39 out of 542 genes, 7.2 per cent | 1.07E-10 |
| small molecule metabolic process | 117 out of 542 genes, 21.6 per cent | 5.46E-09 |
| organic acid metabolic process | 62 out of 542 genes, 11.4 per cent | 4.81E-08 |
| carboxylic acid metabolic process | 61 out of 542 genes, 11.3 per cent | 1.23E-07 |
| oxoacid metabolic process | 61 out of 542 genes, 11.3 per cent | 1.23E-07 |
| carbohydrate metabolic process | 55 out of 542 genes, 10.1 per cent | 4.40E-07 |
| alcohol catabolic process | 20 out of 542 genes, 3.7 per cent | 4.58E-07 |
| cellular ketone metabolic process | 61 out of 542 genes, 11.3 per cent | 7.39E-07 |
| monosaccharide catabolic process | 19 out of 542 genes, 3.5 per cent | 1.08E-06 |
| response to chemical stimulus | 55 out of 542 genes, 10.1 per cent | 2.48E-06 |
| carbohydrate catabolic process | 26 out of 542 genes, 4.8 per cent | 2.89E-06 |
| organic acid catabolic process | 19 out of 542 genes, 3.5 per cent | 3.43E-06 |
| carboxylic acid catabolic process | 19 out of 542 genes, 3.5 per cent | 3.43E-06 |
| cellular carbohydrate catabolic process | 25 out of 542 genes, 4.6 per cent | 6.81E-06 |
| hexose catabolic process | 17 out of 542 genes, 3.1 per cent | 9.16E-06 |
| alcohol metabolic process | 42 out of 542 genes, 7.7 per cent | 1.84E-05 |
| cellular carbohydrate metabolic process | 50 out of 542 genes, 9.2 per cent | 2.15E-05 |
| pyridine nucleotide metabolic process | 17 out of 542 genes, 3.1 per cent | 2.84E-05 |
| hexose metabolic process | 27 out of 542 genes, 5.0 per cent | 3.63E-05 |
| monosaccharide metabolic process | 29 out of 542 genes, 5.4 per cent | 4.16E-05 |
| cellular response to chemical stimulus | 40 out of 542 genes, 7.4 per cent | 5.06E-05 |
| catabolic process | 81 out of 542 genes, 14.9 per cent | 0.00044 |
| glutamate metabolic process | 9 out of 542 genes, 1.7 per cent | 0.00096 |
| coenzyme metabolic process | 27 out of 542 genes, 5.0 per cent | 0.00148 |
| oxidoreduction coenzyme metabolic process | 17 out of 542 genes, 3.1 per cent | 0.00182 |
| nicotinamide nucleotide metabolic process | 14 out of 542 genes, 2.6 per cent | 0.00285 |
| glucose metabolic process | 22 out of 542 genes, 4.1 per cent | 0.00289 |
| monohydric alcohol metabolic process | 7 out of 542 genes, 1.3 per cent | 0.00311 |
| ethanol metabolic process | 7 out of 542 genes, 1.3 per cent | 0.00311 |

Table 3.10. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF4* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| positive regulation of spindle pole body separation | 4 out of 86 genes, 4.7 per cent | 0.00019 |
| galactose catabolic process via UDP-galactose | 3 out of 86 genes, 3.5 per cent | 0.00048 |
| regulation of spindle pole body separation | 4 out of 86 genes, 4.7 per cent | 0.00067 |
| response to chemical stimulus | 15 out of 86 genes, 17.4 per cent | 0.00126 |
| monosaccharide transport | 5 out of 86 genes, 5.8 per cent | 0.00227 |
| hexose transport | 5 out of 86 genes, 5.8 per cent | 0.00227 |
| spindle pole body separation | 4 out of 86 genes, 4.7 per cent | 0.00257 |
| positive regulation of cell cycle process | 4 out of 86 genes, 4.7 per cent | 0.00257 |
| cellular carbohydrate catabolic process | 8 out of 86 genes, 9.3 per cent | 0.00338 |
| carbohydrate catabolic process | 8 out of 86 genes, 9.3 per cent | 0.0043 |
| galactose catabolic process | 3 out of 86 genes, 3.5 per cent | 0.0094 |

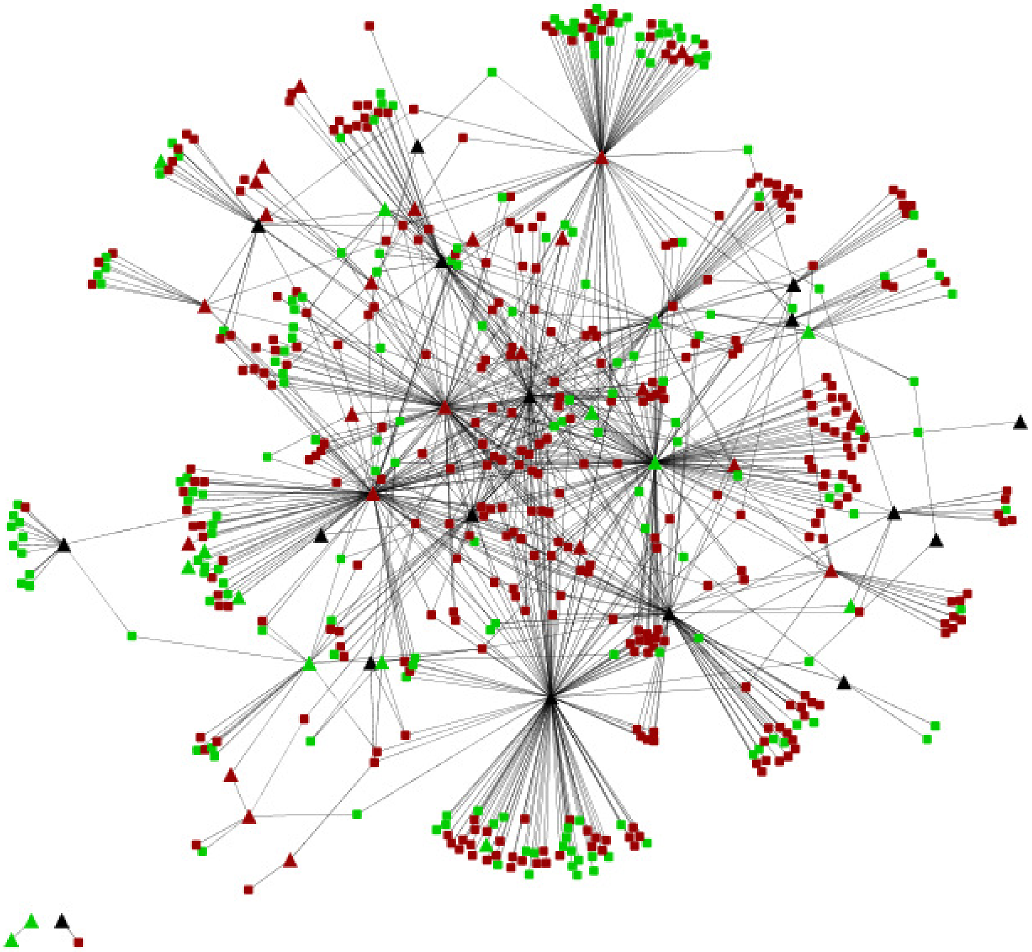

Figure 3.8. Representation of the PRS of *ΔSNF1* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1ΔSNF4* mutant

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| carboxylic acid metabolic process | 55 out of 370 genes, 14.9 per cent | 9.9E-12 |
| oxoacid metabolic process | 55 out of 370 genes, 14.9 per cent | 9.9E-12 |
| organic acid metabolic process | 55 out of 370 genes, 14.9 per cent | 1.12E-11 |
| small molecule metabolic process | 94 out of 370 genes, 25.4 per cent | 2.83E-11 |
| cellular ketone metabolic process | 55 out of 370 genes, 14.9 per cent | 6.34E-11 |
| small molecule catabolic process | 28 out of 370 genes, 7.6 per cent | 0.000000451 |
| glutamate metabolic process | 10 out of 370 genes, 2.7 per cent | 0.00000104 |
| alcohol metabolic process | 35 out of 370 genes, 9.5 per cent | 0.00000144 |
| monocarboxylic acid metabolic process | 26 out of 370 genes, 7.0 per cent | 0.00000321 |
| cellular amino acid and derivative metabolic process | 37 out of 370 genes, 10.0 per cent | 0.00000453 |
| glutamine family amino acid metabolic process | 14 out of 370 genes, 3.8 per cent | 0.0000129 |
| cellular amine metabolic process | 34 out of 370 genes, 9.2 per cent | 0.0000148 |
| carbohydrate metabolic process | 40 out of 370 genes, 10.8 per cent | 0.0000169 |

Table 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1ΔSNF4* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| cellular carbohydrate metabolic process | 39 out of 370 genes, 10.5 per cent | 0.0000184 |
| amine metabolic process | 36 out of 370 genes, 9.7 per cent | 0.0000312 |
| cellular amino acid metabolic process | 31 out of 370 genes, 8.4 per cent | 0.0000538 |
| organic acid biosynthetic process | 25 out of 370 genes, 6.8 per cent | 0.0000544 |
| carboxylic acid biosynthetic process | 25 out of 370 genes, 6.8 per cent | 0.0000544 |
| monosaccharide metabolic process | 23 out of 370 genes, 6.2 per cent | 0.0000626 |
| carbohydrate catabolic process | 19 out of 370 genes, 5.1 per cent | 0.00014 |
| trehalose metabolic process | 7 out of 370 genes, 1.9 per cent | 0.00016 |
| response to oxidative stress | 18 out of 370 genes, 4.9 per cent | 0.0002 |
| small molecule biosynthetic process | 40 out of 370 genes, 10.8 per cent | 0.00025 |
| cellular carbohydrate catabolic process | 18 out of 370 genes, 4.9 per cent | 0.00041 |
| glutamine family amino acid biosynthetic process | 10 out of 370 genes, 2.7 per cent | 0.00042 |
| cellular amino acid biosynthetic process | 20 out of 370 genes, 5.4 per cent | 0.00055 |
| monosaccharide catabolic process | 13 out of 370 genes, 3.5 per cent | 0.00058 |
| alcohol catabolic process | 13 out of 370 genes, 3.5 per cent | 0.00119 |
| pentose catabolic process | 5 out of 370 genes, 1.4 per cent | 0.00127 |
| amine biosynthetic process | 20 out of 370 genes, 5.4 per cent | 0.00169 |
| hexose metabolic process | 19 out of 370 genes, 5.1 per cent | 0.0023 |
| pyridine nucleotide metabolic process | 12 out of 370 genes, 3.2 per cent | 0.00239 |
| carbohydrate transport | 11 out of 370 genes, 3.0 per cent | 0.00289 |
| monohydric alcohol metabolic process | 6 out of 370 genes, 1.6 per cent | 0.00418 |
| ethanol metabolic process | 6 out of 370 genes, 1.6 per cent | 0.00418 |
| glycoside biosynthetic process | 5 out of 370 genes, 1.4 per cent | 0.00427 |
| disaccharide biosynthetic process | 5 out of 370 genes, 1.4 per cent | 0.00427 |
| trehalose biosynthetic process | 5 out of 370 genes, 1.4 per cent | 0.00427 |
| arabinose metabolic process | 4 out of 370 genes, 1.1 per cent | 0.00434 |
| arabinose catabolic process | 4 out of 370 genes, 1.1 per cent | 0.00434 |
| D-xylose metabolic process | 4 out of 370 genes, 1.1 per cent | 0.00434 |
| D-xylose catabolic process | 4 out of 370 genes, 1.1 per cent | 0.00434 |
| glucose metabolic process | 17 out of 370 genes, 4.6 per cent | 0.00634 |
| organic acid catabolic process | 12 out of 370 genes, 3.2 per cent | 0.00724 |
| carboxylic acid catabolic process | 12 out of 370 genes, 3.2 per cent | 0.00724 |
| nicotinamide nucleotide metabolic process | 11 out of 370 genes, 3.0 per cent | 0.00769 |
| response to stress | 54 out of 370 genes, 14.6 per cent | 0.00816 |

By examining the biological process terms of PRSs identified for *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants it can be evaluated how much Snf1p and Snf4p contribute to the functions of the Snf1p kinase complex and whether they have additional functions.

Catabolic processes such as “alcohol catabolic process”, “carbohydrate catabolic process”, “monosaccharide catabolic process”, “organic acid catabolic process”, “small molecule catabolic process” are among the significantly associated GO terms of the PRSs of *ΔSNF1* and *ΔSNF1ΔSNF4* mutants (Figure 3.11). This result is expected since active Snf1p complex switches on ATP-producing catabolic pathways (Usaite *et al*., 2009).

*SNF4* deletion has very little effect compared to *SNF1* deletion (Figure 3.12). "Galactose catabolic process", "hexose transport", "monosaccharide transport" and "regulation of spindle pole body separation" are among the significantly associated GO terms found only for the PRS of *ΔSNF4* mutant.

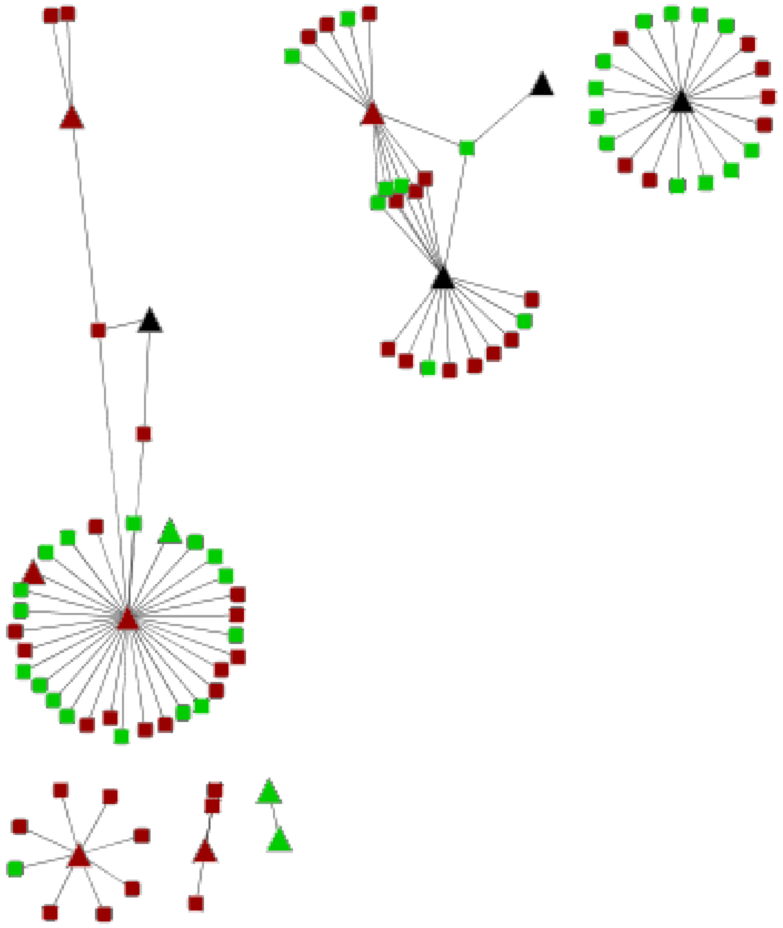

Figure 3.9. Representation of the PRS of *ΔSNF4* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Moreover, deletion of both *SNF1* and *SNF4* genes causes a significant change in the expression of the genes which are significantly associated with the processes "amine biosynthetic process", "amine metabolic process", "arabinose metabolic process", "D-xylose metabolic process", "pentose catabolic process", "trehalose metabolic process", "carboxylic acid biosynthetic process", "cellular amino acid metabolic process", "glutamine family amino acid metabolic process" and "response to stress" (Table 3.12). These terms do not appear among the terms found for *ΔSNF1* and ΔSNF4 mutants. Change in the regulation of nitrogen metabolism in *ΔSNF1ΔSNF4* as a synergistic effect was also reported by Usaite *et al.* (Usaite *et al.*, 2009).

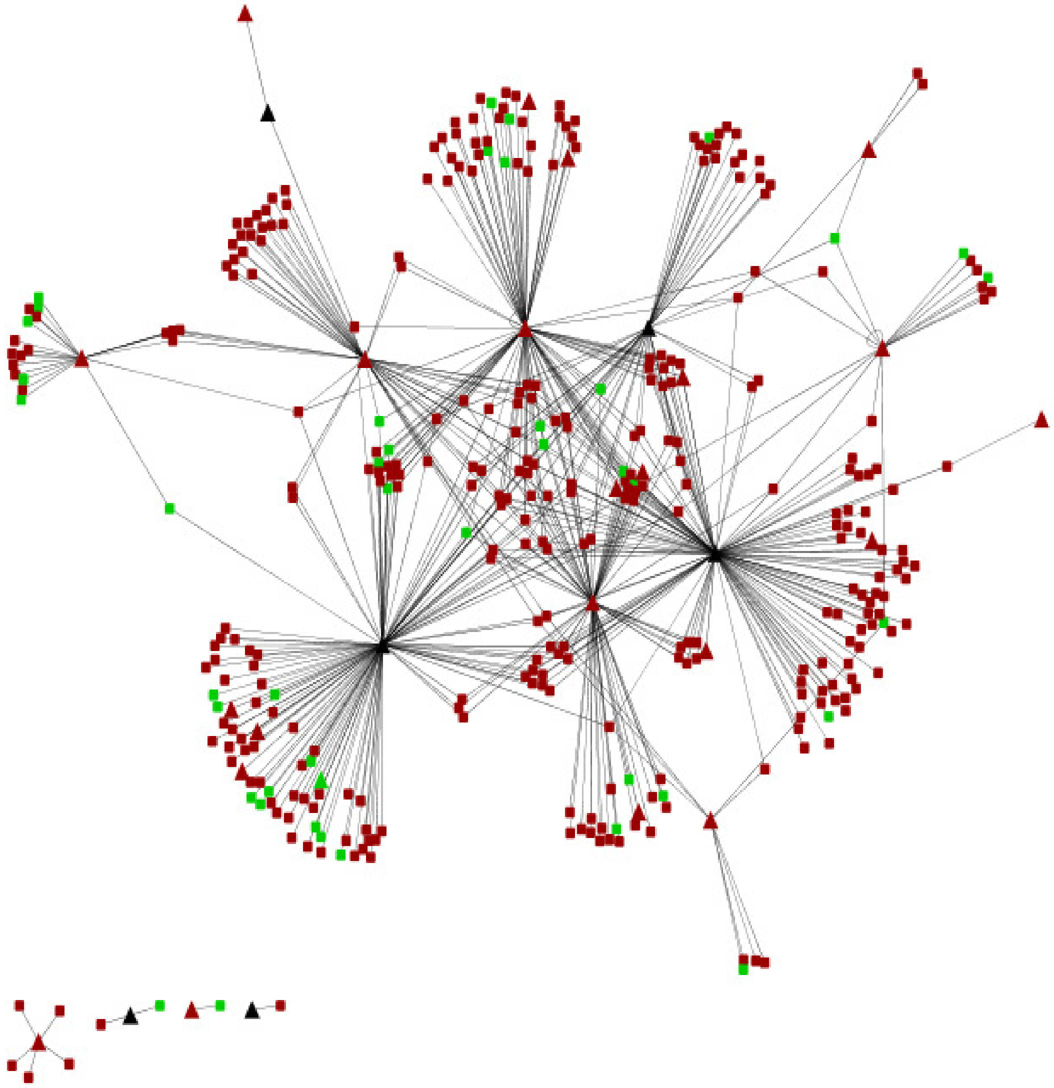

Figure 3.10. Representation of the PRS of *ΔSNF1ΔSNF4* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.12. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants

| **GO Term** | ***ΔSNF1*** | ***ΔSNF4*** | ***ΔSNF1ΔSNF4*** |
|---|---|---|---|
| alcohol catabolic process | 20 | 0 | 13 |
| alcohol metabolic process | 42 | 0 | 35 |
| amine biosynthetic process | 0 | 0 | 20 |
| amine metabolic process | 0 | 0 | 36 |
| arabinose catabolic process | 0 | 0 | 4 |
| arabinose metabolic process | 0 | 0 | 4 |
| carbohydrate catabolic process | 26 | 8 | 19 |
| carbohydrate metabolic process | 55 | 0 | 40 |
| carbohydrate transport | 0 | 0 | 11 |
| carboxylic acid biosynthetic process | 0 | 0 | 25 |
| carboxylic acid catabolic process | 19 | 0 | 12 |
| carboxylic acid metabolic process | 61 | 0 | 55 |
| catabolic process | 81 | 0 | 0 |
| cellular amine metabolic process | 0 | 0 | 34 |
| cellular amino acid and derivative metabolic process | 0 | 0 | 37 |
| cellular amino acid biosynthetic process | 0 | 0 | 20 |
| cellular amino acid metabolic process | 0 | 0 | 31 |
| cellular carbohydrate catabolic process | 25 | 8 | 18 |
| cellular carbohydrate metabolic process | 50 | 0 | 39 |
| cellular ketone metabolic process | 61 | 0 | 55 |
| cellular response to chemical stimulus | 40 | 0 | 0 |
| coenzyme metabolic process | 27 | 0 | 0 |
| disaccharide biosynthetic process | 0 | 0 | 5 |
| D-xylose catabolic process | 0 | 0 | 4 |
| D-xylose metabolic process | 0 | 0 | 4 |
| ethanol metabolic process | 7 | 0 | 6 |
| galactose catabolic process | 0 | 3 | 0 |
| galactose catabolic process via UDP-galactose | 0 | 3 | 0 |
| glucose metabolic process | 22 | 0 | 17 |
| glutamate metabolic process | 9 | 0 | 10 |
| glutamine family amino acid biosynthetic process | 0 | 0 | 10 |
| glutamine family amino acid metabolic process | 0 | 0 | 14 |
| glycoside biosynthetic process | 0 | 0 | 5 |
| hexose catabolic process | 17 | 0 | 0 |
| hexose metabolic process | 27 | 0 | 19 |
| hexose transport | 0 | 5 | 0 |
| monocarboxylic acid metabolic process | 39 | 0 | 26 |
| monohydric alcohol metabolic process | 7 | 0 | 6 |
| monosaccharide catabolic process | 19 | 0 | 13 |
| monosaccharide metabolic process | 29 | 0 | 23 |

Table 3.12. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants (continued)

| **GO Term** | ***ΔSNF1*** | ***ΔSNF4*** | ***ΔSNF1ΔSNF4*** |
|---|---|---|---|
| monosaccharide transport | 0 | 5 | 0 |
| nicotinamide nucleotide metabolic process | 14 | 0 | 11 |
| organic acid biosynthetic process | 0 | 0 | 25 |
| organic acid catabolic process | 19 | 0 | 12 |
| organic acid metabolic process | 62 | 0 | 55 |
| oxidoreduction coenzyme metabolic process | 17 | 0 | 0 |
| oxoacid metabolic process | 61 | 0 | 55 |
| pentose catabolic process | 0 | 0 | 5 |
| positive regulation of cell cycle process | 0 | 4 | 0 |
| positive regulation of spindle pole body separation | 0 | 4 | 0 |
| pyridine nucleotide metabolic process | 17 | 0 | 12 |
| regulation of spindle pole body separation | 0 | 4 | 0 |
| response to chemical stimulus | 55 | 15 | 0 |
| response to oxidative stress | 0 | 0 | 18 |
| response to stress | 0 | 0 | 54 |
| small molecule biosynthetic process | 0 | 0 | 40 |
| small molecule catabolic process | 42 | 0 | 28 |
| small molecule metabolic process | 117 | 0 | 94 |
| spindle pole body separation | 0 | 4 | 0 |
| trehalose biosynthetic process | 0 | 0 | 5 |
| trehalose metabolic process | 0 | 0 | 7 |

Interestingly, fatty acid and lipid metabolism did not appear among the terms significantly associated with the genes of any PRS. This might arise from the *p*-value threshold (0.05) used to identify significantly differentially expressed genes of the PRSs.

As a result, it can be proposed that, Snf1p and Snf4p as a complex are responsible for stress response and the metabolic processes of mono- and disaccharides. Snf4p, by its own, seems to affect sugar transport, and the catabolic processes that Snf1p kinase complex activates are likely because of the contribution of Snf1p.

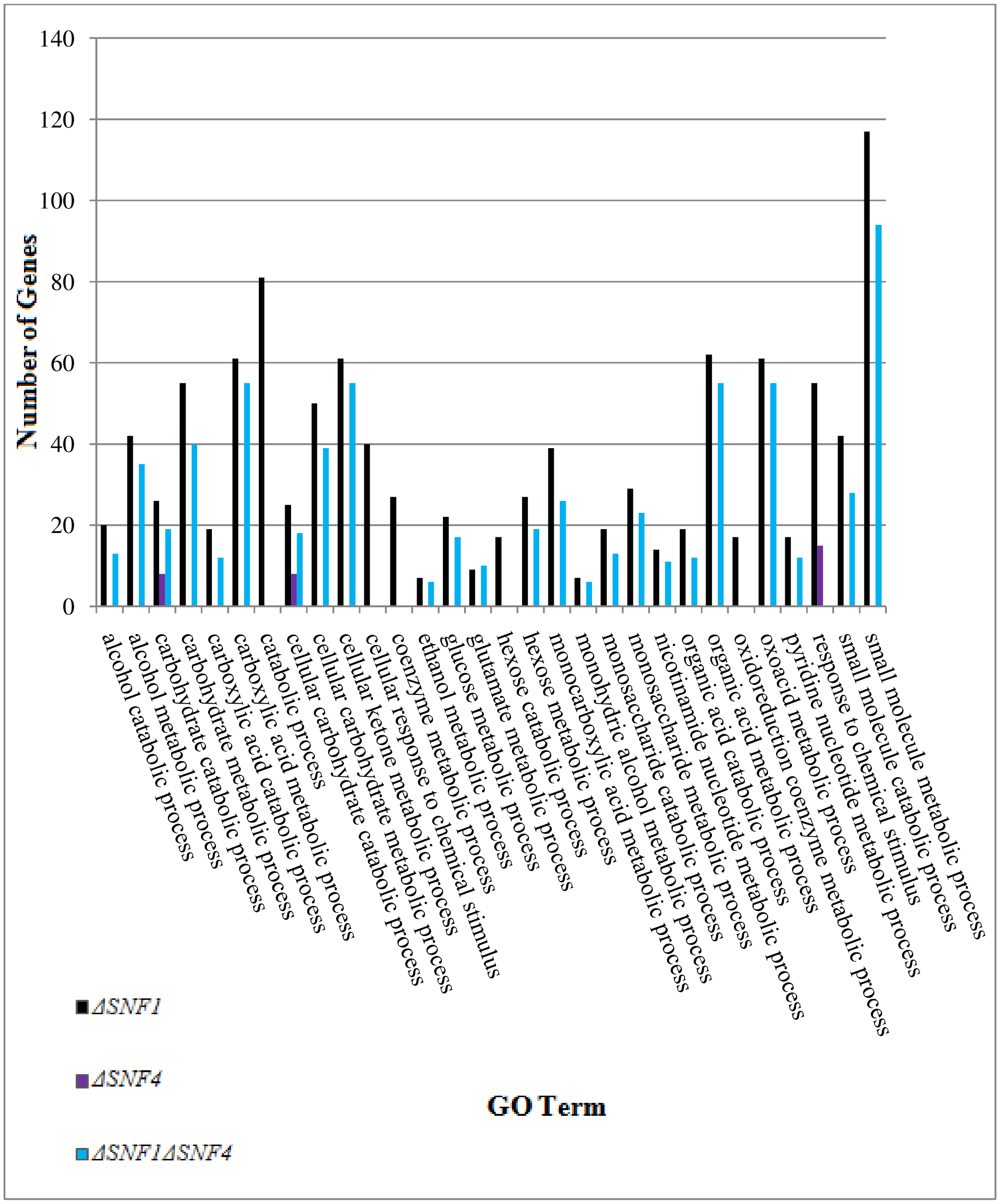

Figure 3.11. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF1* mutant

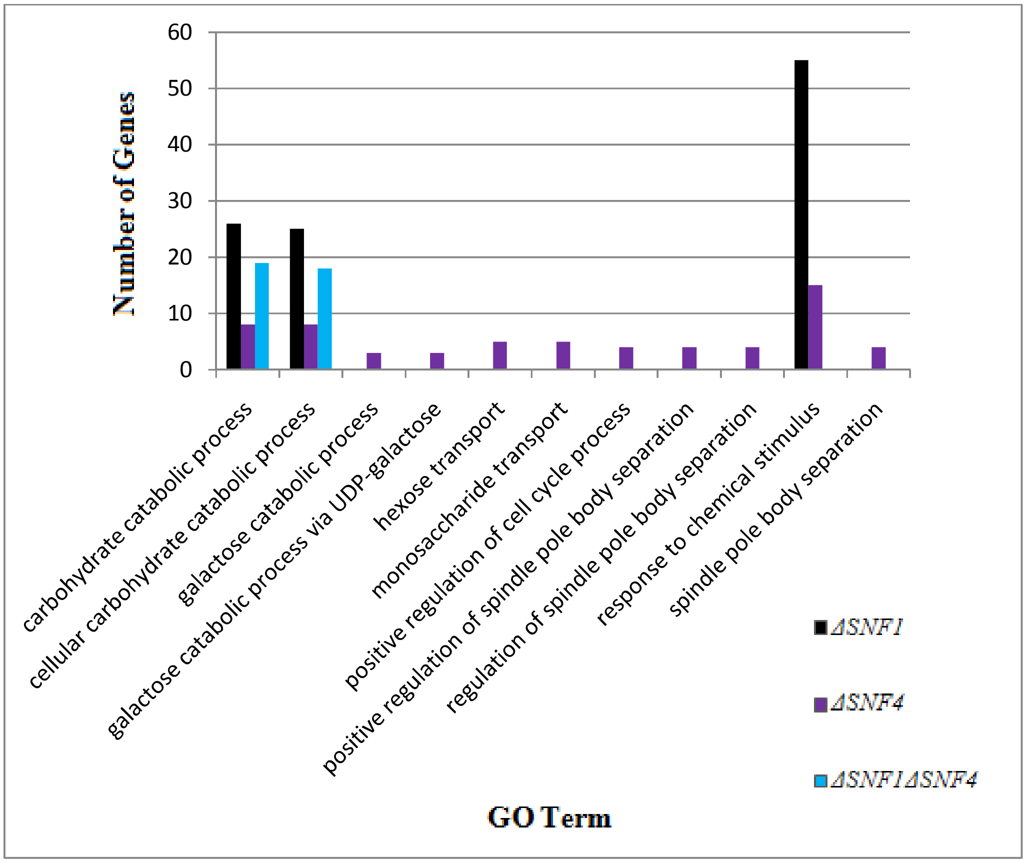

Figure 3.12. Significantly associated GO biological process terms of the target genes of the PRS of *ΔSNF4* mutant

3.2.1.6. Regulation of Key Transcription Factors of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* Mutants. Identification of key TFs demonstrates the change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed, as described in Section 2.4. Most of the key TFs of *ΔSNF4* and *ΔSNF1ΔSNF4* mutants and almost half of the key TFs of *ΔSNF1* mutant were found to be regulated mainly transcriptionally (Table 3.13). In Table 3.14, regulation of each key TF is represented.

Table 3.13. Number of key TFs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4* mutants that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

| **Mutant** | **Number of A** | **Number of B** |
|---|---|---|
| *ΔSNF1* | 16 | 17 |
| *ΔSNF4* | 6 | 4 |
| *ΔSNF1ΔSNF4* | 10 | 6 |

Table 3.14. Regulation of key TFs of *ΔSNF1, ΔSNF4* and *ΔSNF1ΔSNF4* mutants

| **rank** | ***ΔSNF1*** | **Case** | ***ΔSNF4*** | **Case** | ***ΔSNF1ΔSNF4*** | **Case** |
|---|---|---|---|---|---|---|
| 1 | Hpc2p | B | Imp2'p | A | Cdc39p | A |
| 2 | Swi1p | B | Rds3p | B | Rds3p | B |
| 3 | Swi3p | A | Pdr8p | A | Rtg2p | A |
| 4 | Elp6p | B | Yrm1p | B | Lys14p | A |
| 5 | Pdc2p | A | Dig2p | A | Hpc2p | B |
| 6 | Pdr8p | B | Hmlalpha1p | A | Haa1p | A |
| 7 | Rds3p | B | Mig2p | A | Sps18p | B |
| 8 | Rtg2p | B | Gal80p | B | Gis1p | B |
| 9 | Cup2p | A | Haa1p | A | Cup2p | A |
| 10 | Gis1p | A | Ndt80p | B | Gat4p | A |
| 11 | Mig3p | A | | | Hot1p | A |
| 12 | Gat4p | B | | | Ada2p | B |
| 13 | Hot1p | A | | | Elp6p | A |
| 14 | Yrm1p | A | | | Cst6p | B |
| 15 | Xbp1p | A | | | Xbp1p | A |
| 16 | Dig2p | A | | | War1p | A |
| 17 | Cat8p | B | | | | |
| 18 | Bye1p | B | | | | |
| 19 | Opi1p | A | | | | |
| 20 | Imp2'p | A | | | | |
| 21 | Rts2p | B | | | | |
| 22 | Ada2p | B | | | | |
| 23 | Sin3p | A | | | | |
| 24 | Gsm1p | B | | | | |
| 25 | Sps18p | B | | | | |
| 26 | Oaf1p | B | | | | |
| 27 | Sfl1p | B | | | | |
| 28 | Aca1p | A | | | | |
| 29 | Cst6p | A | | | | |
| 30 | Sut1p | B | | | | |
| 31 | Rlm1p | A | | | | |
| 32 | Hmlalpha1p | B | | | | |
| 33 | Hmra1p | A | | | | |

### 3.2.2. Key TFs Responsive to Deletion of the Genes *MIG1*, *MIG2* and *MIG3*

In the presence of glucose, inactive Mig1p gets dephosphorylated by the Glc7p phosphatase via its regulatory subunit Reg1p. Active Mig1p interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes. Mig1p and Mig2p repress a largely overlapping set of genes on 2 per cent glucose and *MIG1* expression is regulated by Mig2p. Mig3p is proposed not to contribute much to the regulation of the genes that are regulated by Mig1p and Mig2p on 2 per cent glucose (Sanz *et al.*, 2000; Westholm *et al.*, 2008).

In the absence of glucose, Mig1p, but not Mig2p, is inactivated by the Snf1p protein kinase. The nuclear localization of Mig1p is regulated by glucose, i. e., Snf1p action causes Mig1p to move to the cytoplasm, but Mig2p is located in the nucleus both in the presence and absence of glucose. The existence of a protein (possibly also a protein kinase) that regulates Mig2p activity in response to glucose has been previously suggested by Lutfiyya *et al.* (Lutfiyya *et al.*, 1998).

Key TFs responsive to the deletions of *MIG1*, *MIG2*, both *MIG1* and *MIG2*, *MIG3* and deletion of all *MIG1*, *MIG2* and *MIG3* genes were identified using the transcriptome data of Westholm *et al.*. In the experiments of Westholm *et al.*, each of which was performed at least in triplicate, *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants and the wild type strain have been grown in the presence of 2 per cent glucose, so that Mig1p and Mig2p are expected to be active in the presence of glucose in the wild type strain (Westholm *et al.*, 2008).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5928, 41905 and 194, respectively. Reporter features algorithm identified 24, 14, 18, 15, 22 key TFs around which most transcriptional changes occur as a response to deletions of *MIG1*, *MIG2*, both *MIG1* and *MIG2*, *MIG3* and deletion of all *MIG1*, *MIG2* and *MIG3* genes, respectively (Table 3.15, Table 3.16, Table 3.17, Table 3.18, Table 3.19). Key TFs were ranked from high to low $Z_{\text{corrected,TF}}$ score. $Z_{\text{corrected,TF}}$ scores, *p*-values and degrees for each key TF are represented in Table C.4, Table C.5, Table C.6, Table C.7 and Table C.8. The deletion of *MIG1* gene possibly is the cause of the largest perturbation at transcriptional response, as it can be concluded from the numbers of key TFs.

3.2.2.1. Response to the Deletion of *MIG1.* Twenty four key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG1* (Table 3.15).

Mig1p appeared as a key TF in *ΔMIG1* mutant as expected, since *MIG1* gene is deleted. The appearance of Mig2p as a key TF in *ΔMIG1* supports the idea that Mig2p acts in a redundant fashion with Mig1p and it can replace the function of Mig1p in case of its deletion. In fact, Mig2p was shown to fine-tune glucose repression by targeting a subset of the Mig1p repressed genes (Westholm *et al.*, 2008).

Mig3p was identified as the top scoring key TF in *ΔMIG1* mutant, which suggest that Mig3p is somehow related to Mig1p and might has a role in glucose repression. Although the function of Mig3p is not well described, it has been reported that Mig3p binds also to the same DNA sequence and contributes modestly to glucose repression (Kaniak *et al.*, 2004).

The algorithm also identified Nrg2p, described in SGD as a transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth, as a key TF in *ΔMIG1* mutant. It was suggested that Nrg1p and Nrg2p are direct or indirect targets of the Snf1p kinase and function in glucose repression of a subset of Snf1p-regulated genes (Vyas *et al.*, 2001). Nrg1p was identified as a third repressor required for glucose repression in addition to Mig1p and Mig2p (Zhou and Winston, 2001).

Rgt1p, which is involved in glucose metabolic process and regulation of glucose import, was also identified as a key TF in *ΔMIG1* mutant. Rgt1p has a role in the glucose induction pathway, in such a way that it functions as a transcriptional repressor in the absence of glucose, it is a transcriptional activator at high concentrations of glucose (4 per cent glucose), and it is neutral (neither represses nor activates transcription) in cells growing on low levels of glucose (0.1 per cent glucose) (Özcan *et al.*, 1996). Glucose repression interacts with the glucose induction pathway through Mig1p (and Mig2p) mediated repression of *MTH1* and *SNF3* expression, which reinforces the inhibitory effect of glucose on Mth1p function and ensures maximal glucose induction of Rgt1p repressed genes (*HXT* s, *MIG2* and *HXK2*) (Johnston and Kim, 2005; Palomino *et al.*, 2005). Rgt1p repressor blocks transcription of glucose-induced genes only when glucose is absent (Johnston *et al.*, 1994).

Gal80p, involved in galactose metabolic process, was also identified as a key TF in response to deletion of *MIG1*. This result is expected, since *GAL* genes are repressed directly by Mig1p (Nehlin *et al.*, 1991).

Mga2p, implemented in fatty acid metabolic process and response to cold, was also identified as a key TF in *ΔMIG1*. Sut1p is involved in stress response and Haa1p regulates the transcription of genes encoding membrane stress proteins. Mig1p sites and STRE motifs occur in the same promoters and it has been reported that dual control of many genes that contain STRE motifs by glucose repression and stress signalling is expected (Westholm *et al.*, 2008).

Mdl2p was among the key TFs identified for *ΔMIG1* and its null mutation shows decreased resistance to oleate, decreased respiratory growth rate and decreased utilization of carbon source.

Twelve key TFs (highlighted in Table 3.15) identified as a response to *SNF1* deletion were also determined as key TFs in *ΔMIG1*.

The algorithm identified Imp2'p, which is required for the rapid glucose derepression of the maltose, galactose, raffinose and ethanol utilization pathways, as a key TF in *ΔMIG1* mutant. Alberti *et al.* have proposed that Imp2'p plays a dual role in the regulation of GAL gene expression, via Mig1p-dependent and Mig1p-independent pathways. The Mig1-independent role of Imp2'p depends on Nrg1p (Alberti *et al.*, 2003).

Rds2p and Gsm1p, implicated in the use of nonfermentable carbon sources and target gluconeogenic genes, were identified as key TFs in *ΔMIG1*. Gluconeogenesis (generation of glucose from non-carbohydrate carbon substrates) is essential for the growth of yeast cells on nonfermentable carbon sources (Turcotte *et al*., 2009). In addition, Aca1p, which is involved in utilization of nonoptimal carbon sources, and Dig2p, involved in invasive growth in response glucose limitation, were found to be key TFs in *ΔMIG1*.

Three key TFs (Ada2p, Swi1p and Swi3p) that are involved in chromatin remodeling were also identified as key TFs in response to deletion of *MIG1*. Moreover, Regulator of Drug Sensitivity, Rds3p, and Rdr1p, controlling multidrug resistance, were among the identified key TFs.

Table 3.15. Key TFs identified for *ΔMIG1* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 2 | Imp2'p<br>(YIL154c) | 8 | Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat<br>• cellular carbohydrate metabolic process<br>• DNA repair |
| 3 | Dig2p<br>(YDR480w) | 5 | Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription<br>• invasive growth in response to glucose limitation |
| 4 | Mig2p<br>(YGL209w) | 61 | Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 5 | Gsm1p<br>(YJL103c) | 25 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 6 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |

Table 3.15. Key TFs identified for *ΔMIG1* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 7 | Rds3p<br>(YPR094w) | 8 | Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance<br>• nuclear mRNA splicing, via spliceosome<br>• response to xenobiotic stimulus<br>• spliceosome assembly |
| 8 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 9 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 10 | Rgt1p<br>(YKL038w) | 67 | Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor<br>• glucose metabolic process<br>• negative regulation of transcription<br>• regulation of glucose import |
| 11 | Mig1p<br>(YGL035c) | 235 | Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 12 | Rdr1p<br>(YOR380w) | 12 | Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins<br>• response to xenobiotic stimulus |
| 13 | Gal80p<br>(YML051w) | 7 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 14 | Stp3p<br>(YLR375w) | 28 | Zinc-finger protein of unknown function, possibly involved in pre-tRNA splicing and in uptake of branched-chain amino acids<br>• biological process unknown |
| 15 | Nrg2p<br>(YBR066c) | 166 | Transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth; has similarity to Nrg1p<br>• biofilm formation<br>• invasive growth in response to glucose limitation<br>• pseudohyphal growth |

Table 3.15. Key TFs identified for *ΔMIG1* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 16 | YPR015c<br>(YPR015c) | 59 | Putative protein of unknown function; overexpression causes a cell cycle delay or arrest<br>• biological process unknown |
| 17 | Aca1p<br>(YER045c) | 29 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources<br>• transcription initiation from RNA polymerase II promoter |
| 18 | Mga2p<br>(YIR033w) | 35 | ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Spt23p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting<br>• fatty acid metabolic process<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to cold |
| 19 | Mdl2p<br>(YPL270w) | 7 | Mitochondrial inner membrane half-type ATP-binding cassette (ABC) transporter, required for respiratory growth at high temperature; similar to human TAP1 and TAP2 implicated in bare lymphocyte syndrome and Wegener-like granulomatosis<br>• oligopeptide transport |
| 20 | Rds2p<br>(YPL133c) | 45 | Zinc cluster transcriptional activator involved in conferring resistance to ketoconazole<br>• positive regulation of gluconeogenesis<br>• response to xenobiotic stimulus |
| 21 | Gat4p<br>(YIR013c) | 129 | Protein containing GATA family zinc finger motifs<br>• transcription |
| 22 | Bye1p<br>(YKL005c) | 24 | Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit<br>• negative regulation of transcription from RNA polymerase II promoter |
| 23 | Sut1p<br>(YGL162w) | 84 | Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression<br>• regulation of transcription<br>• regulation of transcription from RNA polymerase II promoter<br>• sterol transport |
| 24 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |

Key TFs identified in *ΔMIG1*, which are known to be involved in glucose derepression (Gal80p, Imp2'p, Rds2p, Gsm1p and Aca1p) are expected to be inactive in the wild type strain. Identification of them shows that most significant transcriptional changes occur around them, since they are not repressed any more or there are other very high activity repressors suppressing the lack of the functions of Mig1p, respectively. Indeed, the former seems to be true, since deletion of the *MIG1* gene relieves glucose repression of numerous target genes (Santangelo, 2006).

To sum up, the algorithm identified key TFs that are involved in chromatin remodeling, fatty acid metabolic process, oxidative phosphorylation (energy metabolism), alternative carbon source consumption and stress response, as a response to *MIG1* deletion as in *ΔSNF1*. Key TFs involved in glucose repression and drug resistance were also identified. Key TFs Gat4p, Stp3p and YPR015c probably have roles in one or more of the processes mentioned above.

3.2.2.2. Response to the Deletion of *MIG2*. Fourteen key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG2* (Table 3.16).

Mig2p was not found to be a key TF in response to the deletion of the *MIG2* gene, which suggests that there are other factors functioning in place of Mig2p. In this particular case, this other factor is most probably Mig1p, which was not identified as a key TF in *ΔMIG2*. In fact, Westholm *et al.* have found that Mig1p and Mig2p regulate an overlapping set of genes on 2 per cent glucose, with Mig1p being the major regulator (Westholm *et al.*, 2008).

Sin3p, involved in chromatin remodeling like Ada2p, Swi1p and Swi3p, and Hmlalpha1p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG2* deletion.

Although Mga2p, a key TF identified in *ΔMIG1*, did not appear to be a key TF in *ΔMIG2*, Spt23p, homolog of Mga2p, was identified as key TF in *ΔMIG2*. These TFs are involved in fatty acid metabolic process and response to cold.

Nine key TFs (highlighted in Table 3.16) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG2*.

Table 3.16. Key TFs identified for *ΔMIG2* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Dig2p<br>(YDR480w) | 5 | Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription<br>• invasive growth in response to glucose limitation |
| 2 | Gal80p<br>(YML051w) | 7 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 3 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 4 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 5 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 6 | Gsm1p<br>(YJL103c) | 25 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 7 | Sin3p<br>(YOL004w) | 31 | Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity<br>• chromatin silencing at rDNA<br>• chromatin silencing at silent mating-type cassette<br>• chromatin silencing at telomere • histone deacetylation<br>• double-strand break repair via nonhomologous end joining<br>• negative regulation of transcription from RNA polymerase II promoter<br>• negative regulation of transposition, RNA-mediated<br>• positive regulation of gene-specific transcription from RNA polymerase II promoter<br>• positive regulation of transcription from RNA polymerase II promoter |

Table 3.16. Key TFs identified for *ΔMIG2* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 8 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |
| 9 | Hmra2p<br>(YCR096c) | 27 | Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system<br>• biological process unknown |
| 10 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 11 | Hmlalpha1p<br>(YCL066w) | 20 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 12 | Rgt1p<br>(YKL038w) | 67 | Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor<br>• glucose metabolic process<br>• negative regulation of transcription<br>• regulation of glucose import |
| 13 | Spt23p<br>(YKL020c) | 57 | ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Mga2p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting<br>• fatty acid metabolic process<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to cold |
| 14 | Lys14p<br>(YDR034c) | 12 | Transcriptional activator involved in regulation of genes of the lysine biosynthesis pathway; requires 2-aminoadipate semialdehyde as co-inducer<br>• lysine biosynthetic process via aminoadipic acid |

3.2.2.3. Response to the Deletion of both *MIG1* and *MIG2*. Eighteen key TFs around which most transcriptional changes occur were identified as a response to deletion of both *MIG1* and *MIG2* (Table 3.17).

Mig1p and Mig2p were found to be key TFs in response to the deletion of both *MIG1* and *MIG2* genes, as expected.

Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG1* and *MIG2* deletion. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Thirteen key TFs (highlighted in Table 3.17) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG1ΔMIG2*, Mig3p being the top scoring key TF.

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 2 | Mig2p<br>(YGL209w) | 61 | Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 3 | Hmlalpha1p<br>(YCL066w) | 20 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 4 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 5 | Imp2'p<br>(YIL154c) | 8 | Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat<br>• cellular carbohydrate metabolic process<br>• DNA repair |
| 6 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 7 | Gsm1p<br>(YJL103c) | 25 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 8 | Hpc2p<br>(YBR215w) | 3 | Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes<br>• DNA replication-independent nucleosome assembly<br>• regulation of transcription involved in G1/S-phase of mitotic cell cycle<br>• RNA elongation from RNA polymerase II promoter |
| 9 | Rdr1p<br>(YOR380w) | 12 | Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins<br>• response to xenobiotic stimulus |
| 10 | Rpn10p<br>(YHR200w) | 9 | Non-ATPase base subunit of the 19S regulatory particle (RP) of the 26S proteasome; N-terminus plays a role in maintaining the structural integrity of the RP; binds selectively to polyubiquitin chains; homolog of the mammalian S5a protein<br>• ubiquitin-dependent protein catabolic process |
| 11 | Rgt1p<br>(YKL038w) | 67 | Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor<br>• glucose metabolic process<br>• negative regulation of transcription<br>• regulation of glucose import |
| 12 | Mig1p<br>(YGL035c) | 235 | Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 13 | Gat4p<br>(YIR013c) | 129 | Protein containing GATA family zinc finger motifs<br>• transcription |
| 14 | Rds3p<br>(YPR094w) | 8 | Component of the SF3b subcomplex of the U2 snRNP, zinc cluster protein involved in pre-mRNA splicing and cycloheximide resistance<br>• nuclear mRNA splicing, via spliceosome<br>• response to xenobiotic stimulus<br>• spliceosome assembly |
| 15 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |

Table 3.17. Key TFs identified for *ΔMIG1ΔMIG2* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 16 | Gal80p<br>(YML051w) | 7 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 17 | Hmlalpha2p<br>(YCL067c) | 28 | Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression<br>• donor selection<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 18 | Hmra2p<br>(YCR096c) | 27 | Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system<br>• biological process unknown |

3.2.2.4. Comparison of the Responses to Deletions of *MIG1*, *MIG2* and both *MIG1* and *MIG2*. The comparison between the key TFs identified in *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants is shown in Figure 3.13.

Seven key TFs were identified for all three mutants, namely Ada2p, Gal80p, Gsm1p, Mig3p, Rgt1p, Swi1p and Swi3p. These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of transcription" (*p*-value=$3.05\text{x}10^{-5}$), as expected (Table D.7). These key TFs are involved in several biological processes, i.e., galactose metabolic process (Gal80p), chromatin remodeling (Ada2p, Swi1 and Swi3), regulation of energy metabolism (Gsm1p) and regulation of glucose import (Rgt1p).

Nine (Aca1p, Bye1p, Mdl2p, Mga2p, Nrg2p, Rds2p, Stp3p, Sut1p and YPR015c) key TFs that were identified only as a response specifically to the deletion of *MIG1* are involved in several biological processes, i.e., glucose repression (Nrg2p), utilization of nonoptimal/nonfermentable carbon sources (Aca1p, Rds2p), fatty acid metabolic process (Mga2), oligopeptide transport (Mdl2p) and stress response (Sut1p, Mga2p). Three (Lys14p, Sin3p and Spt23p) key TFs that were identified only as a response specifically to the deletion of *MIG2* are involved in several biological processes, i.e., chromatin remodeling (Sin3p), fatty acid metabolic process (Spt23p) and stress response (Spt23p). Three (Hmlalpha2p, Hpc2p and Rpn10p) key TFs that were identified only as a response specifically to the deletion of *MIG1* and *MIG2* are involved in mating-type specific regulation of transcription (Hmlalpha2p) and in chromatin remodeling (Hpc2p). However no significant GO biological process terms could be associated with these sets.

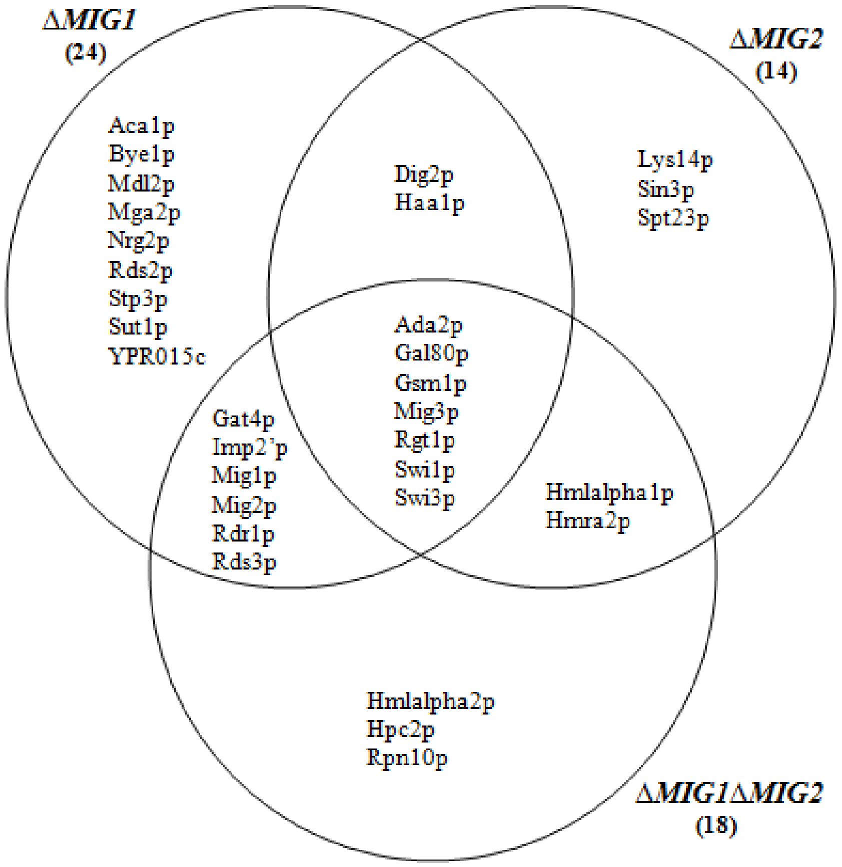

Figure 3.13. Comparison of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants (the number of key TFs for each specific mutant is given in brackets)

When the significant shared GO biological process terms ($p$-value<0.01) of the key TFs identified for the overlaps of any two specific perturbations were further identified excluding the key TFs identified for all three mutants, no significant shared GO biological process terms could be associated with the two key TFs identified for both *ΔMIG1* and *ΔMIG2* mutants (Dig2p and Haa1p) and with the two key TFs identified for both *ΔMIG2* and *ΔMIG1ΔMIG2* mutants (Hmlalpha1p, Hmra2p). Dig2p is involved in invasive growth in response glucose limitation, Haa1p regulates transcription of genes encoding membrane stress proteins, and Hmlalpha1p regulates mating-type specific regulation of transcription.

Six key TFs (Gat4p, Imp2'p, Mig1p, Mig2p, Rdr1p and Rds3p) identified for both *ΔMIG1* and *ΔMIG1ΔMIG2* mutants excluding the key TFs identified for all three mutants were found to be enriched significantly with more specific GO biological process terms, such as "negative regulation of transcription by glucose" (*p*-value=0.00065) and "cellular response to nutrient" (*p*-value=0.00657) (Table D.8). These key TFs are involved in biological processes carbohydrate metabolic processes (Imp2'p) and drug resistance (Rdr1p, Rd3p).

In particular, TFs regulating mating-type specific regulation of transcription did not appear as key TFs in *ΔMIG1* and TFs involved in drug resistance did not appear as key TFs in *ΔMIG2*.

3.2.2.5. Response to the Deletion of *MIG3*. Fifteen key TFs around which most transcriptional changes occur were identified as a response to deletion of *MIG3* (Table 3.18).

Mig3p was found to be a key TF in response to the deletion of *MIG3* gene, as expected.

Maltose fermentation protein, Mal13p, involved in cellular carbohydrate metabolic process, was also among the identified key TFs *ΔMIG3*.

Hmra1p, Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to *MIG3* deletion. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Ten key TFs (highlighted in Table 3.18) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG3*.

Table 3.18. Key TFs identified for *ΔMIG3* mutant

| Rank | TF<br>(ORF Name) | degree<br>(*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 1 | Dig2p<br>(YDR480w) | 5 | Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription<br>• invasive growth in response to glucose limitation |
| 2 | Mdl2p<br>(YPL270w) | 7 | Mitochondrial inner membrane half-type ATP-binding cassette (ABC) transporter, required for respiratory growth at high temperature; similar to human TAP1 and TAP2 implicated in bare lymphocyte syndrome and Wegener-like granulomatosis<br>• oligopeptide transport |
| 3 | Aca1p<br>(YER045c) | 29 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources<br>• transcription initiation from RNA polymerase II promoter |
| 4 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 5 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 6 | Hpc2p<br>(YBR215w) | 3 | Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes<br>• DNA replication-independent nucleosome assembly<br>• regulation of transcription involved in G1/S-phase of mitotic cell cycle<br>• RNA elongation from RNA polymerase II promoter |
| 7 | Gal80p<br>(YML051w) | 7 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 8 | Hmlalpha2p<br>(YCL067c) | 28 | Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression<br>• donor selection<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |

Table 3.18. Key TFs identified for *ΔMIG3* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 9 | Hmlalpha1p<br>(YCL066w) | 20 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 10 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 11 | Gsm1p<br>(YJL103c) | 25 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 12 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |
| 13 | Mal13p<br>(YGR288w) | 12 | MAL-activator protein, part of complex locus MAL1; nonfunctional in genomic reference strain S288C<br>• cellular carbohydrate metabolic process<br>• regulation of transcription, DNA-dependent |
| 14 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 15 | Hmra1p<br>(YCR097w) | 20 | Silenced copy of a1 at HMR; homeobox corepressor that interacts with Alpha2p to repress haploid-specific gene transcription in diploid cells<br>• regulation of transcription, mating-type specific |

3.2.2.6. Comparison of the Responses to Deletions of *MIG1*, *MIG2* and *MIG3*. The comparison between the key TFs identified in *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants is shown in Figure 3.14.

Eight key TFs were identified for all three mutants, namely Ada2p, Dig2p, Gal80p, Gsm1p, Haa1p, Mig3p, Swi1p and Swi3p. These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of macromolecule biosynthetic process" (*p*-value=0.00039) (Table D.11). GO term with the lowest *p*-value was found to be “regulation of transcription, DNA-dependent” (*p*-value=8.28x$10^{-5}$), as expected. These key TFs are involved in several biological processes, i.e., galactose metabolic process (Gal80p), chromatin remodeling (Ada2p, Swi1 and Swi3), regulation of energy metabolism (Gsm1p), invasive growth in response glucose limitation (Dig2p) and transcription of genes encoding membrane stress proteins (Haa1p).

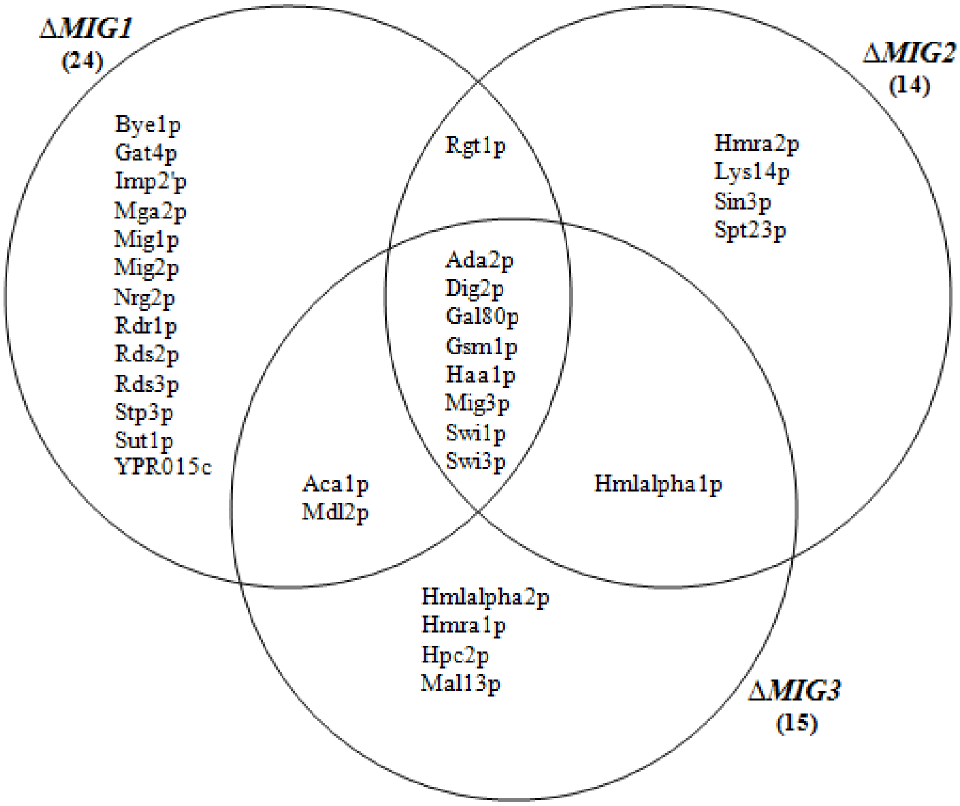

Figure 3.14. Comparison of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants (the number of key TFs for each specific mutant is given in brackets)

Thirteen key TFs were identified only as a response specifically to the deletion of *MIG1* and these key TFs were found to be enriched significantly with GO biological process terms related to glucose repression, such as “negative regulation of transcription by carbon catabolites” (*p*-value=0.00408) and “negative regulation of transcription by glucose” (*p*-value=0.00408) (Table D.9). These key TFs are involved in several biological processes, i.e., glucose repression (Nrg2p), carbohydrate metabolic processes (Imp2’p), use of nonfermentable carbon sources (Rds2p), fatty acid metabolic process (Mga2p), stress response (Mga2p, Sut1p) and drug resistance (Rdr1p, Rd3p).

No significant GO biological process terms could be associated with the four key TFs (Hmra2p, Lys14p, Sin3p and Spt23p) identified only as a response specifically to the deletion of *MIG2*. Sin3p is involved in chromatin remodeling and Spt23p is involved in fatty acid metabolic process and stress response.

Four key TFs (Hmlalpha2p, Hmra1p, Hpc2p and Mal13p) were identified only as a response specifically to the deletion of *MIG3* and these key TFs were found to be enriched significantly with general GO biological process terms, such as “regulation of macromolecule biosynthetic process” (*p*-value=0.00158), as well as with more specific GO biological process terms, such as “cell fate commitment” (*p*-value=0.00363), “sex determination” (*p*-value=0.00363) and “mating type determination” (*p*-value=0.00363) (Table D.10). Hmlalpha2p and Hmra1p regulate mating-type specific transcription and Mal13p is involved in cellular carbohydrate metabolic process.

When the significant shared GO biological process terms (*p*-value<0.01) of the key TFs identified for the overlaps of any two specific perturbations were further investigated excluding the key TFs identified for all three mutants, no significant shared GO biological process terms could be associated with the two key TFs identified for both *ΔMIG1* and *ΔMIG3* mutants (Aca1p and Mdl2p). Aca1p is involved in utilization of nonoptimal carbon sources and Mdl2p in oligopeptide transport.

Rgt1p, involved in glucose induction, was the only key TF identified for both *ΔMIG1* and *ΔMIG2* excluding the key TFs identified for all three mutants and Hmlalpha1p, regulating mating-type specific transcription, was the only key TF identified for both *ΔMIG1* and *ΔMIG3* excluding the key TFs identified for all three mutants.

In particular, TFs regulating mating-type specific regulation of transcription did not appear as key TFs in *ΔMIG1*, TFs involved in drug resistance did not appear as key TFs in *ΔMIG2* and *ΔMIG3*, and TFs involved in fatty acid metabolic process did not appear as key TFs in *ΔMIG3*.

3.2.2.7. Response to the Deletion of all *MIG1*, *MIG2* and *MIG3*. Twenty two key TFs around which most transcriptional changes occur were identified as a response to deletion of all *MIG1*, *MIG2* and *MIG3* genes (Table 3.19).

Mig1p, Mig2p and Mig3p were found to be key TFs in response to the deletion of *MIG1*, *MIG2* and *MIG3* genes, as expected.

Maltose fermentation protein, Mal13p, involved in cellular carbohydrate metabolic process, and Met32p, involved in sulfur amino acid metabolic process, were also among the identified key TFs in *ΔMIG3*.

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways which is important in the regulation of cell growth in response to nutrients was identified as a key TF.

Hmlalpha1p and Hmlalpha2p, involved in mating-type specific regulation of transcription, were also identified as key TFs in response to deletion of all *MIG1*, *MIG2* and *MIG3* genes. Hpc2p is involved in chromatin remodeling like Ada2p, Swi1p and Swi3p.

Thirteen key TFs (highlighted in Table 3.19) identified as a response to *MIG1* deletion were also determined as key TFs in *ΔMIG1ΔMIG2ΔMIG3*.

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 1 | Hmlalpha1p<br>(YCL066w) | 20 | Silenced copy of ALPHA1 at HML, encoding a transcriptional coactivator involved in the regulation of mating-type alpha-specific gene expression<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 2 | Hmra2p<br>(YCR096c) | 27 | Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system<br>• biological process unknown |

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 3 | Mig3p<br>(YER028c) | 26 | Probable transcriptional repressor involved in response to toxic agents such as hydroxyurea that inhibit ribonucleotide reductase; phosphorylation by Snf1p or the Mec1p pathway inactivates Mig3p, allowing induction of damage response genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• response to DNA damage stimulus<br>• transcription initiation |
| 4 | Mig2p<br>(YGL209w) | 61 | Protein containing zinc fingers, involved in repression, along with Mig1p, of SUC2 (invertase) expression by high levels of glucose; binds to Mig1p-binding sites in SUC2 promoter<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 5 | Imp2'p<br>(YIL154c) | 8 | Transcriptional activator involved in maintenance of ion homeostasis and protection against DNA damage caused by bleomycin and other oxidants, contains a C-terminal leucine-rich repeat<br>• cellular carbohydrate metabolic process<br>• DNA repair |
| 6 | Gsm1p<br>(YJL103c) | 25 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 7 | Hpc2p<br>(YBR215w) | 3 | Subunit of the HIR complex, a nucleosome assembly complex involved in regulation of histone gene transcription; mutants display synthetic defects with subunits of FACT, a complex that allows passage of RNA Pol II through nucleosomes<br>• DNA replication-independent nucleosome assembly<br>• regulation of transcription involved in G1/S-phase of mitotic cell cycle<br>• RNA elongation from RNA polymerase II promoter |
| 8 | Gal80p<br>(YML051w) | 7 | Transcriptional regulator involved in the repression of GAL genes in the absence of galactose; inhibits transcriptional activation by Gal4p; inhibition relieved by Gal3p or Gal1p binding<br>• galactose metabolic process<br>• negative regulation of kinase activity<br>• positive regulation of transcription by galactose |
| 9 | Rpn10p<br>(YHR200w) | 9 | Non-ATPase base subunit of the 19S regulatory particle (RP) of the 26S proteasome; N-terminus plays a role in maintaining the structural integrity of the RP; binds selectively to polyubiquitin chains; homolog of the mammalian S5a protein<br>• ubiquitin-dependent protein catabolic process |
| 10 | Rtg2p<br>(YGL252c) | 9 | Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p<br>• extrachromosomal rDNA circle accumulation involved in replicative cell aging<br>• intracellular signaling pathway<br>• mitochondria-nucleus signaling pathway |

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 11 | Haa1p<br>(YPR008w) | 18 | Transcriptional activator involved in the transcription of TPO2, YRO2, and other genes putatively encoding membrane stress proteins; involved in adaptation to weak acid stress<br>• regulation of transcription, DNA-dependent<br>• response to acid<br>• transcription initiation from RNA polymerase II promoter |
| 12 | Mal13p<br>(YGR288w) | 12 | MAL-activator protein, part of complex locus MAL1; nonfunctional in genomic reference strain S288C<br>• cellular carbohydrate metabolic process<br>• regulation of transcription, DNA-dependent |
| 13 | Rgt1p<br>(YKL038w) | 67 | Glucose-responsive transcription factor that regulates expression of several glucose transporter (HXT) genes in response to glucose; binds to promoters and acts both as a transcriptional activator and repressor<br>• glucose metabolic process<br>• negative regulation of transcription<br>• regulation of glucose import |
| 14 | Hmlalpha2p<br>(YCL067c) | 28 | Silenced copy of ALPHA2 at HML; homeobox-domain protein that associates with Mcm1p in haploid cells to repress a-specific gene expression and interacts with a1p in diploid cells to repress haploid-specific gene expression<br>• donor selection<br>• regulation of transcription from RNA polymerase II promoter<br>• regulation of transcription, mating-type specific |
| 15 | Swi3p<br>(YJL176c) | 9 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |
| 16 | Mig1p<br>(YGL035c) | 235 | Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 17 | Gat4p<br>(YIR013c) | 129 | Protein containing GATA family zinc finger motifs<br>• transcription |
| 18 | Swi1p<br>(YPL016w) | 15 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |

Table 3.19. Key TFs identified for *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

| **Rank** | **TF (ORF Name)** | **degree (*k*)** | **SGD Definition & GO Biological Process Terms** |
|---|---|---|---|
| 19 | Kar4p<br>(YCL055w) | 47 | Transcription factor required for gene regulation in response to pheromones; also required during meiosis; exists in two forms, a slower-migrating form more abundant during vegetative growth and a faster-migrating form induced by pheromone<br>• G1 phase of mitotic cell cycle<br>• karyogamy involved in conjugation with cellular fusion<br>• meiosis<br>• negative regulation of transcription from RNA polymerase II promoter by pheromones<br>• positive regulation of transcription from RNA polymerase II promoter by pheromones |
| 20 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 21 | Mga2p<br>(YIR033w) | 35 | ER membrane protein involved in regulation of OLE1 transcription, acts with homolog Spt23p; inactive ER form dimerizes and one subunit is then activated by ubiquitin/proteasome-dependent processing followed by nuclear targeting<br>• fatty acid metabolic process<br>• positive regulation of transcription from RNA polymerase II promoter<br>• response to cold |
| 22 | Met32p<br>(YDR253c) | 99 | Zinc-finger DNA-binding protein, involved in transcriptional regulation of the methionine biosynthetic genes, similar to Met31p<br>• sulfur amino acid metabolic process |

<u>3.2.2.8. Perturbation-Responsive Subnetworks of *ΔMIG1, ΔMIG2, ΔMIG1ΔMIG2, ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants.</u> Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes (*p*-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetworks in *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants are given in Table 3.20. The overviews of these subnetworks produced in Cytoscape are displayed in Figure 3.15, Figure 3.16, Figure 3.17, Figure 3.18 and Figure 3.19, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in the corresponding mutants with respect to wild type strain are indicated. Key TFs indicated in black in these figures were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.27 and Table 3.28). GO

biological process terms significantly associated with the target genes in each PRS (*p*-value<0.01) were identified and represented in Table 3.21, Table 3.22, Table 3.23 and Table 3.24. No significant GO biological process terms could be associated with the target genes of the PRS of *ΔMIG2* mutant.

Table 3.20. The numbers of TFs, their target genes and interactions for the PRSs of *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

| **Mutant** | **Number of Key TFs** | **Number of Target Genes** | **Number of Interactions** |
|---|---|---|---|
| *ΔMIG1* | 21 | 113 | 195 |
| *ΔMIG2* | 8 | 13 | 15 |
| *ΔMIG1ΔMIG2* | 15 | 143 | 209 |
| *ΔMIG3* | 4 | 4 | 4 |
| *ΔMIG1ΔMIG2ΔMIG3* | 19 | 166 | 234 |

Table 3.21. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription by carbon catabolites | 6 out of 113 genes, 5.3 per cent | 0.0000117 |
| monosaccharide transport | 7 out of 113 genes, 6.2 per cent | 0.000018 |
| hexose transport | 7 out of 113 genes, 6.2 per cent | 0.000018 |
| glucose transport | 5 out of 113 genes, 4.4 per cent | 0.0000345 |
| carbohydrate transport | 8 out of 113 genes, 7.1 per cent | 0.0000595 |
| carbohydrate metabolic process | 19 out of 113 genes, 16.8 per cent | 0.000066 |
| cellular response to nutrient | 6 out of 113 genes, 5.3 per cent | 0.0000691 |
| response to nutrient | 6 out of 113 genes, 5.3 per cent | 0.00014 |
| hexose metabolic process | 11 out of 113 genes, 9.7 per cent | 0.00041 |
| alcohol metabolic process | 15 out of 113 genes, 13.3 per cent | 0.0006 |
| cellular carbohydrate metabolic process | 17 out of 113 genes, 15.0 per cent | 0.00087 |
| fructose transport | 3 out of 113 genes, 2.7 per cent | 0.00123 |
| regulation of transcription by glucose | 4 out of 113 genes, 3.5 per cent | 0.00126 |
| monosaccharide metabolic process | 11 out of 113 genes, 9.7 per cent | 0.00142 |
| glucose metabolic process | 9 out of 113 genes, 8.0 per cent | 0.00747 |

Table 3.22. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| carbohydrate transport | 11 out of 143 genes, 7.7 per cent | 0.000000103 |
| monosaccharide transport | 9 out of 143 genes, 6.3 per cent | 0.000000159 |
| hexose transport | 9 out of 143 genes, 6.3 per cent | 0.000000159 |
| glucose transport | 6 out of 143 genes, 4.2 per cent | 0.00000183 |
| carbohydrate metabolic process | 24 out of 143 genes, 16.8 per cent | 0.00000203 |
| cellular carbohydrate metabolic process | 23 out of 143 genes, 16.1 per cent | 0.00000492 |

Table 3.22. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2* mutant (continued)

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| alcohol metabolic process | 20 out of 143 genes, 14.0 per cent | 0.0000055 |
| hexose metabolic process | 14 out of 143 genes, 9.8 per cent | 0.0000152 |
| regulation of transcription by carbon catabolites | 6 out of 143 genes, 4.2 per cent | 0.0000604 |
| monosaccharide metabolic process | 14 out of 143 genes, 9.8 per cent | 0.000076 |
| response to chemical stimulus | 22 out of 143 genes, 15.4 per cent | 0.0001 |
| cellular response to nutrient | 6 out of 143 genes, 4.2 per cent | 0.00035 |
| response to nutrient | 6 out of 143 genes, 4.2 per cent | 0.00071 |
| glucose metabolic process | 11 out of 143 genes, 7.7 per cent | 0.00154 |
| fructose transport | 3 out of 143 genes, 2.1 per cent | 0.00314 |
| regulation of transcription by glucose | 4 out of 143 genes, 2.8 per cent | 0.00404 |
| cellular carbohydrate catabolic process | 10 out of 143 genes, 7.0 per cent | 0.00477 |
| carbohydrate catabolic process | 10 out of 143 genes, 7.0 per cent | 0.00638 |

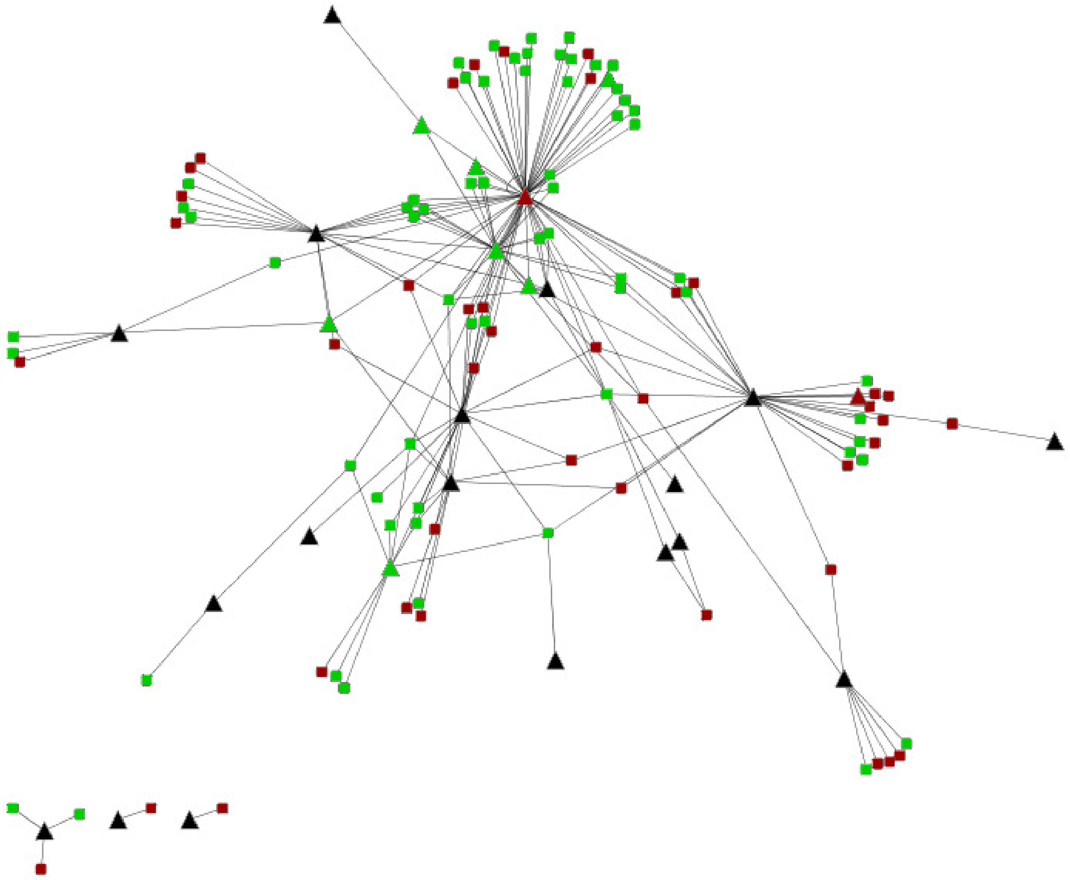

Figure 3.15. Representation of the PRS of *ΔMIG1* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

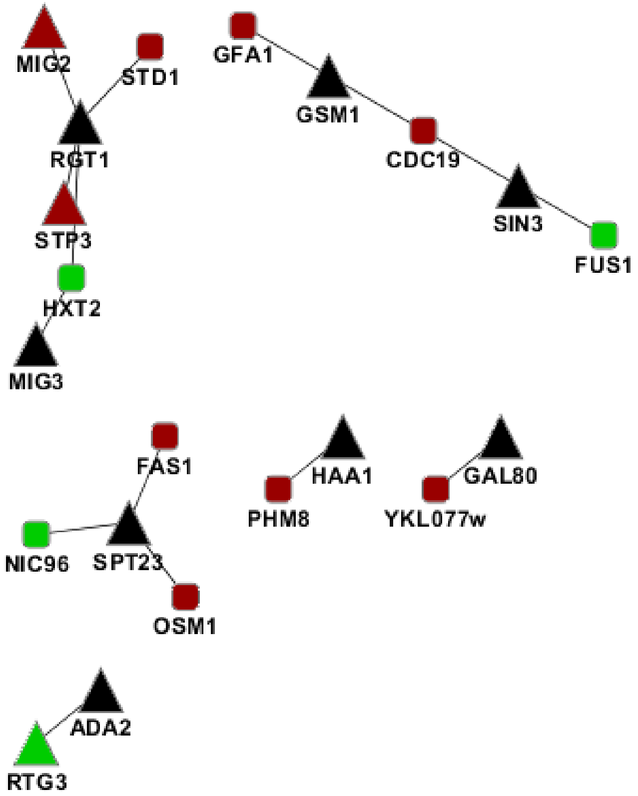

Figure 3.16. Representation of the PRS of *ΔMIG2* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

Table 3.23. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG3* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| cellular process | 2 out of 4 genes, 50.0 per cent | 0 |

Table 3.24. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| carbohydrate transport | 12 out of 166 genes, 7.2 per cent | 3.01E-08 |
| sulfur metabolic process | 16 out of 166 genes, 9.6 per cent | 1.89E-07 |
| monosaccharide transport | 9 out of 166 genes, 5.4 per cent | 6.4E-07 |
| hexose transport | 9 out of 166 genes, 5.4 per cent | 6.4E-07 |
| glucose transport | 6 out of 166 genes, 3.6 per cent | 4.77E-06 |
| carbohydrate metabolic process | 24 out of 166 genes, 14.5 per cent | 0.0000427 |
| sulfur amino acid metabolic process | 9 out of 166 genes, 5.4 per cent | 0.000047 |
| cellular carbohydrate metabolic process | 23 out of 166 genes, 13.9 per cent | 0.00009 |
| regulation of transcription by carbon catabolites | 6 out of 166 genes, 3.6 per cent | 0.00016 |
| alcohol metabolic process | 19 out of 166 genes, 11.4 per cent | 0.00034 |

Table 3.24. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| cellular response to nutrient | 6 out of 166 genes, 3.6 per cent | 0.00089 |
| response to nutrient | 6 out of 166 genes, 3.6 per cent | 0.00178 |
| small molecule metabolic process | 40 out of 166 genes, 24.1 per cent | 0.00208 |
| hexose metabolic process | 12 out of 166 genes, 7.2 per cent | 0.00406 |
| fructose transport | 3 out of 166 genes, 1.8 per cent | 0.00521 |
| regulation of transcription by glucose | 4 out of 166 genes, 2.4 per cent | 0.00772 |
| anion transport | 6 out of 166 genes, 3.6 per cent | 0.00944 |

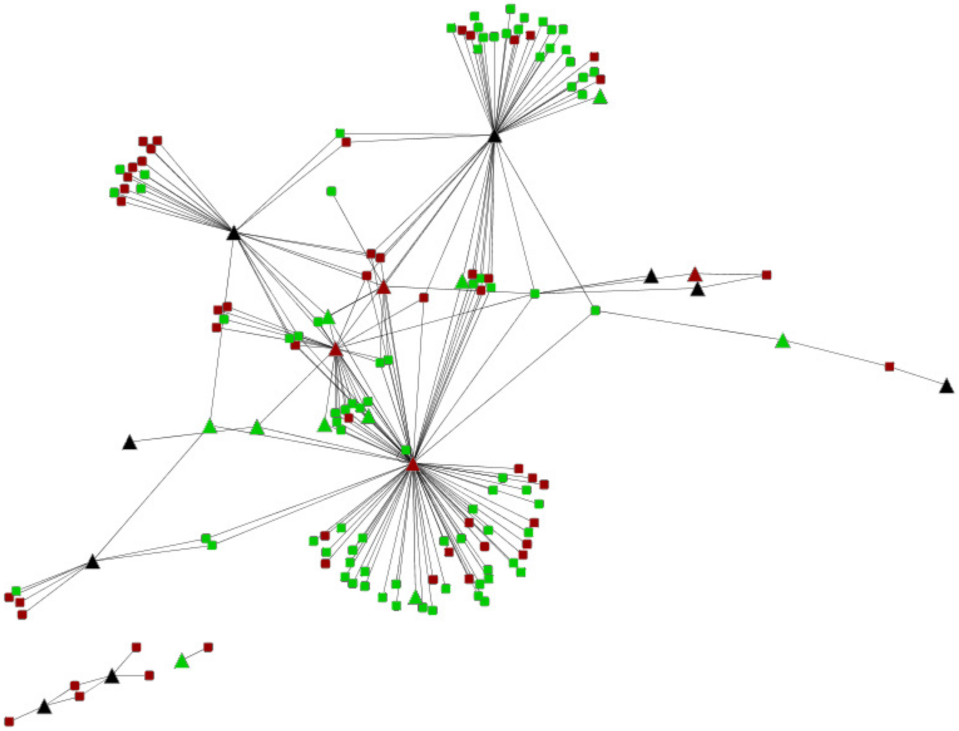

Figure 3.17. Representation of the PRS of *ΔMIG1ΔMIG2* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

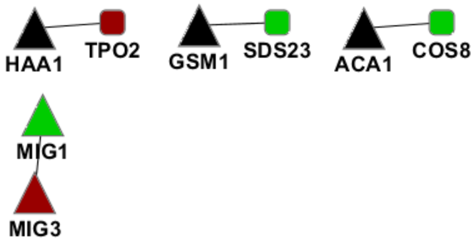

Figure 3.18. Representation of the PRS of *ΔMIG3* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

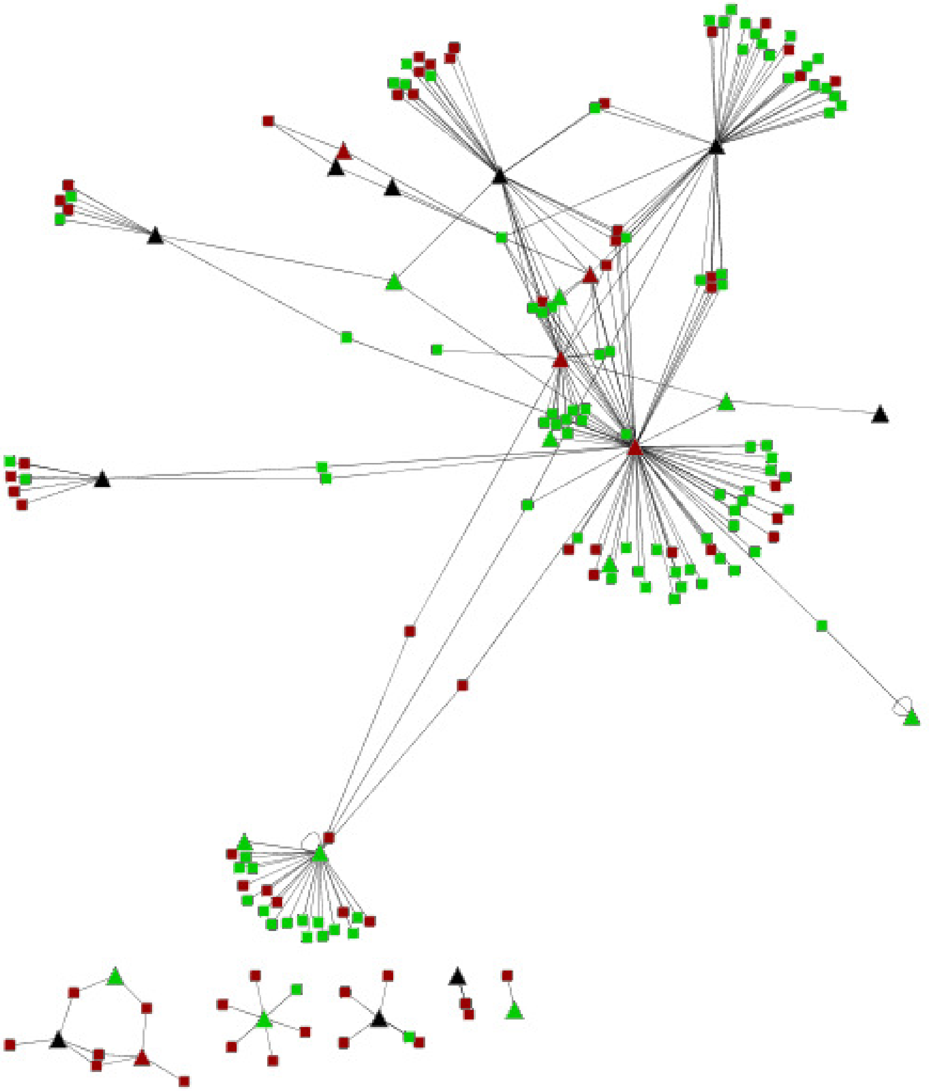

Figure 3.19. Representation of the PRS of *ΔMIG1ΔMIG2ΔMIG3* mutant (triangles and squares represent TFs and non-TF target genes, respectively)

The significantly associated GO terms of the PRSs of *ΔMIG1, ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* strains are very similar. “Regulation of transcription by carbon catabolites”, “regulation of transcription by glucose”, “cellular response to nutrient”, “response to nutrient”, “alcohol metabolic process”, “carbohydrate transport”, “cellular carbohydrate metabolic process”, “glucose transport” and “fructose transport” were among the significantly associated GO terms of the PRSs of all three *MIG1* deletion mutants under investigation, almost with the same number of differentially expressed genes (Figure 3.20). This result is expected since Mig1p has a role in glucose repression pathway and represses genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis (Raghevendran *et al.*, 2005).

*MIG3* deletion has very little effect compared to *MIG1* deletion (Figure 3.20). The only GO term that was significantly associated only with the target genes of the PRS of *ΔMIG3* mutant was "cellular process".

Table 3.25. Number of genes annotated to significantly associated GO biological process terms of the PRS of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

| **GO Term** | ***ΔMIG1*** | ***ΔMIG1ΔMIG2*** | ***ΔMIG3*** | ***ΔMIG1ΔMIG2ΔMIG3*** |
|---|---|---|---|---|
| alcohol metabolic process | 15 | 20 | 0 | 19 |
| anion transport | 0 | 0 | 0 | 6 |
| carbohydrate catabolic process | 0 | 10 | 0 | 0 |
| carbohydrate metabolic process | 19 | 24 | 0 | 24 |
| carbohydrate transport | 8 | 11 | 0 | 12 |
| cellular carbohydrate catabolic process | 0 | 10 | 0 | 0 |
| cellular carbohydrate metabolic process | 17 | 23 | 0 | 23 |
| cellular process | 0 | 0 | 2 | 0 |
| cellular response to nutrient | 6 | 6 | 0 | 6 |
| fructose transport | 3 | 3 | 0 | 3 |
| glucose metabolic process | 9 | 11 | 0 | 0 |
| glucose transport | 5 | 6 | 0 | 6 |
| hexose metabolic process | 11 | 14 | 0 | 12 |
| hexose transport | 7 | 9 | 0 | 9 |
| monosaccharide metabolic process | 11 | 14 | 0 | 0 |
| monosaccharide transport | 7 | 9 | 0 | 9 |
| regulation of transcription by carbon catabolites | 6 | 6 | 0 | 6 |
| regulation of transcription by glucose | 4 | 4 | 0 | 4 |
| response to chemical stimulus | 0 | 22 | 0 | 0 |
| response to nutrient | 6 | 6 | 0 | 6 |
| small molecule metabolic process | 0 | 0 | 0 | 40 |
| sulfur amino acid metabolic process | 0 | 0 | 0 | 9 |
| sulfur metabolic process | 0 | 0 | 0 | 16 |

Deletion of all three *MIG1*, *MIG2* and *MIG3* genes causes a considerable collective change in the expression of the genes which are significantly associated with the processes "anion transport", "small molecule metabolic process", "sulfur amino acid metabolic process" and "sulfur metabolic process" (Table 3.25). These terms do not appear among the terms found for *ΔMIG1*, *ΔMIG3* and *ΔMIG1ΔMIG2* mutants. Moreover, deletion of both *MIG1* and *MIG2* genes causes a significant change in the expression of the genes which are significantly associated with the processes “response to chemical stimulus”, “carbohydrate catabolic process” and “cellular carbohydrate catabolic process”, which do not appear among the terms found for *ΔMIG1* and *ΔMIG2* mutants.

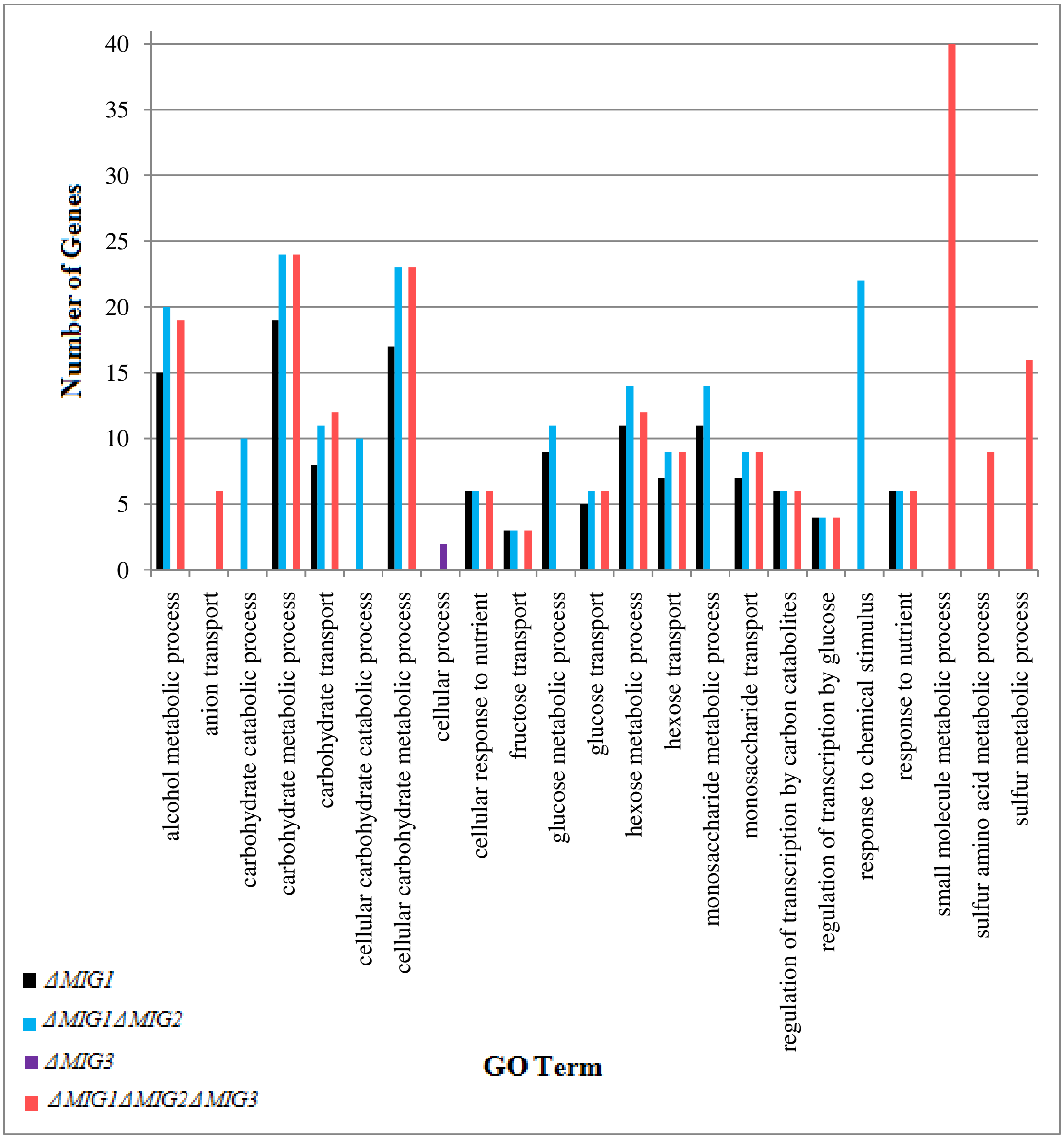

Figure 3.20. Significantly associated GO biological process terms of the target genes of the PRS of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

<u>3.2.2.9. Regulation of Key Transcription Factors of *ΔMIG1*, *ΔMIG2*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants.</u> Identification of key TFs demonstrates the

change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed, as described in Section 2.4. Most of the key TFs of *ΔMIG1*, *ΔMIG2*, *ΔMIG3*, *ΔMIG1ΔMIG2* and *ΔMIG1ΔMIG2ΔMIG3* mutants were found to be regulated mainly post-transcriptionally (Table 3.26). In Table 3.27 and Table 3.28, regulation of each key TF is represented.

Table 3.26. Number of key TFs for *ΔMIG1, ΔMIG2, ΔMIG1ΔMIG2, ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

| **Mutant** | **Number of A** | **Number of B** |
|---|---|---|
| *ΔMIG1* | 3 | 21 |
| *ΔMIG2* | 0 | 14 |
| *ΔMIG1ΔMIG2* | 6 | 12 |
| *ΔMIG3* | 1 | 14 |
| *ΔMIG1ΔMIG2ΔMIG3* | 10 | 12 |

Table 3.27. Regulation of key TFs of *ΔMIG1, ΔMIG2* and *ΔMIG1ΔMIG2* mutants

| **rank** | ***ΔMIG1*** | **Case** | ***ΔMIG2*** | **Case** | ***ΔMIG1ΔMIG2*** | **Case** |
|---|---|---|---|---|---|---|
| 1 | Mig3p | B | Dig2p | B | Mig3p | A |
| 2 | Imp2'p | B | Gal80p | B | Mig2p | A |
| 3 | Dig2p | B | Ada2p | B | Hmlalpha1p | B |
| 4 | Mig2p | A | Mig3p | B | Swi1p | B |
| 5 | Gsm1p | B | Haa1p | B | Imp2'p | B |
| 6 | Swi3p | B | Gsm1p | B | Swi3p | A |
| 7 | Rds3p | B | Sin3p | B | Gsm1p | B |
| 8 | Swi1p | B | Swi3p | B | Hpc2p | B |
| 9 | Haa1p | B | Hmra2p | B | Rdr1p | A |
| 10 | Rgt1p | B | Swi1p | B | Rpn10p | B |
| 11 | Mig1p | A | Hmlalpha1p | B | Rgt1p | B |
| 12 | Rdr1p | B | Rgt1p | B | Mig1p | A |
| 13 | Gal80p | B | Spt23p | B | Gat4p | B |
| 14 | Stp3p | B | Lys14p | B | Rds3p | B |
| 15 | Nrg2p | B | | | Ada2p | B |
| 16 | YPR015c | A | | | Gal80p | A |
| 17 | Aca1p | B | | | Hmlalpha2p | B |
| 18 | Mga2p | B | | | Hmra2p | B |

Table 3.27. Regulation of key TFs of *ΔMIG1, ΔMIG2* and *ΔMIG1ΔMIG2* mutants (continued)

| **rank** | ***ΔMIG1*** | **Case** | ***ΔMIG2*** | **Case** | ***ΔMIG1ΔMIG2*** | **Case** |
|---|---|---|---|---|---|---|
| 19 | Mdl2p | B | | | | |
| 20 | Rds2p | B | | | | |
| 21 | Gat4p | B | | | | |
| 22 | Bye1p | B | | | | |
| 23 | Sut1p | B | | | | |
| 24 | Ada2p | B | | | | |

Table 3.28. Regulation of key TFs of *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants

| **rank** | ***ΔMIG3*** | **Case** | ***ΔMIG1ΔMIG2ΔMIG3*** | **Case** |
|---|---|---|---|---|
| 1 | Dig2p | B | Hmlalpha1p | B |
| 2 | Mdl2p | B | Hmra2p | A |
| 3 | Aca1p | B | Mig3p | A |
| 4 | Haa1p | B | Mig2p | A |
| 5 | Ada2p | B | Imp2'p | B |
| 6 | Hpc2p | B | Gsm1p | B |
| 7 | Gal80p | B | Hpc2p | B |
| 8 | Hmlalpha2p | B | Gal80p | A |
| 9 | Hmlalpha1p | B | Rpn10p | B |
| 10 | Swi1p | B | Rtg2 | B |
| 11 | Gsm1p | B | Haa1p | B |
| 12 | Swi3p | B | Mal13p | A |
| 13 | Mal13p | B | Rgt1p | B |
| 14 | Mig3p | A | Hmlalpha2p | A |
| 15 | Hmra1p | B | Swi3p | A |
| 16 | | | Mig1p | A |
| 17 | | | Gat4p | B |
| 18 | | | Swi1p | B |
| 19 | | | Kar4p | B |
| 20 | | | Ada2p | B |
| 21 | | | Mga2p | A |
| 22 | | | Met32p | A |

### 3.2.3. Key TFs Responsive to Oxygen Availability Under Carbon Limitation Regime

Key TFs responsive to oxygen availability under carbon limitation regime (25 g $L^{-1}$ glucose) were identified using the triplicate transcriptome data of Tai *et al.* (Tai *et al.*, 2005).

When the nodes of the yeast TRN which were not quantified in these transcriptome data were eliminated, the number of the nodes, regulatory interactions and TFs reduced to 5252, 37119 and 185, respectively. By using reporter features algorithm, 46 key TFs around which most transcriptional changes occur were identified as a response to oxygen availability under carbon limitation regime (Table 3.29). Key TFs were ranked from high to low $Z_{\text{corrected,TF}}$ score. $Z_{\text{corrected,TF}}$ scores, *p*-values and degrees for each key TF are represented in Table C.9.

Hap2p/3p/4p/5p complex was among the identified key TFs. The identification of Hap1p as a key TF responsible in cellular respiration is a meaningful result, since Hap1p was shown to be associated with the regulation of aerobiosis and is solely connected to the presence of oxygen. In addition, Hap4p, the regulatory subunit of the complex, has a role in both aerobic regulation and glucose derepression (Knijnenburg *et al.*, 2007).

Sut1p and Upc2p were also among the identified key TFs. These TFs have been shown to regulate anaerobically expressed genes in *S. cerevisiae* (Kwast *et al.*, 2002).

The algorithm also identified Rox1p and Cin5p as key TFs in response to oxygen availability (Clim). Rox1p, a heme-dependent transcriptional repressor of hypoxic genes, constitutes a multi-component TF loop together with Yap6p and Cin5p and these three TFs regulate each other (Knijnenburg *et al.*, 2007). Mot3p, involved in repression of a subset of hypoxic genes by Rox1p, repression of several DAN/TIR genes during aerobic growth, and repression of ergosterol biosynthetic genes, was also identified as a key TF.

Ume6p and Sin3p were found to be key TFs with very close scores. In fact, they are part of a complex formed by Ume6p, Sin3p and Rpd3p which regulates transcription of the phospholipid biosynthetic genes (Elkhaimi *et al.*, 2000).

There are twelve key TFs identified in both *ΔSNF1* and in response to oxygen availability under carbon limitation regime, but not in *ΔMIG1* (Cat8p, Cst6p, Elp6p, Gis1p, Hot1p, Oaf1p, Opi1p, Rtg2p, Sin3p, Sps18p, Xbp1p and Yrm1p) (Figure 3.21).

Cat8p and Adr1p were among the identified key TFs. In the study of Young *et al.* it was reported that Adr1p and Cat8p are active after diauxic transition in the glucose depletion, and when the energy generating metabolism has shifted to aerobic oxidation of non-fermentable carbon sources, which agrees well with the results of the present study (Young *et al.*, 2003).

Oaf1p and Cst6p were also among the identified key TFs in response to oxygen availability (Clim). Oaf1p is an oleate-activated TF, which activates genes involved in β-oxidation of fatty acids, peroxisome organization and biogenesis (Usaite *et al.*, 2009). Cst6p, which is also involved in the regulation of oleate responsive genes and in utilization of nonoptimal carbon sources, was also identified as a key TF.

Pip2p was also identified as a key TF. The promoters of genes encoding peroxisomal proteins and the enzymes of β-oxidation bind both Adr1 and the heterodimeric, oleate-responsive transcription factors Oaf1p and Pip2p (Ratnakumar *et al.*, 2009).

The algorithm identified Opi1p as a key TF. Wagner *et al.* have demonstrated that Opi1p interacts with Sin3p affecting a large number of regulatory systems in yeast and higher eukaryotes (Wagner *et al.*, 2001). Zhang *et al.* have suggested that Snf1p activates Opi1p, which represses phospholipid biosynthesis (Sreenivas and Carman, 2003; Zhang *et al.*, 2010). Gis1p, which is reported to be involved in phospholipid metabolic process and in expression of genes during nutrient limitation, was also identified as a key TF.

Rtg2p, which regulates the subcellular localization of Rtg1p and Rtg3p transcriptional activators of retrograde (RTG) and TOR pathways, and Elp6p, which is involved in protein urmylation, were identified as key TFs. Loss of urmylation pathway was reported to cause invasive growth and confers sensitivity to rapamycin due to genetic interactions with TOR pathway (Goehring et al., 2003). Elp6p may play a role in a pathway related to alternative carbon sources, since Δ*ELP6* strains were shown to be slow to adapt to a change in carbon source from glucose to galactose (Krogan and Greenblatt, 2001).

Xbp1p and Hot1p, TFs that are involved in stress response were also identified as key TFs. The algorithm has also identified Sin3p, which is involved in chromatin remodeling, as a key TF.

Although not identified in *ΔSNF1* as a key TF, Sip4p, activating the carbon source-responsive element (CSRE) of gluconeogenic genes, involved in the positive regulation of gluconeogenesis and regulated by Snf1p protein kinase, was identified as a key TF in response to oxygen availability.

There are six key TFs identified in both *ΔMIG1* and in response to oxygen availability under carbon limitation regime, but not in *ΔSNF1* (Mig1p, Nrg2p, Rdr1p, Rds2p, Stp3p and YPR015c) (Figure 3.21).

Mig1p, Nrg1p and Nrg2p were among the identified key TFs in response to oxygen availability (Clim). It was suggested that Nrg1p and Nrg2p are direct or indirect targets of the Snf1p kinase and function in glucose repression of a subset of Snf1p-regulated genes (Vyas *et al.*, 2001). Nrg1p was identified as a third repressor required for glucose repression in addition to Mig1p and Mig2p (Zhou and Winston, 2001).

Rds2p, involved in the use of nonfermentable carbon sources, and Rdr1p, controlling multidrug resistance, were also identified as key TFs.

Although not identified in *ΔMIG1* as a key TF, Sko1p, which forms a complex with Tup1p and Ssn6p to both activate and repress transcription and which is involved in oxidative stress responses, was identified as a key TF in response to oxygen availability. Active Mig1p interacts with the co-repressors Ssn6p and Tup1p and binds to the promoters of various genes, including genes encoding enzymes of the tricarboxylic acid (TCA) cycle, electron transport chain, alternative carbon sources consumption, gluconeogenesis, and represses the transcription of those genes (Sanz *et al.*, 2000).

There are seven key TFs identified in *ΔSNF1*, *ΔMIG1* and in response to oxygen availability under carbon limitation regime (Aca1p, Ada2p, Bye1, Gsm1p, Sut1p, Swi1p and Swi3p) (Figure 3.21).

The algorithm identified Gsm1p as a key TF, which is implicated in the use of nonfermentable carbon sources and target gluconeogenic genes. Gluconeogenesis (generation of glucose from non-carbohydrate carbon substrates) is essential for the growth of yeast cells on nonfermentable carbon sources (Turcotte *et al.*, 2009). Moreover, Aca1p, involved in utilization of nonoptimal carbon sources, was also among the key TFs identified as a response to oxygen availability under carbon limitation regime (Garcia-Gimeno and Struhl, 2000).

Key TFs Ada2p, Swi1p and Swi3p are involved in chromatin remodeling, and Sut1p is involved in stress response.

The algorithm identified key TFs that are involved in cellular carbohydrate metabolic process (i.e., Adr1p, Hap2p/3p/4p/5p), phospholipid metabolic process (i.e., Gis1p, Opi1p), fatty acid metabolic process (i.e., Oaf1p, Pip2p), oxidative phosphorylation (i.e., Gsm1p), aerobic respiration (i.e., Hap1p) and response to stress (i.e., Xbp1p). Hap2p, Hap3p, Hap4p and Hap5p were counted as one TF because they form a complex. These findings are totally consistent with the study of Kwast *et al.* which showed that half of the anaerobically induced genes fit into four functional categories: cell wall related; lipid, fatty acid, and isoprenoid metabolism; carbohydrate metabolism; and cell stress.

To sum up, as a response to oxygen availability under carbon limitation regime key TFs known to be involved in regulation of aerobiosis/anaerobiosis were identified. In addition, TFs that are involved in glucose repression and derepression and TFs known to be positively regulated by Snf1p kinase (Cat8p, Adr1p and Opi1p) were identified as key TFs. In fact, Snf1p kinase is involved in the switch from fermentative/anaerobic to oxidative metabolism (Sutherland *et al.*, 2003). These results seem to contradict the results of Linde *et al.*, who found that the majority of genes involved in respiratory sugar metabolism (e.g., those encoding enzymes of the tricarboxylic acid cycle or proteins involved in respiration) show little or no repression under anaerobic conditions in glucose-limited chemostat (Linde *et al.*, 1999). On the other hand; even a direct comparison may not be valid, these results confirm the study of Kwast *et al.*, who showed that the effect of oxygen availability (in growth on galactose) on respiratory and TCA cycle genes is exerted at the transcriptional level (Kwast *et al.*, 2002).

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 1 | Elp6p<br>(YMR312w) | 7 | Subunit of Elongator complex, which is required for modification of wobble nucleosides in tRNA; required for Elongator structural integrity<br>• protein urmylation<br>• regulation of transcription from RNA polymerase II promoter<br>• tRNA wobble uridine modification |
| 2 | Ada2p<br>(YDR448w) | 8 | Transcription coactivator, component of the ADA and SAGA transcriptional adaptor/HAT (histone acetyltransferase) complexes<br>• chromatin modification<br>• chromatin silencing at rDNA<br>• chromatin silencing at telomere<br>• positive regulation of histone acetylation<br>• regulation of transcription from RNA polymerase II promoter |
| 3 | Swi1p<br>(YPL016w) | 13 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2; can form the prion [SWI+]<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent<br>• regulation of transcription from RNA polymerase II promoter |
| 4 | Swi3p<br>(YJL176c) | 8 | Subunit of the SWI/SNF chromatin remodeling complex, which regulates transcription by remodeling chromosomes; required for transcription of many genes, including ADH1, ADH2, GAL1, HO, INO1 and SUC2<br>• ATP-dependent chromatin remodeling<br>• positive regulation of transcription, DNA-dependent |
| 5 | Cat8p<br>(YMR280c) | 126 | Zinc cluster transcriptional activator necessary for derepression of a variety of genes under non-fermentative growth conditions, active after diauxic shift, binds carbon source responsive elements<br>• positive regulation of gluconeogenesis<br>• positive regulation of transcription from RNA polymerase II promoter |
| 6 | Pip2p<br>(YOR363c) | 131 | Autoregulatory oleate-specific transcriptional activator of peroxisome proliferation, contains Zn(2)-Cys(6) cluster domain, forms heterodimer with Oaf1p, binds oleate response elements (OREs), activates beta-oxidation genes<br>• fatty acid metabolic process<br>• peroxisome organization<br>• positive regulation of transcription |
| 7 | Aca1p<br>(YER045c) | 26 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, may regulate transcription of genes involved in utilization of non-optimal carbon sources<br>• transcription initiation from RNA polymerase II promoter |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF<br>(ORF Name) | degree<br>(*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 8 | Sut1p<br>(YGL162w) | 77 | Transcription factor of the Zn[II]2Cys6 family involved in sterol uptake; involved in induction of hypoxic gene expression<br>• regulation of transcription<br>• regulation of transcription from RNA polymerase II promoter<br>• sterol transport |
| 9 | Xbp1p<br>(YIL101c) | 168 | Transcriptional repressor that binds to promoter sequences of the cyclin genes, CYS3, and SMF2; expression is induced by stress or starvation during mitosis, and late in meiosis; member of the Swi4p/Mbp1p family; potential Cdc28p substrate<br>• response to stress |
| 10 | Stp3p<br>(YLR375w) | 28 | Zinc-finger protein of unknown function, possibly involved in pre-tRNA splicing and in uptake of branched-chain amino acids<br>• biological process unknown |
| 11 | Gis1p<br>(YDR096w) | 173 | JmjC domain-containing histone demethylase; transcription factor involved in expression of genes during nutrient limitation and in negative regulation of DPP1 and PHR1; activity is modulated by limited proteasome-mediated proteolysis<br>• ascospore wall assembly<br>• histone demethylation<br>• phospholipid metabolic process |
| 12 | Nrg2p<br>(YBR066c) | 156 | Transcriptional repressor that mediates glucose repression and negatively regulates filamentous growth; has similarity to Nrg1p<br>• biofilm formation<br>• invasive growth in response to glucose limitation<br>• pseudohyphal growth |
| 13 | Oaf1p<br>(YAL051w) | 237 | Oleate-activated transcription factor, acts alone and as a heterodimer with Pip2p; activates genes involved in beta-oxidation of fatty acids and peroxisome organization and biogenesis<br>fatty acid metabolic process<br>• negative regulation of transcription<br>• peroxisome organization<br>• positive regulation of transcription |
| 14 | Rds2p<br>(YPL133c) | 42 | Zinc cluster transcriptional activator involved in conferring resistance to ketoconazole<br>• positive regulation of gluconeogenesis<br>• response to xenobiotic stimulus |
| 15 | Cst6p<br>(YIL036w) | 177 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, proposed to be a regulator of oleate responsive genes; involved in utilization of non-optimal carbon sources and chromosome stability<br>• cellular response to oleic acid<br>• DNA metabolic process<br>• transcription initiation from RNA polymerase II promoter |
| 16 | Sps18p<br>(YNL204c) | 58 | Protein of unknown function, contains a putative zinc-binding domain; expressed during sporulation<br>• sporulation resulting in formation of a cellular spore |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF (ORF Name) | degree ($k$) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 17 | Hot1p<br>(YMR172w) | 71 | Transcription factor required for the transient induction of glycerol biosynthetic genes GPD1 and GPP2 in response to high osmolarity; targets Hog1p to osmostress responsive promoters; has similarity to Msn1p and Gcr1p<br>• hyperosmotic response<br>• regulation of transcription from RNA polymerase II promoter |
| 18 | Rtg2p<br>(YGL252c9 | 9 | Sensor of mitochondrial dysfunction; regulates the subcellular location of Rtg1p and Rtg3p, transcriptional activators of the retrograde (RTG) and TOR pathways; Rtg2p is inhibited by the phosphorylated form of Mks1p<br>• extrachromosomal rDNA circle accumulation involved in replicative cell aging<br>• intracellular signaling pathway<br>• mitochondria-nucleus signaling pathway |
| 19 | Gsm1p<br>(YJL103c) | 23 | Putative zinc cluster protein of unknown function; proposed to be involved in the regulation of energy metabolism, based on patterns of expression and sequence analysis<br>• oxidative phosphorylation |
| 20 | Hap1p<br>(YLR256w9 | 176 | Zinc finger transcription factor involved in the complex regulation of gene expression in response to levels of heme and oxygen; the S288C sequence differs from other strain backgrounds due to a Ty1 insertion in the carboxy terminus<br>• aerobic respiration<br>• positive regulation of transcription from RNA polymerase II promoter |
| 21 | Mot3p<br>(YMR070w) | 131 | Nuclear transcription factor with two Cys2-His2 zinc fingers; involved in repression of a subset of hypoxic genes by Rox1p, repression of several DAN/TIR genes during aerobic growth, and repression of ergosterol biosynthetic genes<br>• negative regulation of transcription from RNA polymerase II promoter<br>• transcription |
| 22 | Opi1p<br>(YHL020c) | 30 | Transcriptional regulator of a variety of genes; phosphorylation by protein kinase A stimulates Opi1p function in negative regulation of phospholipid biosynthetic genes; involved in telomere maintenance<br>• endoplasmic reticulum unfolded protein response<br>• negative regulation of transcription from RNA polymerase II promoter<br>• phospholipid biosynthetic process<br>• positive regulation of transcription from RNA polymerase II promoter |
| 23 | Hap4p<br>(YKL109w) | 392 | Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; provides the principal activation function of the complex<br>• regulation of carbohydrate metabolic process<br>• transcription |
| 24 | Bye1p<br>(YKL005c) | 23 | Negative regulator of transcription elongation, contains a TFIIS-like domain and a PHD finger, multicopy suppressor of temperature-sensitive ess1 mutations, probably binds RNA polymerase II large subunit<br>• negative regulation of transcription from RNA polymerase II promoter |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 25 | Cdc14p<br>(YFR028c) | 60 | Protein phosphatase required for mitotic exit; located in the nucleolus until liberated by the FEAR and Mitotic Exit Network in anaphase, enabling it to act on key substrates to effect a decrease in CDK/B-cyclin activity and mitotic exit<br>• mitotic cell cycle<br>• nucleolus organization<br>• protein amino acid dephosphorylation<br>• regulation of exit from mitosis |
| 26 | Nrg1p<br>(YDR043c) | 353 | Transcriptional repressor that recruits the Cyc8p-Tup1p complex to promoters; mediates glucose repression and negatively regulates a variety of processes including filamentous growth and alkaline pH response<br>• biofilm formation<br>• glucose metabolic process<br>• invasive growth in response to glucose limitation<br>• pseudohyphal growth<br>• regulation of transcription from RNA polymerase II promoter<br>• response to pH |
| 27 | Hmra2p<br>(YCR096c) | 25 | Silenced copy of a2 at HMR; similarity to Alpha2p; required along with a1p for inhibiting expression of the HO endonuclease in a/alpha HO/HO diploid cells with an active mating-type interconversion system<br>• biological process unknown |
| 28 | Adr1p<br>(YDR216w) | 421 | Carbon source-responsive zinc-finger transcription factor, required for transcription of the glucose-repressed gene ADH2, of peroxisomal protein genes, and of genes required for ethanol, glycerol, and fatty acid utilization<br>• negative regulation of transcription from RNA polymerase II promoter by glucose<br>• peroxisome organization<br>• regulation of carbohydrate metabolic process<br>• transcription |
| 29 | YPR015c<br>(YPR015c) | 55 | Putative protein of unknown function; overexpression causes a cell cycle delay or arrest<br>• Putative protein of unknown function; overexpression causes a cell cycle delay or arrest<br>• biological process unknown |
| 30 | Upc2p<br>(YDR213w) | 194 | Sterol regulatory element binding protein, induces transcription of sterol biosynthetic genes and of DAN/TIR gene products; Ecm22p homolog; relocates from intracellular membranes to perinuclear foci on sterol depletion<br>• steroid metabolic process<br>• sterol biosynthetic process |
| 31 | Rme1p<br>(YGR044c) | 204 | Zinc finger protein involved in control of meiosis; prevents meiosis by repressing IME1 expression and promotes mitosis by activating CLN2 expression; directly repressed by a1-alpha2 regulator; mediates cell type control of sporulation<br>• meiosis<br>• negative regulation of transcription from RNA polymerase II promoter |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 32 | Hap5p<br>(YOR358w) | 182 | Subunit of the heme-activated, glucose-repressed Hap2/3/4/5 CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; required for assembly and DNA binding activity of the complex<br>• regulation of carbohydrate metabolic process<br>• transcription |
| 33 | Sin3p<br>(YOL004w) | 27 | Component of the Sin3p-Rpd3p histone deacetylase complex, involved in transcriptional repression and activation of diverse processes, including mating-type switching and meiosis; involved in the maintenance of chromosomal integrity<br>• chromatin silencing at rDNA<br>• chromatin silencing at silent mating-type cassette<br>• chromatin silencing at telomere<br>• double-strand break repair via nonhomologous end joining<br>• histone deacetylation<br>• negative regulation of transcription from RNA polymerase II promoter<br>• negative regulation of transposition, RNA-mediated<br>• positive regulation of gene-specific transcription from RNA polymerase II promoter<br>• positive regulation of transcription from RNA polymerase II promoter |
| 34 | Ume6p<br>(YDR207c) | 227 | Key transcriptional regulator of early meiotic genes, binds URS1 upstream regulatory sequence, couples metabolic responses to nutritional cues with initiation and progression of meiosis, forms complex with Ime1p, and also with Sin3p-Rpd3p<br>• ascospore formation<br>• chromosome organization<br>• histone deacetylation<br>• negative regulation of transcription, mitotic<br>• positive regulation of gene-specific transcription from RNA polymerase II promoter<br>• positive regulation of meiosis<br>• reciprocal meiotic recombination |
| 35 | Sip4p<br>(YJL089w) | 104 | C6 zinc cluster transcriptional activator that binds to the carbon source-responsive element (CSRE) of gluconeogenic genes; involved in the positive regulation of gluconeogenesis; regulated by Snf1p protein kinase; localized to the nucleus<br>• invasive growth in response to glucose limitation<br>• positive regulation of gluconeogenesis<br>• regulation of transcription from RNA polymerase II promoter |
| 36 | Hap3p<br>(YBL021c) | 168 | Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences contributing to both complex assembly and DNA binding<br>• regulation of carbohydrate metabolic process<br>• transcription |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF (ORF Name) | degree (*k*) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 37 | Mig1p<br>(YGL035c) | 216 | Transcription factor involved in glucose repression; sequence specific DNA binding protein containing two Cys2His2 zinc finger motifs; regulated by the SNF1 kinase and the GLC7 phosphatase<br>• negative regulation of transcription from RNA polymerase II promoter by glucose |
| 38 | Rox1p<br>(YPR065w) | 339 | Heme-dependent repressor of hypoxic genes; contains an HMG domain that is responsible for DNA bending activity<br>• negative regulation of gene-specific transcription from RNA polymerase II promoter |
| 39 | Rdr1p<br>(YOR380w) | 9 | Transcriptional repressor involved in the control of multidrug resistance; negatively regulates expression of the PDR5 gene; member of the Gal4p family of zinc cluster proteins<br>• response to xenobiotic stimulus |
| 40 | Hms1p<br>(YOR032c) | 205 | Basic helix-loop-helix (bHLH) protein with similarity to myc-family transcription factors; overexpression confers hyperfilamentous growth and suppresses the pseudohyphal filamentation defect of a diploid mep1 mep2 homozygous null mutant<br>• pseudohyphal growth |
| 41 | Cin5p<br>(YOR028c) | 395 | Basic leucine zipper (bZIP) transcription factor of the yAP-1 family, mediates pleiotropic drug resistance and salt tolerance; nuclearly localized under oxidative stress and sequestered in the cytoplasm by Lot6p under reducing conditions<br>• regulation of transcription from RNA polymerase II promoter<br>• response to drug<br>• response to salt stress |
| 42 | Hap2p<br>(YGL237c) | 175 | Subunit of the heme-activated, glucose-repressed Hap2p/3p/4p/5p CCAAT-binding complex, a transcriptional activator and global regulator of respiratory gene expression; contains sequences sufficient for both complex assembly and DNA binding<br>• regulation of carbohydrate metabolic process<br>• transcription |
| 43 | Mac1p<br>(YMR021c) | 92 | Copper-sensing transcription factor involved in regulation of genes required for high affinity copper transport<br>• cellular cadmium ion homeostasis<br>• positive regulation of transcription from RNA polymerase II promoter<br>• regulation of protein catabolic process |
| 44 | Stp2p<br>(YHR006w9 | 293 | Transcription factor, activated by proteolytic processing in response to signals from the SPS sensor system for external amino acids; activates transcription of amino acid permease genes<br>• positive regulation of transcription from RNA polymerase II promoter |
| 45 | Sko1p<br>(YNL167c) | 309 | Basic leucine zipper (bZIP) transcription factor of the ATF/CREB family, forms a complex with Tup1p and Ssn6p to both activate and repress transcription; cytosolic and nuclear protein involved in osmotic and oxidative stress responses<br>• negative regulation of transcription from RNA polymerase II promoter |

Table 3.29. Key TFs identified responsive to oxygen availability under carbon limitation regime (continued)

| Rank | TF (ORF Name) | degree ($k$) | SGD Definition & GO Biological Process Terms |
|---|---|---|---|
| 46 | Yrm1p<br>(YOR172w) | 23 | Zn2-Cys6 zinc-finger transcription factor that activates genes involved in multidrug resistance; paralog of Yrr1p, acting on an overlapping set of target genes<br>• drug transmembrane transport<br>• positive regulation of transcription from RNA polymerase II promoter |

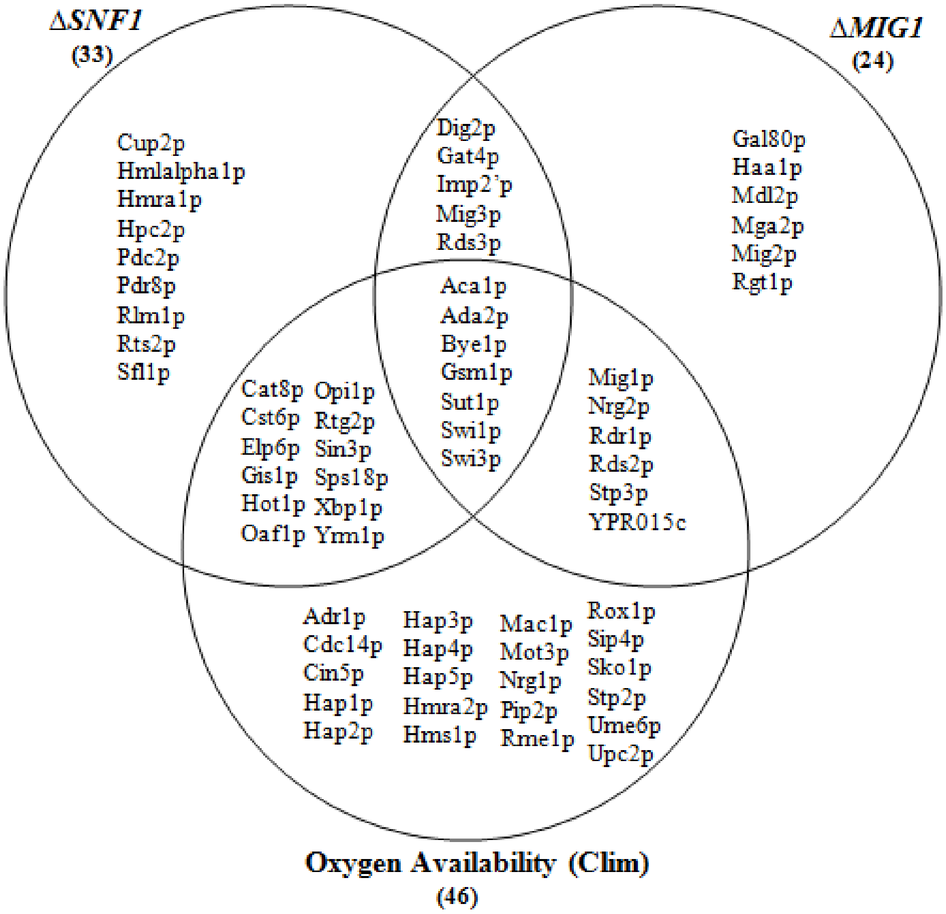

Figure 3.21. Comparison of the key TFs identified for *ΔSNF1*, *ΔMIG1* and as a response to oxygen availability under carbon limitation regime (the number of key TFs for each specific mutant is given in brackets)

Significant shared GO biological process terms ($p$-value<0.01) of 46 key TFs identified as a response to oxygen availability under carbon limitation regime were further identified (Table D.12). These key TFs were found to be enriched significantly with very general GO biological process terms, such as "regulation of cellular biosynthetic process"

($p$-value=9.49x$10^{-18}$), as well as with a more specific GO biological process term, such as "positive regulation of gluconeogenesis" ($p$-value=0.00054), "positive regulation of cellular carbohydrate metabolic process" ($p$-value=0.00299) and "positive regulation of glucose metabolic process" ($p$-value=0.00299). GO term with the lowest $p$-value was found to be "transcription" ($p$-value=2.33x$10^{-23}$), as expected.

### 3.2.3.1. Perturbation-Responsive Subnetwork Responsive to Oxygen Availability (Clim).

Perturbation responsive subnetworks (PRS) were constructed between the key TFs and their differentially expressed target genes ($p$-value<0.05) responsive to the same perturbation. The numbers of key TFs, their target genes and interactions in the perturbation-responsive subnetwork responsive to oxygen availability under carbon limitation regime are given in Table 3.30. The overview of this subnetwork produced in Cytoscape is displayed in Figure 3.22, where the up- (green) or down-regulation (red) of the key TFs and their differentially expressed target genes in aerobic condition with respect to anaerobic condition are indicated. Key TFs indicated in black in this figure were found to be not significantly expressed in this study. Therefore they are considered to be post-transcriptionally regulated (Table 3.33). GO biological process terms significantly associated with the target genes in the PRS ($p$-value<0.01) were identified and represented in Table 3.31.

Table 3.30. The numbers of TFs, their target genes and interactions for the PRS responsive to oxygen availability (Clim)

| Number of Key TFs | Number of Target Genes | Number of Interactions |
|---|---|---|
| 46 | 873 | 2800 |

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim)

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| small molecule metabolic process | 201 out of 873 genes, 23.0 per cent | 2.54E-21 |
| monocarboxylic acid metabolic process | 62 out of 873 genes, 7.1 per cent | 2.63E-19 |
| carboxylic acid metabolic process | 107 out of 873 genes, 12.3 per cent | 1.01E-18 |
| oxoacid metabolic process | 107 out of 873 genes, 12.3 per cent | 1.01E-18 |
| organic acid metabolic process | 107 out of 873 genes, 12.3 per cent | 1.3E-18 |
| cellular ketone metabolic process | 108 out of 873 genes, 12.4 per cent | 1.17E-17 |
| generation of precursor metabolites and energy | 67 out of 873 genes, 7.7 per cent | 1.57E-14 |
| cofactor metabolic process | 61 out of 873 genes, 7.0 per cent | 3.84E-12 |
| energy derivation by oxidation of organic compounds | 54 out of 873 genes, 6.2 per cent | 6.79E-12 |

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim) (continued)

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| oxidative phosphorylation | 27 out of 873 genes, 3.1 per cent | 6.65E-11 |
| small molecule biosynthetic process | 87 out of 873 genes, 10.0 per cent | 1.06E-09 |
| cellular respiration | 39 out of 873 genes, 4.5 per cent | 4.35E-09 |
| small molecule catabolic process | 49 out of 873 genes, 5.6 per cent | 4.78E-09 |
| organic acid catabolic process | 27 out of 873 genes, 3.1 per cent | 6.67E-09 |
| carboxylic acid catabolic process | 27 out of 873 genes, 3.1 per cent | 6.67E-09 |
| electron transport chain | 19 out of 873 genes, 2.2 per cent | 9.3E-09 |
| respiratory electron transport chain | 19 out of 873 genes, 2.2 per cent | 9.3E-09 |
| ATP synthesis coupled electron transport | 19 out of 873 genes, 2.2 per cent | 9.3E-09 |
| mitochondrial ATP synthesis coupled electron transport | 19 out of 873 genes, 2.2 per cent | 9.3E-09 |
| oxidation reduction | 19 out of 873 genes, 2.2 per cent | 9.3E-09 |
| coenzyme metabolic process | 45 out of 873 genes, 5.2 per cent | 4.57E-08 |
| fatty acid metabolic process | 24 out of 873 genes, 2.7 per cent | 0.000000169 |
| nucleoside phosphate metabolic process | 45 out of 873 genes, 5.2 per cent | 0.000000243 |
| nucleotide metabolic process | 45 out of 873 genes, 5.2 per cent | 0.000000243 |
| cellular nitrogen compound biosynthetic process | 66 out of 873 genes, 7.6 per cent | 0.000000659 |
| fatty acid oxidation | 10 out of 873 genes, 1.1 per cent | 0.000000766 |
| lipid oxidation | 10 out of 873 genes, 1.1 per cent | 0.000000766 |
| fatty acid catabolic process | 10 out of 873 genes, 1.1 per cent | 0.000000766 |
| alcohol metabolic process | 60 out of 873 genes, 6.9 per cent | 0.00000112 |
| nicotinamide nucleotide metabolic process | 22 out of 873 genes, 2.5 per cent | 0.00000173 |
| nucleobase, nucleoside and nucleotide metabolic process | 50 out of 873 genes, 5.7 per cent | 0.00000262 |
| transmembrane transport | 48 out of 873 genes, 5.5 per cent | 0.00000548 |
| fatty acid beta-oxidation | 9 out of 873 genes, 1.0 per cent | 0.00000634 |
| pyridine nucleotide metabolic process | 22 out of 873 genes, 2.5 per cent | 0.00000802 |
| lipid metabolic process | 64 out of 873 genes, 7.3 per cent | 0.0000107 |
| ion transport | 39 out of 873 genes, 4.5 per cent | 0.0000128 |
| cofactor catabolic process | 13 out of 873 genes, 1.5 per cent | 0.00011 |
| organic acid transport | 24 out of 873 genes, 2.7 per cent | 0.00013 |
| aerobic respiration | 28 out of 873 genes, 3.2 per cent | 0.00014 |
| organic acid biosynthetic process | 41 out of 873 genes, 4.7 per cent | 0.00015 |
| carboxylic acid biosynthetic process | 41 out of 873 genes, 4.7 per cent | 0.00015 |
| NADH metabolic process | 10 out of 873 genes, 1.1 per cent | 0.00015 |
| acetyl-CoA metabolic process | 14 out of 873 genes, 1.6 per cent | 0.00019 |
| ion transmembrane transport | 16 out of 873 genes, 1.8 per cent | 0.00021 |
| purine ribonucleotide biosynthetic process | 16 out of 873 genes, 1.8 per cent | 0.00021 |
| acetyl-CoA catabolic process | 11 out of 873 genes, 1.3 per cent | 0.00023 |
| tricarboxylic acid cycle | 11 out of 873 genes, 1.3 per cent | 0.00023 |
| ribonucleotide biosynthetic process | 17 out of 873 genes, 1.9 per cent | 0.00025 |
| carboxylic acid transport | 23 out of 873 genes, 2.6 per cent | 0.00043 |
| oxidoreduction coenzyme metabolic process | 23 out of 873 genes, 2.6 per cent | 0.00043 |
| catabolic process | 117 out of 873 genes, 13.4 per cent | 0.00051 |
| coenzyme catabolic process | 12 out of 873 genes, 1.4 per cent | 0.00055 |
| glutamate metabolic process | 11 out of 873 genes, 1.3 per cent | 0.00057 |
| heterocycle metabolic process | 48 out of 873 genes, 5.5 per cent | 0.00074 |
| lipid modification | 14 out of 873 genes, 1.6 per cent | 0.00123 |
| cation transport | 30 out of 873 genes, 3.4 per cent | 0.00127 |

Table 3.31. Significantly associated GO biological process terms of the target genes of the PRS responsive to oxygen availability (Clim) (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| NAD metabolic process | 13 out of 873 genes, 1.5 per cent | 0.00169 |
| NADH oxidation | 8 out of 873 genes, 0.9 per cent | 0.00188 |
| nucleotide biosynthetic process | 23 out of 873 genes, 2.6 per cent | 0.00376 |
| cellular lipid metabolic process | 50 out of 873 genes, 5.7 per cent | 0.0048 |
| purine nucleotide biosynthetic process | 16 out of 873 genes, 1.8 per cent | 0.00564 |
| amine metabolic process | 57 out of 873 genes, 6.5 per cent | 0.00694 |
| amine catabolic process | 17 out of 873 genes, 1.9 per cent | 0.00758 |
| nucleobase, nucleoside and nucleotide biosynthetic process | 26 out of 873 genes, 3.0 per cent | 0.0087 |
| nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process | 26 out of 873 genes, 3.0 per cent | 0.0087 |

As expected, “cellular respiration” and “aerobic respiration” are among the significantly associated GO terms of the PRS responsive to oxygen availability. In addition, the terms “respiratory electron transport chain” and “tricarboxylic acid cycle” are clearly related to the respiration. The appearance of the terms “fatty acid metabolic process” and “lipid metabolic process” is consistent with the study of Kwast *et al.*, which revealed that half of the anaerobically induced genes fit into four functional categories: cell wall related; lipid, fatty acid, and isoprenoid metabolism; carbohydrate metabolism; and cell stress (Kwast *et al.*, 2002).

3.2.3.2. Regulation of Key Transcription Factors Responsive to Oxygen Availability (Clim). Identification of key TFs demonstrates the change in TF activity when passing from one condition to another, without *a priori* requirement of change in the transcription level of the TFs, because many TFs do not respond at transcriptional level per se, but through post-translational regulation. Regulation of key TFs was evaluated based whether the key TFs are significantly differentially expressed. Half of the key TFs responsive to oxygen availability (Clim) were found to be regulated mainly transcriptionally (Table 3.32). In Table 3.33, regulation of each key TF is represented.

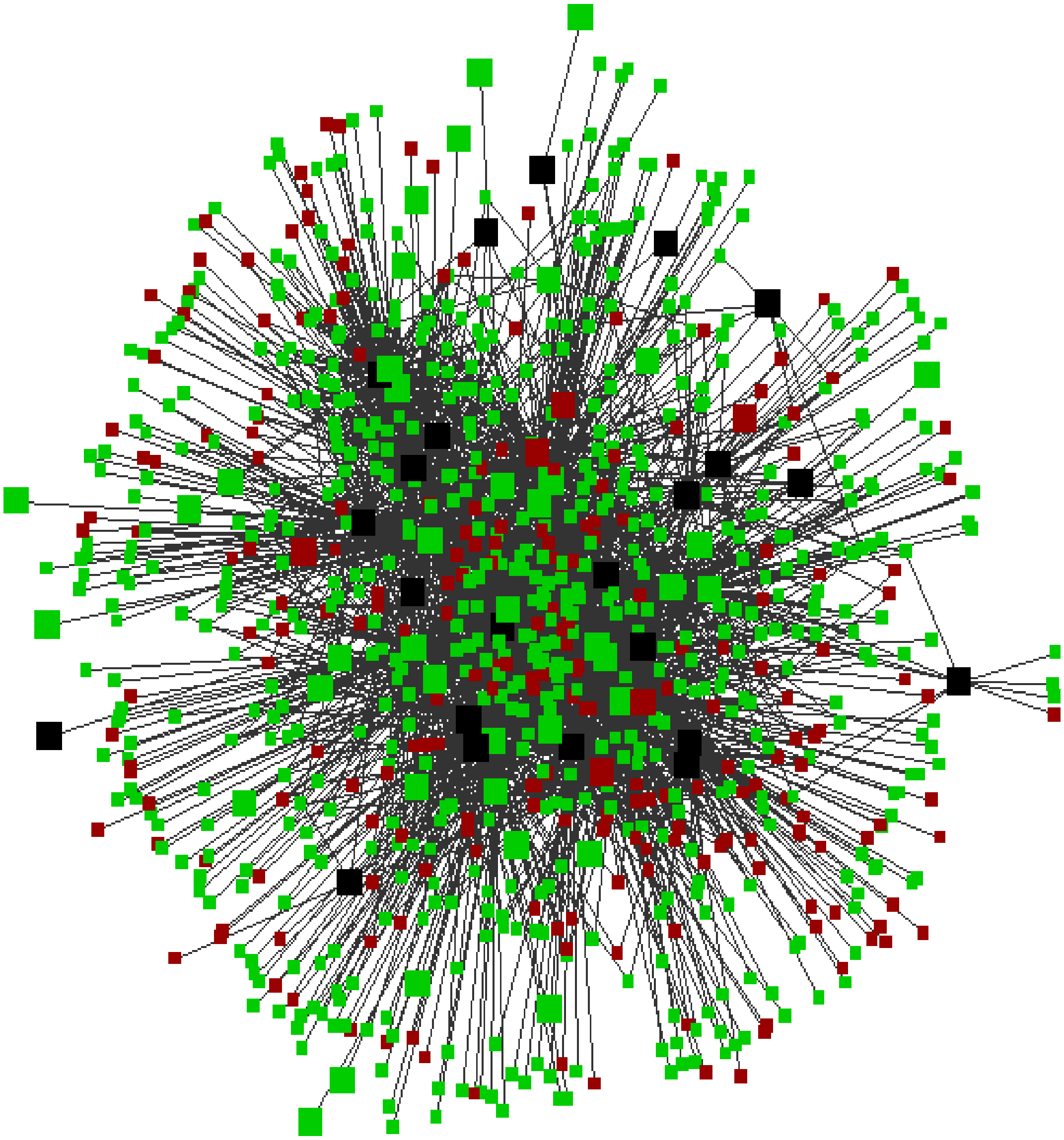

Figure 3.22. Representation of the PRS responsive to oxygen availability (Clim) (big and small squares represent TFs and non-TF target genes, respectively)

Table 3.32. Number of key TFs responsive to oxygen availability (Clim) that were found to be mainly transcriptionally regulated (A) or mainly post-transcriptionally regulated (B)

| **Mutant** | **Number of A** | **Number of B** |
|---|---|---|
| AER vs. ANA (Clim) | 23 | 23 |

Table 3.33. Regulation of key TFs responsive to oxygen availability (Clim)

| rank | AER vs. ANA (Clim) | Case | rank | AER vs. ANA (Clim) | Case | rank | AER vs. ANA (Clim) | Case |
|---|---|---|---|---|---|---|---|---|
| 1 | Elp6p | A | 17 | Hot1p | B | 33 | Sin3p | B |
| 2 | Ada2p | B | 18 | Rtg2p | B | 34 | Ume6p | A |
| 3 | Swi1p | B | 19 | Gsm1p | A | 35 | Sip4p | A |
| 4 | Swi3p | A | 20 | Hap1p | B | 36 | Hap3p | A |
| 5 | Cat8p | A | 21 | Mot3p | A | 37 | Mig1p | A |
| 6 | Pip2p | A | 22 | Opi1p | A | 38 | Rox1p | A |
| 7 | Aca1p | A | 23 | Hap4p | B | 39 | Rdr1p | B |
| 8 | Sut1p | A | 24 | Bye1p | B | 40 | Hms1p | A |
| 9 | Xbp1p | A | 25 | Cdc14p | B | 41 | Cin5p | A |
| 10 | Stp3p | B | 26 | Nrg1p | A | 42 | Hap2p | B |
| 11 | Gis1p | B | 27 | Hmra2p | B | 43 | Mac1p | B |
| 12 | Nrg2p | A | 28 | Adr1p | A | 44 | Stp2p | A |
| 13 | Oaf1p | A | 29 | YPR015c | B | 45 | Sko1p | B |
| 14 | Rds2p | B | 30 | Upc2p | B | 46 | Yrm1p | B |
| 15 | Cst6p | B | 31 | Rme1p | B | | | |
| 16 | Sps18p | B | 32 | Hap5p | A | | | |

# 4. CONCLUSIONS and RECOMMENDATIONS

## 4.1. Conclusions

It is concluded that key TFs (TFs around which a considerable collective change in the expression of the genes occur in response to environmental and genetic perturbations) can be identified using reporter features algorithm developed by Oliveira *et al.* (Oliveira *et al.*, 2008). A genome-scale TRN in *S. cerevisiae* which contains 198 TFs, 6158 non-TF target genes and 44007 interactions was constructed and integrated with the transcriptome data available in literature for the mutants of the glucose signaling pathway of *S. cerevisiae*.

The constructed TRN was found to be scale free and none of the selected hubs (the intersection of the top 20 highest degree and top 20 highest betweenness nodes) were found to be a key TF, showing that identified key TFs were not false-positives resulting from their possible high degree.

Key TFs that are involved in chromatin remodeling, phospholipid biosynthesis, β-oxidation of fatty acids, biogenesis, oxidative phosphorylation (energy metabolism), carbohydrate metabolic process, alternative carbon source consumption and stress response, were identified as a response to *SNF1* deletion. These results are consistent with the predicted role of Snf1p kinase reported in the study of Usaite *et al.*, where three level omics data (genome-wide mRNA, protein profiling and metabolite measurements) has been integrated with different networks (protein-protein interactions, protein-DNA interactions and metabolic reaction stoichiometry) using four computational tools. Key TFs involved in processes, such as oleate response and protein urmylation, were also identified. This result highlights the effectiveness of only using reporter features algorithm with a large genome-scale TRN to investigate the regulatory mechanisms invoked in the cell. The only disadvantage is that reporter features algorithm does not specify the direction of the change but only the significancy of the change.

Key TFs that are involved in chromatin remodeling, fatty acid metabolic process, oxidative phosphorylation (energy metabolism), alternative carbon source consumption and stress response, were identified as a response to *MIG1* deletion as in *ΔSNF1*. Key TFs involved in glucose repression and drug resistance were also identified.

As a response to oxygen availability under carbon limitation regime key TFs known to be involved in regulation of aerobiosis/anaerobiosis were identified, as expected. In addition, TFs that are involved in glucose repression and derepression and TFs known to be positively regulated by Snf1p kinase were identified as key TFs, providing further evidence to the role of Snf1p kinase in the switch from fermentative/anaerobic to oxidative metabolism.

Significant shared GO biological process terms of the key TFs identified as a response to each specific perturbation did not display the expected relationship of the key TFs with the corresponding specific perturbation, generally. However, when combined with the literature, it was observed that key TFs identified reveal the expected changes in response to each specific perturbation.

In this study, it was further showed that once the key TFs are identified, the perturbation-responsive subnetworks might be constructed by interconnecting key TFs and their differentially expressed target genes responsive to the same perturbation. PRSs of *ΔMIG1*, *ΔMIG1ΔMIG2*, *ΔMIG3* and *ΔMIG1ΔMIG2ΔMIG3* mutants do not contain all key TFs identified for each specific mutant, since some of these key TFs do not have significantly differentially expressed (*p*-value<0.05) target genes.

Significant shared GO biological process terms of the target genes in the PRSs display the expected relationship of the key TFs with the corresponding specific perturbation to some extent, but not fully. For example, fatty acid and lipid metabolism did not appear among the terms significantly associated with the genes of the PRSs of *ΔSNF1*, *ΔSNF4* and *ΔSNF1ΔSNF4*. This might arise from the approach used to construct PRSs, i. e., *p*-value threshold (0.05) used to identify significantly differentially expressed genes of the PRSs.

In this study, significant and biologically meaningful key TFs were identified which shed light on the transcriptional regulatory mechanism controlling the glucose signaling in *S. cerevisiae*. The results correlate with prior knowledge of glucose repression/derepression regulatory cascade studies, and they also provide a starting point for potential experimental studies to further investigate the relationships between the identified key TFs and the corresponding perturbations.

## 4.2. Recommendations

The approach used to construct PRSs may be improved or changed. To identify significantly differentially expressed genes a lover threshold value could be used and the larger effects of perturbations could be seen. Alternatively, a protein-protein interaction network could be constructed based on key TFs and differentially expressed target genes and this network could be enlarged by adding first neighbours of the nodes.

Key TFs responsive to carbon availability under aerobic regime could be identified, to further reveal the glucose sensing and signalling mechanism of yeast.

Although not information-preserving, the initial transcriptome data could be filtered to contain only up or down regulated genes. By this way, the identified key TFs can be used to enrich the information about the biological role of a perturbation without considering the directionality.

# APPENDIX A: TOPOLOGICAL STUDY OF THE NETWORK

Table A.1. Topological parameters of individual nodes of the yeast TRN

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A1 | 13 | 0.051 | 2799 | snR17a | 3 | 0.333 | 18 | snR87 | 2 | 0.000 | 9 |
| A2 | 1 | 0.000 | 0 | snR17b | 1 | 0.000 | 0 | SRG1 | 1 | 0.000 | 0 |
| ALD1 | 1 | 0.000 | 0 | snR18 | 1 | 0.000 | 0 | STA1 | 5 | 0.100 | 73 |
| DEX2 | 6 | 0.667 | 20 | snR189 | 1 | 0.000 | 0 | STA2 | 9 | 0.222 | 245 |
| MAL61 | 2 | 0.000 | 19053 | snR190 | 21 | 0.081 | 2692 | STA3 | 3 | 0.333 | 8 |
| MAL62 | 2 | 0.000 | 19053 | snR20 | 1 | 0.000 | 0 | SUC6 | 1 | 0.000 | 0 |
| MALR | 4 | 0.000 | 25415 | snR37 | 13 | 0.103 | 751 | tA(AGC)D | 1 | 0.000 | 0 |
| MALS | 1 | 0.000 | 0 | snR4 | 2 | 0.000 | 18 | tA(AGC)G | 2 | 1.000 | 0 |
| MALT | 1 | 0.000 | 0 | snR42 | 1 | 0.000 | 0 | tA(AGC)K2 | 3 | 0.333 | 27 |
| MEL1 | 2 | 1.000 | 0 | snR44 | 2 | 0.000 | 6 | tA(AGC)P | 3 | 0.000 | 20 |
| MPR1 | 2 | 1.000 | 0 | snR45 | 5 | 0.200 | 168 | tA(UGC)A | 2 | 0.000 | 24 |
| Q0010 | 2 | 0.000 | 15 | snR46 | 2 | 0.000 | 44 | tC(GCA)B | 2 | 0.000 | 131 |
| Q0045 | 3 | 0.333 | 17 | snR47 | 5 | 0.000 | 286 | tC(GCA)P1 | 1 | 0.000 | 0 |
| Q0050 | 5 | 0.200 | 109 | snR53 | 1 | 0.000 | 0 | tC(GCA)P2 | 1 | 0.000 | 0 |
| Q0055 | 4 | 0.667 | 21 | snR54 | 1 | 0.000 | 0 | tD(GUC)B | 1 | 0.000 | 0 |
| Q0060 | 2 | 0.000 | 13 | snR55 | 4 | 0.000 | 42 | tD(GUC)G1 | 1 | 0.000 | 0 |
| Q0065 | 3 | 0.000 | 559 | snR56 | 2 | 0.000 | 3 | tD(GUC)J2 | 2 | 0.000 | 10 |
| Q0070 | 4 | 0.000 | 84 | snR57 | 15 | 0.171 | 2134 | tD(GUC)K | 1 | 0.000 | 0 |
| Q0075 | 5 | 0.300 | 53 | snR59 | 3 | 0.000 | 18 | tD(GUC)L1 | 1 | 0.000 | 0 |
| Q0080 | 7 | 0.429 | 128 | snR6 | 9 | 0.056 | 857 | tD(GUC)L2 | 1 | 0.000 | 0 |
| Q0085 | 3 | 0.667 | 13 | snR60 | 2 | 1.000 | 0 | tE(CUC)D | 9 | 0.111 | 1615 |
| Q0105 | 4 | 0.333 | 77 | snR61 | 9 | 0.056 | 534 | tE(UUC)B | 1 | 0.000 | 0 |
| Q0110 | 2 | 1.000 | 0 | snR63 | 2 | 1.000 | 0 | tE(UUC)C | 1 | 0.000 | 0 |
| Q0115 | 5 | 0.700 | 48 | snR64 | 1 | 0.000 | 0 | tE(UUC)E2 | 1 | 0.000 | 0 |
| Q0120 | 4 | 0.500 | 17 | snR65 | 1 | 0.000 | 0 | tE(UUC)E3 | 2 | 0.000 | 94 |
| Q0130 | 2 | 0.000 | 21 | snR66 | 3 | 0.333 | 47 | tE(UUC)G1 | 1 | 0.000 | 0 |
| Q0140 | 3 | 0.333 | 17 | snR67 | 8 | 0.143 | 295 | tE(UUC)J | 1 | 0.000 | 0 |
| Q0160 | 2 | 0.000 | 13 | snR70 | 9 | 0.056 | 688 | tE(UUC)P | 2 | 1.000 | 0 |
| Q0182 | 1 | 0.000 | 0 | snR71 | 7 | 0.238 | 57 | tF(GAA)B | 1 | 0.000 | 0 |
| Q0250 | 3 | 0.333 | 17 | snR72 | 1 | 0.000 | 0 | tF(GAA)D | 2 | 1.000 | 0 |
| Q0255 | 2 | 0.000 | 10 | snR73 | 1 | 0.000 | 0 | tF(GAA)F | 1 | 0.000 | 0 |
| Q0275 | 2 | 0.000 | 10 | snR74 | 1 | 0.000 | 0 | tF(GAA)H1 | 2 | 1.000 | 0 |
| Q0297 | 2 | 0.000 | 10 | snR75 | 1 | 0.000 | 0 | tF(GAA)P2 | 1 | 0.000 | 0 |
| RDN5 | 3 | 0.333 | 20 | snR76 | 1 | 0.000 | 0 | tG(GCC)F2 | 2 | 0.000 | 6 |
| RPR1 | 2 | 0.000 | 9 | snR77 | 1 | 0.000 | 0 | tG(GCC)G2 | 1 | 0.000 | 0 |
| snR128 | 3 | 0.000 | 67 | snR78 | 1 | 0.000 | 0 | tG(GCC)J1 | 2 | 0.000 | 131 |
| snR13 | 2 | 0.000 | 24 | snR7-S | 1 | 0.000 | 0 | tG(GCC)J2 | 1 | 0.000 | 0 |
| snR14 | 2 | 0.000 | 123 | snR8 | 2 | 0.000 | 13 | tG(GCC)M | 1 | 0.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| tG(GCC)P2 | 1 | 0.000 | 0 | tP(UGG)O2 | 1 | 0.000 | 0 | tY(GUA)M1 | 1 | 0.000 | 0 |
| tG(UCC)G | 2 | 0.000 | 64 | tP(UGG)O3 | 1 | 0.000 | 0 | tY(GUA)O | 1 | 0.000 | 0 |
| tG(UCC)O | 1 | 0.000 | 0 | tQ(CUG)M | 2 | 0.000 | 367 | YAL001c | 5 | 0.100 | 408 |
| tH(GUG)E1 | 6 | 0.133 | 212 | tQ(UUG)D2 | 2 | 1.000 | 0 | YAL002w | 2 | 0.000 | 32 |
| tH(GUG)G2 | 3 | 0.333 | 74 | tQ(UUG)E1 | 4 | 0.000 | 719 | YAL003w | 15 | 0.390 | 928 |
| tH(GUG)H | 1 | 0.000 | 0 | tQ(UUG)E2 | 1 | 0.000 | 0 | YAL004w | 4 | 0.000 | 60 |
| tH(GUG)K | 5 | 0.000 | 489 | tR(ACG)D | 1 | 0.000 | 0 | YAL005c | 28 | 0.243 | 6331 |
| tK(CUU)D1 | 1 | 0.000 | 0 | tR(ACG)K | 1 | 0.000 | 0 | YAL007c | 6 | 0.467 | 78 |
| tK(CUU)G3 | 1 | 0.000 | 0 | tR(CCG)L | 2 | 0.000 | 9 | YAL008w | 2 | 0.000 | 132 |
| tK(CUU)J | 3 | 0.000 | 23 | tR(CCU)J | 1 | 0.000 | 0 | YAL009w | 3 | 0.333 | 134 |
| tK(CUU)K | 1 | 0.000 | 0 | tR(UCU)G2 | 1 | 0.000 | 0 | YAL010c | 4 | 0.333 | 306 |
| tK(CUU)P | 1 | 0.000 | 0 | tS(AGA)D1 | 1 | 0.000 | 0 | YAL011w | 3 | 0.000 | 90 |
| tK(UUU)D | 2 | 1.000 | 0 | tS(AGA)D2 | 1 | 0.000 | 0 | YAL012w | 12 | 0.303 | 646 |
| tK(UUU)G1 | 1 | 0.000 | 0 | tS(AGA)D3 | 2 | 0.000 | 92 | YAL013w | 7 | 0.333 | 277 |
| tK(UUU)L | 1 | 0.000 | 0 | tS(AGA)J | 1 | 0.000 | 0 | YAL014c | 4 | 0.333 | 97 |
| tL(CAA)A | 1 | 0.000 | 0 | tS(CGA)C | 1 | 0.000 | 0 | YAL015c | 6 | 0.200 | 199 |
| tL(CAA)D | 3 | 0.333 | 62 | tS(GCU)L | 2 | 0.000 | 9 | YAL016w | 5 | 0.100 | 87 |
| tL(CAA)G1 | 3 | 0.000 | 13 | tS(UGA)I | 3 | 0.333 | 27 | YAL017w | 10 | 0.244 | 1111 |
| tL(CAA)G2 | 1 | 0.000 | 0 | tS(UGA)P | 2 | 0.000 | 131 | YAL018c | 12 | 0.136 | 1559 |
| tL(CAA)G3 | 2 | 0.000 | 9 | tT(AGU)B | 3 | 0.000 | 12 | YAL019w | 5 | 0.100 | 2780 |
| tL(CAA)K | 1 | 0.000 | 0 | tT(AGU)H | 2 | 0.000 | 4 | YAL020c | 5 | 0.300 | 162 |
| tL(CAA)L | 1 | 0.000 | 0 | tT(AGU)J | 12 | 0.076 | 1447 | YAL021c | 1 | 0.000 | 0 |
| tL(CAA)M | 2 | 1.000 | 0 | tT(AGU)N1 | 2 | 0.000 | 34 | YAL022c | 18 | 0.176 | 2396 |
| tL(GAG)G | 1 | 0.000 | 0 | tT(UGU)G1 | 1 | 0.000 | 0 | YAL023c | 7 | 0.048 | 984 |
| tL(UAA)B1 | 1 | 0.000 | 0 | tT(UGU)G2 | 7 | 0.048 | 515 | YAL024c | 3 | 0.333 | 30 |
| tL(UAA)K | 2 | 1.000 | 0 | tT(UGU)P | 3 | 0.000 | 32 | YAL025c | 9 | 0.139 | 1733 |
| tL(UAG)L1 | 2 | 0.000 | 7 | tV(AAC)E1 | 1 | 0.000 | 0 | YAL026c | 3 | 0.000 | 36 |
| tM(CAU)C | 1 | 0.000 | 0 | tV(AAC)G1 | 1 | 0.000 | 0 | YAL027w | 4 | 0.167 | 29 |
| tM(CAU)D | 1 | 0.000 | 0 | tV(AAC)J | 1 | 0.000 | 0 | YAL028w | 9 | 0.444 | 482 |
| tM(CAU)E | 2 | 0.000 | 41 | tV(AAC)K1 | 1 | 0.000 | 0 | YAL029c | 9 | 0.222 | 271 |
| tM(CAU)J1 | 3 | 0.000 | 43 | tV(AAC)K2 | 2 | 1.000 | 0 | YAL030w | 2 | 0.000 | 7 |
| tM(CAU)J2 | 1 | 0.000 | 0 | tV(AAC)L | 3 | 0.000 | 699 | YAL031c | 4 | 0.667 | 60 |
| tM(CAU)M | 1 | 0.000 | 0 | tV(AAC)O | 1 | 0.000 | 0 | YAL033w | 2 | 1.000 | 0 |
| tM(CAU)O2 | 2 | 0.000 | 10 | tV(CAC)D | 2 | 0.000 | 77 | YAL034c | 4 | 0.500 | 73 |
| tM(CAU)P | 1 | 0.000 | 0 | tV(CAC)H | 2 | 1.000 | 0 | YAL034w-a | 8 | 0.321 | 218 |
| tN(GUU)F | 1 | 0.000 | 0 | tV(UAC)D | 1 | 0.000 | 0 | YAL035w | 5 | 0.100 | 230 |
| tN(GUU)L | 1 | 0.000 | 0 | tW(CCA)G1 | 4 | 0.167 | 252 | YAL036c | 6 | 0.267 | 140 |
| tN(GUU)N1 | 1 | 0.000 | 0 | tW(CCA)G2 | 4 | 0.000 | 78 | YAL037c-a | 2 | 0.000 | 34 |
| tP(AGG)C | 1 | 0.000 | 0 | tW(CCA)J | 12 | 0.015 | 1277 | YAL037w | 9 | 0.361 | 1033 |
| tP(UGG)L | 1 | 0.000 | 0 | tW(CCA)K | 3 | 0.000 | 12 | YAL038w | 25 | 0.247 | 9667 |
| tP(UGG)M | 1 | 0.000 | 0 | tW(CCA)M | 3 | 0.000 | 58 | YAL039c | 15 | 0.371 | 1579 |
| tP(UGG)N1 | 1 | 0.000 | 0 | tY(GUA)F1 | 1 | 0.000 | 0 | YAL040c | 23 | 0.360 | 2146 |
| tP(UGG)O1 | 3 | 0.333 | 7 | tY(GUA)J2 | 1 | 0.000 | 0 | YAL041w | 4 | 0.500 | 178 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YAL042w | 4 | 0.167 | 332 | YAR029w | 5 | 0.100 | 113 | YBL022c | 9 | 0.389 | 600 |
| YAL043c | 3 | 0.000 | 396 | YAR030c | 1 | 0.000 | 0 | YBL023c | 7 | 0.381 | 169 |
| YAL043c-a | 1 | 0.000 | 0 | YAR031w | 4 | 0.000 | 103 | YBL024w | 2 | 0.000 | 28 |
| YAL044c | 11 | 0.327 | 891 | YAR033w | 3 | 0.667 | 19 | YBL025w | 3 | 0.000 | 130 |
| YAL044w-a | 1 | 0.000 | 0 | YAR035w | 16 | 0.300 | 1845 | YBL026w | 7 | 0.238 | 584 |
| YAL045c | 2 | 0.000 | 29 | YAR042w | 12 | 0.212 | 1595 | YBL027w | 11 | 0.455 | 358 |
| YAL046c | 2 | 0.000 | 25 | YAR044w | 1 | 0.000 | 0 | YBL028c | 12 | 0.379 | 472 |
| YAL047c | 1 | 0.000 | 0 | YAR047c | 7 | 0.286 | 542 | YBL029c-a | 19 | 0.444 | 1015 |
| YAL048c | 1 | 0.000 | 0 | YAR050w | 24 | 0.214 | 3248 | YBL029w | 39 | 0.216 | 19187 |
| YAL049c | 4 | 0.167 | 313 | YAR053w | 6 | 0.200 | 86 | YBL030c | 25 | 0.330 | 2001 |
| YAL051w | 264 | 0.008 | 174707 | YAR060c | 1 | 0.000 | 0 | YBL031w | 2 | 0.000 | 14 |
| YAL053w | 14 | 0.176 | 2643 | YAR061w | 5 | 0.400 | 102 | YBL032w | 5 | 0.400 | 203 |
| YAL054c | 18 | 0.190 | 3572 | YAR062w | 4 | 0.167 | 123 | YBL033c | 10 | 0.333 | 1420 |
| YAL055w | 2 | 1.000 | 0 | YAR064w | 5 | 0.700 | 18 | YBL034c | 4 | 0.167 | 109 |
| YAL056w | 2 | 0.000 | 48 | YAR066w | 8 | 0.321 | 103 | YBL035c | 3 | 0.333 | 53 |
| YAL058c-a | 1 | 0.000 | 0 | YAR068w | 13 | 0.244 | 981 | YBL036c | 5 | 0.400 | 135 |
| YAL058w | 2 | 1.000 | 0 | YAR069c | 3 | 0.000 | 72 | YBL037w | 4 | 0.500 | 64 |
| YAL059w | 5 | 0.300 | 82 | YAR070c | 5 | 0.400 | 129 | YBL038w | 5 | 0.100 | 726 |
| YAL060w | 13 | 0.359 | 1106 | YAR071w | 17 | 0.272 | 1260 | YBL039c | 12 | 0.288 | 1402 |
| YAL061w | 14 | 0.264 | 1095 | YAR073w | 10 | 0.444 | 1178 | YBL041w | 13 | 0.231 | 2127 |
| YAL062w | 27 | 0.171 | 5567 | YAR075w | 6 | 0.467 | 108 | YBL042c | 20 | 0.268 | 4609 |
| YAL063c | 22 | 0.281 | 3967 | YBL001c | 14 | 0.121 | 811 | YBL043w | 24 | 0.326 | 2225 |
| YAL064c-a | 14 | 0.440 | 838 | YBL002w | 12 | 0.182 | 1112 | YBL044w | 17 | 0.426 | 551 |
| YAL064w | 14 | 0.385 | 1876 | YBL003c | 7 | 0.238 | 407 | YBL045c | 14 | 0.385 | 295 |
| YAL065c | 5 | 0.100 | 107 | YBL004w | 8 | 0.286 | 465 | YBL046w | 3 | 0.333 | 259 |
| YAL066w | 1 | 0.000 | 0 | YBL005w | 552 | 0.007 | 407305 | YBL047c | 2 | 0.000 | 40 |
| YAL067c | 12 | 0.182 | 1113 | YBL005w-a | 4 | 0.333 | 38 | YBL048w | 4 | 0.167 | 60 |
| YAL068c | 10 | 0.178 | 625 | YBL005w-b | 2 | 1.000 | 0 | YBL049w | 16 | 0.225 | 2475 |
| YAR002c-a | 2 | 0.000 | 42 | YBL006c | 2 | 1.000 | 0 | YBL050w | 3 | 0.333 | 53 |
| YAR002w | 4 | 0.167 | 228 | YBL007c | 6 | 0.267 | 684 | YBL051c | 5 | 0.100 | 330 |
| YAR003w | 6 | 0.067 | 378 | YBL008w | 80 | 0.005 | 44543 | YBL052c | 1 | 0.000 | 0 |
| YAR007c | 8 | 0.214 | 1516 | YBL009w | 1 | 0.000 | 0 | YBL053w | 1 | 0.000 | 0 |
| YAR008w | 6 | 0.267 | 414 | YBL010c | 1 | 0.000 | 0 | YBL054w | 9 | 0.278 | 683 |
| YAR009c | 20 | 0.226 | 3656 | YBL011w | 11 | 0.400 | 330 | YBL055c | 1 | 0.000 | 0 |
| YAR010c | 3 | 0.000 | 41 | YBL013w | 6 | 0.333 | 205 | YBL056w | 5 | 0.100 | 457 |
| YAR014c | 4 | 0.667 | 33 | YBL014c | 5 | 0.400 | 56 | YBL057c | 5 | 0.100 | 268 |
| YAR015w | 11 | 0.436 | 520 | YBL015w | 12 | 0.515 | 481 | YBL058w | 4 | 0.500 | 46 |
| YAR018c | 5 | 0.500 | 67 | YBL016w | 11 | 0.473 | 994 | YBL059c-a | 3 | 0.000 | 90 |
| YAR019c | 7 | 0.286 | 592 | YBL017c | 6 | 0.600 | 283 | YBL059w | 10 | 0.089 | 842 |
| YAR020c | 7 | 0.381 | 211 | YBL018c | 7 | 0.143 | 1158 | YBL060w | 6 | 0.267 | 325 |
| YAR023c | 5 | 0.200 | 75 | YBL019w | 5 | 0.200 | 376 | YBL061c | 3 | 0.333 | 47 |
| YAR027w | 6 | 0.200 | 516 | YBL020w | 7 | 0.333 | 408 | YBL063w | 5 | 0.100 | 320 |
| YAR028w | 7 | 0.333 | 354 | YBL021c | 188 | 0.008 | 81126 | YBL064c | 12 | 0.288 | 630 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YBL066c | 1 | 0.000 | 0 | YBL105c | 5 | 0.600 | 25 | YBR033w | 6 | 0.267 | 278 |
| YBL067c | 2 | 0.000 | 32 | YBL106c | 4 | 0.333 | 229 | YBR034c | 6 | 0.267 | 163 |
| YBL068w | 3 | 0.333 | 222 | YBL107c | 11 | 0.382 | 380 | YBR035c | 5 | 0.500 | 148 |
| YBL069w | 4 | 0.500 | 55 | YBL107w-a | 1 | 0.000 | 0 | YBR036c | 4 | 0.000 | 145 |
| YBL070c | 2 | 1.000 | 0 | YBL108c-a | 3 | 1.000 | 0 | YBR037c | 4 | 0.167 | 50 |
| YBL071c | 5 | 0.500 | 120 | YBL108w | 10 | 0.356 | 224 | YBR038w | 13 | 0.090 | 1654 |
| YBL071c-b | 2 | 0.000 | 9 | YBL109w | 23 | 0.186 | 2108 | YBR039w | 15 | 0.229 | 1002 |
| YBL071w-a | 2 | 0.000 | 9 | YBL111c | 20 | 0.221 | 1212 | YBR040w | 20 | 0.321 | 3739 |
| YBL072c | 7 | 0.619 | 139 | YBL112c | 14 | 0.209 | 912 | YBR041w | 6 | 0.067 | 517 |
| YBL073w | 6 | 0.133 | 369 | YBL113c | 12 | 0.167 | 371 | YBR042c | 3 | 0.000 | 128 |
| YBL074c | 3 | 0.000 | 27 | YBR001c | 4 | 0.500 | 117 | YBR043c | 7 | 0.143 | 656 |
| YBL075c | 18 | 0.248 | 2608 | YBR002c | 4 | 0.000 | 446 | YBR044c | 5 | 0.300 | 149 |
| YBL076c | 4 | 0.500 | 74 | YBR003w | 5 | 0.400 | 371 | YBR045c | 5 | 0.200 | 474 |
| YBL077w | 1 | 0.000 | 0 | YBR004c | 5 | 0.000 | 293 | YBR046c | 9 | 0.278 | 688 |
| YBL078c | 12 | 0.182 | 904 | YBR005w | 6 | 0.333 | 395 | YBR047w | 14 | 0.319 | 912 |
| YBL079w | 6 | 0.200 | 465 | YBR006w | 16 | 0.117 | 1469 | YBR048w | 16 | 0.267 | 2153 |
| YBL080c | 1 | 0.000 | 0 | YBR007c | 14 | 0.308 | 1325 | YBR049c | 324 | 0.007 | 465973 |
| YBL081w | 5 | 0.400 | 270 | YBR008c | 15 | 0.352 | 1582 | YBR050c | 14 | 0.154 | 1199 |
| YBL082c | 4 | 0.500 | 166 | YBR009c | 8 | 0.214 | 924 | YBR051w | 6 | 0.200 | 182 |
| YBL083c | 2 | 0.000 | 86 | YBR010w | 5 | 0.100 | 401 | YBR052c | 7 | 0.190 | 535 |
| YBL085w | 3 | 0.333 | 71 | YBR011c | 8 | 0.357 | 780 | YBR053c | 13 | 0.397 | 755 |
| YBL086c | 5 | 0.400 | 92 | YBR012c | 5 | 0.100 | 194 | YBR054w | 31 | 0.237 | 5667 |
| YBL087c | 15 | 0.314 | 1394 | YBR012w-a | 3 | 0.000 | 41 | YBR055c | 4 | 0.333 | 168 |
| YBL088c | 1 | 0.000 | 0 | YBR012w-b | 3 | 0.000 | 41 | YBR056w | 15 | 0.229 | 2642 |
| YBL089w | 3 | 0.333 | 50 | YBR013c | 6 | 0.333 | 590 | YBR056w-a | 6 | 0.400 | 281 |
| YBL090w | 1 | 0.000 | 0 | YBR014c | 5 | 0.300 | 120 | YBR057c | 11 | 0.073 | 498 |
| YBL091c | 1 | 0.000 | 0 | YBR015c | 5 | 0.400 | 248 | YBR058c | 1 | 0.000 | 0 |
| YBL091c-a | 3 | 0.333 | 241 | YBR016w | 6 | 0.333 | 444 | YBR058c-a | 1 | 0.000 | 0 |
| YBL092w | 10 | 0.422 | 848 | YBR017c | 4 | 0.000 | 399 | YBR059c | 1 | 0.000 | 0 |
| YBL093c | 9 | 0.361 | 693 | YBR018c | 10 | 0.289 | 766 | YBR060c | 7 | 0.238 | 634 |
| YBL094c | 1 | 0.000 | 0 | YBR019c | 20 | 0.116 | 5456 | YBR061c | 4 | 0.333 | 229 |
| YBL095w | 3 | 0.000 | 38 | YBR020w | 24 | 0.138 | 6512 | YBR062c | 5 | 0.500 | 434 |
| YBL096c | 1 | 0.000 | 0 | YBR021w | 10 | 0.244 | 1613 | YBR063c | 2 | 1.000 | 0 |
| YBL097w | 3 | 0.333 | 23 | YBR022w | 1 | 0.000 | 0 | YBR065c | 6 | 0.067 | 517 |
| YBL098w | 13 | 0.179 | 2002 | YBR023c | 4 | 0.333 | 59 | YBR066c | 166 | 0.049 | 134448 |
| YBL099w | 13 | 0.244 | 589 | YBR024w | 5 | 0.200 | 285 | YBR067c | 18 | 0.333 | 1820 |
| YBL101c | 5 | 0.400 | 109 | YBR025c | 14 | 0.264 | 499 | YBR068c | 13 | 0.205 | 1725 |
| YBL101w-a | 3 | 0.333 | 54 | YBR026c | 2 | 0.000 | 8 | YBR069c | 12 | 0.348 | 1036 |
| YBL101w-b | 3 | 0.000 | 92 | YBR028c | 3 | 0.000 | 137 | YBR070c | 8 | 0.321 | 314 |
| YBL101w-c | 1 | 0.000 | 0 | YBR029c | 8 | 0.250 | 1285 | YBR071w | 15 | 0.171 | 1401 |
| YBL102w | 3 | 0.000 | 40 | YBR030w | 5 | 0.200 | 413 | YBR072w | 56 | 0.209 | 16851 |
| YBL103c | 223 | 0.007 | 103327 | YBR031w | 8 | 0.536 | 848 | YBR073w | 6 | 0.333 | 120 |
| YBL104c | 4 | 0.167 | 35 | YBR032w | 4 | 0.000 | 94 | YBR074w | 9 | 0.250 | 942 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YBR075w | 2 | 1.000 | 0 | YBR116c | 16 | 0.283 | 3421 | YBR159w | 9 | 0.111 | 285 |
| YBR076w | 9 | 0.222 | 708 | YBR117c | 30 | 0.232 | 4927 | YBR160w | 6 | 0.200 | 534 |
| YBR077c | 18 | 0.307 | 2061 | YBR118w | 10 | 0.489 | 437 | YBR161w | 6 | 0.200 | 297 |
| YBR078w | 23 | 0.269 | 3945 | YBR119w | 4 | 0.500 | 169 | YBR162c | 9 | 0.444 | 455 |
| YBR079c | 3 | 0.333 | 33 | YBR120c | 3 | 0.333 | 106 | YBR162w-a | 7 | 0.476 | 192 |
| YBR080c | 5 | 0.200 | 1067 | YBR121c | 5 | 0.300 | 698 | YBR163w | 7 | 0.095 | 513 |
| YBR081c | 7 | 0.286 | 551 | YBR122c | 1 | 0.000 | 0 | YBR164c | 5 | 0.100 | 564 |
| YBR082c | 13 | 0.372 | 1526 | YBR123c | 2 | 0.000 | 36 | YBR165w | 2 | 0.000 | 92 |
| YBR083w | 547 | 0.020 | 601548 | YBR124w | 1 | 0.000 | 0 | YBR166c | 8 | 0.107 | 302 |
| YBR084c-a | 6 | 0.533 | 121 | YBR125c | 2 | 1.000 | 0 | YBR167c | 20 | 0.142 | 2031 |
| YBR084w | 3 | 0.333 | 74 | YBR126c | 20 | 0.216 | 2917 | YBR168w | 17 | 0.147 | 1083 |
| YBR085c-a | 10 | 0.356 | 700 | YBR127c | 4 | 0.167 | 90 | YBR169c | 23 | 0.324 | 3270 |
| YBR085w | 17 | 0.294 | 2050 | YBR128c | 1 | 0.000 | 0 | YBR170c | 7 | 0.429 | 483 |
| YBR086c | 13 | 0.090 | 1479 | YBR129c | 6 | 0.333 | 373 | YBR171w | 4 | 0.500 | 217 |
| YBR087w | 11 | 0.091 | 1008 | YBR130c | 3 | 0.333 | 189 | YBR172c | 2 | 1.000 | 0 |
| YBR088c | 3 | 0.667 | 39 | YBR131w | 3 | 0.333 | 189 | YBR173c | 4 | 0.333 | 124 |
| YBR089c-a | 2 | 0.000 | 11 | YBR132c | 7 | 0.381 | 187 | YBR174c | 1 | 0.000 | 0 |
| YBR089w | 2 | 1.000 | 0 | YBR133c | 6 | 0.400 | 97 | YBR175w | 4 | 0.500 | 203 |
| YBR090c | 6 | 0.133 | 133 | YBR134w | 6 | 0.267 | 121 | YBR176w | 3 | 0.000 | 53 |
| YBR091c | 3 | 0.000 | 105 | YBR135w | 7 | 0.143 | 217 | YBR177c | 10 | 0.489 | 874 |
| YBR092c | 21 | 0.176 | 5045 | YBR136w | 2 | 0.000 | 12 | YBR178w | 1 | 0.000 | 0 |
| YBR093c | 24 | 0.130 | 7042 | YBR137w | 6 | 0.533 | 160 | YBR179c | 7 | 0.524 | 536 |
| YBR094w | 6 | 0.133 | 212 | YBR138c | 9 | 0.306 | 572 | YBR180w | 6 | 0.533 | 488 |
| YBR095c | 4 | 0.333 | 315 | YBR139w | 14 | 0.253 | 1520 | YBR181c | 5 | 0.500 | 98 |
| YBR096w | 4 | 0.167 | 305 | YBR140c | 2 | 0.000 | 7 | YBR182c | 167 | 0.020 | 88106 |
| YBR097w | 6 | 0.333 | 596 | YBR141c | 2 | 0.000 | 67 | YBR182c-a | 2 | 1.000 | 0 |
| YBR098w | 10 | 0.067 | 964 | YBR142w | 5 | 0.200 | 151 | YBR183w | 14 | 0.374 | 565 |
| YBR099c | 7 | 0.381 | 253 | YBR143c | 3 | 0.000 | 338 | YBR184w | 5 | 0.000 | 203 |
| YBR101c | 11 | 0.309 | 1165 | YBR144c | 7 | 0.476 | 251 | YBR185c | 3 | 0.333 | 41 |
| YBR102c | 9 | 0.222 | 436 | YBR145w | 17 | 0.279 | 2270 | YBR186w | 2 | 1.000 | 0 |
| YBR103w | 10 | 0.200 | 623 | YBR146w | 2 | 0.000 | 117 | YBR187w | 5 | 0.200 | 176 |
| YBR104w | 8 | 0.286 | 431 | YBR147w | 15 | 0.295 | 1636 | YBR188c | 7 | 0.333 | 958 |
| YBR105c | 16 | 0.267 | 2154 | YBR148w | 5 | 0.300 | 415 | YBR189w | 10 | 0.333 | 1359 |
| YBR106w | 7 | 0.143 | 429 | YBR149w | 11 | 0.273 | 553 | YBR190w | 9 | 0.389 | 439 |
| YBR107c | 2 | 0.000 | 11 | YBR150c | 6 | 0.333 | 153 | YBR191w | 9 | 0.472 | 377 |
| YBR108w | 4 | 0.000 | 154 | YBR151w | 10 | 0.222 | 794 | YBR192w | 1 | 0.000 | 0 |
| YBR109c | 9 | 0.167 | 1283 | YBR152w | 1 | 0.000 | 0 | YBR194w | 1 | 0.000 | 0 |
| YBR110w | 8 | 0.143 | 1235 | YBR153w | 3 | 0.000 | 66 | YBR195c | 4 | 0.333 | 319 |
| YBR111c | 5 | 0.500 | 113 | YBR154c | 4 | 0.167 | 445 | YBR196c | 10 | 0.156 | 677 |
| YBR112c | 8 | 0.464 | 1199 | YBR155w | 4 | 0.333 | 411 | YBR196c-a | 3 | 0.333 | 24 |
| YBR113w | 3 | 0.667 | 12 | YBR156c | 6 | 0.467 | 331 | YBR196c-b | 2 | 0.000 | 9 |
| YBR114w | 11 | 0.382 | 387 | YBR157c | 21 | 0.252 | 1717 | YBR197c | 4 | 0.167 | 54 |
| YBR115c | 10 | 0.289 | 547 | YBR158w | 18 | 0.333 | 1286 | YBR198c | 2 | 0.000 | 206 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YBR199w | 3 | 0.667 | 97 | YBR240c | 85 | 0.040 | 102508 | YBR284w | 8 | 0.357 | 595 |
| YBR200w | 7 | 0.381 | 166 | YBR241c | 14 | 0.242 | 1151 | YBR285w | 15 | 0.276 | 831 |
| YBR201w | 6 | 0.200 | 367 | YBR242w | 1 | 0.000 | 0 | YBR286w | 15 | 0.229 | 2330 |
| YBR202w | 12 | 0.561 | 263 | YBR243c | 10 | 0.311 | 489 | YBR287w | 3 | 0.333 | 132 |
| YBR203w | 11 | 0.436 | 485 | YBR244w | 13 | 0.256 | 1310 | YBR288c | 3 | 0.000 | 90 |
| YBR204c | 2 | 0.000 | 2 | YBR245c | 1 | 0.000 | 0 | YBR289w | 4 | 0.000 | 201 |
| YBR205w | 2 | 0.000 | 2 | YBR246w | 1 | 0.000 | 0 | YBR290w | 3 | 0.000 | 248 |
| YBR206w | 2 | 0.000 | 2 | YBR247c | 10 | 0.244 | 594 | YBR291c | 8 | 0.357 | 940 |
| YBR207w | 7 | 0.286 | 610 | YBR248c | 11 | 0.218 | 1649 | YBR293w | 5 | 0.200 | 784 |
| YBR208c | 14 | 0.286 | 2382 | YBR249c | 9 | 0.444 | 472 | YBR294w | 16 | 0.208 | 2215 |
| YBR209w | 7 | 0.238 | 675 | YBR250w | 11 | 0.164 | 4093 | YBR295w | 9 | 0.306 | 1006 |
| YBR210w | 7 | 0.476 | 1075 | YBR251w | 2 | 1.000 | 0 | YBR296c | 28 | 0.164 | 4784 |
| YBR211c | 3 | 0.000 | 478 | YBR253w | 2 | 1.000 | 0 | YBR297w | 144 | 0.026 | 115072 |
| YBR212w | 3 | 0.000 | 277 | YBR254c | 5 | 0.000 | 174 | YBR298c | 8 | 0.464 | 423 |
| YBR213w | 6 | 0.200 | 306 | YBR255c-a | 1 | 0.000 | 0 | YBR299w | 16 | 0.292 | 2063 |
| YBR214w | 10 | 0.267 | 369 | YBR255w | 3 | 0.000 | 25 | YBR300c | 3 | 0.333 | 32 |
| YBR215w | 3 | 0.000 | 65 | YBR256c | 10 | 0.333 | 426 | YBR301w | 6 | 0.400 | 123 |
| YBR216c | 8 | 0.000 | 214 | YBR257w | 3 | 0.333 | 47 | YBR302c | 7 | 0.524 | 458 |
| YBR217w | 9 | 0.139 | 614 | YBR258c | 3 | 0.000 | 227 | YCL001w | 3 | 0.000 | 283 |
| YBR218c | 3 | 1.000 | 0 | YBR259w | 2 | 0.000 | 20 | YCL001w-a | 1 | 0.000 | 0 |
| YBR219c | 4 | 0.667 | 19 | YBR260c | 5 | 0.400 | 108 | YCL002c | 4 | 0.500 | 66 |
| YBR220c | 1 | 0.000 | 0 | YBR261c | 2 | 0.000 | 42 | YCL004w | 3 | 0.333 | 126 |
| YBR221c | 3 | 0.667 | 48 | YBR262c | 2 | 0.000 | 24 | YCL005w | 1 | 0.000 | 0 |
| YBR222c | 8 | 0.107 | 711 | YBR263w | 2 | 1.000 | 0 | YCL007c | 2 | 1.000 | 0 |
| YBR223c | 2 | 1.000 | 0 | YBR264c | 3 | 0.000 | 164 | YCL008c | 3 | 0.667 | 34 |
| YBR224w | 3 | 0.333 | 57 | YBR265w | 5 | 0.500 | 222 | YCL009c | 8 | 0.357 | 378 |
| YBR225w | 3 | 0.333 | 84 | YBR266c | 4 | 0.000 | 161 | YCL010c | 2 | 1.000 | 0 |
| YBR226c | 1 | 0.000 | 0 | YBR267w | 5 | 0.100 | 229 | YCL011c | 2 | 0.000 | 97 |
| YBR227c | 1 | 0.000 | 0 | YBR268w | 5 | 0.200 | 202 | YCL012w | 1 | 0.000 | 0 |
| YBR228w | 1 | 0.000 | 0 | YBR269c | 1 | 0.000 | 0 | YCL014w | 6 | 0.200 | 460 |
| YBR229c | 6 | 0.200 | 157 | YBR270c | 1 | 0.000 | 0 | YCL016c | 2 | 0.000 | 65 |
| YBR230c | 11 | 0.255 | 517 | YBR271w | 4 | 0.167 | 364 | YCL017c | 4 | 0.167 | 344 |
| YBR230w-a | 1 | 0.000 | 0 | YBR272c | 1 | 0.000 | 0 | YCL018w | 14 | 0.231 | 2236 |
| YBR231c | 3 | 0.333 | 92 | YBR273c | 4 | 0.333 | 133 | YCL019w | 3 | 0.667 | 10 |
| YBR232c | 2 | 1.000 | 0 | YBR274w | 2 | 0.000 | 25 | YCL020w | 3 | 0.333 | 185 |
| YBR233w | 4 | 0.500 | 314 | YBR275c | 14 | 0.099 | 645 | YCL021w-a | 2 | 1.000 | 0 |
| YBR233w-a | 4 | 0.500 | 257 | YBR276c | 1 | 0.000 | 0 | YCL022c | 1 | 0.000 | 0 |
| YBR234c | 2 | 0.000 | 39 | YBR278w | 1 | 0.000 | 0 | YCL023c | 1 | 0.000 | 0 |
| YBR235w | 4 | 0.167 | 171 | YBR279w | 3 | 0.000 | 167 | YCL024w | 11 | 0.218 | 1376 |
| YBR236c | 3 | 0.000 | 50 | YBR280c | 7 | 0.286 | 333 | YCL025c | 26 | 0.237 | 6432 |
| YBR237w | 3 | 0.000 | 50 | YBR281c | 3 | 1.000 | 0 | YCL026c-a | 13 | 0.282 | 1496 |
| YBR238c | 5 | 0.200 | 251 | YBR282w | 3 | 0.667 | 12 | YCL026c-b | 4 | 0.667 | 25 |
| YBR239c | 3 | 0.000 | 161 | YBR283c | 3 | 0.667 | 24 | YCL027w | 21 | 0.329 | 2826 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YCL028w | 5 | 0.300 | 569 | YCR001w | 1 | 0.000 | 0 | YCR039c | 18 | 0.131 | 3141 |
| YCL029c | 5 | 0.500 | 232 | YCR002c | 3 | 0.667 | 42 | YCR040w | 18 | 0.137 | 2441 |
| YCL030c | 14 | 0.264 | 1724 | YCR003w | 1 | 0.000 | 0 | YCR041w | 13 | 0.103 | 1426 |
| YCL031c | 7 | 0.143 | 1038 | YCR004c | 6 | 0.533 | 123 | YCR042c | 3 | 0.000 | 96 |
| YCL032w | 4 | 0.000 | 351 | YCR005c | 30 | 0.161 | 6452 | YCR043c | 3 | 0.000 | 66 |
| YCL033c | 3 | 0.000 | 278 | YCR006c | 6 | 0.267 | 191 | YCR044c | 5 | 0.300 | 339 |
| YCL034w | 3 | 0.667 | 13 | YCR007c | 1 | 0.000 | 0 | YCR045c | 6 | 0.333 | 268 |
| YCL035c | 8 | 0.429 | 302 | YCR008w | 4 | 0.500 | 61 | YCR046c | 1 | 0.000 | 0 |
| YCL036w | 7 | 0.286 | 180 | YCR009c | 4 | 0.500 | 245 | YCR047c | 3 | 0.333 | 48 |
| YCL037c | 8 | 0.250 | 305 | YCR010c | 21 | 0.324 | 5008 | YCR048w | 4 | 0.500 | 49 |
| YCL038c | 1 | 0.000 | 0 | YCR011c | 6 | 0.400 | 358 | YCR049c | 1 | 0.000 | 0 |
| YCL039w | 6 | 0.400 | 378 | YCR012w | 14 | 0.330 | 1131 | YCR050c | 2 | 1.000 | 0 |
| YCL040w | 22 | 0.247 | 3802 | YCR013c | 2 | 0.000 | 15 | YCR051w | 1 | 0.000 | 0 |
| YCL041c | 6 | 0.200 | 257 | YCR014c | 2 | 1.000 | 0 | YCR052w | 4 | 0.167 | 183 |
| YCL042w | 18 | 0.353 | 2052 | YCR015c | 3 | 0.333 | 85 | YCR053w | 8 | 0.214 | 1172 |
| YCL043c | 12 | 0.364 | 1097 | YCR016w | 3 | 0.667 | 87 | YCR057c | 10 | 0.178 | 1313 |
| YCL044c | 5 | 0.300 | 364 | YCR017c | 5 | 0.800 | 103 | YCR059c | 5 | 0.400 | 356 |
| YCL045c | 3 | 0.333 | 8 | YCR018c | 64 | 0.021 | 54006 | YCR060w | 2 | 1.000 | 0 |
| YCL046w | 3 | 0.333 | 13 | YCR018c-a | 36 | 0.159 | 5881 | YCR061w | 14 | 0.341 | 1299 |
| YCL047c | 1 | 0.000 | 0 | YCR019w | 34 | 0.176 | 5868 | YCR063w | 12 | 0.288 | 1222 |
| YCL048w | 2 | 0.000 | 51 | YCR020c | 8 | 0.321 | 1037 | YCR064c | 7 | 0.333 | 128 |
| YCL049c | 11 | 0.345 | 1696 | YCR020c-a | 6 | 0.000 | 452 | YCR065w | 277 | 0.012 | 332117 |
| YCL050c | 9 | 0.389 | 710 | YCR020w-b | 5 | 0.400 | 164 | YCR066w | 2 | 0.000 | 13 |
| YCL051w | 3 | 0.333 | 42 | YCR021c | 39 | 0.247 | 10649 | YCR067c | 3 | 0.333 | 43 |
| YCL052c | 4 | 0.167 | 122 | YCR022c | 5 | 0.200 | 146 | YCR068w | 5 | 0.600 | 88 |
| YCL054w | 12 | 0.227 | 843 | YCR023c | 4 | 0.500 | 128 | YCR069w | 5 | 0.200 | 559 |
| YCL055w | 47 | 0.125 | 44124 | YCR024c | 7 | 0.429 | 110 | YCR071c | 1 | 0.000 | 0 |
| YCL056c | 9 | 0.222 | 1077 | YCR024c-a | 15 | 0.248 | 2020 | YCR072c | 8 | 0.071 | 1771 |
| YCL057c-a | 1 | 0.000 | 0 | YCR024c-b | 3 | 0.333 | 29 | YCR073c | 8 | 0.179 | 441 |
| YCL057w | 8 | 0.286 | 625 | YCR025c | 6 | 0.200 | 338 | YCR073w-a | 3 | 0.333 | 32 |
| YCL058c | 6 | 0.067 | 387 | YCR026c | 3 | 0.333 | 46 | YCR075c | 4 | 0.333 | 127 |
| YCL059c | 5 | 0.500 | 64 | YCR027c | 6 | 0.400 | 228 | YCR075w-a | 1 | 0.000 | 0 |
| YCL061c | 2 | 0.000 | 39 | YCR028c | 15 | 0.143 | 932 | YCR076c | 3 | 0.000 | 39 |
| YCL063w | 9 | 0.083 | 1424 | YCR028c-a | 3 | 0.000 | 102 | YCR077c | 3 | 0.333 | 34 |
| YCL064c | 25 | 0.157 | 5839 | YCR030c | 1 | 0.000 | 0 | YCR079w | 4 | 0.333 | 68 |
| YCL065w | 31 | 0.133 | 7428 | YCR031c | 12 | 0.409 | 1056 | YCR081w | 5 | 0.100 | 263 |
| YCL066w | 23 | 0.170 | 7574 | YCR032w | 9 | 0.167 | 478 | YCR082w | 7 | 0.143 | 1215 |
| YCL067c | 28 | 0.167 | 10786 | YCR033w | 2 | 1.000 | 0 | YCR083w | 5 | 0.600 | 47 |
| YCL068c | 6 | 0.200 | 165 | YCR034w | 4 | 0.000 | 245 | YCR084c | 2 | 0.000 | 35 |
| YCL069w | 8 | 0.214 | 340 | YCR035c | 3 | 0.333 | 191 | YCR086w | 3 | 0.000 | 114 |
| YCL073c | 1 | 0.000 | 0 | YCR036w | 3 | 0.333 | 191 | YCR087c-a | 5 | 0.500 | 105 |
| YCL074w | 9 | 0.250 | 575 | YCR037c | 5 | 0.000 | 397 | YCR087w | 2 | 0.000 | 16 |
| YCL075w | 3 | 0.333 | 10 | YCR038c | 2 | 0.000 | 1 | YCR088w | 5 | 0.500 | 306 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YCR089w | 16 | 0.417 | 1295 | YDL025c | 5 | 0.400 | 157 | YDL069c | 1 | 0.000 | 0 |
| YCR090c | 1 | 0.000 | 0 | YDL026w | 4 | 0.333 | 219 | YDL070w | 11 | 0.145 | 2070 |
| YCR091w | 1 | 0.000 | 0 | YDL027c | 4 | 0.500 | 42 | YDL071c | 7 | 0.048 | 302 |
| YCR092c | 6 | 0.333 | 582 | YDL028c | 2 | 0.000 | 73 | YDL072c | 5 | 0.400 | 654 |
| YCR093w | 9 | 0.250 | 962 | YDL029w | 3 | 0.333 | 16 | YDL073w | 2 | 0.000 | 22 |
| YCR094w | 11 | 0.073 | 1362 | YDL030w | 4 | 0.167 | 188 | YDL074c | 4 | 0.000 | 216 |
| YCR095c | 11 | 0.091 | 661 | YDL031w | 5 | 0.300 | 185 | YDL075w | 23 | 0.213 | 3248 |
| YCR096c | 29 | 0.148 | 6399 | YDL032w | 4 | 0.167 | 181 | YDL076c | 9 | 0.194 | 504 |
| YCR097w | 25 | 0.120 | 25202 | YDL033c | 1 | 0.000 | 0 | YDL078c | 9 | 0.361 | 287 |
| YCR097w-a | 2 | 1.000 | 0 | YDL034w | 8 | 0.107 | 1244 | YDL079c | 8 | 0.286 | 309 |
| YCR098c | 17 | 0.279 | 2699 | YDL035c | 5 | 0.100 | 285 | YDL080c | 3 | 0.333 | 60 |
| YCR099c | 5 | 0.300 | 162 | YDL036c | 6 | 0.067 | 646 | YDL081c | 10 | 0.356 | 1508 |
| YCR100c | 7 | 0.238 | 600 | YDL037c | 17 | 0.257 | 1231 | YDL082w | 14 | 0.407 | 1087 |
| YCR101c | 3 | 0.333 | 69 | YDL038c | 25 | 0.173 | 3006 | YDL083c | 14 | 0.352 | 1186 |
| YCR102c | 20 | 0.358 | 1662 | YDL039c | 16 | 0.200 | 2477 | YDL084w | 10 | 0.156 | 1271 |
| YCR102w-a | 2 | 0.000 | 57 | YDL040c | 1 | 0.000 | 0 | YDL085c-a | 3 | 0.667 | 13 |
| YCR104w | 19 | 0.146 | 1840 | YDL041w | 2 | 0.000 | 9 | YDL085w | 10 | 0.133 | 2398 |
| YCR105w | 35 | 0.134 | 6420 | YDL043c | 2 | 0.000 | 14 | YDL086w | 4 | 0.000 | 361 |
| YCR106w | 58 | 0.052 | 31098 | YDL044c | 7 | 0.000 | 351 | YDL087c | 1 | 0.000 | 0 |
| YCR107w | 27 | 0.191 | 4047 | YDL045w-a | 5 | 0.000 | 257 | YDL088c | 4 | 0.167 | 204 |
| YCR108c | 2 | 1.000 | 0 | YDL046w | 7 | 0.143 | 584 | YDL089w | 8 | 0.214 | 565 |
| YDL001w | 16 | 0.067 | 2035 | YDL047w | 10 | 0.578 | 374 | YDL090c | 9 | 0.167 | 839 |
| YDL003w | 4 | 0.500 | 60 | YDL048c | 16 | 0.550 | 848 | YDL091c | 12 | 0.136 | 1228 |
| YDL004w | 8 | 0.250 | 241 | YDL049c | 15 | 0.324 | 998 | YDL092w | 7 | 0.095 | 596 |
| YDL005c | 2 | 0.000 | 12 | YDL050c | 2 | 0.000 | 15 | YDL093w | 2 | 1.000 | 0 |
| YDL006w | 3 | 0.000 | 68 | YDL051w | 5 | 0.300 | 219 | YDL094c | 4 | 0.000 | 68 |
| YDL007w | 7 | 0.619 | 160 | YDL052c | 8 | 0.107 | 873 | YDL095w | 2 | 0.000 | 26 |
| YDL008w | 2 | 0.000 | 32 | YDL053c | 4 | 0.333 | 158 | YDL096c | 1 | 0.000 | 0 |
| YDL009c | 1 | 0.000 | 0 | YDL054c | 3 | 0.333 | 222 | YDL097c | 3 | 1.000 | 0 |
| YDL010w | 7 | 0.381 | 583 | YDL055c | 17 | 0.471 | 854 | YDL098c | 3 | 0.333 | 128 |
| YDL011c | 1 | 0.000 | 0 | YDL056w | 506 | 0.010 | 605184 | YDL099w | 4 | 0.500 | 86 |
| YDL012c | 6 | 0.267 | 825 | YDL057w | 5 | 0.500 | 206 | YDL100c | 4 | 0.167 | 87 |
| YDL013w | 4 | 0.000 | 67 | YDL058w | 6 | 0.400 | 268 | YDL101c | 5 | 0.400 | 37 |
| YDL014w | 8 | 0.286 | 734 | YDL059c | 8 | 0.286 | 264 | YDL102w | 11 | 0.200 | 1253 |
| YDL016c | 1 | 0.000 | 0 | YDL060w | 11 | 0.345 | 428 | YDL104c | 2 | 0.000 | 12 |
| YDL017w | 9 | 0.083 | 1254 | YDL061c | 9 | 0.472 | 530 | YDL105w | 3 | 0.000 | 207 |
| YDL018c | 10 | 0.178 | 805 | YDL062w | 3 | 0.000 | 152 | YDL106c | 170 | 0.010 | 169704 |
| YDL019c | 6 | 0.333 | 1179 | YDL063c | 8 | 0.286 | 772 | YDL107w | 3 | 0.000 | 72 |
| YDL020c | 1033 | 0.007 | 1949936 | YDL064w | 4 | 0.167 | 381 | YDL108w | 3 | 0.333 | 25 |
| YDL021w | 26 | 0.280 | 2864 | YDL065c | 2 | 0.000 | 48 | YDL109c | 2 | 1.000 | 0 |
| YDL022w | 17 | 0.294 | 1523 | YDL066w | 9 | 0.250 | 195 | YDL110c | 15 | 0.200 | 1199 |
| YDL023c | 2 | 0.000 | 26 | YDL067c | 9 | 0.167 | 190 | YDL111c | 1 | 0.000 | 0 |
| YDL024c | 12 | 0.242 | 952 | YDL068w | 8 | 0.107 | 401 | YDL112w | 4 | 0.333 | 300 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDL113c | 2 | 0.000 | 48 | YDL154w | 9 | 0.028 | 588 | YDL197c | 3 | 0.333 | 130 |
| YDL114w | 8 | 0.250 | 629 | YDL155w | 12 | 0.182 | 1850 | YDL198c | 5 | 0.200 | 106 |
| YDL115c | 10 | 0.289 | 414 | YDL156w | 7 | 0.190 | 766 | YDL199c | 4 | 0.000 | 69 |
| YDL116w | 6 | 0.067 | 461 | YDL157c | 3 | 0.000 | 159 | YDL201w | 2 | 1.000 | 0 |
| YDL117w | 5 | 0.400 | 475 | YDL158c | 2 | 1.000 | 0 | YDL202w | 3 | 0.333 | 57 |
| YDL118w | 1 | 0.000 | 0 | YDL159w | 12 | 0.227 | 2088 | YDL203c | 1 | 0.000 | 0 |
| YDL119c | 4 | 0.000 | 78 | YDL159w-a | 4 | 0.333 | 38 | YDL204w | 13 | 0.449 | 854 |
| YDL120w | 6 | 0.333 | 287 | YDL160c | 11 | 0.200 | 1331 | YDL205c | 9 | 0.111 | 478 |
| YDL121c | 7 | 0.429 | 333 | YDL161w | 5 | 0.200 | 232 | YDL206w | 7 | 0.048 | 458 |
| YDL122w | 2 | 1.000 | 0 | YDL164c | 6 | 0.067 | 656 | YDL207w | 4 | 0.167 | 89 |
| YDL123w | 4 | 0.333 | 345 | YDL165w | 5 | 0.500 | 84 | YDL208w | 5 | 0.100 | 601 |
| YDL124w | 18 | 0.248 | 2471 | YDL166c | 4 | 0.500 | 47 | YDL209c | 3 | 0.000 | 225 |
| YDL125c | 9 | 0.194 | 855 | YDL167c | 6 | 0.467 | 147 | YDL210w | 14 | 0.242 | 1665 |
| YDL126c | 11 | 0.291 | 1215 | YDL168w | 9 | 0.500 | 256 | YDL211c | 8 | 0.321 | 784 |
| YDL127w | 14 | 0.516 | 550 | YDL169c | 7 | 0.476 | 232 | YDL212w | 2 | 0.000 | 7 |
| YDL128w | 7 | 0.333 | 273 | YDL170w | 122 | 0.033 | 125393 | YDL213c | 5 | 0.500 | 139 |
| YDL129w | 11 | 0.200 | 1198 | YDL171c | 11 | 0.164 | 1798 | YDL214c | 12 | 0.515 | 358 |
| YDL130w | 11 | 0.382 | 960 | YDL172c | 1 | 0.000 | 0 | YDL215c | 10 | 0.222 | 1479 |
| YDL130w-a | 7 | 0.190 | 1002 | YDL173w | 10 | 0.356 | 526 | YDL216c | 4 | 0.333 | 190 |
| YDL131w | 7 | 0.429 | 1003 | YDL174c | 19 | 0.257 | 1702 | YDL217c | 5 | 0.100 | 163 |
| YDL132w | 4 | 0.000 | 140 | YDL175c | 4 | 0.000 | 244 | YDL218w | 6 | 0.533 | 295 |
| YDL133c-a | 5 | 0.300 | 71 | YDL176w | 9 | 0.056 | 598 | YDL219w | 3 | 0.333 | 50 |
| YDL133w | 5 | 0.400 | 111 | YDL177c | 5 | 0.100 | 479 | YDL220c | 5 | 0.300 | 140 |
| YDL134c | 4 | 0.333 | 124 | YDL178w | 5 | 0.200 | 379 | YDL221w | 1 | 0.000 | 0 |
| YDL135c | 21 | 0.171 | 3141 | YDL179w | 4 | 0.167 | 50 | YDL222c | 16 | 0.333 | 913 |
| YDL136w | 12 | 0.303 | 1268 | YDL180w | 10 | 0.178 | 516 | YDL223c | 21 | 0.233 | 1811 |
| YDL137w | 11 | 0.182 | 2516 | YDL181w | 13 | 0.192 | 490 | YDL224c | 7 | 0.333 | 233 |
| YDL138w | 5 | 0.200 | 466 | YDL182w | 17 | 0.338 | 1924 | YDL225w | 6 | 0.133 | 313 |
| YDL139c | 4 | 0.500 | 28 | YDL183c | 12 | 0.439 | 791 | YDL226c | 4 | 0.167 | 123 |
| YDL140c | 5 | 0.500 | 315 | YDL184c | 10 | 0.356 | 837 | YDL227c | 22 | 0.203 | 7286 |
| YDL141w | 7 | 0.286 | 332 | YDL185c-a | 2 | 0.000 | 10 | YDL228c | 1 | 0.000 | 0 |
| YDL142c | 7 | 0.286 | 409 | YDL185w | 7 | 0.238 | 357 | YDL229w | 6 | 0.267 | 237 |
| YDL143w | 4 | 0.167 | 107 | YDL186w | 5 | 0.200 | 446 | YDL230w | 9 | 0.222 | 322 |
| YDL144c | 3 | 0.333 | 37 | YDL187c | 2 | 0.000 | 12 | YDL231c | 2 | 0.000 | 15 |
| YDL145c | 10 | 0.311 | 1102 | YDL188c | 4 | 0.333 | 315 | YDL232w | 2 | 0.000 | 88 |
| YDL146w | 5 | 0.100 | 207 | YDL189w | 6 | 0.067 | 676 | YDL233w | 5 | 0.200 | 292 |
| YDL147w | 7 | 0.476 | 890 | YDL190c | 4 | 0.500 | 357 | YDL234c | 5 | 0.000 | 189 |
| YDL148c | 6 | 0.400 | 421 | YDL191w | 11 | 0.291 | 916 | YDL235c | 4 | 0.333 | 85 |
| YDL149w | 11 | 0.091 | 896 | YDL192w | 10 | 0.289 | 654 | YDL236w | 1 | 0.000 | 0 |
| YDL150w | 2 | 0.000 | 145 | YDL193w | 10 | 0.089 | 972 | YDL237w | 7 | 0.333 | 580 |
| YDL151c | 3 | 0.333 | 35 | YDL194w | 4 | 0.333 | 272 | YDL238c | 7 | 0.333 | 723 |
| YDL152w | 2 | 0.000 | 5 | YDL195w | 2 | 0.000 | 9 | YDL239c | 8 | 0.214 | 416 |
| YDL153c | 3 | 0.333 | 45 | YDL196w | 5 | 0.300 | 92 | YDL240w | 6 | 0.533 | 110 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDL241w | 15 | 0.171 | 930 | YDR034c-c | 1 | 0.000 | 0 | YDR076w | 9 | 0.528 | 100 |
| YDL242w | 5 | 0.500 | 92 | YDR034w-b | 28 | 0.172 | 5741 | YDR077w | 43 | 0.244 | 8960 |
| YDL243c | 6 | 0.333 | 225 | YDR035w | 7 | 0.238 | 483 | YDR078c | 6 | 0.067 | 287 |
| YDL244w | 11 | 0.273 | 2198 | YDR036c | 6 | 0.533 | 180 | YDR079w | 7 | 0.190 | 275 |
| YDL245c | 16 | 0.292 | 1919 | YDR037w | 7 | 0.571 | 260 | YDR080w | 4 | 0.333 | 79 |
| YDL246c | 19 | 0.351 | 678 | YDR038c | 9 | 0.222 | 914 | YDR081c | 19 | 0.082 | 13056 |
| YDL247w | 6 | 0.133 | 381 | YDR039c | 9 | 0.222 | 634 | YDR082w | 1 | 0.000 | 0 |
| YDL248w | 8 | 0.321 | 1110 | YDR040c | 30 | 0.239 | 4332 | YDR083w | 9 | 0.167 | 676 |
| YDR001c | 12 | 0.197 | 1622 | YDR041w | 24 | 0.308 | 2230 | YDR084c | 31 | 0.118 | 5438 |
| YDR002w | 4 | 0.167 | 231 | YDR042c | 46 | 0.132 | 17451 | YDR085c | 11 | 0.236 | 998 |
| YDR003w | 9 | 0.194 | 4399 | YDR043c | 425 | 0.028 | 474296 | YDR086c | 11 | 0.200 | 1616 |
| YDR004w | 7 | 0.095 | 694 | YDR044w | 20 | 0.326 | 2612 | YDR087c | 1 | 0.000 | 0 |
| YDR005c | 1 | 0.000 | 0 | YDR045c | 5 | 0.000 | 198 | YDR088c | 5 | 0.200 | 2217 |
| YDR006c | 6 | 0.000 | 353 | YDR046c | 12 | 0.167 | 2089 | YDR089w | 15 | 0.381 | 2423 |
| YDR007w | 8 | 0.214 | 768 | YDR047w | 5 | 0.100 | 217 | YDR090c | 3 | 0.000 | 67 |
| YDR008c | 4 | 0.000 | 199 | YDR048c | 9 | 0.083 | 661 | YDR091c | 4 | 0.333 | 110 |
| YDR009w | 9 | 0.306 | 929 | YDR049w | 8 | 0.107 | 273 | YDR092w | 6 | 0.467 | 218 |
| YDR010c | 14 | 0.220 | 1115 | YDR050c | 11 | 0.291 | 1634 | YDR093w | 4 | 0.667 | 50 |
| YDR011w | 26 | 0.246 | 5038 | YDR051c | 3 | 0.333 | 95 | YDR094w | 1 | 0.000 | 0 |
| YDR012w | 9 | 0.500 | 619 | YDR052c | 6 | 0.133 | 150 | YDR096w | 194 | 0.022 | 76429 |
| YDR013w | 5 | 0.400 | 88 | YDR053w | 2 | 0.000 | 6 | YDR097c | 4 | 0.000 | 301 |
| YDR014w | 1 | 0.000 | 0 | YDR054c | 9 | 0.194 | 641 | YDR098c | 7 | 0.476 | 2454 |
| YDR015c | 2 | 1.000 | 0 | YDR055w | 19 | 0.281 | 1664 | YDR098c-a | 6 | 0.267 | 214 |
| YDR016c | 2 | 1.000 | 0 | YDR056c | 2 | 0.000 | 11 | YDR098c-b | 6 | 0.267 | 214 |
| YDR017c | 2 | 0.000 | 28 | YDR057w | 4 | 0.333 | 213 | YDR099w | 3 | 0.667 | 3 |
| YDR018c | 7 | 0.095 | 334 | YDR058c | 9 | 0.250 | 3626 | YDR100w | 6 | 0.200 | 441 |
| YDR019c | 9 | 0.389 | 759 | YDR059c | 3 | 0.000 | 44 | YDR101c | 7 | 0.143 | 771 |
| YDR020c | 3 | 0.333 | 62 | YDR060w | 5 | 0.500 | 109 | YDR102c | 7 | 0.190 | 426 |
| YDR021w | 4 | 0.500 | 89 | YDR061w | 8 | 0.179 | 536 | YDR103w | 11 | 0.145 | 1166 |
| YDR022c | 3 | 0.000 | 178 | YDR062w | 3 | 0.667 | 17 | YDR104c | 4 | 0.167 | 148 |
| YDR023w | 7 | 0.286 | 567 | YDR063w | 10 | 0.200 | 851 | YDR105c | 1 | 0.000 | 0 |
| YDR024w | 3 | 0.333 | 27 | YDR064w | 12 | 0.258 | 2418 | YDR106w | 2 | 0.000 | 31 |
| YDR025w | 9 | 0.222 | 621 | YDR065w | 9 | 0.222 | 798 | YDR107c | 5 | 0.200 | 112 |
| YDR026c | 3 | 0.000 | 105 | YDR066c | 4 | 0.167 | 127 | YDR108w | 2 | 0.000 | 86 |
| YDR027c | 3 | 0.000 | 326 | YDR067c | 12 | 0.167 | 1068 | YDR109c | 2 | 0.000 | 61 |
| YDR028c | 8 | 0.143 | 772 | YDR068w | 12 | 0.167 | 1068 | YDR110w | 5 | 0.100 | 387 |
| YDR029w | 4 | 0.000 | 372 | YDR069c | 2 | 1.000 | 0 | YDR111c | 6 | 0.467 | 148 |
| YDR030c | 19 | 0.187 | 1489 | YDR070c | 19 | 0.228 | 2064 | YDR112w | 2 | 1.000 | 0 |
| YDR031w | 15 | 0.124 | 757 | YDR071c | 4 | 0.000 | 72 | YDR113c | 9 | 0.278 | 2002 |
| YDR032c | 9 | 0.194 | 257 | YDR072c | 8 | 0.321 | 364 | YDR114c | 2 | 0.000 | 11 |
| YDR033w | 13 | 0.231 | 1365 | YDR073w | 8 | 0.429 | 179 | YDR115w | 4 | 0.167 | 45 |
| YDR034c | 12 | 0.288 | 664 | YDR074w | 15 | 0.200 | 1511 | YDR117c | 2 | 0.000 | 163 |
| YDR034c-a | 1 | 0.000 | 0 | YDR075w | 6 | 0.067 | 742 | YDR118w | 5 | 0.100 | 248 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDR119w | 3 | 0.333 | 110 | YDR164c | 3 | 0.000 | 158 | YDR205w | 1 | 0.000 | 0 |
| YDR120c | 2 | 0.000 | 10 | YDR165w | 6 | 0.267 | 519 | YDR207c | 266 | 0.015 | 339144 |
| YDR121w | 1 | 0.000 | 0 | YDR166c | 1 | 0.000 | 0 | YDR208w | 11 | 0.164 | 1580 |
| YDR122w | 4 | 0.333 | 67 | YDR167w | 2 | 0.000 | 175 | YDR210c-c | 3 | 0.667 | 6 |
| YDR123c | 168 | 0.021 | 77869 | YDR168w | 3 | 0.000 | 77 | YDR210c-d | 19 | 0.111 | 1533 |
| YDR124w | 7 | 0.333 | 251 | YDR169c | 8 | 0.393 | 423 | YDR210w | 10 | 0.289 | 760 |
| YDR125c | 6 | 0.200 | 385 | YDR169c-a | 3 | 0.667 | 31 | YDR210w-c | 2 | 1.000 | 0 |
| YDR126w | 3 | 0.000 | 51 | YDR170c | 4 | 0.333 | 50 | YDR210w-d | 5 | 0.300 | 92 |
| YDR127w | 10 | 0.178 | 598 | YDR170w-a | 3 | 0.333 | 31 | YDR211w | 5 | 0.500 | 100 |
| YDR128w | 3 | 0.333 | 47 | YDR171w | 30 | 0.260 | 6233 | YDR212w | 3 | 0.333 | 30 |
| YDR129c | 5 | 0.000 | 172 | YDR172w | 4 | 0.167 | 799 | YDR213w | 215 | 0.018 | 151526 |
| YDR130c | 2 | 1.000 | 0 | YDR173c | 2 | 1.000 | 0 | YDR214w | 11 | 0.218 | 1800 |
| YDR131c | 8 | 0.107 | 434 | YDR174w | 4 | 0.333 | 81 | YDR215c | 3 | 0.333 | 80 |
| YDR132c | 13 | 0.321 | 844 | YDR175c | 1 | 0.000 | 0 | YDR216w | 458 | 0.013 | 589228 |
| YDR133c | 9 | 0.333 | 292 | YDR176w | 2 | 0.000 | 19 | YDR217c | 2 | 1.000 | 0 |
| YDR134c | 12 | 0.379 | 387 | YDR177w | 1 | 0.000 | 0 | YDR218c | 3 | 0.667 | 8 |
| YDR135c | 8 | 0.393 | 504 | YDR178w | 10 | 0.222 | 557 | YDR219c | 2 | 0.000 | 33 |
| YDR136c | 5 | 0.700 | 97 | YDR179c | 22 | 0.126 | 2877 | YDR220c | 2 | 0.000 | 10 |
| YDR137w | 6 | 0.333 | 357 | YDR179w-a | 16 | 0.150 | 1603 | YDR221w | 3 | 1.000 | 0 |
| YDR138w | 5 | 0.400 | 144 | YDR180w | 2 | 0.000 | 1 | YDR222w | 11 | 0.218 | 1004 |
| YDR139c | 2 | 1.000 | 0 | YDR181c | 3 | 0.333 | 34 | YDR223w | 7 | 0.143 | 466 |
| YDR140w | 2 | 0.000 | 27 | YDR182w | 3 | 0.333 | 40 | YDR224c | 6 | 0.133 | 261 |
| YDR141c | 2 | 0.000 | 63 | YDR182w-a | 2 | 0.000 | 31 | YDR225w | 7 | 0.143 | 2504 |
| YDR142c | 3 | 0.000 | 52 | YDR183w | 12 | 0.121 | 1235 | YDR226w | 7 | 0.333 | 229 |
| YDR143c | 2 | 0.000 | 65 | YDR184c | 7 | 0.238 | 586 | YDR227w | 8 | 0.179 | 858 |
| YDR144c | 16 | 0.175 | 3404 | YDR185c | 5 | 0.500 | 204 | YDR228c | 5 | 0.200 | 149 |
| YDR145w | 14 | 0.110 | 1930 | YDR186c | 11 | 0.255 | 2334 | YDR229w | 6 | 0.400 | 133 |
| YDR146c | 240 | 0.028 | 286695 | YDR187c | 3 | 0.000 | 84 | YDR231c | 3 | 0.667 | 15 |
| YDR147w | 10 | 0.200 | 773 | YDR188w | 8 | 0.357 | 269 | YDR232w | 8 | 0.036 | 189 |
| YDR148c | 8 | 0.071 | 207 | YDR189w | 6 | 0.400 | 359 | YDR233c | 3 | 0.333 | 212 |
| YDR150w | 4 | 0.167 | 107 | YDR190c | 6 | 0.267 | 231 | YDR234w | 7 | 0.286 | 771 |
| YDR151c | 8 | 0.429 | 259 | YDR191w | 8 | 0.214 | 623 | YDR235w | 3 | 0.333 | 131 |
| YDR152w | 10 | 0.333 | 4641 | YDR192c | 6 | 0.267 | 122 | YDR236c | 2 | 1.000 | 0 |
| YDR153c | 3 | 0.333 | 18 | YDR193w | 1 | 0.000 | 0 | YDR237w | 2 | 1.000 | 0 |
| YDR154c | 12 | 0.333 | 874 | YDR194c | 3 | 0.000 | 135 | YDR239c | 2 | 0.000 | 89 |
| YDR155c | 16 | 0.158 | 2389 | YDR195w | 3 | 0.333 | 97 | YDR240c | 6 | 0.400 | 188 |
| YDR156w | 14 | 0.253 | 1769 | YDR197w | 3 | 0.333 | 213 | YDR241w | 1 | 0.000 | 0 |
| YDR157w | 9 | 0.194 | 561 | YDR198c | 1 | 0.000 | 0 | YDR242w | 4 | 0.167 | 63 |
| YDR158w | 12 | 0.227 | 884 | YDR199w | 1 | 0.000 | 0 | YDR243c | 2 | 0.000 | 15 |
| YDR159w | 3 | 0.000 | 99 | YDR200c | 2 | 1.000 | 0 | YDR244w | 14 | 0.099 | 5278 |
| YDR160w | 3 | 0.333 | 67 | YDR201w | 3 | 0.667 | 51 | YDR245w | 8 | 0.107 | 1258 |
| YDR161w | 5 | 0.300 | 196 | YDR202c | 1 | 0.000 | 0 | YDR246w | 9 | 0.306 | 854 |
| YDR163w | 3 | 1.000 | 0 | YDR204w | 2 | 0.000 | 15 | YDR246w-a | 4 | 0.500 | 21 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDR247w | 4 | 0.333 | 66 | YDR290w | 1 | 0.000 | 0 | YDR332w | 5 | 0.000 | 57 |
| YDR248c | 2 | 1.000 | 0 | YDR291w | 1 | 0.000 | 0 | YDR333c | 3 | 0.667 | 57 |
| YDR249c | 3 | 0.667 | 36 | YDR292c | 4 | 0.000 | 91 | YDR334w | 4 | 0.833 | 24 |
| YDR250c | 4 | 0.500 | 96 | YDR293c | 3 | 0.667 | 23 | YDR335w | 1 | 0.000 | 0 |
| YDR251w | 6 | 0.400 | 157 | YDR294c | 10 | 0.089 | 1213 | YDR336w | 1 | 0.000 | 0 |
| YDR252w | 1 | 0.000 | 0 | YDR295c | 1 | 0.000 | 0 | YDR337w | 2 | 0.000 | 8 |
| YDR253c | 102 | 0.024 | 31538 | YDR296w | 2 | 1.000 | 0 | YDR338c | 2 | 1.000 | 0 |
| YDR254w | 6 | 0.267 | 105 | YDR297w | 16 | 0.275 | 1877 | YDR339c | 3 | 0.000 | 325 |
| YDR255c | 2 | 0.000 | 19 | YDR298c | 9 | 0.222 | 168 | YDR340w | 2 | 0.000 | 37 |
| YDR256c | 13 | 0.154 | 1199 | YDR299w | 6 | 0.133 | 82 | YDR341c | 7 | 0.048 | 524 |
| YDR257c | 6 | 0.200 | 537 | YDR300c | 7 | 0.381 | 388 | YDR342c | 19 | 0.304 | 4026 |
| YDR258c | 17 | 0.324 | 2688 | YDR301w | 6 | 0.200 | 336 | YDR343c | 25 | 0.330 | 2492 |
| YDR259c | 358 | 0.034 | 219573 | YDR302w | 2 | 1.000 | 0 | YDR345c | 28 | 0.302 | 3768 |
| YDR260c | 6 | 0.467 | 297 | YDR303c | 3 | 0.333 | 44 | YDR346c | 1 | 0.000 | 0 |
| YDR261c | 11 | 0.291 | 292 | YDR304c | 1 | 0.000 | 0 | YDR347w | 1 | 0.000 | 0 |
| YDR261w-b | 1 | 0.000 | 0 | YDR305c | 1 | 0.000 | 0 | YDR348c | 2 | 1.000 | 0 |
| YDR262w | 7 | 0.429 | 239 | YDR307w | 2 | 0.000 | 77 | YDR350c | 2 | 1.000 | 0 |
| YDR263c | 8 | 0.250 | 238 | YDR308c | 4 | 0.500 | 43 | YDR351w | 3 | 0.333 | 42 |
| YDR264c | 5 | 0.700 | 83 | YDR309c | 26 | 0.286 | 3026 | YDR352w | 1 | 0.000 | 0 |
| YDR265w | 5 | 0.400 | 129 | YDR310c | 162 | 0.009 | 226036 | YDR353w | 9 | 0.500 | 253 |
| YDR266c | 6 | 0.267 | 1207 | YDR311w | 7 | 0.286 | 1679 | YDR354w | 10 | 0.400 | 566 |
| YDR267c | 4 | 0.167 | 203 | YDR312w | 9 | 0.278 | 1337 | YDR355c | 2 | 1.000 | 0 |
| YDR268w | 4 | 0.167 | 174 | YDR313c | 7 | 0.238 | 224 | YDR356w | 4 | 0.167 | 398 |
| YDR270w | 5 | 0.400 | 34 | YDR314c | 5 | 0.100 | 166 | YDR357c | 3 | 0.333 | 32 |
| YDR271c | 2 | 1.000 | 0 | YDR315c | 5 | 0.200 | 218 | YDR358w | 3 | 0.333 | 21 |
| YDR272w | 5 | 0.500 | 52 | YDR316w | 4 | 0.000 | 173 | YDR359c | 2 | 0.000 | 25 |
| YDR273w | 5 | 0.000 | 514 | YDR316w-a | 5 | 0.600 | 51 | YDR360w | 1 | 0.000 | 0 |
| YDR274c | 7 | 0.476 | 173 | YDR316w-b | 5 | 0.600 | 51 | YDR361c | 7 | 0.333 | 720 |
| YDR275w | 8 | 0.536 | 215 | YDR317w | 15 | 0.105 | 1682 | YDR362c | 1 | 0.000 | 0 |
| YDR276c | 5 | 0.300 | 120 | YDR318w | 1 | 0.000 | 0 | YDR363w | 2 | 0.000 | 15 |
| YDR277c | 90 | 0.039 | 110053 | YDR319c | 3 | 0.667 | 19 | YDR363w-a | 7 | 0.476 | 791 |
| YDR278c | 10 | 0.133 | 597 | YDR320c | 2 | 0.000 | 14 | YDR364c | 1 | 0.000 | 0 |
| YDR279w | 11 | 0.164 | 831 | YDR321w | 6 | 0.267 | 1163 | YDR365c | 3 | 0.333 | 152 |
| YDR280w | 3 | 0.000 | 157 | YDR322c-a | 7 | 0.238 | 127 | YDR366c | 3 | 0.333 | 7 |
| YDR281c | 6 | 0.333 | 381 | YDR322w | 2 | 1.000 | 0 | YDR367w | 5 | 0.300 | 119 |
| YDR282c | 13 | 0.115 | 1182 | YDR323c | 8 | 0.036 | 498 | YDR368w | 7 | 0.190 | 270 |
| YDR283c | 5 | 0.200 | 481 | YDR324c | 8 | 0.286 | 505 | YDR369c | 3 | 0.000 | 61 |
| YDR284c | 12 | 0.121 | 1352 | YDR325w | 6 | 0.200 | 542 | YDR370c | 13 | 0.090 | 2442 |
| YDR285w | 6 | 0.267 | 267 | YDR326c | 2 | 0.000 | 64 | YDR371w | 10 | 0.067 | 919 |
| YDR286c | 11 | 0.109 | 910 | YDR327w | 2 | 0.000 | 103 | YDR372c | 24 | 0.072 | 2904 |
| YDR287w | 9 | 0.111 | 768 | YDR328c | 5 | 0.100 | 242 | YDR373w | 17 | 0.147 | 1112 |
| YDR288w | 2 | 0.000 | 36 | YDR329c | 2 | 0.000 | 42 | YDR374c | 3 | 0.333 | 50 |
| YDR289c | 1 | 0.000 | 0 | YDR330w | 2 | 0.000 | 70 | YDR375c | 3 | 0.000 | 105 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDR376w | 6 | 0.067 | 241 | YDR419w | 4 | 0.000 | 1619 | YDR463w | 238 | 0.012 | 200667 |
| YDR377w | 13 | 0.103 | 738 | YDR420w | 4 | 0.333 | 271 | YDR464w | 3 | 0.000 | 147 |
| YDR378c | 6 | 0.267 | 420 | YDR421w | 99 | 0.011 | 91373 | YDR465c | 8 | 0.143 | 326 |
| YDR379c-a | 3 | 0.333 | 122 | YDR422c | 3 | 0.333 | 189 | YDR466w | 2 | 0.000 | 7 |
| YDR379w | 8 | 0.286 | 618 | YDR423c | 492 | 0.007 | 562971 | YDR467c | 1 | 0.000 | 0 |
| YDR380w | 22 | 0.212 | 4591 | YDR424c | 4 | 0.167 | 104 | YDR468c | 6 | 0.067 | 378 |
| YDR381c-a | 2 | 1.000 | 0 | YDR425w | 1 | 0.000 | 0 | YDR469w | 4 | 0.167 | 142 |
| YDR381w | 2 | 1.000 | 0 | YDR426c | 3 | 0.000 | 88 | YDR470c | 8 | 0.321 | 611 |
| YDR382w | 9 | 0.472 | 655 | YDR427w | 4 | 0.667 | 98 | YDR471w | 20 | 0.284 | 3248 |
| YDR383c | 3 | 0.333 | 17 | YDR428c | 1 | 0.000 | 0 | YDR472w | 7 | 0.143 | 521 |
| YDR384c | 20 | 0.237 | 5504 | YDR429c | 2 | 0.000 | 88 | YDR473c | 25 | 0.140 | 3953 |
| YDR385w | 13 | 0.321 | 1607 | YDR430c | 1 | 0.000 | 0 | YDR474c | 3 | 0.000 | 105 |
| YDR386w | 1 | 0.000 | 0 | YDR432w | 4 | 0.667 | 46 | YDR475c | 4 | 0.333 | 50 |
| YDR387c | 2 | 0.000 | 17 | YDR433w | 4 | 0.167 | 63 | YDR476c | 6 | 0.200 | 559 |
| YDR388w | 3 | 0.333 | 27 | YDR434w | 6 | 0.133 | 528 | YDR477w | 2 | 0.000 | 17 |
| YDR389w | 6 | 0.533 | 98 | YDR435c | 3 | 0.667 | 6 | YDR478w | 1 | 0.000 | 0 |
| YDR390c | 2 | 0.000 | 36 | YDR436w | 2 | 1.000 | 0 | YDR479c | 2 | 0.000 | 87 |
| YDR391c | 9 | 0.389 | 1501 | YDR437w | 2 | 0.000 | 22 | YDR480w | 5 | 0.300 | 648 |
| YDR392w | 2 | 0.000 | 23 | YDR438w | 5 | 0.300 | 142 | YDR481c | 8 | 0.286 | 977 |
| YDR393w | 9 | 0.111 | 668 | YDR439w | 5 | 0.300 | 341 | YDR482c | 4 | 0.333 | 115 |
| YDR394w | 5 | 0.600 | 74 | YDR440w | 1 | 0.000 | 0 | YDR483w | 5 | 0.100 | 298 |
| YDR395w | 3 | 0.000 | 140 | YDR441c | 26 | 0.317 | 2094 | YDR484w | 4 | 0.167 | 108 |
| YDR396w | 2 | 0.000 | 43 | YDR442w | 19 | 0.287 | 1112 | YDR485c | 1 | 0.000 | 0 |
| YDR397c | 2 | 0.000 | 47 | YDR443c | 2 | 0.000 | 26 | YDR486c | 7 | 0.286 | 591 |
| YDR398w | 4 | 0.500 | 23 | YDR444w | 2 | 0.000 | 189 | YDR487c | 8 | 0.500 | 472 |
| YDR399w | 10 | 0.378 | 325 | YDR445c | 1 | 0.000 | 0 | YDR488c | 4 | 0.167 | 94 |
| YDR400w | 3 | 0.333 | 27 | YDR446w | 8 | 0.357 | 247 | YDR489w | 2 | 0.000 | 9 |
| YDR401w | 1 | 0.000 | 0 | YDR447c | 10 | 0.444 | 392 | YDR490c | 3 | 0.333 | 32 |
| YDR402c | 12 | 0.167 | 1224 | YDR448w | 8 | 0.179 | 349 | YDR491c | 1 | 0.000 | 0 |
| YDR403w | 20 | 0.226 | 3717 | YDR449c | 12 | 0.288 | 802 | YDR492w | 13 | 0.154 | 973 |
| YDR404c | 5 | 0.300 | 360 | YDR450w | 10 | 0.356 | 913 | YDR493w | 3 | 0.667 | 19 |
| YDR405w | 6 | 0.333 | 492 | YDR451c | 326 | 0.023 | 443477 | YDR494w | 7 | 0.048 | 251 |
| YDR406w | 20 | 0.174 | 2926 | YDR452w | 17 | 0.287 | 1356 | YDR495c | 12 | 0.152 | 709 |
| YDR407c | 5 | 0.100 | 164 | YDR453c | 19 | 0.251 | 950 | YDR496c | 8 | 0.357 | 547 |
| YDR408c | 8 | 0.321 | 794 | YDR454c | 7 | 0.333 | 602 | YDR497c | 8 | 0.321 | 419 |
| YDR409w | 3 | 0.000 | 71 | YDR455c | 5 | 0.100 | 369 | YDR498c | 6 | 0.267 | 582 |
| YDR410c | 5 | 0.100 | 474 | YDR456w | 4 | 0.500 | 127 | YDR499w | 4 | 0.333 | 294 |
| YDR411c | 4 | 0.167 | 167 | YDR457w | 10 | 0.200 | 996 | YDR500c | 17 | 0.316 | 1902 |
| YDR412w | 4 | 0.333 | 202 | YDR458c | 1 | 0.000 | 0 | YDR501w | 210 | 0.015 | 363000 |
| YDR415c | 3 | 0.000 | 37 | YDR459c | 3 | 0.000 | 26 | YDR502c | 7 | 0.143 | 760 |
| YDR416w | 6 | 0.133 | 203 | YDR460w | 3 | 0.333 | 237 | YDR503c | 4 | 0.167 | 102 |
| YDR417c | 3 | 0.667 | 13 | YDR461w | 19 | 0.374 | 1769 | YDR504c | 3 | 0.667 | 2 |
| YDR418w | 11 | 0.382 | 1207 | YDR462w | 2 | 0.000 | 45 | YDR505c | 2 | 0.000 | 9 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YDR506c | 3 | 0.000 | 36 | YDR545w | 28 | 0.183 | 2188 | YEL041w | 13 | 0.359 | 478 |
| YDR507c | 6 | 0.400 | 144 | YEL001c | 15 | 0.286 | 1715 | YEL042w | 5 | 0.100 | 132 |
| YDR508c | 17 | 0.279 | 1671 | YEL002c | 7 | 0.048 | 885 | YEL043w | 3 | 0.000 | 69 |
| YDR509w | 9 | 0.167 | 548 | YEL003w | 3 | 1.000 | 0 | YEL044w | 25 | 0.260 | 4523 |
| YDR510w | 21 | 0.290 | 2622 | YEL004w | 11 | 0.182 | 1312 | YEL045c | 22 | 0.208 | 3602 |
| YDR511w | 4 | 0.000 | 230 | YEL005c | 9 | 0.083 | 742 | YEL046c | 25 | 0.207 | 5077 |
| YDR512c | 7 | 0.095 | 337 | YEL006w | 1 | 0.000 | 0 | YEL047c | 11 | 0.291 | 547 |
| YDR513w | 5 | 0.600 | 37 | YEL007w | 19 | 0.433 | 1716 | YEL048c | 1 | 0.000 | 0 |
| YDR514c | 5 | 0.500 | 292 | YEL008w | 10 | 0.311 | 323 | YEL049w | 5 | 0.100 | 169 |
| YDR515w | 5 | 0.300 | 238 | YEL009c | 585 | 0.012 | 839314 | YEL050c | 12 | 0.227 | 971 |
| YDR516c | 14 | 0.374 | 843 | YEL010w | 8 | 0.143 | 173 | YEL051w | 3 | 0.667 | 11 |
| YDR517w | 4 | 0.333 | 63 | YEL011w | 21 | 0.400 | 1207 | YEL052w | 5 | 0.600 | 89 |
| YDR518w | 6 | 0.600 | 92 | YEL012w | 10 | 0.156 | 689 | YEL053c | 4 | 1.000 | 0 |
| YDR519w | 4 | 0.000 | 247 | YEL013w | 4 | 0.000 | 210 | YEL054c | 14 | 0.363 | 872 |
| YDR520c | 4 | 0.167 | 98 | YEL014c | 1 | 0.000 | 0 | YEL055c | 7 | 0.238 | 720 |
| YDR521w | 2 | 0.000 | 9 | YEL015w | 3 | 0.000 | 97 | YEL056w | 7 | 0.190 | 860 |
| YDR522c | 22 | 0.134 | 2395 | YEL016c | 6 | 0.133 | 562 | YEL057c | 8 | 0.357 | 466 |
| YDR523c | 17 | 0.221 | 5698 | YEL017c-a | 9 | 0.361 | 789 | YEL058w | 6 | 0.267 | 240 |
| YDR524c | 4 | 0.500 | 9 | YEL017w | 7 | 0.619 | 293 | YEL059c-a | 3 | 1.000 | 0 |
| YDR524c-b | 9 | 0.417 | 220 | YEL018w | 3 | 0.000 | 422 | YEL059w | 7 | 0.190 | 212 |
| YDR524w-a | 1 | 0.000 | 0 | YEL019c | 2 | 0.000 | 4 | YEL060c | 29 | 0.148 | 5192 |
| YDR524w-c | 1 | 0.000 | 0 | YEL020c | 3 | 0.333 | 96 | YEL061c | 5 | 0.300 | 661 |
| YDR525w | 9 | 0.111 | 255 | YEL020w-a | 10 | 0.444 | 441 | YEL062w | 14 | 0.220 | 1383 |
| YDR525w-a | 19 | 0.333 | 1810 | YEL021w | 18 | 0.248 | 2828 | YEL063c | 10 | 0.422 | 619 |
| YDR526c | 7 | 0.333 | 189 | YEL022w | 6 | 0.200 | 598 | YEL064c | 2 | 0.000 | 7 |
| YDR527w | 12 | 0.212 | 715 | YEL023c | 6 | 0.200 | 598 | YEL065w | 20 | 0.205 | 2595 |
| YDR528w | 15 | 0.238 | 990 | YEL024w | 15 | 0.238 | 834 | YEL066w | 2 | 1.000 | 0 |
| YDR529c | 9 | 0.139 | 254 | YEL025c | 8 | 0.071 | 234 | YEL067c | 3 | 0.333 | 119 |
| YDR530c | 5 | 0.300 | 225 | YEL026w | 7 | 0.524 | 177 | YEL068c | 2 | 0.000 | 20 |
| YDR531w | 7 | 0.381 | 355 | YEL027w | 4 | 0.167 | 148 | YEL069c | 11 | 0.418 | 517 |
| YDR532c | 2 | 0.000 | 48 | YEL028w | 1 | 0.000 | 0 | YEL070w | 22 | 0.316 | 1639 |
| YDR533c | 32 | 0.280 | 3844 | YEL029c | 2 | 0.000 | 36 | YEL071w | 22 | 0.294 | 2757 |
| YDR534c | 9 | 0.306 | 428 | YEL030w | 4 | 0.333 | 98 | YEL072w | 14 | 0.165 | 1155 |
| YDR535c | 5 | 0.100 | 139 | YEL031w | 3 | 0.000 | 138 | YEL073c | 10 | 0.267 | 742 |
| YDR536w | 17 | 0.147 | 1594 | YEL032w | 5 | 0.500 | 77 | YEL074w | 12 | 0.348 | 840 |
| YDR537c | 1 | 0.000 | 0 | YEL033w | 4 | 0.167 | 38 | YEL075c | 7 | 0.476 | 90 |
| YDR538w | 1 | 0.000 | 0 | YEL034w | 7 | 0.667 | 151 | YEL076c | 5 | 0.100 | 78 |
| YDR539w | 4 | 0.000 | 51 | YEL035c | 13 | 0.359 | 1005 | YEL076c-a | 6 | 0.133 | 134 |
| YDR540c | 5 | 0.300 | 229 | YEL036c | 6 | 0.733 | 32 | YEL076w-c | 2 | 0.000 | 2 |
| YDR541c | 10 | 0.200 | 464 | YEL037c | 4 | 0.333 | 314 | YEL077c | 5 | 0.100 | 85 |
| YDR542w | 21 | 0.214 | 3645 | YEL038w | 4 | 0.167 | 83 | YER001w | 25 | 0.247 | 3715 |
| YDR543c | 25 | 0.207 | 2146 | YEL039c | 19 | 0.275 | 1545 | YER002w | 12 | 0.227 | 1633 |
| YDR544c | 28 | 0.201 | 2430 | YEL040w | 30 | 0.264 | 5558 | YER003c | 4 | 0.667 | 50 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YER004w | 7 | 0.333 | 362 | YER044c-a | 8 | 0.357 | 244 | YER081w | 12 | 0.212 | 5143 |
| YER006w | 9 | 0.278 | 831 | YER045c | 29 | 0.305 | 8796 | YER082c | 3 | 0.333 | 127 |
| YER007c-a | 19 | 0.088 | 1870 | YER046w | 14 | 0.374 | 1857 | YER083c | 2 | 0.000 | 7 |
| YER007w | 4 | 0.333 | 215 | YER047c | 4 | 0.333 | 189 | YER084w | 3 | 0.000 | 47 |
| YER008c | 1 | 0.000 | 0 | YER048c | 5 | 0.600 | 15 | YER085c | 3 | 0.333 | 28 |
| YER009w | 1 | 0.000 | 0 | YER048w-a | 7 | 0.095 | 510 | YER086w | 6 | 0.267 | 254 |
| YER010c | 9 | 0.361 | 407 | YER049w | 6 | 0.067 | 182 | YER087c-a | 1 | 0.000 | 0 |
| YER011w | 20 | 0.342 | 1602 | YER050c | 1 | 0.000 | 0 | YER087c-b | 3 | 0.000 | 26 |
| YER012w | 11 | 0.182 | 981 | YER052c | 9 | 0.333 | 621 | YER087w | 2 | 1.000 | 0 |
| YER013w | 17 | 0.066 | 3439 | YER053c | 18 | 0.275 | 1568 | YER088c | 269 | 0.007 | 551939 |
| YER014w | 5 | 0.400 | 124 | YER053c-a | 6 | 0.600 | 50 | YER089c | 9 | 0.472 | 507 |
| YER015w | 5 | 0.200 | 98 | YER054c | 13 | 0.308 | 551 | YER090w | 5 | 0.500 | 90 |
| YER016w | 2 | 0.000 | 28 | YER055c | 18 | 0.327 | 2610 | YER091c | 19 | 0.205 | 2226 |
| YER017c | 6 | 0.400 | 153 | YER056c | 8 | 0.536 | 328 | YER091c-a | 6 | 0.267 | 196 |
| YER018c | 9 | 0.278 | 461 | YER056c-a | 8 | 0.464 | 297 | YER092w | 13 | 0.179 | 2494 |
| YER019c-a | 5 | 0.700 | 28 | YER057c | 4 | 0.000 | 112 | YER093c-a | 3 | 0.333 | 50 |
| YER019w | 8 | 0.357 | 397 | YER058w | 2 | 1.000 | 0 | YER094c | 14 | 0.319 | 1161 |
| YER020w | 5 | 0.700 | 28 | YER059w | 4 | 0.333 | 105 | YER095w | 10 | 0.222 | 524 |
| YER021w | 6 | 0.400 | 408 | YER060w | 6 | 0.133 | 410 | YER096w | 19 | 0.316 | 1677 |
| YER022w | 4 | 0.167 | 198 | YER060w-a | 7 | 0.333 | 235 | YER097w | 2 | 0.000 | 26 |
| YER023w | 3 | 0.000 | 150 | YER061c | 5 | 0.400 | 93 | YER098w | 5 | 0.300 | 91 |
| YER024w | 10 | 0.178 | 745 | YER062c | 28 | 0.249 | 4741 | YER099c | 4 | 0.333 | 78 |
| YER025w | 5 | 0.200 | 176 | YER063w | 7 | 0.190 | 442 | YER100w | 7 | 0.333 | 227 |
| YER026c | 8 | 0.321 | 1010 | YER064c | 8 | 0.250 | 580 | YER101c | 6 | 0.600 | 153 |
| YER027c | 1 | 0.000 | 0 | YER065c | 13 | 0.256 | 2288 | YER102w | 11 | 0.491 | 729 |
| YER028c | 30 | 0.257 | 5256 | YER066c-a | 5 | 0.200 | 114 | YER103w | 30 | 0.216 | 5042 |
| YER029c | 4 | 0.500 | 73 | YER066w | 3 | 0.000 | 23 | YER104w | 3 | 0.667 | 94 |
| YER030w | 3 | 0.333 | 39 | YER067w | 14 | 0.297 | 1100 | YER105c | 3 | 0.333 | 253 |
| YER031c | 7 | 0.524 | 459 | YER068w | 45 | 0.057 | 68574 | YER106w | 5 | 0.400 | 518 |
| YER032w | 8 | 0.321 | 1242 | YER069w | 21 | 0.162 | 3459 | YER107c | 3 | 0.000 | 177 |
| YER033c | 13 | 0.436 | 798 | YER070w | 18 | 0.118 | 3038 | YER109c | 236 | 0.040 | 104710 |
| YER034w | 9 | 0.472 | 401 | YER071c | 3 | 0.333 | 100 | YER110c | 7 | 0.238 | 259 |
| YER035w | 12 | 0.318 | 1533 | YER072w | 15 | 0.295 | 1155 | YER111c | 594 | 0.014 | 861633 |
| YER036c | 5 | 0.300 | 143 | YER073w | 23 | 0.383 | 2090 | YER112w | 15 | 0.286 | 1404 |
| YER037w | 19 | 0.257 | 2389 | YER074w | 14 | 0.352 | 1230 | YER114c | 3 | 0.667 | 21 |
| YER038c | 5 | 0.400 | 113 | YER074w-a | 3 | 0.333 | 27 | YER115c | 1 | 0.000 | 0 |
| YER039c | 7 | 0.333 | 332 | YER075c | 8 | 0.500 | 144 | YER116c | 9 | 0.333 | 470 |
| YER039c-a | 3 | 0.000 | 119 | YER076c | 4 | 0.500 | 59 | YER117w | 11 | 0.473 | 773 |
| YER040w | 184 | 0.023 | 136327 | YER077c | 4 | 0.167 | 74 | YER118c | 3 | 0.333 | 24 |
| YER041w | 2 | 0.000 | 47 | YER078c | 14 | 0.297 | 836 | YER119c | 5 | 0.400 | 119 |
| YER042w | 5 | 0.200 | 94 | YER078w-a | 3 | 0.000 | 13 | YER119c-a | 1 | 0.000 | 0 |
| YER043c | 5 | 0.200 | 201 | YER079w | 18 | 0.222 | 1539 | YER120w | 5 | 0.400 | 72 |
| YER044c | 25 | 0.210 | 5928 | YER080w | 5 | 0.600 | 95 | YER121w | 6 | 0.600 | 86 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YER122c | 1 | 0.000 | 0 | YER162c | 4 | 0.500 | 139 | YFL010w-a | 3 | 0.333 | 154 |
| YER123w | 6 | 0.133 | 223 | YER163c | 5 | 0.200 | 354 | YFL011w | 15 | 0.171 | 2837 |
| YER124c | 14 | 0.308 | 1752 | YER164w | 2 | 0.000 | 82 | YFL012w | 8 | 0.250 | 689 |
| YER125w | 9 | 0.417 | 681 | YER165w | 2 | 0.000 | 43 | YFL013c | 6 | 0.333 | 207 |
| YER126c | 6 | 0.333 | 133 | YER166w | 1 | 0.000 | 0 | YFL013w-a | 2 | 0.000 | 5 |
| YER127w | 3 | 0.333 | 33 | YER167w | 2 | 0.000 | 23 | YFL014w | 57 | 0.203 | 18951 |
| YER128w | 6 | 0.067 | 146 | YER168c | 3 | 1.000 | 0 | YFL015c | 2 | 1.000 | 0 |
| YER129w | 4 | 0.167 | 58 | YER169w | 96 | 0.019 | 94209 | YFL016c | 15 | 0.295 | 1196 |
| YER130c | 12 | 0.333 | 1273 | YER170w | 4 | 0.167 | 51 | YFL017c | 4 | 0.167 | 174 |
| YER131w | 14 | 0.385 | 1492 | YER171w | 3 | 0.000 | 33 | YFL017w-a | 4 | 0.167 | 273 |
| YER132c | 4 | 0.500 | 77 | YER172c | 3 | 0.333 | 38 | YFL018c | 9 | 0.167 | 690 |
| YER133w | 16 | 0.167 | 2202 | YER173w | 3 | 0.000 | 111 | YFL020c | 15 | 0.267 | 1218 |
| YER134c | 7 | 0.238 | 147 | YER174c | 9 | 0.278 | 178 | YFL021w | 167 | 0.039 | 200969 |
| YER135c | 4 | 0.167 | 76 | YER175c | 9 | 0.361 | 227 | YFL022c | 17 | 0.272 | 2888 |
| YER136w | 7 | 0.286 | 682 | YER176w | 10 | 0.200 | 416 | YFL023w | 14 | 0.209 | 1268 |
| YER137c | 6 | 0.333 | 221 | YER177w | 18 | 0.294 | 1354 | YFL024c | 13 | 0.218 | 869 |
| YER137c-a | 3 | 0.333 | 29 | YER178w | 2 | 1.000 | 0 | YFL025c | 4 | 0.333 | 75 |
| YER138c | 15 | 0.133 | 1711 | YER179w | 8 | 0.214 | 500 | YFL026w | 11 | 0.236 | 894 |
| YER138w-a | 7 | 0.333 | 119 | YER180c | 2 | 0.000 | 27 | YFL027c | 9 | 0.306 | 293 |
| YER139c | 6 | 0.267 | 188 | YER180c-a | 1 | 0.000 | 0 | YFL028c | 6 | 0.267 | 125 |
| YER140w | 6 | 0.400 | 198 | YER181c | 3 | 0.333 | 107 | YFL029c | 5 | 0.200 | 282 |
| YER141w | 10 | 0.200 | 939 | YER182w | 2 | 0.000 | 134 | YFL030w | 12 | 0.258 | 757 |
| YER142c | 11 | 0.218 | 497 | YER183c | 6 | 0.133 | 610 | YFL031w | 223 | 0.017 | 382509 |
| YER143w | 9 | 0.333 | 303 | YER184c | 6 | 0.267 | 293 | YFL032w | 1 | 0.000 | 0 |
| YER144c | 4 | 0.333 | 165 | YER185w | 9 | 0.167 | 786 | YFL033c | 4 | 0.167 | 967 |
| YER145c | 20 | 0.332 | 2177 | YER186c | 1 | 0.000 | 0 | YFL034c-a | 15 | 0.238 | 2518 |
| YER146w | 19 | 0.292 | 2373 | YER187w | 5 | 0.400 | 369 | YFL034c-b | 3 | 0.667 | 9 |
| YER147c | 4 | 0.167 | 184 | YER188c-a | 6 | 0.267 | 59 | YFL034w | 9 | 0.250 | 653 |
| YER148w | 4 | 0.167 | 541 | YER188w | 5 | 0.300 | 438 | YFL036w | 1 | 0.000 | 0 |
| YER149c | 10 | 0.267 | 472 | YER189w | 29 | 0.158 | 3910 | YFL037w | 6 | 0.200 | 797 |
| YER150w | 39 | 0.177 | 9189 | YER190w | 26 | 0.182 | 2789 | YFL038c | 3 | 0.000 | 276 |
| YER151c | 1 | 0.000 | 0 | YFL001w | 1 | 0.000 | 0 | YFL039c | 10 | 0.356 | 577 |
| YER152c | 4 | 0.167 | 81 | YFL002c | 2 | 0.000 | 11 | YFL040w | 3 | 0.333 | 130 |
| YER153c | 9 | 0.222 | 356 | YFL002w-a | 1 | 0.000 | 0 | YFL041w | 5 | 0.300 | 297 |
| YER154w | 8 | 0.393 | 210 | YFL002w-b | 4 | 0.167 | 192 | YFL042c | 6 | 0.600 | 84 |
| YER155c | 17 | 0.279 | 2129 | YFL003c | 5 | 0.100 | 414 | YFL044c | 98 | 0.016 | 141988 |
| YER156c | 5 | 0.500 | 189 | YFL004w | 6 | 0.467 | 229 | YFL045c | 7 | 0.429 | 552 |
| YER157w | 4 | 0.167 | 121 | YFL005w | 6 | 0.400 | 111 | YFL046w | 1 | 0.000 | 0 |
| YER158c | 18 | 0.359 | 2277 | YFL006w | 1 | 0.000 | 0 | YFL047w | 7 | 0.286 | 830 |
| YER159c | 7 | 0.429 | 268 | YFL007w | 6 | 0.267 | 432 | YFL048c | 5 | 0.400 | 467 |
| YER159c-a | 3 | 0.667 | 69 | YFL008w | 3 | 0.000 | 91 | YFL049w | 2 | 1.000 | 0 |
| YER160c | 4 | 0.500 | 218 | YFL009w | 2 | 0.000 | 21 | YFL050c | 2 | 1.000 | 0 |
| YER161c | 24 | 0.065 | 6118 | YFL010c | 2 | 0.000 | 21 | YFL051c | 4 | 0.833 | 6 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YFL052w | 5 | 0.300 | 217 | YFR027w | 2 | 0.000 | 14 | YGL009c | 13 | 0.282 | 934 |
| YFL053w | 10 | 0.267 | 709 | YFR028c | 77 | 0.004 | 125739 | YGL010w | 6 | 0.333 | 154 |
| YFL054c | 8 | 0.357 | 326 | YFR029w | 6 | 0.067 | 591 | YGL011c | 5 | 0.500 | 139 |
| YFL055w | 12 | 0.424 | 504 | YFR030w | 13 | 0.333 | 1473 | YGL012w | 11 | 0.255 | 771 |
| YFL056c | 9 | 0.361 | 315 | YFR031c | 1 | 0.000 | 0 | YGL013c | 666 | 0.015 | 779413 |
| YFL057c | 10 | 0.511 | 285 | YFR031c-a | 14 | 0.374 | 1747 | YGL014w | 2 | 1.000 | 0 |
| YFL058w | 10 | 0.178 | 1879 | YFR032c | 8 | 0.107 | 1026 | YGL015c | 6 | 0.067 | 572 |
| YFL059w | 13 | 0.244 | 1122 | YFR032c-a | 15 | 0.229 | 1310 | YGL017w | 2 | 0.000 | 17 |
| YFL060c | 11 | 0.036 | 770 | YFR032c-b | 2 | 0.000 | 9 | YGL018c | 1 | 0.000 | 0 |
| YFL061w | 4 | 0.167 | 134 | YFR033c | 15 | 0.248 | 1049 | YGL021w | 7 | 0.286 | 435 |
| YFL062w | 10 | 0.222 | 266 | YFR034c | 377 | 0.011 | 523332 | YGL022w | 1 | 0.000 | 0 |
| YFL063w | 11 | 0.218 | 664 | YFR035c | 7 | 0.143 | 324 | YGL023c | 2 | 0.000 | 17 |
| YFL064c | 10 | 0.400 | 322 | YFR036w | 4 | 0.167 | 108 | YGL025c | 1 | 0.000 | 0 |
| YFL065c | 4 | 0.667 | 33 | YFR037c | 6 | 0.133 | 353 | YGL026c | 4 | 0.500 | 70 |
| YFL066c | 3 | 0.000 | 34 | YFR038w | 5 | 0.300 | 243 | YGL027c | 2 | 0.000 | 35 |
| YFL067w | 5 | 0.100 | 114 | YFR039c | 6 | 0.200 | 521 | YGL028c | 10 | 0.422 | 364 |
| YFL068w | 1 | 0.000 | 0 | YFR040w | 4 | 0.333 | 139 | YGL029w | 8 | 0.357 | 298 |
| YFR001w | 9 | 0.222 | 2615 | YFR041c | 4 | 0.333 | 69 | YGL030w | 9 | 0.417 | 325 |
| YFR002w | 3 | 0.000 | 56 | YFR042w | 2 | 0.000 | 41 | YGL031c | 11 | 0.400 | 624 |
| YFR003c | 6 | 0.333 | 383 | YFR043c | 5 | 0.200 | 315 | YGL032c | 15 | 0.448 | 628 |
| YFR004w | 5 | 0.300 | 303 | YFR044c | 7 | 0.143 | 729 | YGL033w | 3 | 0.000 | 44 |
| YFR005c | 3 | 0.000 | 41 | YFR045w | 4 | 0.167 | 75 | YGL034c | 2 | 0.000 | 10 |
| YFR006w | 5 | 0.400 | 42 | YFR047c | 7 | 0.286 | 321 | YGL035c | 247 | 0.015 | 263790 |
| YFR007w | 10 | 0.089 | 612 | YFR048w | 2 | 1.000 | 0 | YGL036w | 7 | 0.524 | 115 |
| YFR008w | 4 | 0.167 | 43 | YFR049w | 3 | 0.333 | 110 | YGL037c | 20 | 0.279 | 1919 |
| YFR009w | 7 | 0.238 | 970 | YFR050c | 4 | 0.833 | 52 | YGL038c | 11 | 0.273 | 940 |
| YFR010w | 5 | 0.300 | 469 | YFR051c | 1 | 0.000 | 0 | YGL039w | 7 | 0.381 | 317 |
| YFR011c | 7 | 0.381 | 326 | YFR052w | 5 | 0.200 | 223 | YGL040c | 2 | 0.000 | 36 |
| YFR012w | 8 | 0.214 | 700 | YFR053c | 27 | 0.296 | 2857 | YGL041c | 1 | 0.000 | 0 |
| YFR013w | 1 | 0.000 | 0 | YFR054c | 6 | 0.200 | 207 | YGL043w | 4 | 0.500 | 55 |
| YFR014c | 2 | 1.000 | 0 | YFR055w | 8 | 0.393 | 548 | YGL044c | 2 | 0.000 | 36 |
| YFR015c | 23 | 0.233 | 5291 | YFR056c | 1 | 0.000 | 0 | YGL045w | 7 | 0.381 | 102 |
| YFR016c | 3 | 0.333 | 56 | YFR057w | 6 | 0.133 | 336 | YGL046w | 1 | 0.000 | 0 |
| YFR017c | 32 | 0.254 | 5615 | YGL001c | 40 | 0.147 | 8647 | YGL047w | 4 | 0.333 | 292 |
| YFR018c | 9 | 0.306 | 1259 | YGL002w | 2 | 0.000 | 17 | YGL048c | 5 | 0.600 | 505 |
| YFR019w | 6 | 0.133 | 201 | YGL003c | 4 | 0.167 | 433 | YGL050w | 3 | 0.000 | 94 |
| YFR020w | 5 | 0.500 | 248 | YGL004c | 4 | 0.167 | 26 | YGL051w | 1 | 0.000 | 0 |
| YFR021w | 1 | 0.000 | 0 | YGL005c | 4 | 0.000 | 1145 | YGL052w | 3 | 0.000 | 162 |
| YFR022w | 14 | 0.264 | 1956 | YGL006w | 7 | 0.143 | 345 | YGL053w | 12 | 0.364 | 683 |
| YFR023w | 13 | 0.115 | 1964 | YGL006w-a | 14 | 0.385 | 699 | YGL054c | 1 | 0.000 | 0 |
| YFR024c-a | 5 | 0.300 | 90 | YGL007c-a | 15 | 0.400 | 796 | YGL055w | 23 | 0.281 | 9792 |
| YFR025c | 5 | 0.400 | 183 | YGL007w | 15 | 0.162 | 1540 | YGL056c | 8 | 0.179 | 312 |
| YFR026c | 8 | 0.179 | 951 | YGL008c | 16 | 0.192 | 1487 | YGL057c | 1 | 0.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YGL058w | 2 | 0.000 | 33 | YGL104c | 13 | 0.346 | 892 | YGL151w | 4 | 0.167 | 98 |
| YGL059w | 4 | 0.000 | 96 | YGL105w | 1 | 0.000 | 0 | YGL152c | 3 | 0.000 | 50 |
| YGL060w | 4 | 0.500 | 56 | YGL106w | 1 | 0.000 | 0 | YGL153w | 5 | 0.400 | 94 |
| YGL061c | 6 | 0.400 | 96 | YGL107c | 2 | 0.000 | 171 | YGL154c | 6 | 0.533 | 67 |
| YGL062w | 17 | 0.279 | 1083 | YGL108c | 4 | 0.333 | 167 | YGL155w | 1 | 0.000 | 0 |
| YGL063w | 7 | 0.190 | 608 | YGL110c | 1 | 0.000 | 0 | YGL156w | 21 | 0.181 | 4276 |
| YGL064c | 3 | 0.000 | 80 | YGL111w | 3 | 0.667 | 12 | YGL157w | 27 | 0.205 | 4561 |
| YGL065c | 2 | 0.000 | 17 | YGL113w | 1 | 0.000 | 0 | YGL158w | 17 | 0.338 | 1426 |
| YGL066w | 2 | 0.000 | 7 | YGL114w | 9 | 0.361 | 480 | YGL159w | 10 | 0.111 | 708 |
| YGL067w | 1 | 0.000 | 0 | YGL115w | 6 | 0.267 | 233 | YGL160w | 7 | 0.095 | 607 |
| YGL068w | 4 | 0.500 | 56 | YGL116w | 20 | 0.179 | 2954 | YGL161c | 5 | 0.200 | 252 |
| YGL069c | 1 | 0.000 | 0 | YGL117w | 17 | 0.250 | 2655 | YGL162w | 84 | 0.116 | 44305 |
| YGL070c | 4 | 0.333 | 116 | YGL118c | 2 | 0.000 | 36 | YGL163c | 11 | 0.455 | 393 |
| YGL071w | 756 | 0.008 | 1414625 | YGL119w | 4 | 0.167 | 88 | YGL164c | 1 | 0.000 | 0 |
| YGL072c | 6 | 0.400 | 174 | YGL120c | 5 | 0.400 | 133 | YGL165c | 1 | 0.000 | 0 |
| YGL073w | 577 | 0.008 | 804470 | YGL121c | 22 | 0.216 | 4057 | YGL166w | 30 | 0.115 | 8658 |
| YGL074c | 4 | 0.667 | 17 | YGL122c | 2 | 1.000 | 0 | YGL167c | 8 | 0.393 | 636 |
| YGL075c | 3 | 0.333 | 54 | YGL123w | 10 | 0.378 | 703 | YGL169w | 2 | 0.000 | 16 |
| YGL076c | 9 | 0.472 | 291 | YGL124c | 5 | 0.400 | 110 | YGL170c | 1 | 0.000 | 0 |
| YGL077c | 7 | 0.143 | 795 | YGL125w | 14 | 0.297 | 1310 | YGL171w | 10 | 0.200 | 1909 |
| YGL078c | 5 | 0.500 | 64 | YGL126w | 9 | 0.333 | 854 | YGL172w | 2 | 1.000 | 0 |
| YGL079w | 4 | 0.000 | 198 | YGL127c | 5 | 0.300 | 193 | YGL173c | 5 | 0.300 | 401 |
| YGL080w | 2 | 0.000 | 54 | YGL128c | 7 | 0.286 | 512 | YGL174w | 4 | 0.500 | 100 |
| YGL081w | 2 | 0.000 | 11 | YGL130w | 2 | 0.000 | 158 | YGL175c | 3 | 0.333 | 92 |
| YGL083w | 4 | 0.167 | 80 | YGL131c | 2 | 1.000 | 0 | YGL176c | 1 | 0.000 | 0 |
| YGL084c | 3 | 0.667 | 17 | YGL133w | 12 | 0.136 | 956 | YGL177w | 6 | 0.200 | 158 |
| YGL085w | 1 | 0.000 | 0 | YGL134w | 11 | 0.073 | 904 | YGL178w | 6 | 0.733 | 35 |
| YGL087c | 1 | 0.000 | 0 | YGL135w | 20 | 0.142 | 3252 | YGL179c | 9 | 0.472 | 264 |
| YGL088w | 4 | 0.500 | 36 | YGL136c | 10 | 0.244 | 836 | YGL180w | 10 | 0.267 | 1382 |
| YGL089c | 10 | 0.244 | 842 | YGL137w | 1 | 0.000 | 0 | YGL181w | 69 | 0.022 | 46596 |
| YGL091c | 2 | 0.000 | 22 | YGL138c | 4 | 0.000 | 367 | YGL182c | 6 | 0.267 | 310 |
| YGL092w | 1 | 0.000 | 0 | YGL139w | 3 | 0.000 | 211 | YGL183c | 4 | 0.000 | 207 |
| YGL093w | 3 | 0.000 | 57 | YGL140c | 3 | 0.333 | 32 | YGL184c | 21 | 0.233 | 3021 |
| YGL094c | 3 | 0.333 | 70 | YGL141w | 5 | 0.200 | 230 | YGL185c | 3 | 0.667 | 121 |
| YGL095c | 4 | 0.667 | 62 | YGL142c | 3 | 0.667 | 18 | YGL186c | 9 | 0.250 | 1362 |
| YGL096w | 326 | 0.024 | 594587 | YGL143c | 7 | 0.238 | 147 | YGL187c | 14 | 0.220 | 756 |
| YGL097w | 5 | 0.600 | 25 | YGL144c | 4 | 0.167 | 513 | YGL188c | 10 | 0.356 | 573 |
| YGL098w | 2 | 1.000 | 0 | YGL145w | 14 | 0.341 | 1090 | YGL188c-a | 2 | 0.000 | 9 |
| YGL099w | 4 | 0.500 | 115 | YGL146c | 6 | 0.333 | 181 | YGL189c | 11 | 0.455 | 524 |
| YGL100w | 5 | 0.700 | 60 | YGL147c | 13 | 0.372 | 1007 | YGL190c | 5 | 0.000 | 180 |
| YGL101w | 8 | 0.214 | 372 | YGL148w | 10 | 0.200 | 840 | YGL191w | 12 | 0.121 | 1280 |
| YGL102c | 5 | 0.000 | 203 | YGL149w | 1 | 0.000 | 0 | YGL192w | 118 | 0.012 | 70076 |
| YGL103w | 9 | 0.556 | 294 | YGL150c | 1 | 0.000 | 0 | YGL193c | 10 | 0.267 | 344 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YGL194c | 16 | 0.117 | 2986 | YGL239c | 1 | 0.000 | 0 | YGR019w | 14 | 0.209 | 1375 |
| YGL195w | 7 | 0.286 | 1302 | YGL240w | 4 | 0.667 | 43 | YGR020c | 4 | 0.167 | 193 |
| YGL196w | 8 | 0.143 | 863 | YGL241w | 2 | 0.000 | 46 | YGR021w | 3 | 0.333 | 57 |
| YGL197w | 6 | 0.200 | 190 | YGL242c | 5 | 0.300 | 297 | YGR022c | 2 | 0.000 | 76 |
| YGL198w | 5 | 0.200 | 145 | YGL243w | 2 | 1.000 | 0 | YGR024c | 6 | 0.467 | 193 |
| YGL199c | 2 | 0.000 | 14 | YGL244w | 3 | 0.000 | 72 | YGR025w | 1 | 0.000 | 0 |
| YGL200c | 4 | 0.333 | 64 | YGL245w | 5 | 0.100 | 533 | YGR026w | 11 | 0.091 | 933 |
| YGL201c | 5 | 0.400 | 54 | YGL246c | 4 | 0.167 | 374 | YGR027c | 8 | 0.429 | 445 |
| YGL202w | 8 | 0.286 | 694 | YGL247w | 4 | 0.167 | 169 | YGR028w | 6 | 0.333 | 142 |
| YGL203c | 1 | 0.000 | 0 | YGL248w | 8 | 0.500 | 404 | YGR029w | 2 | 0.000 | 26 |
| YGL204c | 2 | 1.000 | 0 | YGL249w | 6 | 0.000 | 162 | YGR030c | 2 | 0.000 | 30 |
| YGL205w | 13 | 0.128 | 1072 | YGL250w | 5 | 0.100 | 615 | YGR031c-a | 1 | 0.000 | 0 |
| YGL206c | 3 | 0.667 | 156 | YGL251c | 3 | 0.333 | 65 | YGR031w | 4 | 0.500 | 68 |
| YGL207w | 6 | 0.200 | 357 | YGL252c | 9 | 0.139 | 362 | YGR032w | 20 | 0.226 | 3145 |
| YGL208w | 4 | 0.000 | 107 | YGL253w | 14 | 0.264 | 1679 | YGR033c | 5 | 0.600 | 65 |
| YGL209w | 66 | 0.082 | 39033 | YGL254w | 104 | 0.023 | 89297 | YGR034w | 7 | 0.381 | 4655 |
| YGL210w | 2 | 0.000 | 14 | YGL255w | 29 | 0.180 | 6227 | YGR035c | 21 | 0.262 | 2428 |
| YGL213c | 1 | 0.000 | 0 | YGL256w | 13 | 0.154 | 1387 | YGR035w-a | 4 | 0.833 | 6 |
| YGL214w | 1 | 0.000 | 0 | YGL257c | 7 | 0.143 | 170 | YGR036c | 5 | 0.100 | 111 |
| YGL215w | 4 | 0.333 | 280 | YGL258w | 16 | 0.283 | 2564 | YGR037c | 4 | 0.667 | 70 |
| YGL216w | 1 | 0.000 | 0 | YGL259w | 10 | 0.222 | 382 | YGR038c-a | 6 | 0.467 | 301 |
| YGL217c | 2 | 0.000 | 54 | YGL260w | 4 | 0.333 | 29 | YGR038c-b | 2 | 1.000 | 0 |
| YGL218w | 1 | 0.000 | 0 | YGL261c | 13 | 0.295 | 566 | YGR038w | 1 | 0.000 | 0 |
| YGL219c | 3 | 0.333 | 66 | YGL262w | 1 | 0.000 | 0 | YGR039w | 6 | 0.267 | 110 |
| YGL220w | 1 | 0.000 | 0 | YGL263w | 7 | 0.095 | 674 | YGR040w | 11 | 0.327 | 435 |
| YGL221c | 2 | 0.000 | 35 | YGR001c | 1 | 0.000 | 0 | YGR041w | 15 | 0.381 | 1474 |
| YGL222c | 2 | 0.000 | 80 | YGR002c | 2 | 1.000 | 0 | YGR042w | 1 | 0.000 | 0 |
| YGL223c | 3 | 0.000 | 89 | YGR003w | 2 | 0.000 | 151 | YGR043c | 30 | 0.214 | 7926 |
| YGL224c | 6 | 0.267 | 198 | YGR004w | 1 | 0.000 | 0 | YGR044c | 247 | 0.014 | 168884 |
| YGL225w | 7 | 0.143 | 321 | YGR005c | 3 | 0.333 | 38 | YGR045c | 9 | 0.250 | 277 |
| YGL226c-a | 6 | 0.267 | 279 | YGR006w | 2 | 0.000 | 205 | YGR046w | 3 | 0.333 | 51 |
| YGL226w | 8 | 0.321 | 277 | YGR007w | 3 | 0.000 | 226 | YGR047c | 2 | 0.000 | 12 |
| YGL227w | 12 | 0.182 | 997 | YGR008c | 13 | 0.256 | 897 | YGR048w | 4 | 0.500 | 53 |
| YGL228w | 8 | 0.214 | 527 | YGR009c | 9 | 0.444 | 424 | YGR049w | 10 | 0.289 | 751 |
| YGL229c | 6 | 0.133 | 274 | YGR010w | 8 | 0.393 | 222 | YGR050c | 17 | 0.294 | 1087 |
| YGL230c | 8 | 0.250 | 1390 | YGR011w | 9 | 0.361 | 438 | YGR051c | 3 | 0.333 | 26 |
| YGL231c | 5 | 0.100 | 148 | YGR012w | 8 | 0.250 | 732 | YGR052w | 32 | 0.264 | 5059 |
| YGL232w | 2 | 0.000 | 57 | YGR013w | 4 | 0.500 | 60 | YGR053c | 5 | 0.200 | 259 |
| YGL234w | 12 | 0.212 | 1404 | YGR014w | 11 | 0.455 | 662 | YGR054w | 2 | 0.000 | 14 |
| YGL235w | 4 | 0.167 | 52 | YGR015c | 6 | 0.133 | 549 | YGR055w | 12 | 0.182 | 1897 |
| YGL236c | 5 | 0.400 | 123 | YGR016w | 8 | 0.107 | 957 | YGR056w | 2 | 0.000 | 171 |
| YGL237c | 201 | 0.007 | 70496 | YGR017w | 2 | 0.000 | 22 | YGR057c | 4 | 0.167 | 223 |
| YGL238w | 4 | 0.167 | 167 | YGR018c | 4 | 0.000 | 144 | YGR058w | 5 | 0.000 | 905 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YGR059w | 12 | 0.076 | 1658 | YGR105w | 2 | 1.000 | 0 | YGR146c | 18 | 0.333 | 1275 |
| YGR060w | 20 | 0.300 | 3181 | YGR106c | 7 | 0.190 | 484 | YGR146c-a | 2 | 0.000 | 26 |
| YGR061c | 8 | 0.143 | 1157 | YGR107w | 6 | 0.200 | 225 | YGR147c | 3 | 0.000 | 122 |
| YGR063c | 1 | 0.000 | 0 | YGR108w | 21 | 0.314 | 2622 | YGR148c | 15 | 0.286 | 1569 |
| YGR065c | 11 | 0.327 | 513 | YGR109c | 11 | 0.127 | 1054 | YGR149w | 15 | 0.286 | 1298 |
| YGR066c | 14 | 0.143 | 1065 | YGR109w-a | 6 | 0.267 | 141 | YGR150c | 6 | 0.133 | 292 |
| YGR067c | 14 | 0.253 | 971 | YGR109w-b | 5 | 0.400 | 97 | YGR151c | 3 | 0.667 | 20 |
| YGR068c | 3 | 0.000 | 137 | YGR110w | 13 | 0.218 | 838 | YGR152c | 9 | 0.306 | 1095 |
| YGR069w | 5 | 0.300 | 88 | YGR111w | 4 | 0.500 | 84 | YGR153w | 5 | 0.500 | 83 |
| YGR070w | 7 | 0.333 | 507 | YGR112w | 7 | 0.238 | 1131 | YGR154c | 10 | 0.156 | 1336 |
| YGR071c | 12 | 0.106 | 623 | YGR113w | 6 | 0.267 | 346 | YGR155w | 10 | 0.267 | 1627 |
| YGR072w | 13 | 0.154 | 1296 | YGR115c | 1 | 0.000 | 0 | YGR156w | 4 | 0.500 | 55 |
| YGR073c | 4 | 0.000 | 107 | YGR116w | 4 | 0.167 | 256 | YGR157w | 12 | 0.258 | 2032 |
| YGR074w | 1 | 0.000 | 0 | YGR117c | 8 | 0.571 | 218 | YGR158c | 2 | 0.000 | 94 |
| YGR075c | 6 | 0.000 | 388 | YGR118w | 13 | 0.282 | 3171 | YGR159c | 9 | 0.333 | 449 |
| YGR076c | 2 | 0.000 | 26 | YGR119c | 2 | 0.000 | 47 | YGR160w | 2 | 0.000 | 14 |
| YGR077c | 2 | 1.000 | 0 | YGR120c | 6 | 0.133 | 602 | YGR161c | 27 | 0.291 | 4157 |
| YGR078c | 8 | 0.143 | 436 | YGR121c | 12 | 0.303 | 1418 | YGR161w-a | 2 | 0.000 | 51 |
| YGR079w | 19 | 0.164 | 2817 | YGR121w-a | 3 | 1.000 | 0 | YGR161w-b | 1 | 0.000 | 0 |
| YGR080w | 3 | 0.000 | 45 | YGR122w | 5 | 0.300 | 76 | YGR161w-c | 1 | 0.000 | 0 |
| YGR081c | 4 | 0.333 | 100 | YGR123c | 9 | 0.250 | 623 | YGR162w | 7 | 0.429 | 163 |
| YGR082w | 3 | 0.333 | 27 | YGR124w | 11 | 0.164 | 1343 | YGR163w | 1 | 0.000 | 0 |
| YGR084c | 9 | 0.250 | 1047 | YGR125w | 8 | 0.250 | 356 | YGR164w | 1 | 0.000 | 0 |
| YGR085c | 9 | 0.444 | 361 | YGR126w | 4 | 0.167 | 221 | YGR165w | 6 | 0.133 | 413 |
| YGR086c | 17 | 0.309 | 1168 | YGR127w | 9 | 0.222 | 1066 | YGR166w | 8 | 0.036 | 771 |
| YGR087c | 16 | 0.200 | 1550 | YGR128c | 5 | 0.300 | 674 | YGR168c | 7 | 0.190 | 174 |
| YGR088w | 45 | 0.191 | 10227 | YGR129w | 4 | 0.000 | 522 | YGR169c | 2 | 0.000 | 70 |
| YGR089w | 9 | 0.278 | 214 | YGR130c | 10 | 0.400 | 502 | YGR169c-a | 1 | 0.000 | 0 |
| YGR090w | 4 | 0.667 | 43 | YGR131w | 6 | 0.467 | 66 | YGR170w | 9 | 0.083 | 960 |
| YGR091w | 5 | 0.200 | 146 | YGR132c | 3 | 0.333 | 21 | YGR171c | 3 | 0.000 | 55 |
| YGR092w | 14 | 0.319 | 1221 | YGR133w | 4 | 0.500 | 44 | YGR172c | 2 | 0.000 | 121 |
| YGR093w | 3 | 0.000 | 396 | YGR134w | 5 | 0.500 | 428 | YGR173w | 6 | 0.067 | 660 |
| YGR094w | 6 | 0.333 | 1069 | YGR135w | 7 | 0.238 | 673 | YGR174c | 2 | 1.000 | 0 |
| YGR095c | 3 | 0.333 | 37 | YGR136w | 4 | 0.167 | 184 | YGR174w-a | 1 | 0.000 | 0 |
| YGR096w | 2 | 1.000 | 0 | YGR137w | 4 | 0.333 | 110 | YGR175c | 16 | 0.233 | 1415 |
| YGR097w | 5 | 0.900 | 3 | YGR138c | 13 | 0.244 | 1331 | YGR176w | 9 | 0.250 | 373 |
| YGR098c | 9 | 0.139 | 744 | YGR139w | 3 | 0.333 | 26 | YGR177c | 11 | 0.164 | 804 |
| YGR099w | 8 | 0.107 | 1029 | YGR140w | 8 | 0.571 | 127 | YGR178c | 3 | 0.333 | 62 |
| YGR100w | 2 | 0.000 | 8 | YGR141w | 5 | 0.400 | 221 | YGR179c | 4 | 0.333 | 112 |
| YGR101w | 2 | 1.000 | 0 | YGR142w | 21 | 0.224 | 3403 | YGR180c | 24 | 0.373 | 2167 |
| YGR102c | 1 | 0.000 | 0 | YGR143w | 10 | 0.311 | 355 | YGR181w | 6 | 0.800 | 41 |
| YGR103w | 13 | 0.128 | 1258 | YGR144w | 14 | 0.308 | 2160 | YGR182c | 2 | 0.000 | 47 |
| YGR104c | 1 | 0.000 | 0 | YGR145w | 6 | 0.467 | 90 | YGR183c | 15 | 0.152 | 1582 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YGR184c | 5 | 0.200 | 230 | YGR229c | 8 | 0.250 | 456 | YGR271w | 13 | 0.179 | 480 |
| YGR185c | 3 | 0.333 | 274 | YGR230w | 10 | 0.356 | 707 | YGR272c | 7 | 0.190 | 246 |
| YGR186w | 1 | 0.000 | 0 | YGR231c | 5 | 0.100 | 651 | YGR273c | 5 | 0.000 | 362 |
| YGR187c | 7 | 0.286 | 547 | YGR232w | 6 | 0.133 | 819 | YGR274c | 2 | 1.000 | 0 |
| YGR188c | 17 | 0.096 | 1779 | YGR233c | 18 | 0.261 | 2097 | YGR275w | 3 | 0.333 | 142 |
| YGR189c | 19 | 0.269 | 2707 | YGR234w | 34 | 0.212 | 7972 | YGR276c | 3 | 0.333 | 310 |
| YGR190c | 4 | 0.000 | 95 | YGR235c | 4 | 0.000 | 202 | YGR277c | 4 | 0.000 | 73 |
| YGR191w | 12 | 0.409 | 450 | YGR236c | 8 | 0.179 | 464 | YGR278w | 4 | 0.000 | 73 |
| YGR192c | 21 | 0.333 | 4028 | YGR237c | 4 | 0.333 | 63 | YGR279c | 14 | 0.396 | 628 |
| YGR193c | 5 | 0.500 | 24 | YGR238c | 13 | 0.321 | 795 | YGR280c | 9 | 0.389 | 355 |
| YGR194c | 5 | 0.200 | 114 | YGR239c | 5 | 0.400 | 143 | YGR281w | 10 | 0.156 | 698 |
| YGR195w | 3 | 0.333 | 41 | YGR240c | 11 | 0.309 | 851 | YGR282c | 11 | 0.182 | 819 |
| YGR196c | 3 | 0.333 | 98 | YGR240c-a | 1 | 0.000 | 0 | YGR283c | 10 | 0.311 | 524 |
| YGR197c | 12 | 0.197 | 1496 | YGR241c | 6 | 0.467 | 187 | YGR284c | 3 | 0.667 | 57 |
| YGR198w | 7 | 0.333 | 849 | YGR242w | 3 | 0.333 | 33 | YGR285c | 3 | 0.333 | 66 |
| YGR199w | 6 | 0.267 | 538 | YGR243w | 11 | 0.218 | 686 | YGR286c | 10 | 0.378 | 372 |
| YGR200c | 5 | 0.100 | 574 | YGR244c | 10 | 0.200 | 944 | YGR287c | 17 | 0.265 | 1009 |
| YGR201c | 8 | 0.286 | 258 | YGR245c | 6 | 0.467 | 95 | YGR288w | 11 | 0.182 | 929 |
| YGR202c | 4 | 0.667 | 183 | YGR246c | 4 | 0.333 | 100 | YGR289c | 9 | 0.306 | 861 |
| YGR203w | 8 | 0.214 | 926 | YGR247w | 4 | 0.500 | 306 | YGR292w | 10 | 0.200 | 1214 |
| YGR204c-a | 1 | 0.000 | 0 | YGR248w | 45 | 0.231 | 10533 | YGR294w | 5 | 0.300 | 132 |
| YGR204w | 17 | 0.235 | 3260 | YGR249w | 316 | 0.049 | 365525 | YGR295c | 16 | 0.250 | 972 |
| YGR205w | 4 | 0.167 | 190 | YGR250c | 11 | 0.345 | 697 | YGR296w | 19 | 0.228 | 1132 |
| YGR206w | 2 | 0.000 | 11 | YGR251w | 10 | 0.444 | 1002 | YHL001w | 14 | 0.264 | 1863 |
| YGR208w | 4 | 0.500 | 80 | YGR252w | 2 | 0.000 | 126 | YHL002w | 3 | 0.333 | 29 |
| YGR209c | 11 | 0.309 | 319 | YGR253c | 14 | 0.319 | 1595 | YHL003c | 1 | 0.000 | 0 |
| YGR210c | 6 | 0.533 | 83 | YGR254w | 25 | 0.217 | 3498 | YHL004w | 3 | 0.000 | 54 |
| YGR211w | 9 | 0.444 | 392 | YGR255c | 6 | 0.333 | 325 | YHL005c | 2 | 0.000 | 93 |
| YGR212w | 4 | 0.333 | 173 | YGR256w | 22 | 0.229 | 4368 | YHL006c | 3 | 0.000 | 165 |
| YGR213c | 13 | 0.231 | 940 | YGR257c | 1 | 0.000 | 0 | YHL007c | 2 | 0.000 | 19 |
| YGR214w | 14 | 0.308 | 2366 | YGR258c | 8 | 0.179 | 1013 | YHL008c | 5 | 0.100 | 569 |
| YGR215w | 4 | 0.333 | 228 | YGR259c | 2 | 0.000 | 27 | YHL009c | 43 | 0.012 | 29212 |
| YGR216c | 5 | 0.200 | 217 | YGR260w | 6 | 0.133 | 897 | YHL009w-a | 1 | 0.000 | 0 |
| YGR217w | 7 | 0.333 | 608 | YGR261c | 3 | 0.667 | 94 | YHL010c | 2 | 0.000 | 4 |
| YGR218w | 14 | 0.187 | 823 | YGR263c | 3 | 0.333 | 262 | YHL011c | 3 | 1.000 | 0 |
| YGR220c | 3 | 0.000 | 71 | YGR264c | 5 | 0.500 | 184 | YHL012w | 7 | 0.048 | 204 |
| YGR221c | 16 | 0.433 | 1549 | YGR265w | 3 | 0.000 | 42 | YHL013c | 9 | 0.250 | 325 |
| YGR222w | 10 | 0.511 | 332 | YGR266w | 4 | 0.167 | 129 | YHL015w | 18 | 0.327 | 1612 |
| YGR223c | 6 | 0.733 | 66 | YGR267c | 5 | 0.300 | 216 | YHL015w-a | 5 | 0.700 | 26 |
| YGR224w | 12 | 0.333 | 769 | YGR268c | 9 | 0.278 | 1548 | YHL016c | 19 | 0.257 | 3084 |
| YGR225w | 2 | 0.000 | 4 | YGR269w | 3 | 0.667 | 61 | YHL017w | 3 | 0.000 | 69 |
| YGR226c | 1 | 0.000 | 0 | YGR270w | 9 | 0.250 | 2199 | YHL019c | 1 | 0.000 | 0 |
| YGR227w | 2 | 0.000 | 10 | YGR271c-a | 4 | 0.167 | 147 | YHL020c | 30 | 0.124 | 3625 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YHL021c | 16 | 0.342 | 1584 | YHR011w | 3 | 0.000 | 41 | YHR050w | 8 | 0.214 | 388 |
| YHL022c | 6 | 0.133 | 400 | YHR012w | 5 | 0.300 | 98 | YHR050w-a | 3 | 0.000 | 71 |
| YHL023c | 4 | 0.167 | 185 | YHR013c | 4 | 0.000 | 163 | YHR051w | 12 | 0.152 | 761 |
| YHL024w | 20 | 0.389 | 2203 | YHR014w | 7 | 0.190 | 620 | YHR052w | 10 | 0.267 | 3417 |
| YHL025w | 5 | 0.500 | 31 | YHR015w | 6 | 0.133 | 1117 | YHR053c | 13 | 0.205 | 1220 |
| YHL026c | 10 | 0.400 | 283 | YHR016c | 10 | 0.400 | 822 | YHR054c | 6 | 0.200 | 333 |
| YHL027w | 218 | 0.027 | 146339 | YHR017w | 2 | 0.000 | 11 | YHR055c | 13 | 0.167 | 973 |
| YHL028w | 29 | 0.276 | 5211 | YHR018c | 21 | 0.195 | 3035 | YHR056c | 24 | 0.040 | 12856 |
| YHL029c | 18 | 0.275 | 1931 | YHR019c | 8 | 0.286 | 562 | YHR058c | 5 | 0.000 | 289 |
| YHL030w | 10 | 0.244 | 689 | YHR020w | 7 | 0.429 | 475 | YHR059w | 3 | 0.000 | 32 |
| YHL031c | 3 | 0.000 | 57 | YHR021c | 10 | 0.400 | 454 | YHR060w | 3 | 0.667 | 22 |
| YHL032c | 10 | 0.267 | 1052 | YHR021w-a | 4 | 0.167 | 103 | YHR061c | 9 | 0.333 | 1076 |
| YHL033c | 9 | 0.528 | 233 | YHR022c | 14 | 0.385 | 1336 | YHR062c | 9 | 0.278 | 889 |
| YHL034c | 13 | 0.218 | 766 | YHR022c-a | 4 | 0.167 | 222 | YHR063c | 4 | 0.667 | 102 |
| YHL035c | 6 | 0.400 | 474 | YHR023w | 12 | 0.318 | 1673 | YHR064c | 4 | 0.500 | 233 |
| YHL036w | 19 | 0.222 | 3383 | YHR024c | 2 | 0.000 | 36 | YHR065c | 5 | 0.400 | 374 |
| YHL037c | 3 | 0.000 | 37 | YHR025w | 6 | 0.333 | 279 | YHR066w | 6 | 0.400 | 554 |
| YHL038c | 6 | 0.533 | 509 | YHR026w | 3 | 0.333 | 28 | YHR067w | 7 | 0.333 | 587 |
| YHL039w | 8 | 0.143 | 395 | YHR027c | 2 | 1.000 | 0 | YHR068w | 4 | 0.167 | 415 |
| YHL040c | 19 | 0.363 | 1987 | YHR028c | 10 | 0.111 | 927 | YHR069c | 1 | 0.000 | 0 |
| YHL041w | 7 | 0.286 | 117 | YHR029c | 13 | 0.346 | 748 | YHR070w | 6 | 0.333 | 197 |
| YHL042w | 9 | 0.417 | 451 | YHR030c | 5 | 0.100 | 71 | YHR071w | 18 | 0.320 | 2608 |
| YHL043w | 1 | 0.000 | 0 | YHR031c | 7 | 0.238 | 169 | YHR072w | 4 | 0.500 | 43 |
| YHL044w | 7 | 0.429 | 72 | YHR032w | 6 | 0.467 | 77 | YHR072w-a | 3 | 0.667 | 10 |
| YHL045w | 8 | 0.357 | 300 | YHR033w | 20 | 0.447 | 1088 | YHR073w | 3 | 0.667 | 31 |
| YHL046c | 15 | 0.267 | 1160 | YHR034c | 3 | 0.667 | 9 | YHR074w | 2 | 0.000 | 118 |
| YHL047c | 9 | 0.222 | 1252 | YHR035w | 6 | 0.200 | 108 | YHR076w | 3 | 0.000 | 70 |
| YHL048w | 20 | 0.200 | 1786 | YHR036w | 3 | 0.000 | 31 | YHR077c | 3 | 0.333 | 58 |
| YHL049c | 17 | 0.294 | 1467 | YHR037w | 11 | 0.145 | 805 | YHR078w | 4 | 0.667 | 54 |
| YHL050c | 6 | 0.400 | 234 | YHR038w | 2 | 0.000 | 30 | YHR079c | 3 | 0.000 | 187 |
| YHR001w | 14 | 0.121 | 1359 | YHR039c | 3 | 0.000 | 53 | YHR079c-a | 3 | 0.333 | 15 |
| YHR001w-a | 12 | 0.136 | 562 | YHR039c-a | 5 | 0.200 | 180 | YHR080c | 5 | 0.100 | 253 |
| YHR002w | 5 | 0.200 | 265 | YHR040w | 3 | 0.333 | 38 | YHR081w | 6 | 0.000 | 646 |
| YHR003c | 4 | 0.167 | 73 | YHR041c | 9 | 0.250 | 744 | YHR082c | 4 | 0.000 | 168 |
| YHR004c | 5 | 0.200 | 147 | YHR042w | 11 | 0.218 | 638 | YHR083w | 8 | 0.107 | 1116 |
| YHR005c | 10 | 0.467 | 658 | YHR043c | 9 | 0.222 | 537 | YHR084w | 1375 | 0.007 | 3379020 |
| YHR005c-a | 7 | 0.333 | 216 | YHR044c | 5 | 0.000 | 334 | YHR085w | 6 | 0.333 | 637 |
| YHR006w | 345 | 0.008 | 467778 | YHR045w | 2 | 0.000 | 30 | YHR086w | 9 | 0.333 | 756 |
| YHR007c | 17 | 0.397 | 1160 | YHR046c | 3 | 0.333 | 111 | YHR087w | 39 | 0.189 | 13913 |
| YHR007c-a | 3 | 0.000 | 100 | YHR047c | 11 | 0.309 | 1073 | YHR088w | 10 | 0.311 | 311 |
| YHR008c | 17 | 0.294 | 924 | YHR048w | 17 | 0.360 | 2271 | YHR089c | 6 | 0.333 | 351 |
| YHR009c | 4 | 0.500 | 49 | YHR049c-a | 1 | 0.000 | 0 | YHR090c | 5 | 0.100 | 931 |
| YHR010w | 9 | 0.417 | 1024 | YHR049w | 18 | 0.275 | 1725 | YHR091c | 25 | 0.173 | 2580 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YHR092c | 25 | 0.307 | 3198 | YHR135c | 7 | 0.095 | 380 | YHR178w | 343 | 0.012 | 420044 |
| YHR093w | 2 | 0.000 | 2 | YHR136c | 27 | 0.188 | 5322 | YHR179w | 25 | 0.223 | 4314 |
| YHR094c | 32 | 0.226 | 7223 | YHR137w | 32 | 0.185 | 8960 | YHR180w | 3 | 0.000 | 69 |
| YHR095w | 8 | 0.179 | 670 | YHR138c | 25 | 0.147 | 6429 | YHR181w | 4 | 0.167 | 109 |
| YHR096c | 33 | 0.208 | 7296 | YHR139c | 21 | 0.238 | 2590 | YHR182w | 7 | 0.048 | 551 |
| YHR097c | 13 | 0.308 | 1414 | YHR139c-a | 4 | 0.333 | 288 | YHR183w | 8 | 0.250 | 1291 |
| YHR098c | 4 | 0.000 | 123 | YHR140w | 17 | 0.213 | 2628 | YHR184w | 9 | 0.528 | 1013 |
| YHR099w | 5 | 0.000 | 193 | YHR141c | 16 | 0.292 | 2574 | YHR185c | 6 | 0.067 | 1892 |
| YHR100c | 1 | 0.000 | 0 | YHR142w | 15 | 0.371 | 2201 | YHR186c | 6 | 0.267 | 456 |
| YHR101c | 1 | 0.000 | 0 | YHR143w | 10 | 0.244 | 419 | YHR187w | 1 | 0.000 | 0 |
| YHR102w | 1 | 0.000 | 0 | YHR143w-a | 4 | 0.333 | 83 | YHR189w | 3 | 0.000 | 50 |
| YHR103w | 4 | 0.500 | 166 | YHR144c | 5 | 0.500 | 162 | YHR190w | 24 | 0.185 | 2626 |
| YHR104w | 17 | 0.331 | 1205 | YHR145c | 6 | 0.267 | 196 | YHR191c | 5 | 0.300 | 482 |
| YHR105w | 2 | 0.000 | 29 | YHR146w | 5 | 0.200 | 211 | YHR192w | 5 | 0.400 | 132 |
| YHR106w | 1 | 0.000 | 0 | YHR147c | 4 | 0.000 | 330 | YHR193c | 19 | 0.111 | 1590 |
| YHR107c | 6 | 0.333 | 317 | YHR148w | 11 | 0.291 | 1510 | YHR194w | 18 | 0.098 | 907 |
| YHR108w | 4 | 0.333 | 119 | YHR149c | 10 | 0.400 | 503 | YHR195w | 7 | 0.000 | 321 |
| YHR109w | 3 | 0.333 | 76 | YHR150w | 8 | 0.500 | 105 | YHR196w | 8 | 0.500 | 259 |
| YHR110w | 5 | 0.200 | 426 | YHR151c | 9 | 0.333 | 539 | YHR197w | 4 | 0.667 | 17 |
| YHR111w | 6 | 0.267 | 290 | YHR152w | 16 | 0.300 | 2249 | YHR198c | 2 | 1.000 | 0 |
| YHR112c | 4 | 0.167 | 153 | YHR153c | 8 | 0.071 | 851 | YHR199c | 11 | 0.164 | 1640 |
| YHR113w | 4 | 0.167 | 87 | YHR154w | 10 | 0.111 | 1439 | YHR200w | 9 | 0.306 | 1277 |
| YHR114w | 2 | 0.000 | 31 | YHR155w | 19 | 0.058 | 3804 | YHR201c | 3 | 0.000 | 114 |
| YHR115c | 3 | 0.333 | 114 | YHR156c | 21 | 0.114 | 2351 | YHR202w | 8 | 0.286 | 519 |
| YHR116w | 5 | 0.200 | 344 | YHR157w | 18 | 0.157 | 2118 | YHR203c | 12 | 0.379 | 680 |
| YHR117w | 6 | 0.267 | 153 | YHR159w | 1 | 0.000 | 0 | YHR204w | 7 | 0.190 | 298 |
| YHR118c | 6 | 0.067 | 467 | YHR160c | 14 | 0.220 | 725 | YHR205w | 2 | 0.000 | 21 |
| YHR119w | 4 | 0.000 | 137 | YHR161c | 7 | 0.286 | 574 | YHR206w | 420 | 0.014 | 380453 |
| YHR120w | 4 | 0.167 | 139 | YHR162w | 9 | 0.250 | 851 | YHR207c | 5 | 0.500 | 72 |
| YHR121w | 5 | 0.200 | 385 | YHR163w | 2 | 1.000 | 0 | YHR208w | 10 | 0.400 | 549 |
| YHR122w | 5 | 0.400 | 225 | YHR164c | 4 | 0.333 | 127 | YHR209w | 13 | 0.295 | 1217 |
| YHR123w | 7 | 0.190 | 1168 | YHR165c | 2 | 0.000 | 139 | YHR210c | 13 | 0.308 | 975 |
| YHR124w | 40 | 0.050 | 46293 | YHR166c | 1 | 0.000 | 0 | YHR211w | 7 | 0.524 | 161 |
| YHR126c | 5 | 0.200 | 290 | YHR167w | 1 | 0.000 | 0 | YHR212c | 1 | 0.000 | 0 |
| YHR127w | 2 | 0.000 | 16 | YHR169w | 8 | 0.214 | 328 | YHR212w-a | 5 | 0.700 | 101 |
| YHR128w | 10 | 0.378 | 622 | YHR170w | 9 | 0.389 | 308 | YHR213w | 6 | 0.333 | 394 |
| YHR129c | 2 | 1.000 | 0 | YHR171w | 6 | 0.133 | 159 | YHR213w-a | 2 | 1.000 | 0 |
| YHR130c | 2 | 0.000 | 21 | YHR172w | 2 | 1.000 | 0 | YHR213w-b | 3 | 1.000 | 0 |
| YHR131c | 1 | 0.000 | 0 | YHR173c | 4 | 0.167 | 100 | YHR214c-b | 2 | 0.000 | 34 |
| YHR132c | 2 | 0.000 | 9 | YHR174w | 15 | 0.333 | 1470 | YHR214c-c | 1 | 0.000 | 0 |
| YHR132w-a | 1 | 0.000 | 0 | YHR175w | 8 | 0.179 | 424 | YHR214w | 7 | 0.333 | 68 |
| YHR133c | 4 | 0.333 | 66 | YHR176w | 6 | 0.267 | 182 | YHR214w-a | 9 | 0.278 | 472 |
| YHR134w | 7 | 0.524 | 471 | YHR177w | 3 | 1.000 | 0 | YHR215w | 15 | 0.133 | 1583 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YHR216w | 8 | 0.429 | 754 | YIL041w | 5 | 0.100 | 95 | YIL086c | 1 | 0.000 | 0 |
| YHR217c | 2 | 1.000 | 0 | YIL042c | 6 | 0.267 | 675 | YIL087c | 8 | 0.429 | 198 |
| YHR218w | 4 | 0.333 | 54 | YIL043c | 2 | 0.000 | 11 | YIL088c | 5 | 0.300 | 254 |
| YHR219w | 3 | 0.333 | 37 | YIL044c | 4 | 0.167 | 119 | YIL089w | 4 | 0.500 | 20 |
| YIL001w | 4 | 0.667 | 18 | YIL045w | 11 | 0.200 | 723 | YIL090w | 4 | 0.333 | 172 |
| YIL002c | 2 | 1.000 | 0 | YIL046w | 11 | 0.345 | 955 | YIL091c | 9 | 0.306 | 453 |
| YIL002w-a | 6 | 0.267 | 242 | YIL046w-a | 5 | 0.400 | 123 | YIL092w | 2 | 1.000 | 0 |
| YIL003w | 21 | 0.124 | 5310 | YIL047c | 8 | 0.321 | 411 | YIL094c | 5 | 0.300 | 229 |
| YIL004c | 1 | 0.000 | 0 | YIL048w | 10 | 0.178 | 1018 | YIL095w | 5 | 0.500 | 64 |
| YIL005w | 1 | 0.000 | 0 | YIL049w | 2 | 1.000 | 0 | YIL096c | 9 | 0.444 | 4329 |
| YIL006w | 3 | 0.667 | 2 | YIL050w | 10 | 0.333 | 933 | YIL097w | 4 | 0.167 | 152 |
| YIL008w | 3 | 0.667 | 70 | YIL051c | 15 | 0.200 | 1877 | YIL098c | 7 | 0.238 | 236 |
| YIL009c-a | 3 | 0.333 | 60 | YIL052c | 13 | 0.295 | 1237 | YIL099w | 42 | 0.262 | 9463 |
| YIL009w | 10 | 0.444 | 280 | YIL053w | 21 | 0.267 | 2425 | YIL100w | 12 | 0.348 | 286 |
| YIL010w | 1 | 0.000 | 0 | YIL054w | 3 | 0.000 | 46 | YIL101c | 201 | 0.057 | 97533 |
| YIL011w | 18 | 0.359 | 1513 | YIL055c | 8 | 0.393 | 341 | YIL102c | 8 | 0.321 | 548 |
| YIL012w | 3 | 0.333 | 9 | YIL056w | 17 | 0.426 | 3136 | YIL103w | 3 | 1.000 | 0 |
| YIL013c | 18 | 0.412 | 1187 | YIL057c | 16 | 0.508 | 1405 | YIL104c | 4 | 0.500 | 48 |
| YIL014c-a | 3 | 0.667 | 6 | YIL060w | 2 | 0.000 | 26 | YIL105c | 2 | 0.000 | 11 |
| YIL014w | 7 | 0.143 | 152 | YIL061c | 2 | 0.000 | 16 | YIL106w | 6 | 0.400 | 139 |
| YIL015c-a | 2 | 0.000 | 9 | YIL062c | 3 | 0.667 | 24 | YIL107c | 9 | 0.278 | 390 |
| YIL015w | 16 | 0.283 | 4558 | YIL063c | 2 | 0.000 | 39 | YIL108w | 7 | 0.333 | 257 |
| YIL016w | 4 | 0.500 | 179 | YIL064w | 3 | 0.000 | 46 | YIL109c | 3 | 0.333 | 27 |
| YIL018w | 11 | 0.309 | 1331 | YIL065c | 5 | 0.400 | 64 | YIL110w | 2 | 0.000 | 75 |
| YIL019w | 14 | 0.308 | 1573 | YIL066c | 28 | 0.230 | 3927 | YIL111w | 11 | 0.182 | 975 |
| YIL020c | 7 | 0.190 | 710 | YIL067c | 1 | 0.000 | 0 | YIL112w | 6 | 0.200 | 264 |
| YIL022w | 4 | 0.333 | 206 | YIL069c | 13 | 0.321 | 1122 | YIL113w | 14 | 0.275 | 1808 |
| YIL023c | 6 | 0.067 | 382 | YIL070c | 5 | 0.200 | 110 | YIL114c | 7 | 0.381 | 257 |
| YIL024c | 3 | 0.333 | 38 | YIL071c | 1 | 0.000 | 0 | YIL115c | 4 | 0.333 | 41 |
| YIL026c | 5 | 0.400 | 175 | YIL072w | 9 | 0.250 | 582 | YIL116w | 13 | 0.359 | 860 |
| YIL027c | 1 | 0.000 | 0 | YIL073c | 4 | 0.333 | 106 | YIL117c | 28 | 0.238 | 4419 |
| YIL029c | 2 | 0.000 | 5 | YIL074c | 7 | 0.476 | 345 | YIL118w | 23 | 0.415 | 2509 |
| YIL030c | 7 | 0.429 | 437 | YIL075c | 8 | 0.571 | 183 | YIL119c | 34 | 0.360 | 4432 |
| YIL031w | 4 | 0.167 | 284 | YIL076w | 4 | 0.000 | 299 | YIL120w | 6 | 0.467 | 184 |
| YIL032c | 3 | 0.333 | 97 | YIL077c | 4 | 0.000 | 137 | YIL121w | 15 | 0.324 | 1643 |
| YIL033c | 8 | 0.393 | 249 | YIL078w | 3 | 0.667 | 14 | YIL122w | 111 | 0.029 | 185444 |
| YIL034c | 1 | 0.000 | 0 | YIL079c | 2 | 0.000 | 158 | YIL123w | 21 | 0.338 | 2159 |
| YIL035c | 5 | 0.000 | 386 | YIL080w | 2 | 1.000 | 0 | YIL124w | 7 | 0.190 | 584 |
| YIL036w | 199 | 0.028 | 117431 | YIL082w | 2 | 1.000 | 0 | YIL125w | 6 | 0.200 | 69 |
| YIL037c | 18 | 0.340 | 3478 | YIL082w-a | 2 | 0.000 | 16 | YIL126w | 4 | 0.333 | 156 |
| YIL038c | 4 | 0.167 | 100 | YIL083c | 4 | 0.333 | 165 | YIL127c | 4 | 0.333 | 103 |
| YIL039w | 1 | 0.000 | 0 | YIL084c | 2 | 0.000 | 62 | YIL128w | 3 | 0.667 | 5 |
| YIL040w | 4 | 0.167 | 297 | YIL085c | 1 | 0.000 | 0 | YIL129c | 7 | 0.143 | 421 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YIL130w | 4 | 0.833 | 16 | YIL175w | 12 | 0.212 | 597 | YIR038c | 18 | 0.320 | 1942 |
| YIL131c | 242 | 0.010 | 199990 | YIL176c | 13 | 0.218 | 766 | YIR039c | 12 | 0.152 | 1034 |
| YIL132c | 4 | 0.333 | 38 | YIL177c | 17 | 0.309 | 1258 | YIR040c | 7 | 0.095 | 278 |
| YIL133c | 14 | 0.308 | 1793 | YIR001c | 2 | 0.000 | 19 | YIR041w | 11 | 0.236 | 725 |
| YIL134w | 2 | 0.000 | 94 | YIR002c | 5 | 0.600 | 83 | YIR042c | 7 | 0.238 | 621 |
| YIL135c | 7 | 0.143 | 801 | YIR003w | 5 | 0.400 | 95 | YIR043c | 5 | 0.500 | 127 |
| YIL136w | 23 | 0.316 | 2417 | YIR004w | 4 | 0.500 | 75 | YIR044c | 6 | 0.133 | 221 |
| YIL137c | 5 | 0.200 | 611 | YIR005w | 4 | 0.167 | 50 | YJL001w | 7 | 0.333 | 357 |
| YIL138c | 3 | 0.000 | 214 | YIR006c | 6 | 0.667 | 123 | YJL002c | 3 | 0.667 | 7 |
| YIL139c | 6 | 0.333 | 159 | YIR007w | 2 | 1.000 | 0 | YJL003w | 4 | 0.167 | 17 |
| YIL140w | 7 | 0.095 | 243 | YIR008c | 2 | 0.000 | 28 | YJL004c | 2 | 0.000 | 36 |
| YIL141w | 5 | 0.300 | 91 | YIR009w | 3 | 0.000 | 269 | YJL005w | 4 | 0.333 | 80 |
| YIL142w | 3 | 0.333 | 34 | YIR010w | 2 | 0.000 | 68 | YJL006c | 2 | 0.000 | 6 |
| YIL143c | 2 | 0.000 | 19 | YIR011c | 2 | 0.000 | 34 | YJL007c | 1 | 0.000 | 0 |
| YIL144w | 3 | 0.000 | 75 | YIR012w | 5 | 0.200 | 153 | YJL008c | 8 | 0.286 | 826 |
| YIL145c | 4 | 0.167 | 261 | YIR013c | 135 | 0.037 | 15803 | YJL009w | 1 | 0.000 | 0 |
| YIL146c | 1 | 0.000 | 0 | YIR014w | 7 | 0.429 | 148 | YJL010c | 2 | 0.000 | 36 |
| YIL147c | 2 | 0.000 | 27 | YIR015w | 4 | 0.333 | 57 | YJL011c | 4 | 0.167 | 104 |
| YIL148w | 8 | 0.429 | 365 | YIR016w | 10 | 0.333 | 1010 | YJL012c | 11 | 0.109 | 1682 |
| YIL149c | 9 | 0.333 | 564 | YIR017c | 63 | 0.088 | 45517 | YJL012c-a | 2 | 0.000 | 13 |
| YIL150c | 1 | 0.000 | 0 | YIR018c-a | 5 | 0.900 | 2 | YJL013c | 1 | 0.000 | 0 |
| YIL152w | 2 | 0.000 | 36 | YIR018w | 504 | 0.012 | 614058 | YJL014w | 2 | 1.000 | 0 |
| YIL153w | 6 | 0.533 | 119 | YIR019c | 31 | 0.314 | 3668 | YJL016w | 11 | 0.309 | 768 |
| YIL154c | 8 | 0.250 | 736 | YIR020c | 18 | 0.373 | 562 | YJL017w | 2 | 0.000 | 8 |
| YIL155c | 25 | 0.253 | 4466 | YIR020w-a | 1 | 0.000 | 0 | YJL019w | 1 | 0.000 | 0 |
| YIL156w | 4 | 0.667 | 85 | YIR020w-b | 10 | 0.489 | 89 | YJL020c | 3 | 1.000 | 0 |
| YIL157c | 1 | 0.000 | 0 | YIR021w | 15 | 0.590 | 363 | YJL022w | 6 | 0.067 | 169 |
| YIL158w | 9 | 0.139 | 454 | YIR022w | 2 | 0.000 | 17 | YJL023c | 10 | 0.200 | 953 |
| YIL159w | 7 | 0.286 | 288 | YIR023w | 254 | 0.003 | 248926 | YJL024c | 2 | 0.000 | 46 |
| YIL160c | 14 | 0.264 | 1711 | YIR024c | 2 | 0.000 | 31 | YJL025w | 5 | 0.200 | 277 |
| YIL161w | 2 | 1.000 | 0 | YIR025w | 3 | 0.000 | 242 | YJL026w | 19 | 0.398 | 1351 |
| YIL162w | 27 | 0.188 | 3473 | YIR026c | 7 | 0.286 | 1667 | YJL027c | 5 | 0.400 | 84 |
| YIL164c | 5 | 0.500 | 130 | YIR027c | 19 | 0.269 | 4591 | YJL028w | 6 | 0.333 | 257 |
| YIL165c | 4 | 0.833 | 16 | YIR028w | 14 | 0.220 | 3231 | YJL029c | 7 | 0.524 | 121 |
| YIL166c | 7 | 0.143 | 411 | YIR029w | 17 | 0.257 | 2615 | YJL030w | 6 | 0.400 | 180 |
| YIL167w | 4 | 0.500 | 32 | YIR030c | 6 | 0.067 | 388 | YJL031c | 9 | 0.278 | 390 |
| YIL168w | 9 | 0.472 | 166 | YIR031c | 14 | 0.198 | 1950 | YJL032w | 1 | 0.000 | 0 |
| YIL169c | 22 | 0.260 | 1945 | YIR032c | 17 | 0.184 | 2345 | YJL033w | 5 | 0.200 | 160 |
| YIL170w | 19 | 0.380 | 1504 | YIR033w | 35 | 0.062 | 11992 | YJL034w | 8 | 0.321 | 952 |
| YIL171w | 14 | 0.473 | 496 | YIR034c | 17 | 0.191 | 2194 | YJL035c | 3 | 1.000 | 0 |
| YIL172c | 17 | 0.485 | 783 | YIR035c | 5 | 0.100 | 251 | YJL036w | 2 | 1.000 | 0 |
| YIL173w | 8 | 0.250 | 632 | YIR036c | 6 | 0.400 | 125 | YJL037w | 6 | 0.200 | 572 |
| YIL174w | 11 | 0.236 | 439 | YIR037w | 1 | 0.000 | 0 | YJL038c | 7 | 0.190 | 560 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YJL041w | 1 | 0.000 | 0 | YJL083w | 5 | 0.200 | 150 | YJL126w | 2 | 0.000 | 29 |
| YJL042w | 7 | 0.381 | 204 | YJL084c | 7 | 0.238 | 230 | YJL127c | 3 | 0.667 | 28 |
| YJL043w | 9 | 0.306 | 996 | YJL085w | 6 | 0.267 | 167 | YJL127c-b | 2 | 1.000 | 0 |
| YJL044c | 8 | 0.321 | 995 | YJL086c | 1 | 0.000 | 0 | YJL129c | 2 | 0.000 | 33 |
| YJL045w | 17 | 0.228 | 1845 | YJL087c | 1 | 0.000 | 0 | YJL130c | 6 | 0.533 | 113 |
| YJL047c | 1 | 0.000 | 0 | YJL088w | 24 | 0.210 | 3279 | YJL131c | 1 | 0.000 | 0 |
| YJL047c-a | 6 | 0.467 | 149 | YJL089w | 116 | 0.027 | 142180 | YJL132w | 4 | 0.500 | 45 |
| YJL048c | 15 | 0.267 | 1307 | YJL090c | 4 | 0.167 | 79 | YJL133c-a | 2 | 0.000 | 24 |
| YJL049w | 7 | 0.429 | 318 | YJL091c | 4 | 0.000 | 93 | YJL133w | 5 | 0.000 | 484 |
| YJL050w | 9 | 0.278 | 501 | YJL092w | 6 | 0.200 | 283 | YJL134w | 9 | 0.361 | 671 |
| YJL051w | 9 | 0.167 | 768 | YJL093c | 3 | 1.000 | 0 | YJL135w | 6 | 0.333 | 260 |
| YJL052c-a | 2 | 1.000 | 0 | YJL094c | 6 | 0.267 | 762 | YJL136c | 12 | 0.318 | 1069 |
| YJL052w | 17 | 0.176 | 1876 | YJL095w | 5 | 0.200 | 247 | YJL136w-a | 1 | 0.000 | 0 |
| YJL053w | 2 | 0.000 | 22 | YJL096w | 4 | 0.333 | 71 | YJL137c | 1 | 0.000 | 0 |
| YJL054w | 2 | 0.000 | 15 | YJL097w | 3 | 0.333 | 67 | YJL138c | 6 | 0.333 | 275 |
| YJL055w | 3 | 0.667 | 103 | YJL098w | 5 | 0.500 | 61 | YJL139c | 7 | 0.143 | 171 |
| YJL056c | 191 | 0.011 | 115335 | YJL099w | 2 | 0.000 | 82 | YJL140w | 4 | 0.333 | 70 |
| YJL057c | 7 | 0.238 | 1288 | YJL100w | 10 | 0.356 | 770 | YJL141c | 9 | 0.306 | 403 |
| YJL058c | 3 | 0.667 | 37 | YJL101c | 17 | 0.221 | 1926 | YJL142c | 5 | 0.100 | 105 |
| YJL059w | 1 | 0.000 | 0 | YJL102w | 5 | 0.100 | 2051 | YJL143w | 4 | 0.000 | 184 |
| YJL060w | 14 | 0.077 | 1108 | YJL103c | 23 | 0.123 | 9756 | YJL144w | 15 | 0.171 | 1497 |
| YJL061w | 3 | 0.000 | 35 | YJL104w | 9 | 0.194 | 1550 | YJL145w | 8 | 0.250 | 149 |
| YJL062w | 1 | 0.000 | 0 | YJL105w | 13 | 0.231 | 2763 | YJL146w | 3 | 0.000 | 72 |
| YJL063c | 2 | 1.000 | 0 | YJL106w | 18 | 0.242 | 2666 | YJL147c | 1 | 0.000 | 0 |
| YJL064w | 1 | 0.000 | 0 | YJL107c | 16 | 0.308 | 852 | YJL148w | 45 | 0.139 | 16159 |
| YJL066c | 2 | 0.000 | 13 | YJL108c | 5 | 0.100 | 896 | YJL149w | 12 | 0.182 | 1315 |
| YJL067w | 4 | 0.333 | 48 | YJL109c | 3 | 0.000 | 106 | YJL150w | 4 | 0.167 | 160 |
| YJL068c | 7 | 0.238 | 390 | YJL110c | 152 | 0.022 | 86457 | YJL151c | 9 | 0.278 | 774 |
| YJL069c | 5 | 0.200 | 524 | YJL111w | 2 | 0.000 | 139 | YJL152w | 8 | 0.250 | 360 |
| YJL070c | 2 | 1.000 | 0 | YJL112w | 6 | 0.333 | 543 | YJL153c | 27 | 0.154 | 7813 |
| YJL071w | 4 | 0.667 | 68 | YJL113w | 2 | 0.000 | 13 | YJL154c | 1 | 0.000 | 0 |
| YJL072c | 1 | 0.000 | 0 | YJL114w | 3 | 0.333 | 43 | YJL155c | 5 | 0.200 | 131 |
| YJL073w | 8 | 0.107 | 860 | YJL115w | 13 | 0.359 | 790 | YJL156c | 3 | 0.000 | 63 |
| YJL074c | 5 | 0.100 | 406 | YJL116c | 24 | 0.301 | 3231 | YJL156w-a | 2 | 1.000 | 0 |
| YJL075c | 3 | 0.333 | 12 | YJL117w | 5 | 0.400 | 128 | YJL157c | 7 | 0.429 | 53 |
| YJL076w | 7 | 0.381 | 510 | YJL118w | 4 | 0.000 | 113 | YJL158c | 21 | 0.290 | 2626 |
| YJL077c | 8 | 0.321 | 691 | YJL119c | 3 | 0.333 | 22 | YJL159w | 22 | 0.303 | 3531 |
| YJL077w-b | 4 | 0.333 | 18 | YJL120w | 1 | 0.000 | 0 | YJL160c | 12 | 0.242 | 582 |
| YJL078c | 17 | 0.390 | 1212 | YJL121c | 4 | 0.000 | 122 | YJL161w | 11 | 0.182 | 700 |
| YJL079c | 25 | 0.317 | 3664 | YJL122w | 4 | 0.500 | 50 | YJL162c | 5 | 0.400 | 1272 |
| YJL080c | 6 | 0.267 | 216 | YJL123c | 2 | 0.000 | 39 | YJL163c | 12 | 0.227 | 514 |
| YJL081c | 2 | 0.000 | 20 | YJL124c | 2 | 0.000 | 9 | YJL164c | 9 | 0.139 | 813 |
| YJL082w | 9 | 0.361 | 238 | YJL125c | 1 | 0.000 | 0 | YJL165c | 1 | 0.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YJL166w | 9 | 0.111 | 656 | YJL213w | 12 | 0.288 | 1009 | YJR035w | 2 | 0.000 | 20 |
| YJL167w | 4 | 0.167 | 216 | YJL214w | 5 | 0.800 | 16 | YJR036c | 1 | 0.000 | 0 |
| YJL168c | 4 | 0.000 | 617 | YJL215c | 1 | 0.000 | 0 | YJR038c | 1 | 0.000 | 0 |
| YJL169w | 1 | 0.000 | 0 | YJL216c | 16 | 0.317 | 1439 | YJR039w | 2 | 0.000 | 40 |
| YJL170c | 17 | 0.434 | 761 | YJL217w | 13 | 0.154 | 1062 | YJR040w | 3 | 0.000 | 89 |
| YJL171c | 10 | 0.178 | 444 | YJL218w | 17 | 0.279 | 1868 | YJR041c | 7 | 0.190 | 614 |
| YJL172w | 10 | 0.200 | 878 | YJL219w | 20 | 0.347 | 1656 | YJR042w | 3 | 0.333 | 43 |
| YJL173c | 5 | 0.000 | 290 | YJL220w | 11 | 0.455 | 330 | YJR043c | 6 | 0.533 | 1050 |
| YJL174w | 2 | 0.000 | 110 | YJL221c | 19 | 0.480 | 1045 | YJR044c | 23 | 0.103 | 4296 |
| YJL175w | 4 | 0.333 | 200 | YJL222w | 4 | 0.000 | 268 | YJR045c | 7 | 0.143 | 859 |
| YJL176c | 9 | 0.306 | 692 | YJL223c | 14 | 0.187 | 1765 | YJR046w | 9 | 0.139 | 500 |
| YJL177w | 9 | 0.444 | 411 | YJL225c | 18 | 0.261 | 1184 | YJR047c | 12 | 0.379 | 576 |
| YJL178c | 4 | 0.333 | 35 | YJR001w | 3 | 0.000 | 227 | YJR048w | 19 | 0.234 | 2310 |
| YJL179w | 3 | 0.000 | 91 | YJR002w | 5 | 0.300 | 327 | YJR049c | 4 | 0.167 | 162 |
| YJL180c | 4 | 0.500 | 324 | YJR003c | 5 | 0.300 | 58 | YJR050w | 3 | 0.000 | 31 |
| YJL183w | 1 | 0.000 | 0 | YJR004c | 7 | 0.190 | 466 | YJR051w | 4 | 0.333 | 68 |
| YJL184w | 3 | 1.000 | 0 | YJR005w | 2 | 0.000 | 80 | YJR052w | 2 | 0.000 | 31 |
| YJL185c | 7 | 0.238 | 236 | YJR006w | 6 | 0.200 | 436 | YJR053w | 5 | 0.300 | 116 |
| YJL186w | 8 | 0.250 | 322 | YJR007w | 8 | 0.071 | 811 | YJR054w | 10 | 0.289 | 637 |
| YJL187c | 7 | 0.333 | 287 | YJR008w | 12 | 0.227 | 923 | YJR055w | 2 | 0.000 | 36 |
| YJL188c | 6 | 0.267 | 60 | YJR009c | 10 | 0.378 | 426 | YJR056c | 3 | 0.000 | 171 |
| YJL189w | 14 | 0.308 | 1262 | YJR010c-a | 2 | 0.000 | 12 | YJR057w | 3 | 0.000 | 76 |
| YJL190c | 14 | 0.297 | 1289 | YJR010w | 16 | 0.200 | 2691 | YJR058c | 4 | 0.167 | 235 |
| YJL191w | 11 | 0.291 | 1088 | YJR011c | 23 | 0.142 | 3858 | YJR059w | 7 | 0.381 | 199 |
| YJL192c | 10 | 0.244 | 456 | YJR013w | 4 | 0.167 | 307 | YJR060w | 334 | 0.009 | 432706 |
| YJL194w | 17 | 0.250 | 1549 | YJR015w | 6 | 0.067 | 321 | YJR061w | 8 | 0.357 | 509 |
| YJL196c | 21 | 0.200 | 2232 | YJR016c | 8 | 0.357 | 412 | YJR062c | 1 | 0.000 | 0 |
| YJL197w | 1 | 0.000 | 0 | YJR017c | 2 | 0.000 | 11 | YJR063w | 2 | 0.000 | 171 |
| YJL198w | 8 | 0.429 | 337 | YJR018w | 3 | 0.667 | 11 | YJR064w | 3 | 0.333 | 60 |
| YJL199c | 1 | 0.000 | 0 | YJR019c | 9 | 0.389 | 404 | YJR065c | 3 | 0.333 | 230 |
| YJL200c | 10 | 0.333 | 520 | YJR020w | 1 | 0.000 | 0 | YJR066w | 4 | 0.167 | 319 |
| YJL201w | 5 | 0.100 | 281 | YJR021c | 2 | 1.000 | 0 | YJR067c | 1 | 0.000 | 0 |
| YJL202c | 1 | 0.000 | 0 | YJR022w | 2 | 0.000 | 19 | YJR068w | 1 | 0.000 | 0 |
| YJL203w | 11 | 0.145 | 1243 | YJR023c | 2 | 1.000 | 0 | YJR069c | 3 | 0.333 | 34 |
| YJL204c | 11 | 0.073 | 946 | YJR025c | 12 | 0.439 | 1461 | YJR070c | 4 | 0.500 | 68 |
| YJL205c | 5 | 0.400 | 614 | YJR026w | 3 | 0.333 | 231 | YJR071w | 5 | 0.200 | 142 |
| YJL206c | 52 | 0.010 | 33077 | YJR027w | 4 | 0.333 | 285 | YJR072c | 1 | 0.000 | 0 |
| YJL207c | 4 | 0.667 | 5 | YJR028w | 3 | 0.333 | 231 | YJR073c | 11 | 0.255 | 1004 |
| YJL208c | 3 | 0.667 | 30 | YJR029w | 4 | 0.333 | 285 | YJR074w | 4 | 0.333 | 116 |
| YJL209w | 6 | 0.000 | 790 | YJR030c | 8 | 0.357 | 410 | YJR075w | 4 | 0.500 | 883 |
| YJL210w | 13 | 0.295 | 1379 | YJR032w | 1 | 0.000 | 0 | YJR076c | 1 | 0.000 | 0 |
| YJL211c | 1 | 0.000 | 0 | YJR033c | 4 | 0.500 | 58 | YJR077c | 7 | 0.048 | 341 |
| YJL212c | 13 | 0.205 | 1900 | YJR034w | 1 | 0.000 | 0 | YJR078w | 12 | 0.136 | 2811 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YJR079w | 7 | 0.143 | 209 | YJR121w | 12 | 0.318 | 550 | YKL004w | 5 | 0.300 | 752 |
| YJR080c | 2 | 0.000 | 19 | YJR122w | 10 | 0.267 | 831 | YKL005c | 26 | 0.031 | 5471 |
| YJR082c | 5 | 0.000 | 92 | YJR123w | 13 | 0.397 | 1153 | YKL006c-a | 8 | 0.179 | 817 |
| YJR083c | 1 | 0.000 | 0 | YJR124c | 2 | 0.000 | 4 | YKL006w | 11 | 0.327 | 1850 |
| YJR084w | 1 | 0.000 | 0 | YJR127c | 68 | 0.084 | 115913 | YKL007w | 15 | 0.229 | 4247 |
| YJR085c | 5 | 0.200 | 323 | YJR128w | 5 | 0.000 | 436 | YKL008c | 16 | 0.217 | 3046 |
| YJR086w | 5 | 0.200 | 188 | YJR129c | 6 | 0.333 | 755 | YKL009w | 11 | 0.273 | 1186 |
| YJR087w | 2 | 0.000 | 7 | YJR130c | 2 | 1.000 | 0 | YKL010c | 5 | 0.200 | 391 |
| YJR088c | 9 | 0.278 | 320 | YJR131w | 3 | 0.667 | 20 | YKL011c | 3 | 0.333 | 222 |
| YJR089w | 10 | 0.311 | 586 | YJR132w | 6 | 0.467 | 124 | YKL012w | 1 | 0.000 | 0 |
| YJR090c | 4 | 0.000 | 71 | YJR133w | 4 | 0.167 | 419 | YKL013c | 3 | 0.000 | 162 |
| YJR091c | 10 | 0.222 | 527 | YJR134c | 3 | 0.667 | 33 | YKL014c | 4 | 0.167 | 488 |
| YJR092w | 8 | 0.286 | 296 | YJR135c | 6 | 0.133 | 628 | YKL015w | 170 | 0.023 | 186446 |
| YJR093c | 3 | 0.000 | 152 | YJR135w-a | 2 | 0.000 | 57 | YKL016c | 14 | 0.209 | 1124 |
| YJR094c | 45 | 0.180 | 51329 | YJR136c | 3 | 0.667 | 14 | YKL017c | 1 | 0.000 | 0 |
| YJR094w-a | 14 | 0.462 | 695 | YJR137c | 15 | 0.267 | 2393 | YKL018w | 1 | 0.000 | 0 |
| YJR095w | 19 | 0.310 | 2164 | YJR138w | 9 | 0.167 | 1106 | YKL019w | 5 | 0.400 | 105 |
| YJR096w | 18 | 0.288 | 2322 | YJR139c | 6 | 0.467 | 147 | YKL020c | 59 | 0.046 | 24449 |
| YJR097w | 5 | 0.200 | 196 | YJR140c | 2 | 0.000 | 17 | YKL021c | 2 | 0.000 | 88 |
| YJR098c | 7 | 0.095 | 825 | YJR141w | 2 | 1.000 | 0 | YKL022c | 1 | 0.000 | 0 |
| YJR099w | 4 | 0.000 | 178 | YJR144w | 13 | 0.154 | 1580 | YKL023w | 1 | 0.000 | 0 |
| YJR100c | 19 | 0.058 | 1426 | YJR145c | 18 | 0.412 | 1284 | YKL024c | 2 | 1.000 | 0 |
| YJR101w | 3 | 0.000 | 15 | YJR146w | 13 | 0.359 | 700 | YKL025c | 3 | 1.000 | 0 |
| YJR102c | 6 | 0.400 | 189 | YJR147w | 58 | 0.078 | 70404 | YKL026c | 8 | 0.464 | 687 |
| YJR103w | 8 | 0.286 | 624 | YJR148w | 19 | 0.333 | 2506 | YKL027w | 3 | 0.667 | 13 |
| YJR104c | 14 | 0.286 | 1585 | YJR149w | 6 | 0.133 | 91 | YKL028w | 6 | 0.333 | 447 |
| YJR105w | 9 | 0.250 | 899 | YJR150c | 11 | 0.291 | 598 | YKL029c | 19 | 0.374 | 2373 |
| YJR106w | 2 | 1.000 | 0 | YJR151c | 9 | 0.194 | 723 | YKL030w | 5 | 0.300 | 84 |
| YJR107w | 4 | 0.333 | 274 | YJR151w-a | 1 | 0.000 | 0 | YKL031w | 2 | 0.000 | 9 |
| YJR108w | 3 | 0.667 | 11 | YJR152w | 19 | 0.234 | 2565 | YKL032c | 129 | 0.024 | 135771 |
| YJR109c | 16 | 0.267 | 1532 | YJR153w | 6 | 0.800 | 3 | YKL033w | 5 | 0.400 | 261 |
| YJR110w | 11 | 0.273 | 922 | YJR154w | 7 | 0.286 | 333 | YKL033w-a | 4 | 0.000 | 106 |
| YJR111c | 4 | 0.333 | 170 | YJR155w | 7 | 0.571 | 181 | YKL034w | 5 | 0.300 | 367 |
| YJR112w | 5 | 0.200 | 277 | YJR156c | 16 | 0.242 | 4596 | YKL035w | 17 | 0.301 | 1270 |
| YJR112w-a | 1 | 0.000 | 0 | YJR157w | 11 | 0.473 | 350 | YKL036c | 2 | 0.000 | 15 |
| YJR113c | 5 | 0.500 | 92 | YJR158w | 21 | 0.405 | 1000 | YKL037w | 8 | 0.250 | 239 |
| YJR114w | 3 | 0.000 | 506 | YJR159w | 17 | 0.441 | 691 | YKL038w | 67 | 0.027 | 34011 |
| YJR115w | 14 | 0.341 | 1650 | YJR160c | 3 | 0.333 | 171 | YKL039w | 13 | 0.244 | 786 |
| YJR116w | 7 | 0.333 | 536 | YJR161c | 9 | 0.222 | 736 | YKL040c | 18 | 0.222 | 2054 |
| YJR117w | 1 | 0.000 | 0 | YJR162c | 1 | 0.000 | 0 | YKL041w | 2 | 0.000 | 76 |
| YJR118c | 4 | 0.167 | 145 | YKL001c | 15 | 0.286 | 1853 | YKL042w | 7 | 0.286 | 1193 |
| YJR119c | 5 | 0.400 | 130 | YKL002w | 3 | 0.333 | 48 | YKL043w | 534 | 0.021 | 578631 |
| YJR120w | 7 | 0.429 | 273 | YKL003c | 3 | 0.333 | 118 | YKL044w | 15 | 0.410 | 712 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YKL045w | 13 | 0.359 | 738 | YKL086w | 18 | 0.235 | 2340 | YKL128c | 3 | 0.000 | 137 |
| YKL046c | 1 | 0.000 | 0 | YKL087c | 8 | 0.321 | 545 | YKL129c | 4 | 0.500 | 292 |
| YKL047w | 5 | 0.200 | 310 | YKL088w | 2 | 1.000 | 0 | YKL130c | 1 | 0.000 | 0 |
| YKL048c | 2 | 0.000 | 32 | YKL089w | 2 | 0.000 | 36 | YKL131w | 1 | 0.000 | 0 |
| YKL049c | 5 | 0.000 | 518 | YKL090w | 6 | 0.333 | 121 | YKL132c | 5 | 0.400 | 49 |
| YKL050c | 1 | 0.000 | 0 | YKL091c | 11 | 0.309 | 543 | YKL133c | 2 | 0.000 | 2 |
| YKL051w | 13 | 0.128 | 1405 | YKL092c | 2 | 0.000 | 27 | YKL134c | 3 | 0.333 | 88 |
| YKL052c | 9 | 0.222 | 890 | YKL093w | 6 | 0.333 | 244 | YKL135c | 4 | 0.333 | 425 |
| YKL053c-a | 3 | 0.333 | 48 | YKL095w | 7 | 0.524 | 334 | YKL136w | 1 | 0.000 | 0 |
| YKL053w | 1 | 0.000 | 0 | YKL096c-b | 8 | 0.464 | 144 | YKL137w | 1 | 0.000 | 0 |
| YKL054c | 5 | 0.700 | 41 | YKL096w | 34 | 0.273 | 7123 | YKL138c | 5 | 0.200 | 427 |
| YKL055c | 5 | 0.200 | 148 | YKL096w-a | 31 | 0.280 | 5872 | YKL138c-a | 6 | 0.000 | 304 |
| YKL056c | 3 | 0.667 | 13 | YKL097c | 21 | 0.324 | 3335 | YKL139w | 6 | 0.200 | 181 |
| YKL057c | 4 | 0.333 | 148 | YKL098w | 7 | 0.286 | 373 | YKL140w | 2 | 0.000 | 27 |
| YKL058w | 6 | 0.200 | 199 | YKL099c | 3 | 0.000 | 277 | YKL141w | 10 | 0.200 | 607 |
| YKL059c | 5 | 0.300 | 77 | YKL100c | 4 | 0.167 | 164 | YKL142w | 10 | 0.244 | 846 |
| YKL060c | 12 | 0.227 | 1492 | YKL101w | 11 | 0.382 | 465 | YKL143w | 9 | 0.194 | 1561 |
| YKL061w | 2 | 1.000 | 0 | YKL102c | 4 | 0.500 | 38 | YKL144c | 5 | 0.100 | 614 |
| YKL062w | 522 | 0.016 | 493176 | YKL103c | 27 | 0.225 | 5053 | YKL145w | 5 | 0.600 | 63 |
| YKL063c | 9 | 0.222 | 809 | YKL104c | 9 | 0.278 | 483 | YKL146w | 5 | 0.200 | 169 |
| YKL064w | 4 | 0.333 | 199 | YKL105c | 2 | 0.000 | 19 | YKL147c | 3 | 0.667 | 19 |
| YKL065c | 4 | 0.500 | 138 | YKL106w | 3 | 0.000 | 122 | YKL148c | 12 | 0.167 | 890 |
| YKL066w | 4 | 0.167 | 78 | YKL107w | 11 | 0.164 | 2618 | YKL149c | 2 | 0.000 | 27 |
| YKL067w | 8 | 0.357 | 412 | YKL108w | 2 | 0.000 | 23 | YKL150w | 15 | 0.352 | 762 |
| YKL068w | 7 | 0.524 | 320 | YKL109w | 448 | 0.018 | 510855 | YKL151c | 11 | 0.382 | 420 |
| YKL068w-a | 1 | 0.000 | 0 | YKL110c | 18 | 0.477 | 940 | YKL152c | 9 | 0.278 | 729 |
| YKL069w | 6 | 0.067 | 807 | YKL111c | 2 | 0.000 | 71 | YKL153w | 3 | 0.000 | 64 |
| YKL070w | 7 | 0.286 | 251 | YKL112w | 688 | 0.003 | 1544447 | YKL154w | 3 | 0.333 | 67 |
| YKL071w | 17 | 0.250 | 1390 | YKL113c | 5 | 0.400 | 30 | YKL155c | 2 | 0.000 | 20 |
| YKL072w | 10 | 0.067 | 1058 | YKL114c | 4 | 0.000 | 122 | YKL156w | 9 | 0.417 | 619 |
| YKL073w | 14 | 0.121 | 1370 | YKL115c | 2 | 0.000 | 14 | YKL157w | 14 | 0.308 | 1072 |
| YKL074c | 4 | 0.333 | 193 | YKL116c | 2 | 0.000 | 23 | YKL159c | 3 | 0.333 | 151 |
| YKL075c | 3 | 0.000 | 118 | YKL117w | 3 | 1.000 | 0 | YKL160w | 4 | 0.167 | 451 |
| YKL076c | 1 | 0.000 | 0 | YKL118w | 4 | 0.167 | 382 | YKL161c | 11 | 0.164 | 1271 |
| YKL077w | 10 | 0.133 | 1355 | YKL119c | 2 | 0.000 | 36 | YKL162c | 3 | 0.667 | 14 |
| YKL078w | 11 | 0.091 | 2393 | YKL120w | 15 | 0.114 | 1733 | YKL162c-a | 9 | 0.417 | 247 |
| YKL079w | 3 | 0.000 | 212 | YKL121w | 2 | 1.000 | 0 | YKL163w | 35 | 0.249 | 5275 |
| YKL080w | 4 | 0.500 | 77 | YKL122c | 5 | 0.600 | 122 | YKL164c | 16 | 0.358 | 865 |
| YKL081w | 9 | 0.417 | 572 | YKL123w | 2 | 0.000 | 73 | YKL165c | 10 | 0.200 | 4382 |
| YKL082c | 10 | 0.400 | 3137 | YKL124w | 4 | 0.000 | 222 | YKL167c | 4 | 0.333 | 165 |
| YKL083w | 3 | 0.667 | 23 | YKL125w | 2 | 0.000 | 163 | YKL168c | 2 | 1.000 | 0 |
| YKL084w | 10 | 0.200 | 768 | YKL126w | 1 | 0.000 | 0 | YKL169c | 1 | 0.000 | 0 |
| YKL085w | 10 | 0.156 | 801 | YKL127w | 3 | 0.667 | 3 | YKL171w | 1 | 0.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YKL172w | 4 | 0.000 | 469 | YKL217w | 15 | 0.248 | 1180 | YKR038c | 6 | 0.267 | 287 |
| YKL173w | 4 | 0.167 | 276 | YKL218c | 8 | 0.357 | 817 | YKR039w | 25 | 0.273 | 2966 |
| YKL174c | 6 | 0.133 | 565 | YKL219w | 11 | 0.109 | 797 | YKR040c | 19 | 0.234 | 1739 |
| YKL175w | 3 | 0.333 | 15 | YKL220c | 22 | 0.221 | 4897 | YKR041w | 14 | 0.264 | 1249 |
| YKL176c | 6 | 0.333 | 286 | YKL221w | 17 | 0.199 | 2886 | YKR042w | 32 | 0.282 | 4862 |
| YKL177w | 13 | 0.231 | 2052 | YKL222c | 1 | 0.000 | 0 | YKR043c | 4 | 0.000 | 165 |
| YKL178c | 13 | 0.218 | 2315 | YKL223w | 4 | 0.500 | 10 | YKR044w | 5 | 0.100 | 311 |
| YKL179c | 21 | 0.205 | 4292 | YKL224c | 12 | 0.348 | 420 | YKR045c | 1 | 0.000 | 0 |
| YKL180w | 8 | 0.536 | 278 | YKL225w | 8 | 0.179 | 257 | YKR046c | 11 | 0.309 | 1028 |
| YKL181w | 5 | 0.600 | 74 | YKR002w | 1 | 0.000 | 0 | YKR047w | 1 | 0.000 | 0 |
| YKL182w | 17 | 0.250 | 2827 | YKR003w | 1 | 0.000 | 0 | YKR048c | 1 | 0.000 | 0 |
| YKL183c-a | 1 | 0.000 | 0 | YKR004c | 4 | 0.000 | 80 | YKR049c | 9 | 0.417 | 342 |
| YKL183w | 7 | 0.286 | 763 | YKR005c | 3 | 0.333 | 29 | YKR051w | 1 | 0.000 | 0 |
| YKL184w | 3 | 0.000 | 71 | YKR006c | 1 | 0.000 | 0 | YKR052c | 12 | 0.364 | 708 |
| YKL185w | 120 | 0.028 | 48262 | YKR007w | 2 | 0.000 | 31 | YKR053c | 11 | 0.255 | 1622 |
| YKL186c | 5 | 0.600 | 18 | YKR008w | 2 | 0.000 | 18 | YKR054c | 5 | 0.400 | 249 |
| YKL187c | 15 | 0.181 | 1141 | YKR009c | 13 | 0.167 | 1313 | YKR055w | 8 | 0.107 | 907 |
| YKL188c | 4 | 0.500 | 57 | YKR010c | 5 | 0.100 | 254 | YKR056w | 9 | 0.167 | 714 |
| YKL189w | 6 | 0.400 | 393 | YKR011c | 6 | 0.600 | 65 | YKR057w | 12 | 0.439 | 865 |
| YKL190w | 2 | 0.000 | 171 | YKR012c | 4 | 0.000 | 138 | YKR058w | 12 | 0.212 | 2059 |
| YKL191w | 2 | 0.000 | 77 | YKR013w | 10 | 0.333 | 452 | YKR059w | 8 | 0.286 | 1114 |
| YKL192c | 2 | 1.000 | 0 | YKR014c | 3 | 0.667 | 5 | YKR060w | 4 | 0.333 | 85 |
| YKL193c | 1 | 0.000 | 0 | YKR015c | 4 | 0.000 | 432 | YKR061w | 10 | 0.356 | 584 |
| YKL194c | 1 | 0.000 | 0 | YKR016w | 3 | 0.333 | 27 | YKR062w | 6 | 0.067 | 330 |
| YKL195w | 4 | 0.167 | 240 | YKR018c | 2 | 0.000 | 30 | YKR063c | 2 | 1.000 | 0 |
| YKL196c | 5 | 0.400 | 451 | YKR019c | 2 | 1.000 | 0 | YKR064w | 1 | 0.000 | 0 |
| YKL197c | 8 | 0.286 | 646 | YKR020w | 1 | 0.000 | 0 | YKR065c | 5 | 0.400 | 126 |
| YKL198c | 8 | 0.321 | 234 | YKR021w | 1 | 0.000 | 0 | YKR066c | 9 | 0.361 | 625 |
| YKL201c | 15 | 0.314 | 1357 | YKR022c | 4 | 0.167 | 307 | YKR067w | 9 | 0.306 | 684 |
| YKL202w | 2 | 0.000 | 14 | YKR023w | 3 | 0.000 | 187 | YKR068c | 6 | 0.267 | 678 |
| YKL203c | 7 | 0.143 | 714 | YKR024c | 8 | 0.464 | 313 | YKR069w | 6 | 0.200 | 166 |
| YKL204w | 5 | 0.400 | 211 | YKR025w | 3 | 0.667 | 22 | YKR070w | 6 | 0.533 | 406 |
| YKL205w | 5 | 0.400 | 133 | YKR026c | 9 | 0.139 | 1860 | YKR071c | 6 | 0.333 | 156 |
| YKL207w | 1 | 0.000 | 0 | YKR027w | 3 | 0.000 | 80 | YKR072c | 3 | 0.333 | 57 |
| YKL208w | 3 | 0.333 | 29 | YKR028w | 1 | 0.000 | 0 | YKR073c | 5 | 0.200 | 202 |
| YKL209c | 8 | 0.393 | 188 | YKR029c | 2 | 0.000 | 80 | YKR074w | 2 | 1.000 | 0 |
| YKL210w | 8 | 0.571 | 156 | YKR030w | 2 | 0.000 | 171 | YKR075c | 17 | 0.199 | 1849 |
| YKL211c | 7 | 0.238 | 839 | YKR031c | 3 | 0.667 | 5 | YKR076w | 14 | 0.253 | 1624 |
| YKL212w | 1 | 0.000 | 0 | YKR033c | 1 | 0.000 | 0 | YKR077w | 4 | 0.333 | 51 |
| YKL213c | 3 | 0.333 | 146 | YKR034w | 85 | 0.044 | 23689 | YKR078w | 2 | 0.000 | 160 |
| YKL214c | 2 | 0.000 | 30 | YKR035w-a | 1 | 0.000 | 0 | YKR079c | 4 | 0.500 | 92 |
| YKL215c | 1 | 0.000 | 0 | YKR036c | 2 | 0.000 | 10 | YKR080w | 13 | 0.256 | 961 |
| YKL216w | 18 | 0.203 | 3026 | YKR037c | 2 | 0.000 | 44 | YKR081c | 6 | 0.400 | 540 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YKR082w | 1 | 0.000 | 0 | YLL018c | 7 | 0.238 | 870 | YLL063c | 7 | 0.429 | 236 |
| YKR083c | 5 | 0.400 | 192 | YLL018c-a | 7 | 0.095 | 547 | YLL064c | 10 | 0.178 | 423 |
| YKR084c | 3 | 0.333 | 251 | YLL019c | 12 | 0.333 | 977 | YLL065w | 23 | 0.202 | 2888 |
| YKR085c | 2 | 0.000 | 46 | YLL020c | 4 | 0.000 | 76 | YLL066c | 21 | 0.252 | 2191 |
| YKR086w | 3 | 0.000 | 101 | YLL021w | 2 | 0.000 | 35 | YLL066w-b | 2 | 1.000 | 0 |
| YKR087c | 4 | 0.500 | 91 | YLL022c | 2 | 1.000 | 0 | YLL067c | 24 | 0.268 | 3206 |
| YKR088c | 1 | 0.000 | 0 | YLL023c | 6 | 0.400 | 155 | YLR001c | 3 | 0.333 | 36 |
| YKR089c | 6 | 0.267 | 369 | YLL024c | 10 | 0.267 | 695 | YLR002c | 6 | 0.133 | 663 |
| YKR090w | 5 | 0.300 | 215 | YLL025w | 13 | 0.192 | 1934 | YLR003c | 5 | 0.300 | 466 |
| YKR091w | 13 | 0.244 | 694 | YLL026w | 26 | 0.271 | 5848 | YLR004c | 8 | 0.321 | 1324 |
| YKR092c | 16 | 0.250 | 1943 | YLL027w | 15 | 0.276 | 759 | YLR005w | 5 | 0.600 | 120 |
| YKR093w | 24 | 0.225 | 3466 | YLL028w | 17 | 0.287 | 1319 | YLR006c | 4 | 0.167 | 126 |
| YKR094c | 8 | 0.536 | 320 | YLL029w | 3 | 0.000 | 100 | YLR007w | 2 | 0.000 | 36 |
| YKR095w | 4 | 0.333 | 67 | YLL030c | 3 | 0.000 | 66 | YLR008c | 1 | 0.000 | 0 |
| YKR095w-a | 1 | 0.000 | 0 | YLL032c | 9 | 0.056 | 1194 | YLR009w | 8 | 0.214 | 368 |
| YKR096w | 10 | 0.244 | 862 | YLL033w | 12 | 0.136 | 1686 | YLR010c | 1 | 0.000 | 0 |
| YKR097w | 24 | 0.246 | 2906 | YLL034c | 15 | 0.067 | 1843 | YLR011w | 3 | 0.000 | 9 |
| YKR098c | 6 | 0.067 | 211 | YLL035w | 3 | 0.333 | 58 | YLR012c | 13 | 0.269 | 831 |
| YKR099w | 146 | 0.016 | 99176 | YLL036c | 1 | 0.000 | 0 | YLR013w | 200 | 0.012 | 79517 |
| YKR100c | 3 | 0.667 | 36 | YLL037w | 4 | 0.500 | 72 | YLR014c | 31 | 0.049 | 38866 |
| YKR101w | 10 | 0.622 | 190 | YLL038c | 2 | 0.000 | 19 | YLR016c | 2 | 0.000 | 90 |
| YKR102w | 20 | 0.300 | 2060 | YLL039c | 18 | 0.333 | 1215 | YLR017w | 2 | 1.000 | 0 |
| YKR103w | 5 | 0.200 | 58 | YLL040c | 4 | 0.000 | 357 | YLR018c | 2 | 0.000 | 12 |
| YKR104w | 1 | 0.000 | 0 | YLL041c | 6 | 0.200 | 327 | YLR019w | 3 | 0.333 | 28 |
| YKR105c | 8 | 0.286 | 471 | YLL042c | 3 | 0.667 | 37 | YLR020c | 5 | 0.300 | 130 |
| YKR106w | 6 | 0.200 | 142 | YLL043w | 9 | 0.250 | 575 | YLR021w | 2 | 0.000 | 6 |
| YLL001w | 15 | 0.152 | 1974 | YLL045c | 10 | 0.422 | 531 | YLR022c | 8 | 0.286 | 1435 |
| YLL002w | 3 | 0.667 | 22 | YLL046c | 5 | 0.300 | 169 | YLR023c | 16 | 0.267 | 1096 |
| YLL004w | 10 | 0.267 | 1457 | YLL048c | 7 | 0.238 | 768 | YLR024c | 3 | 0.333 | 109 |
| YLL005c | 11 | 0.218 | 1274 | YLL049w | 5 | 0.900 | 25 | YLR025w | 3 | 0.000 | 427 |
| YLL006w | 8 | 0.000 | 697 | YLL050c | 5 | 0.500 | 73 | YLR026c | 1 | 0.000 | 0 |
| YLL006w-a | 2 | 0.000 | 48 | YLL051c | 8 | 0.500 | 591 | YLR027c | 6 | 0.200 | 135 |
| YLL007c | 5 | 0.100 | 272 | YLL052c | 16 | 0.350 | 986 | YLR028c | 3 | 0.000 | 77 |
| YLL008w | 7 | 0.143 | 388 | YLL053c | 8 | 0.179 | 684 | YLR029c | 12 | 0.348 | 811 |
| YLL009c | 7 | 0.238 | 218 | YLL054c | 6 | 0.267 | 144 | YLR030w | 9 | 0.194 | 738 |
| YLL010c | 3 | 0.333 | 14 | YLL055w | 18 | 0.288 | 1793 | YLR031w | 6 | 0.000 | 840 |
| YLL011w | 12 | 0.333 | 1338 | YLL056c | 15 | 0.286 | 1491 | YLR032w | 6 | 0.133 | 247 |
| YLL012w | 5 | 0.300 | 434 | YLL057c | 11 | 0.218 | 1740 | YLR033w | 6 | 0.200 | 354 |
| YLL013c | 4 | 0.167 | 367 | YLL058w | 6 | 0.333 | 183 | YLR034c | 10 | 0.244 | 498 |
| YLL014w | 3 | 0.333 | 65 | YLL059c | 2 | 0.000 | 77 | YLR035c | 6 | 0.333 | 231 |
| YLL015w | 10 | 0.222 | 629 | YLL060c | 8 | 0.214 | 375 | YLR035c-a | 18 | 0.229 | 2136 |
| YLL016w | 4 | 0.000 | 40 | YLL061w | 12 | 0.182 | 1467 | YLR037c | 5 | 0.100 | 199 |
| YLL017w | 2 | 0.000 | 4 | YLL062c | 7 | 0.095 | 382 | YLR038c | 9 | 0.111 | 692 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YLR039c | 2 | 1.000 | 0 | YLR082c | 9 | 0.028 | 1110 | YLR126c | 8 | 0.250 | 272 |
| YLR040c | 6 | 0.267 | 518 | YLR083c | 6 | 0.200 | 357 | YLR127c | 4 | 0.500 | 53 |
| YLR041w | 3 | 0.000 | 463 | YLR084c | 11 | 0.345 | 1405 | YLR128w | 3 | 0.333 | 111 |
| YLR042c | 25 | 0.300 | 2428 | YLR086w | 4 | 0.000 | 62 | YLR129w | 4 | 0.167 | 68 |
| YLR043c | 7 | 0.238 | 264 | YLR087c | 2 | 0.000 | 99 | YLR130c | 11 | 0.145 | 699 |
| YLR044c | 29 | 0.222 | 7571 | YLR088w | 1 | 0.000 | 0 | YLR131c | 169 | 0.032 | 148567 |
| YLR045c | 2 | 1.000 | 0 | YLR089c | 16 | 0.200 | 2830 | YLR132c | 2 | 1.000 | 0 |
| YLR046c | 10 | 0.133 | 1905 | YLR090w | 12 | 0.197 | 1139 | YLR133w | 5 | 0.400 | 148 |
| YLR047c | 20 | 0.205 | 1998 | YLR091w | 3 | 0.000 | 41 | YLR134w | 13 | 0.308 | 2365 |
| YLR048w | 19 | 0.275 | 1873 | YLR092w | 10 | 0.333 | 785 | YLR136c | 17 | 0.191 | 3276 |
| YLR049c | 9 | 0.194 | 445 | YLR093c | 4 | 0.500 | 71 | YLR137w | 9 | 0.389 | 462 |
| YLR050c | 4 | 0.167 | 215 | YLR094c | 4 | 0.167 | 238 | YLR138w | 1 | 0.000 | 0 |
| YLR051c | 6 | 0.333 | 217 | YLR095c | 3 | 0.333 | 181 | YLR139c | 7 | 0.286 | 567 |
| YLR052w | 4 | 0.000 | 89 | YLR096w | 3 | 0.667 | 38 | YLR140w | 4 | 0.000 | 88 |
| YLR053c | 9 | 0.389 | 237 | YLR097c | 4 | 0.000 | 109 | YLR141w | 10 | 0.178 | 732 |
| YLR054c | 9 | 0.111 | 432 | YLR098c | 100 | 0.003 | 63988 | YLR142w | 24 | 0.225 | 5080 |
| YLR055c | 8 | 0.214 | 699 | YLR099c | 10 | 0.089 | 1153 | YLR143w | 3 | 0.333 | 119 |
| YLR056w | 20 | 0.211 | 3651 | YLR099w-a | 1 | 0.000 | 0 | YLR144c | 3 | 0.333 | 114 |
| YLR057w | 2 | 0.000 | 17 | YLR100w | 4 | 0.500 | 52 | YLR145w | 4 | 0.333 | 74 |
| YLR058c | 17 | 0.279 | 2089 | YLR102c | 5 | 0.200 | 111 | YLR146c | 2 | 1.000 | 0 |
| YLR059c | 2 | 0.000 | 21 | YLR103c | 3 | 0.333 | 20 | YLR147c | 2 | 0.000 | 35 |
| YLR060w | 8 | 0.286 | 678 | YLR104w | 4 | 0.167 | 123 | YLR148w | 1 | 0.000 | 0 |
| YLR061w | 13 | 0.346 | 1861 | YLR105c | 13 | 0.192 | 1069 | YLR149c | 14 | 0.253 | 1591 |
| YLR062c | 3 | 0.333 | 203 | YLR106c | 8 | 0.250 | 704 | YLR149c-a | 2 | 0.000 | 19 |
| YLR063w | 3 | 0.000 | 140 | YLR107w | 10 | 0.133 | 1521 | YLR150w | 9 | 0.333 | 666 |
| YLR064w | 5 | 0.000 | 138 | YLR108c | 19 | 0.287 | 1734 | YLR151c | 3 | 0.000 | 84 |
| YLR065c | 7 | 0.048 | 1067 | YLR109w | 24 | 0.268 | 3005 | YLR152c | 8 | 0.179 | 404 |
| YLR066w | 8 | 0.107 | 1303 | YLR110c | 23 | 0.296 | 3116 | YLR153c | 12 | 0.212 | 967 |
| YLR067c | 3 | 0.000 | 18 | YLR111w | 9 | 0.194 | 671 | YLR154c | 11 | 0.309 | 658 |
| YLR068w | 1 | 0.000 | 0 | YLR112w | 13 | 0.269 | 1392 | YLR154c-g | 2 | 0.000 | 10 |
| YLR069c | 3 | 0.000 | 178 | YLR113w | 24 | 0.254 | 3907 | YLR154w-c | 1 | 0.000 | 0 |
| YLR070c | 6 | 0.200 | 127 | YLR114c | 5 | 0.000 | 364 | YLR155c | 7 | 0.000 | 280 |
| YLR071c | 2 | 0.000 | 254 | YLR115w | 4 | 0.000 | 217 | YLR156w | 4 | 0.500 | 86 |
| YLR072w | 4 | 0.500 | 84 | YLR116w | 1 | 0.000 | 0 | YLR157c | 4 | 0.000 | 56 |
| YLR073c | 9 | 0.361 | 459 | YLR117c | 1 | 0.000 | 0 | YLR157c-a | 1 | 0.000 | 0 |
| YLR074c | 12 | 0.409 | 665 | YLR118c | 3 | 0.333 | 112 | YLR157c-b | 1 | 0.000 | 0 |
| YLR075w | 12 | 0.455 | 732 | YLR119w | 1 | 0.000 | 0 | YLR157w-c | 2 | 1.000 | 0 |
| YLR076c | 6 | 0.133 | 576 | YLR120c | 17 | 0.176 | 2226 | YLR158c | 5 | 0.000 | 145 |
| YLR077w | 5 | 0.400 | 456 | YLR121c | 21 | 0.229 | 3191 | YLR159w | 4 | 0.167 | 77 |
| YLR078c | 3 | 0.333 | 230 | YLR122c | 3 | 0.000 | 60 | YLR160c | 6 | 0.133 | 604 |
| YLR079w | 3 | 0.000 | 51 | YLR123c | 3 | 0.333 | 83 | YLR161w | 3 | 0.000 | 39 |
| YLR080w | 14 | 0.198 | 1747 | YLR124w | 1 | 0.000 | 0 | YLR162w | 15 | 0.219 | 1585 |
| YLR081w | 11 | 0.236 | 1271 | YLR125w | 6 | 0.067 | 351 | YLR162w-a | 5 | 0.400 | 104 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YLR163c | 4 | 0.167 | 307 | YLR209c | 4 | 0.167 | 221 | YLR252w | 7 | 0.381 | 182 |
| YLR164w | 9 | 0.333 | 336 | YLR210w | 6 | 0.067 | 188 | YLR253w | 2 | 0.000 | 19 |
| YLR165c | 1 | 0.000 | 0 | YLR211c | 2 | 0.000 | 23 | YLR254c | 10 | 0.378 | 957 |
| YLR166c | 8 | 0.357 | 1207 | YLR212c | 5 | 0.500 | 140 | YLR255c | 8 | 0.321 | 189 |
| YLR167w | 13 | 0.244 | 2650 | YLR213c | 13 | 0.308 | 1707 | YLR256w | 198 | 0.037 | 162005 |
| YLR168c | 10 | 0.178 | 763 | YLR214w | 27 | 0.205 | 5700 | YLR256w-a | 3 | 0.333 | 195 |
| YLR169w | 7 | 0.143 | 138 | YLR215c | 2 | 0.000 | 14 | YLR257w | 11 | 0.291 | 1448 |
| YLR170c | 2 | 0.000 | 7 | YLR216c | 10 | 0.333 | 446 | YLR258w | 18 | 0.288 | 2517 |
| YLR171w | 7 | 0.048 | 253 | YLR217w | 3 | 0.333 | 38 | YLR259c | 8 | 0.321 | 959 |
| YLR172c | 3 | 0.000 | 82 | YLR218c | 3 | 0.000 | 134 | YLR260w | 5 | 0.500 | 132 |
| YLR173w | 5 | 0.100 | 532 | YLR219w | 3 | 0.000 | 2 | YLR261c | 7 | 0.095 | 307 |
| YLR174w | 20 | 0.168 | 2747 | YLR220w | 8 | 0.214 | 132 | YLR262c | 9 | 0.139 | 320 |
| YLR175w | 5 | 0.400 | 174 | YLR221c | 3 | 0.000 | 125 | YLR262c-a | 2 | 0.000 | 33 |
| YLR176c | 199 | 0.007 | 126921 | YLR222c | 9 | 0.306 | 773 | YLR263w | 7 | 0.381 | 560 |
| YLR177w | 9 | 0.278 | 276 | YLR223c | 314 | 0.018 | 327148 | YLR264c-a | 1 | 0.000 | 0 |
| YLR178c | 32 | 0.192 | 6866 | YLR224w | 3 | 0.667 | 41 | YLR264w | 9 | 0.278 | 987 |
| YLR179c | 14 | 0.187 | 2097 | YLR225c | 6 | 0.133 | 674 | YLR265c | 4 | 0.500 | 36 |
| YLR180w | 17 | 0.243 | 1923 | YLR226w | 2 | 0.000 | 26 | YLR266c | 24 | 0.083 | 3128 |
| YLR181c | 1 | 0.000 | 0 | YLR227c | 6 | 0.333 | 166 | YLR267w | 15 | 0.114 | 2056 |
| YLR182w | 222 | 0.014 | 134248 | YLR228c | 275 | 0.011 | 205404 | YLR268w | 1 | 0.000 | 0 |
| YLR183c | 240 | 0.014 | 481010 | YLR229c | 3 | 0.000 | 180 | YLR270w | 10 | 0.356 | 493 |
| YLR184w | 3 | 0.000 | 33 | YLR230w | 2 | 0.000 | 118 | YLR271w | 1 | 0.000 | 0 |
| YLR185w | 14 | 0.308 | 1171 | YLR231c | 6 | 0.200 | 693 | YLR272c | 7 | 0.286 | 202 |
| YLR186w | 5 | 0.300 | 119 | YLR232w | 1 | 0.000 | 0 | YLR273c | 5 | 0.200 | 118 |
| YLR187w | 4 | 0.500 | 47 | YLR233c | 6 | 0.267 | 240 | YLR274w | 5 | 0.300 | 169 |
| YLR188w | 3 | 0.000 | 98 | YLR234w | 3 | 0.333 | 23 | YLR275w | 3 | 0.667 | 36 |
| YLR189c | 8 | 0.179 | 368 | YLR235c | 1 | 0.000 | 0 | YLR276c | 8 | 0.321 | 888 |
| YLR190w | 7 | 0.143 | 251 | YLR236c | 2 | 0.000 | 22 | YLR277c | 6 | 0.267 | 163 |
| YLR191w | 1 | 0.000 | 0 | YLR237w | 16 | 0.200 | 2193 | YLR278c | 5 | 0.300 | 110 |
| YLR192c | 7 | 0.476 | 497 | YLR238w | 5 | 0.100 | 320 | YLR279w | 1 | 0.000 | 0 |
| YLR193c | 2 | 0.000 | 42 | YLR239c | 1 | 0.000 | 0 | YLR280c | 2 | 0.000 | 63 |
| YLR194c | 10 | 0.333 | 666 | YLR240w | 2 | 0.000 | 24 | YLR281c | 7 | 0.286 | 400 |
| YLR195c | 3 | 0.333 | 41 | YLR241w | 3 | 0.333 | 96 | YLR283w | 3 | 0.000 | 46 |
| YLR196w | 3 | 0.333 | 34 | YLR242c | 4 | 0.333 | 174 | YLR284c | 8 | 0.143 | 721 |
| YLR197w | 7 | 0.476 | 237 | YLR243w | 3 | 0.333 | 208 | YLR285w | 7 | 0.286 | 853 |
| YLR198c | 2 | 1.000 | 0 | YLR244c | 2 | 0.000 | 27 | YLR286c | 19 | 0.298 | 2951 |
| YLR199c | 5 | 0.300 | 100 | YLR245c | 1 | 0.000 | 0 | YLR287c | 9 | 0.111 | 647 |
| YLR200w | 7 | 0.190 | 262 | YLR246w | 4 | 0.167 | 370 | YLR287c-a | 10 | 0.378 | 629 |
| YLR203c | 1 | 0.000 | 0 | YLR247c | 2 | 1.000 | 0 | YLR288c | 3 | 0.000 | 35 |
| YLR205c | 14 | 0.198 | 1284 | YLR248w | 3 | 0.333 | 75 | YLR289w | 3 | 0.333 | 19 |
| YLR206w | 13 | 0.218 | 941 | YLR249w | 7 | 0.381 | 326 | YLR290c | 3 | 0.333 | 38 |
| YLR207w | 6 | 0.333 | 385 | YLR250w | 5 | 0.500 | 219 | YLR291c | 1 | 0.000 | 0 |
| YLR208w | 1 | 0.000 | 0 | YLR251w | 11 | 0.218 | 1071 | YLR292c | 5 | 0.100 | 782 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YLR293c | 3 | 0.000 | 207 | YLR338w | 3 | 0.333 | 29 | YLR382c | 3 | 0.000 | 51 |
| YLR294c | 9 | 0.222 | 137 | YLR339c | 5 | 0.400 | 170 | YLR383w | 1 | 0.000 | 0 |
| YLR295c | 8 | 0.286 | 80 | YLR340w | 9 | 0.472 | 413 | YLR384c | 5 | 0.100 | 836 |
| YLR296w | 6 | 0.067 | 23 | YLR341w | 5 | 0.100 | 240 | YLR385c | 2 | 0.000 | 32 |
| YLR297w | 18 | 0.281 | 2453 | YLR342w | 13 | 0.308 | 1195 | YLR386w | 3 | 0.000 | 141 |
| YLR298c | 3 | 0.667 | 42 | YLR343w | 7 | 0.286 | 552 | YLR387c | 8 | 0.536 | 264 |
| YLR299w | 16 | 0.267 | 1232 | YLR344w | 8 | 0.536 | 284 | YLR388w | 9 | 0.417 | 410 |
| YLR300w | 18 | 0.261 | 1836 | YLR345w | 6 | 0.267 | 263 | YLR389c | 2 | 1.000 | 0 |
| YLR301w | 13 | 0.179 | 1245 | YLR346c | 15 | 0.238 | 2104 | YLR390w | 4 | 0.500 | 15 |
| YLR302c | 10 | 0.244 | 475 | YLR347c | 6 | 0.467 | 461 | YLR390w-a | 6 | 0.467 | 117 |
| YLR303w | 15 | 0.362 | 1229 | YLR348c | 7 | 0.286 | 263 | YLR392c | 5 | 0.200 | 192 |
| YLR304c | 24 | 0.181 | 4185 | YLR349w | 5 | 0.200 | 615 | YLR393w | 3 | 0.667 | 8 |
| YLR305c | 2 | 0.000 | 30 | YLR350w | 11 | 0.091 | 867 | YLR394w | 3 | 0.333 | 42 |
| YLR306w | 5 | 0.300 | 276 | YLR351c | 4 | 0.167 | 401 | YLR395c | 9 | 0.083 | 294 |
| YLR307w | 7 | 0.095 | 1356 | YLR352w | 6 | 0.133 | 386 | YLR396c | 2 | 0.000 | 171 |
| YLR308w | 4 | 0.167 | 201 | YLR353w | 3 | 0.667 | 6 | YLR397c | 22 | 0.190 | 4100 |
| YLR309c | 3 | 0.000 | 169 | YLR354c | 7 | 0.238 | 368 | YLR398c | 1 | 0.000 | 0 |
| YLR310c | 3 | 0.333 | 38 | YLR355c | 7 | 0.429 | 212 | YLR399c | 11 | 0.364 | 1128 |
| YLR311c | 2 | 0.000 | 19 | YLR356w | 10 | 0.311 | 565 | YLR400w | 6 | 0.467 | 311 |
| YLR312c | 12 | 0.409 | 516 | YLR357w | 3 | 0.333 | 142 | YLR401c | 8 | 0.286 | 301 |
| YLR312w-a | 10 | 0.489 | 454 | YLR358c | 3 | 0.667 | 29 | YLR402w | 3 | 1.000 | 0 |
| YLR313c | 3 | 0.000 | 84 | YLR359w | 8 | 0.179 | 391 | YLR403w | 2188 | 0.003 | 7721326 |
| YLR314c | 3 | 0.667 | 171 | YLR360w | 3 | 0.333 | 8 | YLR405w | 1 | 0.000 | 0 |
| YLR315w | 1 | 0.000 | 0 | YLR362w | 4 | 0.167 | 216 | YLR406c | 11 | 0.400 | 929 |
| YLR316c | 2 | 0.000 | 20 | YLR363c | 6 | 0.200 | 3313 | YLR406c-a | 2 | 0.000 | 9 |
| YLR317w | 2 | 0.000 | 12 | YLR364w | 2 | 0.000 | 405 | YLR407w | 7 | 0.381 | 382 |
| YLR318w | 4 | 0.000 | 191 | YLR365w | 1 | 0.000 | 0 | YLR408c | 2 | 0.000 | 42 |
| YLR320w | 2 | 0.000 | 59 | YLR366w | 7 | 0.095 | 764 | YLR409c | 8 | 0.286 | 843 |
| YLR322w | 1 | 0.000 | 0 | YLR367w | 18 | 0.176 | 3598 | YLR410w | 4 | 0.167 | 330 |
| YLR323c | 3 | 0.667 | 8 | YLR368w | 4 | 0.333 | 80 | YLR410w-a | 5 | 0.000 | 165 |
| YLR324w | 3 | 0.667 | 12 | YLR369w | 2 | 0.000 | 23 | YLR410w-b | 4 | 0.000 | 108 |
| YLR325c | 7 | 0.238 | 836 | YLR370c | 1 | 0.000 | 0 | YLR411w | 6 | 0.467 | 139 |
| YLR326w | 6 | 0.267 | 741 | YLR371w | 3 | 0.667 | 22 | YLR412c-a | 5 | 0.800 | 15 |
| YLR327c | 19 | 0.257 | 2845 | YLR372w | 6 | 0.333 | 334 | YLR412w | 6 | 0.667 | 29 |
| YLR328w | 4 | 0.500 | 30 | YLR373c | 6 | 0.000 | 611 | YLR413w | 17 | 0.412 | 1050 |
| YLR329w | 5 | 0.200 | 433 | YLR374c | 1 | 0.000 | 0 | YLR414c | 11 | 0.218 | 845 |
| YLR330w | 7 | 0.429 | 274 | YLR375w | 28 | 0.082 | 9467 | YLR415c | 5 | 0.300 | 251 |
| YLR332w | 10 | 0.467 | 197 | YLR376c | 1 | 0.000 | 0 | YLR416c | 2 | 0.000 | 11 |
| YLR333c | 8 | 0.536 | 284 | YLR377c | 15 | 0.229 | 1236 | YLR417w | 10 | 0.267 | 934 |
| YLR334c | 2 | 0.000 | 15 | YLR378c | 2 | 0.000 | 7 | YLR418c | 3 | 0.333 | 146 |
| YLR335w | 6 | 0.267 | 134 | YLR379w | 2 | 1.000 | 0 | YLR419w | 5 | 0.100 | 400 |
| YLR336c | 2 | 1.000 | 0 | YLR380w | 4 | 0.000 | 203 | YLR420w | 8 | 0.214 | 742 |
| YLR337c | 3 | 0.333 | 39 | YLR381w | 2 | 1.000 | 0 | YLR421c | 4 | 0.833 | 31 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YLR422w | 3 | 1.000 | 0 | YLR466w | 13 | 0.192 | 776 | YML043c | 4 | 0.333 | 120 |
| YLR423c | 5 | 0.000 | 190 | YLR467w | 23 | 0.233 | 815 | YML045w | 3 | 0.000 | 1373 |
| YLR424w | 3 | 0.333 | 1645 | YML001w | 3 | 0.000 | 43 | YML045w-a | 1 | 0.000 | 0 |
| YLR425w | 4 | 0.333 | 238 | YML002w | 4 | 0.333 | 118 | YML046w | 4 | 0.500 | 66 |
| YLR426w | 2 | 1.000 | 0 | YML003w | 4 | 0.500 | 31 | YML047c | 9 | 0.444 | 302 |
| YLR427w | 1 | 0.000 | 0 | YML004c | 14 | 0.308 | 1056 | YML047w-a | 2 | 0.000 | 14 |
| YLR428c | 9 | 0.167 | 850 | YML005w | 6 | 0.267 | 209 | YML048w | 2 | 1.000 | 0 |
| YLR429w | 5 | 0.200 | 226 | YML006c | 2 | 0.000 | 19 | YML048w-a | 1 | 0.000 | 0 |
| YLR430w | 8 | 0.179 | 422 | YML007c-a | 2 | 1.000 | 0 | YML049c | 3 | 0.000 | 46 |
| YLR432w | 3 | 0.667 | 26 | YML007w | 1829 | 0.004 | 5162138 | YML050w | 6 | 0.267 | 220 |
| YLR435w | 4 | 0.500 | 70 | YML008c | 16 | 0.325 | 1135 | YML051w | 7 | 0.286 | 543 |
| YLR436c | 5 | 0.200 | 474 | YML009c | 2 | 1.000 | 0 | YML052w | 16 | 0.150 | 1945 |
| YLR437c | 11 | 0.255 | 1315 | YML010c-b | 1 | 0.000 | 0 | YML053c | 11 | 0.164 | 820 |
| YLR438c-a | 13 | 0.282 | 829 | YML010w | 3 | 1.000 | 0 | YML054c | 22 | 0.234 | 1710 |
| YLR438w | 17 | 0.213 | 3562 | YML011c | 2 | 1.000 | 0 | YML054c-a | 2 | 1.000 | 0 |
| YLR439w | 24 | 0.192 | 4450 | YML012w | 2 | 1.000 | 0 | YML055w | 3 | 0.000 | 27 |
| YLR440c | 3 | 0.667 | 5 | YML013c-a | 1 | 0.000 | 0 | YML056c | 11 | 0.309 | 639 |
| YLR441c | 9 | 0.500 | 410 | YML013w | 5 | 0.300 | 393 | YML057w | 5 | 0.200 | 197 |
| YLR442c | 1 | 0.000 | 0 | YML014w | 2 | 0.000 | 9 | YML058w | 5 | 0.400 | 80 |
| YLR443w | 1 | 0.000 | 0 | YML015c | 1 | 0.000 | 0 | YML058w-a | 9 | 0.306 | 776 |
| YLR444c | 1 | 0.000 | 0 | YML017w | 2 | 0.000 | 36 | YML059c | 5 | 0.200 | 94 |
| YLR445w | 2 | 1.000 | 0 | YML018c | 4 | 0.167 | 202 | YML060w | 2 | 1.000 | 0 |
| YLR446w | 5 | 0.400 | 123 | YML019w | 3 | 0.333 | 34 | YML061c | 1 | 0.000 | 0 |
| YLR447c | 8 | 0.214 | 492 | YML021c | 1 | 0.000 | 0 | YML062c | 2 | 0.000 | 86 |
| YLR448w | 11 | 0.364 | 704 | YML022w | 2 | 1.000 | 0 | YML063w | 12 | 0.409 | 724 |
| YLR449w | 6 | 0.333 | 160 | YML023c | 1 | 0.000 | 0 | YML064c | 9 | 0.333 | 390 |
| YLR450w | 7 | 0.143 | 658 | YML024w | 9 | 0.472 | 413 | YML065w | 2 | 0.000 | 17 |
| YLR451w | 510 | 0.010 | 643610 | YML025c | 6 | 0.333 | 162 | YML066c | 2 | 1.000 | 0 |
| YLR452c | 13 | 0.410 | 1051 | YML026c | 11 | 0.382 | 581 | YML067c | 1 | 0.000 | 0 |
| YLR453c | 6 | 0.133 | 1369 | YML027w | 482 | 0.011 | 752603 | YML068w | 2 | 0.000 | 28 |
| YLR454w | 9 | 0.389 | 473 | YML028w | 18 | 0.190 | 1734 | YML069w | 2 | 0.000 | 36 |
| YLR455w | 2 | 1.000 | 0 | YML029w | 5 | 0.600 | 69 | YML070w | 9 | 0.389 | 356 |
| YLR456w | 4 | 0.167 | 43 | YML030w | 1 | 0.000 | 0 | YML071c | 3 | 0.333 | 20 |
| YLR457c | 5 | 0.700 | 82 | YML032c | 3 | 0.667 | 10 | YML072c | 7 | 0.048 | 141 |
| YLR458w | 3 | 0.333 | 83 | YML034w | 3 | 0.333 | 75 | YML073c | 11 | 0.400 | 622 |
| YLR459w | 2 | 0.000 | 46 | YML035c | 5 | 0.500 | 136 | YML074c | 4 | 0.500 | 163 |
| YLR460c | 18 | 0.235 | 2044 | YML036w | 1 | 0.000 | 0 | YML075c | 11 | 0.345 | 729 |
| YLR461w | 22 | 0.212 | 3286 | YML037c | 1 | 0.000 | 0 | YML076c | 33 | 0.042 | 14407 |
| YLR462w | 12 | 0.333 | 488 | YML038c | 2 | 0.000 | 16 | YML077w | 4 | 0.667 | 68 |
| YLR463c | 21 | 0.205 | 730 | YML039w | 2 | 0.000 | 34 | YML078w | 4 | 0.500 | 114 |
| YLR464w | 6 | 0.400 | 111 | YML040w | 3 | 0.333 | 59 | YML081c-a | 5 | 0.400 | 349 |
| YLR465c | 18 | 0.242 | 544 | YML041c | 6 | 0.333 | 150 | YML081w | 3 | 0.000 | 167 |
| YLR466c-b | 1 | 0.000 | 0 | YML042w | 14 | 0.209 | 1928 | YML082w | 6 | 0.333 | 171 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YML083c | 11 | 0.091 | 557 | YML124c | 5 | 0.200 | 130 | YMR035w | 7 | 0.238 | 188 |
| YML085c | 1 | 0.000 | 0 | YML125c | 8 | 0.393 | 394 | YMR036c | 2 | 1.000 | 0 |
| YML086c | 4 | 0.833 | 10 | YML126c | 7 | 0.429 | 246 | YMR037c | 916 | 0.007 | 1230908 |
| YML087c | 7 | 0.429 | 59 | YML128c | 24 | 0.279 | 3149 | YMR038c | 6 | 0.267 | 164 |
| YML088w | 11 | 0.309 | 296 | YML129c | 4 | 0.000 | 243 | YMR039c | 6 | 0.133 | 1347 |
| YML089c | 9 | 0.111 | 302 | YML130c | 14 | 0.242 | 1197 | YMR040w | 11 | 0.109 | 954 |
| YML090w | 1 | 0.000 | 0 | YML131w | 23 | 0.360 | 2205 | YMR041c | 8 | 0.429 | 325 |
| YML091c | 13 | 0.385 | 284 | YML132w | 26 | 0.258 | 4009 | YMR042w | 106 | 0.024 | 57111 |
| YML092c | 5 | 0.400 | 110 | YML133c | 19 | 0.310 | 2076 | YMR043w | 407 | 0.009 | 345552 |
| YML093w | 6 | 0.333 | 188 | YMR001c | 7 | 0.238 | 318 | YMR044w | 2 | 0.000 | 7 |
| YML094w | 1 | 0.000 | 0 | YMR001c-a | 1 | 0.000 | 0 | YMR045c | 3 | 0.667 | 34 |
| YML095c | 1 | 0.000 | 0 | YMR002w | 4 | 0.333 | 83 | YMR046c | 3 | 1.000 | 0 |
| YML096w | 3 | 0.333 | 19 | YMR003w | 6 | 0.200 | 229 | YMR046w-a | 1 | 0.000 | 0 |
| YML097c | 3 | 0.000 | 15 | YMR004w | 7 | 0.333 | 797 | YMR047c | 4 | 0.333 | 57 |
| YML098w | 10 | 0.333 | 713 | YMR005w | 1 | 0.000 | 0 | YMR048w | 4 | 0.000 | 149 |
| YML099c | 97 | 0.012 | 19891 | YMR006c | 12 | 0.348 | 823 | YMR049c | 9 | 0.417 | 361 |
| YML100w | 29 | 0.241 | 4045 | YMR007w | 3 | 0.000 | 124 | YMR050c | 2 | 0.000 | 18 |
| YML100w-a | 5 | 0.200 | 123 | YMR008c | 14 | 0.352 | 2131 | YMR051c | 3 | 0.333 | 52 |
| YML101c | 17 | 0.235 | 1820 | YMR009w | 7 | 0.476 | 229 | YMR052c-a | 1 | 0.000 | 0 |
| YML101c-a | 2 | 0.000 | 9 | YMR010w | 3 | 0.000 | 34 | YMR052w | 7 | 0.429 | 451 |
| YML102c-a | 7 | 0.333 | 199 | YMR011w | 30 | 0.324 | 5097 | YMR053c | 4 | 0.167 | 172 |
| YML102w | 3 | 0.000 | 42 | YMR012w | 2 | 0.000 | 38 | YMR054w | 2 | 0.000 | 11 |
| YML103c | 2 | 0.000 | 13 | YMR013c | 8 | 0.429 | 198 | YMR055c | 3 | 0.000 | 90 |
| YML104c | 2 | 0.000 | 68 | YMR013w-a | 1 | 0.000 | 0 | YMR056c | 16 | 0.158 | 1483 |
| YML105c | 2 | 0.000 | 21 | YMR014w | 10 | 0.200 | 524 | YMR057c | 1 | 0.000 | 0 |
| YML106w | 4 | 0.500 | 182 | YMR015c | 12 | 0.379 | 597 | YMR058w | 16 | 0.317 | 914 |
| YML107c | 2 | 0.000 | 27 | YMR016c | 1055 | 0.011 | 1491427 | YMR059w | 1 | 0.000 | 0 |
| YML108w | 2 | 0.000 | 48 | YMR017w | 22 | 0.394 | 1537 | YMR060c | 2 | 0.000 | 65 |
| YML109w | 1 | 0.000 | 0 | YMR018w | 7 | 0.190 | 140 | YMR061w | 1 | 0.000 | 0 |
| YML110c | 9 | 0.167 | 577 | YMR019w | 17 | 0.199 | 2119 | YMR062c | 14 | 0.286 | 1639 |
| YML111w | 3 | 0.000 | 10 | YMR020w | 6 | 0.333 | 259 | YMR063w | 3 | 0.000 | 26 |
| YML112w | 3 | 0.667 | 5 | YMR021c | 112 | 0.008 | 74302 | YMR064w | 5 | 0.300 | 342 |
| YML113w | 2 | 1.000 | 0 | YMR023c | 2 | 0.000 | 35 | YMR065w | 11 | 0.236 | 1435 |
| YML115c | 5 | 0.800 | 2 | YMR026c | 5 | 0.300 | 531 | YMR066w | 4 | 0.333 | 217 |
| YML116w | 19 | 0.333 | 1836 | YMR027w | 2 | 0.000 | 85 | YMR067c | 5 | 0.500 | 88 |
| YML116w-a | 2 | 0.000 | 14 | YMR028w | 4 | 0.500 | 68 | YMR068w | 3 | 0.000 | 80 |
| YML117w | 1 | 0.000 | 0 | YMR029c | 5 | 0.600 | 156 | YMR069w | 9 | 0.194 | 427 |
| YML118w | 1 | 0.000 | 0 | YMR030w | 3 | 1.000 | 0 | YMR070w | 150 | 0.048 | 81167 |
| YML119w | 14 | 0.220 | 1167 | YMR031c | 9 | 0.306 | 351 | YMR071c | 7 | 0.333 | 182 |
| YML120c | 18 | 0.222 | 2398 | YMR031w-a | 1 | 0.000 | 0 | YMR072w | 5 | 0.300 | 71 |
| YML121w | 14 | 0.253 | 1029 | YMR032w | 7 | 0.238 | 743 | YMR073c | 1 | 0.000 | 0 |
| YML122c | 5 | 0.300 | 148 | YMR033w | 2 | 0.000 | 33 | YMR074c | 2 | 1.000 | 0 |
| YML123c | 28 | 0.169 | 4695 | YMR034c | 4 | 0.667 | 24 | YMR075w | 1 | 0.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YMR076c | 9 | 0.167 | 363 | YMR119w | 7 | 0.333 | 561 | YMR159c | 1 | 0.000 | 0 |
| YMR077c | 3 | 0.333 | 44 | YMR119w-a | 6 | 0.333 | 373 | YMR160w | 1 | 0.000 | 0 |
| YMR078c | 5 | 0.400 | 400 | YMR120c | 12 | 0.258 | 967 | YMR162c | 4 | 0.167 | 52 |
| YMR079w | 9 | 0.194 | 1650 | YMR121c | 14 | 0.429 | 816 | YMR163c | 4 | 0.000 | 315 |
| YMR080c | 3 | 0.333 | 356 | YMR122c | 1 | 0.000 | 0 | YMR164c | 78 | 0.033 | 57802 |
| YMR081c | 13 | 0.244 | 1121 | YMR122w-a | 12 | 0.379 | 652 | YMR165c | 16 | 0.200 | 1015 |
| YMR082c | 2 | 0.000 | 8 | YMR123w | 3 | 0.667 | 28 | YMR166c | 3 | 0.000 | 117 |
| YMR083w | 16 | 0.342 | 2274 | YMR124w | 7 | 0.286 | 795 | YMR167w | 3 | 0.000 | 220 |
| YMR084w | 6 | 0.200 | 682 | YMR125w | 7 | 0.095 | 261 | YMR169c | 35 | 0.237 | 6563 |
| YMR085w | 7 | 0.143 | 720 | YMR126c | 5 | 0.000 | 192 | YMR170c | 6 | 0.267 | 112 |
| YMR086c-a | 11 | 0.145 | 893 | YMR127c | 1 | 0.000 | 0 | YMR171c | 4 | 0.167 | 43 |
| YMR086w | 6 | 0.133 | 317 | YMR128w | 8 | 0.357 | 812 | YMR172c-a | 15 | 0.333 | 1162 |
| YMR087w | 14 | 0.165 | 1743 | YMR129w | 2 | 1.000 | 0 | YMR172w | 76 | 0.020 | 22083 |
| YMR088c | 5 | 0.100 | 391 | YMR130w | 3 | 0.000 | 98 | YMR173w | 29 | 0.246 | 3749 |
| YMR089c | 5 | 0.700 | 52 | YMR131c | 6 | 0.067 | 538 | YMR173w-a | 12 | 0.394 | 267 |
| YMR090w | 14 | 0.363 | 1493 | YMR132c | 1 | 0.000 | 0 | YMR174c | 18 | 0.235 | 1578 |
| YMR091c | 1 | 0.000 | 0 | YMR133w | 6 | 0.133 | 376 | YMR175w | 17 | 0.250 | 4320 |
| YMR092c | 3 | 0.333 | 217 | YMR134w | 16 | 0.208 | 1687 | YMR176w | 5 | 0.000 | 399 |
| YMR093w | 5 | 0.600 | 479 | YMR135c | 21 | 0.419 | 1865 | YMR177w | 14 | 0.198 | 1914 |
| YMR094w | 3 | 0.000 | 118 | YMR135w-a | 25 | 0.180 | 4044 | YMR178w | 9 | 0.194 | 427 |
| YMR095c | 12 | 0.288 | 1079 | YMR136w | 28 | 0.320 | 3449 | YMR179w | 5 | 0.500 | 105 |
| YMR096w | 18 | 0.288 | 3604 | YMR137c | 5 | 0.400 | 56 | YMR180c | 2 | 0.000 | 16 |
| YMR097c | 2 | 1.000 | 0 | YMR138w | 6 | 0.200 | 507 | YMR181c | 5 | 0.300 | 122 |
| YMR098c | 13 | 0.179 | 745 | YMR139w | 4 | 0.167 | 129 | YMR182c | 134 | 0.015 | 49648 |
| YMR099c | 2 | 0.000 | 19 | YMR140w | 6 | 0.467 | 146 | YMR182w-a | 2 | 0.000 | 14 |
| YMR100w | 1 | 0.000 | 0 | YMR141c | 1 | 0.000 | 0 | YMR183c | 5 | 0.500 | 260 |
| YMR101c | 5 | 0.300 | 52 | YMR142c | 11 | 0.382 | 581 | YMR184w | 6 | 0.267 | 280 |
| YMR102c | 9 | 0.250 | 432 | YMR143w | 13 | 0.346 | 1065 | YMR185w | 8 | 0.214 | 482 |
| YMR103c | 11 | 0.309 | 463 | YMR144w | 12 | 0.227 | 1874 | YMR186w | 18 | 0.255 | 3685 |
| YMR104c | 4 | 0.667 | 40 | YMR145c | 14 | 0.352 | 617 | YMR187c | 8 | 0.143 | 1051 |
| YMR105c | 28 | 0.212 | 4181 | YMR146c | 3 | 0.667 | 57 | YMR188c | 6 | 0.333 | 111 |
| YMR106c | 1 | 0.000 | 0 | YMR147w | 6 | 0.200 | 372 | YMR189w | 18 | 0.301 | 2861 |
| YMR107w | 19 | 0.211 | 1668 | YMR148w | 1 | 0.000 | 0 | YMR190c | 1 | 0.000 | 0 |
| YMR108w | 9 | 0.333 | 618 | YMR149w | 2 | 0.000 | 19 | YMR191w | 5 | 0.400 | 145 |
| YMR110c | 6 | 0.333 | 253 | YMR150c | 2 | 1.000 | 0 | YMR192w | 9 | 0.028 | 735 |
| YMR111c | 1 | 0.000 | 0 | YMR151w | 2 | 1.000 | 0 | YMR193c-a | 2 | 0.000 | 9 |
| YMR112c | 1 | 0.000 | 0 | YMR152w | 4 | 0.833 | 2 | YMR193w | 28 | 0.161 | 4610 |
| YMR113w | 3 | 0.333 | 51 | YMR153w | 2 | 0.000 | 37 | YMR194c-a | 10 | 0.267 | 313 |
| YMR114c | 1 | 0.000 | 0 | YMR154c | 3 | 0.000 | 178 | YMR194c-b | 6 | 0.533 | 131 |
| YMR115w | 2 | 0.000 | 19 | YMR155w | 4 | 0.167 | 211 | YMR194w | 21 | 0.195 | 2926 |
| YMR116c | 10 | 0.467 | 531 | YMR156c | 1 | 0.000 | 0 | YMR195w | 28 | 0.270 | 4973 |
| YMR117c | 4 | 0.167 | 152 | YMR157c | 3 | 0.667 | 2 | YMR196w | 18 | 0.281 | 1353 |
| YMR118c | 9 | 0.167 | 901 | YMR158w-b | 1 | 0.000 | 0 | YMR197c | 6 | 0.267 | 572 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YMR198w | 12 | 0.364 | 1200 | YMR240c | 7 | 0.476 | 204 | YMR280c | 128 | 0.029 | 117015 |
| YMR199w | 22 | 0.273 | 2871 | YMR241w | 6 | 0.467 | 365 | YMR281w | 4 | 0.000 | 103 |
| YMR200w | 5 | 0.500 | 299 | YMR242c | 8 | 0.536 | 278 | YMR282c | 2 | 1.000 | 0 |
| YMR201c | 6 | 0.467 | 109 | YMR242w-a | 2 | 0.000 | 9 | YMR283c | 4 | 0.000 | 88 |
| YMR202w | 9 | 0.444 | 262 | YMR243c | 4 | 0.000 | 85 | YMR284w | 2 | 0.000 | 7 |
| YMR203w | 2 | 1.000 | 0 | YMR244c-a | 6 | 0.667 | 48 | YMR285c | 1 | 0.000 | 0 |
| YMR204c | 2 | 0.000 | 24 | YMR244w | 6 | 0.467 | 152 | YMR286w | 2 | 1.000 | 0 |
| YMR205c | 8 | 0.536 | 200 | YMR245w | 3 | 0.333 | 27 | YMR287c | 2 | 0.000 | 17 |
| YMR206w | 7 | 0.286 | 406 | YMR246w | 10 | 0.267 | 502 | YMR288w | 2 | 0.000 | 17 |
| YMR207c | 2 | 0.000 | 36 | YMR247c | 4 | 0.500 | 50 | YMR289w | 2 | 0.000 | 8 |
| YMR208w | 2 | 0.000 | 76 | YMR247w-a | 2 | 1.000 | 0 | YMR290c | 7 | 0.286 | 338 |
| YMR209c | 1 | 0.000 | 0 | YMR250w | 27 | 0.222 | 3962 | YMR290w-a | 2 | 0.000 | 10 |
| YMR210w | 2 | 0.000 | 13 | YMR251w | 11 | 0.309 | 543 | YMR291w | 9 | 0.222 | 345 |
| YMR211w | 4 | 0.000 | 261 | YMR251w-a | 32 | 0.264 | 6818 | YMR292w | 2 | 0.000 | 122 |
| YMR212c | 1 | 0.000 | 0 | YMR252c | 11 | 0.273 | 871 | YMR294w | 1 | 0.000 | 0 |
| YMR213w | 2 | 0.000 | 37 | YMR253c | 5 | 0.300 | 225 | YMR294w-a | 1 | 0.000 | 0 |
| YMR214w | 8 | 0.107 | 538 | YMR254c | 1 | 0.000 | 0 | YMR295c | 3 | 1.000 | 0 |
| YMR215w | 11 | 0.127 | 865 | YMR255w | 5 | 0.200 | 111 | YMR296c | 3 | 0.667 | 171 |
| YMR216c | 4 | 0.167 | 449 | YMR256c | 14 | 0.176 | 1048 | YMR297w | 4 | 0.333 | 204 |
| YMR217w | 5 | 0.200 | 508 | YMR257c | 13 | 0.090 | 2019 | YMR298w | 2 | 0.000 | 18 |
| YMR218c | 3 | 0.333 | 51 | YMR258c | 25 | 0.157 | 2698 | YMR299c | 1 | 0.000 | 0 |
| YMR219w | 6 | 0.400 | 302 | YMR259c | 8 | 0.036 | 431 | YMR300c | 10 | 0.267 | 872 |
| YMR220w | 6 | 0.200 | 538 | YMR260c | 7 | 0.286 | 1101 | YMR301c | 6 | 0.333 | 351 |
| YMR221c | 6 | 0.400 | 239 | YMR261c | 10 | 0.156 | 831 | YMR302c | 6 | 0.467 | 139 |
| YMR222c | 2 | 0.000 | 26 | YMR262w | 4 | 0.000 | 57 | YMR303c | 16 | 0.225 | 1941 |
| YMR223w | 4 | 0.333 | 152 | YMR263w | 3 | 0.000 | 89 | YMR304c-a | 9 | 0.306 | 226 |
| YMR224c | 3 | 0.333 | 349 | YMR264w | 1 | 0.000 | 0 | YMR304w | 4 | 0.167 | 88 |
| YMR225c | 3 | 0.333 | 41 | YMR265c | 9 | 0.528 | 237 | YMR305c | 16 | 0.358 | 1311 |
| YMR226c | 4 | 0.333 | 183 | YMR266w | 12 | 0.500 | 405 | YMR306c-a | 6 | 0.133 | 98 |
| YMR227c | 7 | 0.190 | 135 | YMR267w | 5 | 0.200 | 415 | YMR306w | 12 | 0.364 | 302 |
| YMR228w | 7 | 0.238 | 92 | YMR268c | 1 | 0.000 | 0 | YMR307w | 11 | 0.145 | 809 |
| YMR229c | 31 | 0.120 | 5170 | YMR269w | 4 | 0.000 | 281 | YMR308c | 5 | 0.400 | 260 |
| YMR230w | 12 | 0.318 | 1633 | YMR270c | 4 | 0.167 | 126 | YMR309c | 4 | 0.333 | 162 |
| YMR230w-a | 3 | 0.667 | 9 | YMR271c | 9 | 0.250 | 325 | YMR310c | 2 | 1.000 | 0 |
| YMR231w | 12 | 0.197 | 2105 | YMR272c | 9 | 0.056 | 1472 | YMR311c | 1 | 0.000 | 0 |
| YMR232w | 5 | 0.400 | 84 | YMR272w-b | 1 | 0.000 | 0 | YMR312w | 7 | 0.571 | 172 |
| YMR233w | 2 | 0.000 | 36 | YMR273c | 1 | 0.000 | 0 | YMR313c | 3 | 0.000 | 190 |
| YMR234w | 2 | 0.000 | 48 | YMR274c | 1 | 0.000 | 0 | YMR314w | 3 | 1.000 | 0 |
| YMR235c | 7 | 0.333 | 760 | YMR275c | 7 | 0.429 | 939 | YMR315w | 14 | 0.242 | 942 |
| YMR236w | 3 | 0.333 | 152 | YMR276w | 9 | 0.389 | 1428 | YMR316c-a | 2 | 0.000 | 60 |
| YMR237w | 3 | 0.333 | 104 | YMR277w | 6 | 0.333 | 198 | YMR316c-b | 3 | 0.333 | 63 |
| YMR238w | 4 | 0.000 | 183 | YMR278w | 1 | 0.000 | 0 | YMR316w | 9 | 0.194 | 705 |
| YMR239c | 7 | 0.429 | 290 | YMR279c | 6 | 0.267 | 121 | YMR317w | 2 | 1.000 | 0 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YMR318c | 9 | 0.222 | 668 | YNL034w | 3 | 0.000 | 35 | YNL073w | 6 | 0.467 | 363 |
| YMR319c | 24 | 0.341 | 3295 | YNL035c | 5 | 0.400 | 66 | YNL074c | 3 | 0.333 | 84 |
| YMR320w | 7 | 0.238 | 732 | YNL036w | 26 | 0.182 | 4558 | YNL075w | 5 | 0.400 | 122 |
| YMR321c | 1 | 0.000 | 0 | YNL037c | 23 | 0.138 | 3552 | YNL076w | 4 | 0.000 | 258 |
| YMR322c | 22 | 0.216 | 2992 | YNL038w | 4 | 0.000 | 51 | YNL077w | 10 | 0.289 | 591 |
| YMR323w | 7 | 0.286 | 125 | YNL039w | 2 | 0.000 | 9 | YNL078w | 13 | 0.385 | 662 |
| YMR324c | 10 | 0.111 | 469 | YNL040w | 5 | 0.400 | 101 | YNL079c | 9 | 0.417 | 270 |
| YMR325w | 18 | 0.137 | 2565 | YNL041c | 6 | 0.267 | 306 | YNL080c | 4 | 0.167 | 202 |
| YMR326c | 1 | 0.000 | 0 | YNL042w | 5 | 0.500 | 90 | YNL081c | 2 | 0.000 | 64 |
| YNL001w | 11 | 0.109 | 591 | YNL042w-b | 1 | 0.000 | 0 | YNL082w | 5 | 0.300 | 186 |
| YNL002c | 9 | 0.111 | 504 | YNL043c | 6 | 0.200 | 1052 | YNL083w | 1 | 0.000 | 0 |
| YNL003c | 2 | 0.000 | 1 | YNL044w | 6 | 0.333 | 712 | YNL084c | 3 | 0.333 | 159 |
| YNL004w | 5 | 0.300 | 440 | YNL045w | 8 | 0.214 | 596 | YNL085w | 4 | 0.167 | 642 |
| YNL005c | 5 | 0.300 | 664 | YNL046w | 4 | 0.667 | 52 | YNL086w | 3 | 0.333 | 310 |
| YNL006w | 7 | 0.190 | 421 | YNL047c | 2 | 0.000 | 16 | YNL087w | 16 | 0.433 | 1299 |
| YNL007c | 8 | 0.357 | 316 | YNL048w | 4 | 0.000 | 120 | YNL088w | 4 | 0.667 | 18 |
| YNL008c | 5 | 0.100 | 186 | YNL049c | 2 | 0.000 | 7 | YNL089c | 2 | 0.000 | 3 |
| YNL009w | 14 | 0.143 | 733 | YNL050c | 4 | 0.167 | 177 | YNL090w | 8 | 0.357 | 454 |
| YNL010w | 13 | 0.077 | 1330 | YNL051w | 4 | 0.833 | 14 | YNL091w | 9 | 0.306 | 1028 |
| YNL011c | 6 | 0.200 | 684 | YNL052w | 13 | 0.154 | 340 | YNL092w | 8 | 0.250 | 993 |
| YNL012w | 10 | 0.156 | 998 | YNL053w | 6 | 0.400 | 148 | YNL093w | 3 | 0.333 | 97 |
| YNL013c | 1 | 0.000 | 0 | YNL054w | 3 | 1.000 | 0 | YNL094w | 6 | 0.333 | 290 |
| YNL014w | 10 | 0.267 | 1183 | YNL054w-a | 3 | 0.667 | 8 | YNL095c | 3 | 0.000 | 97 |
| YNL015w | 14 | 0.275 | 1053 | YNL054w-b | 1 | 0.000 | 0 | YNL096c | 11 | 0.327 | 861 |
| YNL016w | 8 | 0.286 | 625 | YNL055c | 7 | 0.429 | 189 | YNL097c | 10 | 0.200 | 818 |
| YNL017c | 4 | 0.167 | 225 | YNL056w | 4 | 0.167 | 50 | YNL097c-b | 1 | 0.000 | 0 |
| YNL018c | 5 | 0.300 | 29 | YNL057w | 4 | 0.167 | 335 | YNL098c | 3 | 0.333 | 13 |
| YNL019c | 3 | 0.000 | 55 | YNL058c | 6 | 0.200 | 131 | YNL100w | 7 | 0.000 | 1437 |
| YNL020c | 2 | 0.000 | 54 | YNL059c | 4 | 0.167 | 300 | YNL101w | 12 | 0.227 | 1359 |
| YNL021w | 1 | 0.000 | 0 | YNL061w | 10 | 0.267 | 1187 | YNL102w | 11 | 0.109 | 1177 |
| YNL022c | 4 | 0.167 | 216 | YNL062c | 5 | 0.500 | 110 | YNL103w | 1156 | 0.006 | 2489871 |
| YNL023c | 1 | 0.000 | 0 | YNL063w | 5 | 0.300 | 172 | YNL104c | 11 | 0.255 | 1309 |
| YNL024c | 2 | 0.000 | 77 | YNL064c | 5 | 0.200 | 601 | YNL105w | 1 | 0.000 | 0 |
| YNL024c-a | 1 | 0.000 | 0 | YNL065w | 22 | 0.255 | 2876 | YNL106c | 1 | 0.000 | 0 |
| YNL025c | 5 | 0.000 | 319 | YNL066w | 10 | 0.289 | 935 | YNL107w | 3 | 0.000 | 124 |
| YNL026w | 1 | 0.000 | 0 | YNL067w | 13 | 0.385 | 1234 | YNL108c | 4 | 0.333 | 132 |
| YNL027w | 301 | 0.007 | 334676 | YNL067w-a | 1 | 0.000 | 0 | YNL109w | 1 | 0.000 | 0 |
| YNL028w | 5 | 0.200 | 173 | YNL067w-b | 2 | 1.000 | 0 | YNL110c | 3 | 0.333 | 45 |
| YNL029c | 4 | 0.333 | 91 | YNL068c | 315 | 0.013 | 309200 | YNL111c | 14 | 0.264 | 1596 |
| YNL030w | 13 | 0.205 | 1568 | YNL069c | 12 | 0.455 | 586 | YNL112w | 10 | 0.244 | 1810 |
| YNL031c | 11 | 0.273 | 1189 | YNL070w | 6 | 0.000 | 762 | YNL113w | 5 | 0.200 | 165 |
| YNL032w | 4 | 0.500 | 72 | YNL071w | 4 | 0.333 | 70 | YNL114c | 2 | 1.000 | 0 |
| YNL033w | 5 | 0.300 | 65 | YNL072w | 5 | 0.600 | 128 | YNL115c | 11 | 0.309 | 1221 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YNL116w | 2 | 0.000 | 64 | YNL159c | 2 | 1.000 | 0 | YNL203c | 1 | 0.000 | 0 |
| YNL117w | 19 | 0.187 | 4427 | YNL160w | 33 | 0.184 | 7806 | YNL204c | 63 | 0.008 | 11439 |
| YNL118c | 7 | 0.095 | 1046 | YNL161w | 5 | 0.400 | 82 | YNL205c | 4 | 0.333 | 51 |
| YNL119w | 1 | 0.000 | 0 | YNL162w | 11 | 0.418 | 772 | YNL206c | 2 | 0.000 | 63 |
| YNL121c | 1 | 0.000 | 0 | YNL162w-a | 2 | 0.000 | 9 | YNL207w | 5 | 0.300 | 416 |
| YNL122c | 6 | 0.267 | 618 | YNL163c | 6 | 0.333 | 183 | YNL208w | 9 | 0.194 | 1091 |
| YNL123w | 3 | 0.333 | 27 | YNL164c | 4 | 0.333 | 371 | YNL209w | 6 | 0.333 | 219 |
| YNL124w | 9 | 0.556 | 434 | YNL165w | 3 | 0.667 | 30 | YNL210w | 5 | 0.400 | 679 |
| YNL125c | 7 | 0.524 | 352 | YNL166c | 4 | 0.500 | 51 | YNL211c | 4 | 0.333 | 455 |
| YNL126w | 4 | 0.000 | 79 | YNL167c | 339 | 0.018 | 226233 | YNL212w | 5 | 0.200 | 822 |
| YNL127w | 1 | 0.000 | 0 | YNL168c | 6 | 0.467 | 242 | YNL213c | 5 | 0.100 | 786 |
| YNL128w | 5 | 0.100 | 307 | YNL169c | 8 | 0.393 | 449 | YNL214w | 1 | 0.000 | 0 |
| YNL129w | 6 | 0.133 | 248 | YNL170w | 2 | 0.000 | 8 | YNL216w | 1230 | 0.007 | 2988666 |
| YNL130c | 7 | 0.286 | 274 | YNL171c | 4 | 0.167 | 118 | YNL217w | 5 | 0.600 | 44 |
| YNL130c-a | 1 | 0.000 | 0 | YNL172w | 5 | 0.000 | 148 | YNL218w | 5 | 0.300 | 196 |
| YNL131w | 1 | 0.000 | 0 | YNL173c | 8 | 0.286 | 253 | YNL219c | 2 | 1.000 | 0 |
| YNL132w | 9 | 0.556 | 403 | YNL174w | 6 | 0.200 | 429 | YNL220w | 10 | 0.267 | 1192 |
| YNL133c | 6 | 0.467 | 245 | YNL175c | 8 | 0.321 | 550 | YNL221c | 3 | 0.333 | 146 |
| YNL134c | 17 | 0.228 | 1792 | YNL176c | 5 | 0.300 | 245 | YNL224c | 5 | 0.400 | 147 |
| YNL135c | 7 | 0.286 | 632 | YNL178w | 22 | 0.403 | 2215 | YNL225c | 1 | 0.000 | 0 |
| YNL136w | 3 | 0.333 | 29 | YNL179c | 8 | 0.429 | 341 | YNL226w | 2 | 0.000 | 14 |
| YNL137c | 2 | 0.000 | 17 | YNL180c | 17 | 0.493 | 1062 | YNL227c | 1 | 0.000 | 0 |
| YNL138w | 3 | 0.667 | 39 | YNL181w | 3 | 0.000 | 161 | YNL229c | 3 | 0.000 | 37 |
| YNL139c | 3 | 0.000 | 467 | YNL182c | 9 | 0.194 | 678 | YNL230c | 5 | 0.200 | 141 |
| YNL141w | 11 | 0.182 | 1044 | YNL183c | 5 | 0.300 | 351 | YNL231c | 20 | 0.221 | 3051 |
| YNL142w | 13 | 0.346 | 1918 | YNL185c | 1 | 0.000 | 0 | YNL232w | 10 | 0.222 | 400 |
| YNL143c | 7 | 0.333 | 502 | YNL186w | 5 | 0.400 | 116 | YNL233w | 4 | 0.000 | 166 |
| YNL144c | 13 | 0.423 | 770 | YNL187w | 3 | 0.667 | 14 | YNL234w | 22 | 0.225 | 2644 |
| YNL145w | 20 | 0.321 | 3328 | YNL188w | 4 | 0.000 | 293 | YNL235c | 3 | 1.000 | 0 |
| YNL146c-a | 5 | 0.100 | 325 | YNL189w | 7 | 0.143 | 841 | YNL236w | 3 | 0.000 | 29 |
| YNL146w | 16 | 0.158 | 1892 | YNL190w | 7 | 0.333 | 609 | YNL237w | 14 | 0.363 | 545 |
| YNL147w | 6 | 0.000 | 362 | YNL191w | 4 | 0.333 | 283 | YNL238w | 2 | 1.000 | 0 |
| YNL148c | 6 | 0.267 | 248 | YNL192w | 16 | 0.250 | 1460 | YNL239w | 13 | 0.244 | 1954 |
| YNL149c | 7 | 0.333 | 576 | YNL193w | 5 | 0.500 | 87 | YNL240c | 6 | 0.267 | 356 |
| YNL150w | 2 | 1.000 | 0 | YNL194c | 20 | 0.284 | 1895 | YNL241c | 33 | 0.195 | 7065 |
| YNL151c | 5 | 0.300 | 348 | YNL195c | 14 | 0.352 | 695 | YNL242w | 2 | 0.000 | 88 |
| YNL152w | 2 | 0.000 | 55 | YNL196c | 4 | 0.000 | 84 | YNL243w | 3 | 0.333 | 190 |
| YNL153c | 3 | 0.333 | 154 | YNL197c | 1 | 0.000 | 0 | YNL244c | 4 | 0.500 | 398 |
| YNL154c | 5 | 0.700 | 68 | YNL198c | 1 | 0.000 | 0 | YNL245c | 1 | 0.000 | 0 |
| YNL155w | 9 | 0.444 | 344 | YNL199c | 189 | 0.013 | 78263 | YNL246w | 1 | 0.000 | 0 |
| YNL156c | 5 | 0.600 | 64 | YNL200c | 14 | 0.516 | 284 | YNL247w | 3 | 1.000 | 0 |
| YNL157w | 3 | 0.667 | 52 | YNL201c | 2 | 0.000 | 30 | YNL248c | 3 | 0.333 | 38 |
| YNL158w | 2 | 0.000 | 19 | YNL202w | 9 | 0.194 | 425 | YNL249c | 2 | 0.000 | 16 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YNL250w | 2 | 0.000 | 38 | YNL293w | 6 | 0.267 | 269 | YNL337w | 35 | 0.173 | 6085 |
| YNL251c | 6 | 0.200 | 462 | YNL294c | 8 | 0.214 | 389 | YNL338w | 30 | 0.195 | 2838 |
| YNL252c | 2 | 0.000 | 14 | YNL295w | 4 | 0.333 | 93 | YNL339c | 30 | 0.221 | 3452 |
| YNL253w | 5 | 0.300 | 212 | YNL296w | 4 | 0.333 | 136 | YNR001c | 21 | 0.114 | 3252 |
| YNL254c | 5 | 0.500 | 69 | YNL297c | 2 | 1.000 | 0 | YNR002c | 11 | 0.291 | 802 |
| YNL255c | 23 | 0.075 | 33211 | YNL298w | 9 | 0.278 | 1283 | YNR003c | 4 | 0.167 | 253 |
| YNL256w | 4 | 0.167 | 69 | YNL299w | 6 | 0.200 | 169 | YNR004w | 5 | 0.100 | 206 |
| YNL257c | 3 | 0.000 | 33 | YNL300w | 9 | 0.194 | 537 | YNR006w | 3 | 0.000 | 25 |
| YNL258c | 6 | 0.133 | 1031 | YNL301c | 11 | 0.327 | 1244 | YNR007c | 1 | 0.000 | 0 |
| YNL259c | 9 | 0.167 | 886 | YNL302c | 8 | 0.536 | 225 | YNR008w | 4 | 0.000 | 167 |
| YNL260c | 7 | 0.190 | 508 | YNL303w | 1 | 0.000 | 0 | YNR009w | 9 | 0.278 | 419 |
| YNL261w | 2 | 0.000 | 16 | YNL304w | 2 | 0.000 | 11 | YNR010w | 2 | 0.000 | 36 |
| YNL262w | 5 | 0.200 | 494 | YNL305c | 7 | 0.476 | 227 | YNR011c | 4 | 0.333 | 167 |
| YNL263c | 2 | 0.000 | 7 | YNL306w | 6 | 0.200 | 335 | YNR012w | 6 | 0.333 | 278 |
| YNL265c | 3 | 0.000 | 27 | YNL307c | 5 | 0.100 | 355 | YNR013c | 9 | 0.306 | 960 |
| YNL267w | 3 | 0.333 | 123 | YNL308c | 6 | 0.467 | 107 | YNR014w | 22 | 0.273 | 3047 |
| YNL268w | 7 | 0.429 | 436 | YNL309w | 58 | 0.038 | 74754 | YNR016c | 14 | 0.242 | 1944 |
| YNL269w | 5 | 0.300 | 108 | YNL310c | 3 | 0.333 | 67 | YNR017w | 20 | 0.284 | 3223 |
| YNL270c | 11 | 0.273 | 813 | YNL311c | 4 | 0.500 | 68 | YNR018w | 15 | 0.343 | 1970 |
| YNL271c | 6 | 0.067 | 1028 | YNL312w | 8 | 0.286 | 814 | YNR019w | 12 | 0.227 | 1139 |
| YNL272c | 1 | 0.000 | 0 | YNL313c | 7 | 0.238 | 730 | YNR020c | 3 | 0.667 | 103 |
| YNL273w | 4 | 0.333 | 99 | YNL314w | 167 | 0.004 | 147336 | YNR021w | 1 | 0.000 | 0 |
| YNL274c | 16 | 0.250 | 1050 | YNL315c | 1 | 0.000 | 0 | YNR022c | 1 | 0.000 | 0 |
| YNL275w | 1 | 0.000 | 0 | YNL317w | 1 | 0.000 | 0 | YNR024w | 3 | 0.333 | 118 |
| YNL276c | 1 | 0.000 | 0 | YNL318c | 3 | 0.000 | 120 | YNR025c | 2 | 0.000 | 20 |
| YNL277w | 18 | 0.275 | 1697 | YNL319w | 1 | 0.000 | 0 | YNR026c | 3 | 0.000 | 166 |
| YNL277w-a | 2 | 0.000 | 9 | YNL320w | 1 | 0.000 | 0 | YNR027w | 5 | 0.200 | 333 |
| YNL278w | 9 | 0.194 | 798 | YNL321w | 6 | 0.267 | 611 | YNR028w | 12 | 0.394 | 459 |
| YNL279w | 21 | 0.352 | 3408 | YNL322c | 5 | 0.300 | 308 | YNR029c | 3 | 0.000 | 8 |
| YNL280c | 7 | 0.286 | 827 | YNL323w | 1 | 0.000 | 0 | YNR030w | 3 | 0.000 | 29 |
| YNL281w | 3 | 0.333 | 36 | YNL324w | 4 | 0.167 | 65 | YNR031c | 4 | 0.167 | 100 |
| YNL282w | 7 | 0.381 | 207 | YNL325c | 2 | 1.000 | 0 | YNR032c-a | 2 | 0.000 | 63 |
| YNL283c | 8 | 0.357 | 324 | YNL326c | 3 | 0.333 | 51 | YNR032w | 5 | 0.500 | 165 |
| YNL284c | 6 | 0.267 | 254 | YNL327w | 12 | 0.333 | 416 | YNR033w | 3 | 0.000 | 153 |
| YNL284c-a | 2 | 0.000 | 7 | YNL328c | 7 | 0.571 | 133 | YNR034w | 10 | 0.267 | 849 |
| YNL285w | 3 | 0.667 | 12 | YNL329c | 6 | 0.067 | 253 | YNR034w-a | 8 | 0.500 | 145 |
| YNL286w | 2 | 0.000 | 17 | YNL330c | 2 | 0.000 | 12 | YNR035c | 4 | 0.167 | 635 |
| YNL287w | 3 | 0.000 | 176 | YNL331c | 7 | 0.476 | 176 | YNR036c | 5 | 0.400 | 378 |
| YNL288w | 6 | 0.600 | 312 | YNL332w | 6 | 0.333 | 422 | YNR037c | 3 | 0.333 | 257 |
| YNL289w | 29 | 0.204 | 3470 | YNL333w | 12 | 0.333 | 874 | YNR038w | 3 | 0.000 | 268 |
| YNL290w | 6 | 0.200 | 208 | YNL334c | 6 | 0.333 | 284 | YNR039c | 6 | 0.067 | 692 |
| YNL291c | 1 | 0.000 | 0 | YNL335w | 11 | 0.236 | 950 | YNR040w | 7 | 0.000 | 829 |
| YNL292w | 3 | 0.333 | 32 | YNL336w | 17 | 0.213 | 1692 | YNR041c | 4 | 0.500 | 144 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YNR042w | 1 | 0.000 | 0 | YOL008w | 1 | 0.000 | 0 | YOL049w | 5 | 0.500 | 101 |
| YNR043w | 8 | 0.357 | 370 | YOL009c | 1 | 0.000 | 0 | YOL050c | 4 | 0.167 | 123 |
| YNR044w | 24 | 0.290 | 3307 | YOL010w | 8 | 0.429 | 417 | YOL052c | 2 | 1.000 | 0 |
| YNR045w | 2 | 1.000 | 0 | YOL011w | 8 | 0.286 | 522 | YOL052c-a | 32 | 0.302 | 4625 |
| YNR046w | 5 | 0.100 | 420 | YOL012c | 7 | 0.286 | 352 | YOL053w | 2 | 0.000 | 8 |
| YNR047w | 4 | 0.333 | 122 | YOL013c | 6 | 0.467 | 150 | YOL054w | 2 | 0.000 | 8 |
| YNR049c | 6 | 0.267 | 162 | YOL013w-a | 5 | 0.000 | 215 | YOL055c | 7 | 0.381 | 908 |
| YNR050c | 19 | 0.246 | 2131 | YOL014w | 10 | 0.222 | 1379 | YOL056w | 4 | 0.333 | 89 |
| YNR051c | 4 | 0.333 | 101 | YOL016c | 9 | 0.306 | 630 | YOL057w | 8 | 0.357 | 320 |
| YNR052c | 1 | 0.000 | 0 | YOL017w | 3 | 0.333 | 70 | YOL058w | 35 | 0.217 | 7254 |
| YNR053c | 10 | 0.333 | 1056 | YOL018c | 4 | 0.667 | 70 | YOL059w | 9 | 0.250 | 439 |
| YNR054c | 11 | 0.145 | 1018 | YOL019w | 10 | 0.444 | 559 | YOL060c | 7 | 0.429 | 243 |
| YNR055c | 4 | 0.167 | 133 | YOL019w-a | 4 | 0.667 | 4 | YOL061w | 1 | 0.000 | 0 |
| YNR056c | 9 | 0.278 | 603 | YOL020w | 7 | 0.190 | 887 | YOL063c | 1 | 0.000 | 0 |
| YNR057c | 5 | 0.400 | 322 | YOL021c | 4 | 0.167 | 487 | YOL064c | 7 | 0.286 | 208 |
| YNR058w | 8 | 0.357 | 776 | YOL022c | 5 | 0.200 | 782 | YOL065c | 3 | 0.000 | 84 |
| YNR059w | 5 | 0.200 | 397 | YOL023w | 9 | 0.083 | 721 | YOL066c | 1 | 0.000 | 0 |
| YNR060w | 23 | 0.360 | 1183 | YOL024w | 12 | 0.030 | 1677 | YOL067c | 130 | 0.016 | 42378 |
| YNR061c | 3 | 0.000 | 27 | YOL025w | 1 | 0.000 | 0 | YOL068c | 3 | 0.333 | 274 |
| YNR062c | 7 | 0.143 | 485 | YOL026c | 4 | 0.000 | 294 | YOL069w | 1 | 0.000 | 0 |
| YNR063w | 3 | 0.000 | 160 | YOL027c | 3 | 0.667 | 13 | YOL070c | 1 | 0.000 | 0 |
| YNR064c | 13 | 0.218 | 2040 | YOL028c | 188 | 0.018 | 110219 | YOL071w | 5 | 0.300 | 65 |
| YNR065c | 6 | 0.267 | 156 | YOL029c | 5 | 0.200 | 165 | YOL072w | 2 | 1.000 | 0 |
| YNR066c | 3 | 0.000 | 94 | YOL030w | 10 | 0.311 | 657 | YOL073c | 3 | 0.333 | 58 |
| YNR067c | 13 | 0.359 | 534 | YOL031c | 10 | 0.356 | 621 | YOL075c | 6 | 0.200 | 1356 |
| YNR068c | 11 | 0.200 | 887 | YOL032w | 5 | 0.200 | 97 | YOL076w | 6 | 0.067 | 873 |
| YNR069c | 7 | 0.429 | 211 | YOL033w | 2 | 0.000 | 87 | YOL077c | 9 | 0.278 | 1432 |
| YNR070w | 6 | 0.267 | 369 | YOL034w | 7 | 0.143 | 494 | YOL077w-a | 7 | 0.286 | 289 |
| YNR071c | 16 | 0.125 | 1273 | YOL035c | 3 | 0.000 | 131 | YOL078w | 8 | 0.214 | 306 |
| YNR072w | 24 | 0.217 | 2859 | YOL036w | 1 | 0.000 | 0 | YOL079w | 7 | 0.095 | 448 |
| YNR073c | 8 | 0.536 | 183 | YOL037c | 2 | 0.000 | 14 | YOL080c | 7 | 0.190 | 475 |
| YNR074c | 2 | 1.000 | 0 | YOL038c-a | 3 | 0.667 | 30 | YOL081w | 9 | 0.417 | 290 |
| YNR075c-a | 2 | 1.000 | 0 | YOL038w | 8 | 0.500 | 932 | YOL082w | 14 | 0.308 | 2186 |
| YNR075w | 10 | 0.244 | 716 | YOL039w | 16 | 0.325 | 1959 | YOL083w | 14 | 0.176 | 1137 |
| YNR076w | 24 | 0.254 | 4122 | YOL040c | 15 | 0.381 | 1102 | YOL084w | 31 | 0.252 | 4654 |
| YNR081w | 1 | 0.000 | 0 | YOL041c | 8 | 0.321 | 945 | YOL085c | 5 | 0.300 | 117 |
| YOL001w | 9 | 0.167 | 343 | YOL042w | 7 | 0.143 | 457 | YOL086c | 22 | 0.299 | 4244 |
| YOL002c | 6 | 0.133 | 209 | YOL043c | 3 | 0.000 | 249 | YOL087c | 1 | 0.000 | 0 |
| YOL003c | 3 | 0.000 | 166 | YOL044w | 1 | 0.000 | 0 | YOL088c | 1 | 0.000 | 0 |
| YOL004w | 32 | 0.081 | 4363 | YOL045w | 2 | 1.000 | 0 | YOL089c | 111 | 0.013 | 68468 |
| YOL005c | 3 | 0.000 | 76 | YOL046c | 1 | 0.000 | 0 | YOL090w | 2 | 1.000 | 0 |
| YOL006c | 6 | 0.400 | 169 | YOL047c | 4 | 0.167 | 510 | YOL091w | 10 | 0.044 | 1046 |
| YOL007c | 9 | 0.250 | 450 | YOL048c | 5 | 0.300 | 141 | YOL092w | 4 | 0.500 | 91 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YOL093w | 3 | 0.000 | 785 | YOL137w | 5 | 0.300 | 327 | YOR010c | 9 | 0.361 | 267 |
| YOL095c | 1 | 0.000 | 0 | YOL138c | 5 | 0.000 | 381 | YOR011w | 9 | 0.333 | 845 |
| YOL096c | 2 | 0.000 | 36 | YOL139c | 4 | 0.333 | 174 | YOR012w | 1 | 0.000 | 0 |
| YOL097c | 1 | 0.000 | 0 | YOL140w | 12 | 0.227 | 1436 | YOR014w | 3 | 0.333 | 26 |
| YOL098c | 2 | 1.000 | 0 | YOL141w | 4 | 0.167 | 48 | YOR015w | 2 | 0.000 | 22 |
| YOL099c | 1 | 0.000 | 0 | YOL142w | 4 | 0.000 | 156 | YOR016c | 1 | 0.000 | 0 |
| YOL100w | 5 | 0.400 | 165 | YOL143c | 6 | 0.467 | 229 | YOR017w | 4 | 0.000 | 116 |
| YOL101c | 14 | 0.154 | 1199 | YOL144w | 5 | 0.300 | 462 | YOR018w | 10 | 0.378 | 474 |
| YOL102c | 4 | 0.167 | 588 | YOL145c | 5 | 0.000 | 257 | YOR019w | 5 | 0.300 | 177 |
| YOL103w | 3 | 0.333 | 44 | YOL146w | 4 | 0.000 | 83 | YOR020c | 10 | 0.222 | 738 |
| YOL103w-a | 1 | 0.000 | 0 | YOL147c | 7 | 0.238 | 164 | YOR020w-a | 3 | 0.000 | 69 |
| YOL103w-b | 1 | 0.000 | 0 | YOL148c | 5 | 0.300 | 276 | YOR021c | 8 | 0.214 | 744 |
| YOL104c | 5 | 0.300 | 331 | YOL149w | 4 | 0.167 | 117 | YOR022c | 2 | 0.000 | 16 |
| YOL105c | 8 | 0.214 | 662 | YOL150c | 8 | 0.500 | 193 | YOR023c | 9 | 0.167 | 893 |
| YOL106w | 1 | 0.000 | 0 | YOL151w | 28 | 0.233 | 2919 | YOR024w | 3 | 0.000 | 83 |
| YOL107w | 5 | 0.400 | 303 | YOL152w | 14 | 0.418 | 1869 | YOR025w | 12 | 0.152 | 1636 |
| YOL108c | 637 | 0.004 | 836047 | YOL153c | 12 | 0.258 | 887 | YOR026w | 3 | 0.667 | 11 |
| YOL109w | 21 | 0.290 | 1829 | YOL154w | 24 | 0.236 | 2472 | YOR027w | 16 | 0.433 | 1792 |
| YOL110w | 10 | 0.422 | 503 | YOL155c | 31 | 0.228 | 5805 | YOR028c | 459 | 0.024 | 705126 |
| YOL111c | 3 | 0.000 | 69 | YOL155w-a | 3 | 1.000 | 0 | YOR029w | 6 | 0.467 | 67 |
| YOL112w | 6 | 0.533 | 121 | YOL156w | 29 | 0.239 | 3901 | YOR030w | 8 | 0.750 | 29 |
| YOL113w | 9 | 0.222 | 420 | YOL157c | 25 | 0.267 | 3185 | YOR031w | 8 | 0.179 | 456 |
| YOL114c | 9 | 0.222 | 420 | YOL158c | 16 | 0.308 | 1177 | YOR032c | 247 | 0.039 | 258854 |
| YOL115w | 6 | 0.133 | 153 | YOL159c | 15 | 0.171 | 1085 | YOR032w-a | 8 | 0.786 | 43 |
| YOL116w | 53 | 0.032 | 42977 | YOL160w | 8 | 0.250 | 472 | YOR033c | 2 | 0.000 | 84 |
| YOL117w | 8 | 0.250 | 1597 | YOL161c | 16 | 0.250 | 1507 | YOR034c | 4 | 0.500 | 52 |
| YOL118c | 2 | 0.000 | 156 | YOL162w | 6 | 0.067 | 741 | YOR035c | 7 | 0.143 | 1280 |
| YOL119c | 17 | 0.228 | 3461 | YOL163w | 5 | 0.100 | 233 | YOR036w | 8 | 0.250 | 2112 |
| YOL120c | 10 | 0.489 | 487 | YOL164w | 11 | 0.200 | 1018 | YOR037w | 3 | 0.333 | 247 |
| YOL121c | 19 | 0.246 | 2429 | YOL164w-a | 2 | 1.000 | 0 | YOR038c | 80 | 0.021 | 32991 |
| YOL122c | 9 | 0.333 | 372 | YOL165c | 8 | 0.250 | 438 | YOR039w | 5 | 0.200 | 229 |
| YOL123w | 5 | 0.000 | 218 | YOL166c | 4 | 0.333 | 44 | YOR040w | 8 | 0.321 | 369 |
| YOL124c | 9 | 0.278 | 550 | YOL166w-a | 1 | 0.000 | 0 | YOR041c | 1 | 0.000 | 0 |
| YOL125w | 12 | 0.106 | 880 | YOR001w | 3 | 0.667 | 35 | YOR042w | 5 | 0.300 | 157 |
| YOL126c | 27 | 0.199 | 7420 | YOR003w | 7 | 0.143 | 900 | YOR043w | 6 | 0.400 | 248 |
| YOL127w | 12 | 0.333 | 850 | YOR004w | 4 | 0.167 | 154 | YOR044w | 7 | 0.048 | 746 |
| YOL128c | 8 | 0.250 | 504 | YOR005c | 8 | 0.179 | 796 | YOR045w | 3 | 0.000 | 234 |
| YOL130w | 7 | 0.286 | 426 | YOR006c | 2 | 0.000 | 14 | YOR046c | 2 | 0.000 | 9 |
| YOL131w | 3 | 0.333 | 13 | YOR007c | 5 | 0.600 | 66 | YOR047c | 5 | 0.500 | 128 |
| YOL132w | 3 | 0.333 | 22 | YOR008c | 5 | 0.400 | 164 | YOR048c | 5 | 0.200 | 132 |
| YOL133w | 4 | 0.667 | 35 | YOR008c-a | 3 | 0.667 | 22 | YOR049c | 22 | 0.433 | 770 |
| YOL135c | 3 | 0.333 | 35 | YOR008w-b | 1 | 0.000 | 0 | YOR050c | 7 | 0.333 | 220 |
| YOL136c | 12 | 0.227 | 1332 | YOR009w | 11 | 0.309 | 1078 | YOR051c | 4 | 0.667 | 57 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YOR052c | 16 | 0.275 | 1615 | YOR097c | 1 | 0.000 | 0 | YOR140w | 65 | 0.069 | 52553 |
| YOR053w | 1 | 0.000 | 0 | YOR098c | 7 | 0.190 | 638 | YOR141c | 2 | 0.000 | 88 |
| YOR054c | 5 | 0.200 | 208 | YOR099w | 8 | 0.250 | 458 | YOR142w | 2 | 0.000 | 15 |
| YOR055w | 1 | 0.000 | 0 | YOR100c | 19 | 0.257 | 1831 | YOR142w-a | 1 | 0.000 | 0 |
| YOR056c | 7 | 0.286 | 656 | YOR101w | 12 | 0.348 | 837 | YOR143c | 8 | 0.250 | 1018 |
| YOR057w | 4 | 0.333 | 346 | YOR102w | 1 | 0.000 | 0 | YOR144c | 3 | 0.333 | 101 |
| YOR058c | 13 | 0.179 | 1674 | YOR103c | 1 | 0.000 | 0 | YOR145c | 4 | 0.500 | 413 |
| YOR059c | 4 | 0.500 | 53 | YOR104w | 1 | 0.000 | 0 | YOR146w | 1 | 0.000 | 0 |
| YOR060c | 3 | 0.000 | 81 | YOR105w | 3 | 0.000 | 23 | YOR147w | 1 | 0.000 | 0 |
| YOR061w | 2 | 0.000 | 39 | YOR106w | 5 | 0.100 | 89 | YOR148c | 7 | 0.095 | 242 |
| YOR062c | 11 | 0.327 | 624 | YOR107w | 14 | 0.341 | 788 | YOR149c | 3 | 0.333 | 35 |
| YOR063w | 16 | 0.350 | 2353 | YOR108w | 8 | 0.357 | 468 | YOR150w | 3 | 0.000 | 52 |
| YOR064c | 8 | 0.107 | 219 | YOR109w | 3 | 0.333 | 27 | YOR151c | 3 | 0.667 | 12 |
| YOR065w | 15 | 0.143 | 798 | YOR110w | 5 | 0.700 | 73 | YOR152c | 9 | 0.222 | 596 |
| YOR066w | 7 | 0.476 | 308 | YOR111w | 4 | 0.000 | 158 | YOR153w | 30 | 0.193 | 6987 |
| YOR067c | 4 | 0.167 | 398 | YOR112w | 3 | 0.000 | 90 | YOR154w | 7 | 0.095 | 38 |
| YOR068c | 1 | 0.000 | 0 | YOR113w | 130 | 0.023 | 111303 | YOR155c | 2 | 0.000 | 17 |
| YOR070c | 4 | 0.167 | 153 | YOR114w | 2 | 1.000 | 0 | YOR156c | 1 | 0.000 | 0 |
| YOR071c | 8 | 0.321 | 700 | YOR115c | 7 | 0.143 | 381 | YOR157c | 6 | 0.400 | 622 |
| YOR072w | 3 | 0.000 | 298 | YOR116c | 6 | 0.467 | 504 | YOR158w | 3 | 0.667 | 23 |
| YOR072w-b | 1 | 0.000 | 0 | YOR117w | 7 | 0.238 | 1260 | YOR159c | 1 | 0.000 | 0 |
| YOR073w | 4 | 0.333 | 65 | YOR118w | 2 | 0.000 | 18 | YOR160w | 1 | 0.000 | 0 |
| YOR074c | 11 | 0.291 | 1244 | YOR119c | 5 | 0.100 | 142 | YOR161c | 21 | 0.310 | 1653 |
| YOR075w | 7 | 0.143 | 727 | YOR120w | 14 | 0.275 | 2050 | YOR161c-c | 3 | 0.667 | 9 |
| YOR076c | 3 | 0.333 | 74 | YOR121c | 1 | 0.000 | 0 | YOR162c | 97 | 0.037 | 109267 |
| YOR077w | 50 | 0.017 | 171958 | YOR122c | 4 | 0.333 | 115 | YOR163w | 5 | 0.300 | 146 |
| YOR078w | 6 | 0.133 | 470 | YOR123c | 1 | 0.000 | 0 | YOR164c | 3 | 0.667 | 24 |
| YOR080w | 2 | 1.000 | 0 | YOR124c | 4 | 0.500 | 66 | YOR165w | 2 | 0.000 | 22 |
| YOR081c | 4 | 0.333 | 91 | YOR125c | 5 | 0.300 | 121 | YOR166c | 2 | 0.000 | 23 |
| YOR082c | 4 | 0.167 | 73 | YOR126c | 4 | 0.333 | 211 | YOR167c | 8 | 0.536 | 877 |
| YOR083w | 3 | 0.000 | 76 | YOR127w | 3 | 0.333 | 64 | YOR168w | 3 | 0.667 | 30 |
| YOR084w | 12 | 0.182 | 1149 | YOR128c | 16 | 0.375 | 1437 | YOR171c | 1 | 0.000 | 0 |
| YOR085w | 2 | 1.000 | 0 | YOR129c | 6 | 0.267 | 177 | YOR172w | 24 | 0.011 | 950 |
| YOR086c | 7 | 0.238 | 687 | YOR130c | 5 | 0.900 | 13 | YOR173w | 29 | 0.185 | 6242 |
| YOR087w | 6 | 0.400 | 247 | YOR131c | 4 | 0.333 | 153 | YOR174w | 3 | 0.000 | 74 |
| YOR089c | 2 | 0.000 | 72 | YOR132w | 1 | 0.000 | 0 | YOR175c | 1 | 0.000 | 0 |
| YOR090c | 4 | 0.167 | 157 | YOR133w | 5 | 0.500 | 468 | YOR176w | 3 | 0.667 | 11 |
| YOR091w | 5 | 0.400 | 540 | YOR134w | 12 | 0.121 | 775 | YOR177c | 5 | 0.500 | 129 |
| YOR092w | 5 | 0.700 | 32 | YOR135c | 3 | 0.000 | 34 | YOR178c | 30 | 0.363 | 2670 |
| YOR093c | 12 | 0.182 | 1665 | YOR136w | 17 | 0.257 | 1466 | YOR179c | 12 | 0.439 | 845 |
| YOR094w | 11 | 0.182 | 963 | YOR137c | 4 | 0.167 | 192 | YOR180c | 8 | 0.393 | 171 |
| YOR095c | 16 | 0.358 | 1587 | YOR138c | 18 | 0.261 | 1995 | YOR181w | 6 | 0.600 | 75 |
| YOR096w | 13 | 0.410 | 1077 | YOR139c | 2 | 1.000 | 0 | YOR182c | 12 | 0.273 | 1180 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YOR183w | 4 | 0.167 | 63 | YOR224c | 5 | 0.200 | 595 | YOR268c | 13 | 0.154 | 527 |
| YOR184w | 14 | 0.286 | 1253 | YOR225w | 6 | 0.267 | 137 | YOR269w | 13 | 0.192 | 752 |
| YOR185c | 3 | 0.667 | 9 | YOR226c | 16 | 0.358 | 978 | YOR270c | 3 | 0.667 | 63 |
| YOR186w | 8 | 0.179 | 639 | YOR227w | 12 | 0.348 | 545 | YOR271c | 2 | 0.000 | 35 |
| YOR187w | 7 | 0.429 | 171 | YOR228c | 3 | 0.000 | 23 | YOR272w | 8 | 0.286 | 387 |
| YOR188w | 3 | 0.000 | 73 | YOR229w | 7 | 0.190 | 290 | YOR273c | 26 | 0.240 | 4521 |
| YOR189w | 2 | 0.000 | 424 | YOR230w | 18 | 0.255 | 1799 | YOR274w | 9 | 0.222 | 1375 |
| YOR190w | 2 | 0.000 | 14 | YOR231w | 1 | 0.000 | 0 | YOR275c | 2 | 0.000 | 3 |
| YOR191w | 2 | 1.000 | 0 | YOR232w | 1 | 0.000 | 0 | YOR276w | 6 | 0.667 | 92 |
| YOR192c | 16 | 0.158 | 959 | YOR233w | 5 | 0.400 | 83 | YOR279c | 1 | 0.000 | 0 |
| YOR192c-a | 1 | 0.000 | 0 | YOR234c | 14 | 0.297 | 1447 | YOR280c | 7 | 0.238 | 430 |
| YOR192c-b | 1 | 0.000 | 0 | YOR235w | 11 | 0.218 | 852 | YOR281c | 1 | 0.000 | 0 |
| YOR192c-c | 2 | 1.000 | 0 | YOR236w | 20 | 0.263 | 4767 | YOR282w | 3 | 0.000 | 57 |
| YOR193w | 4 | 0.167 | 145 | YOR237w | 6 | 0.267 | 326 | YOR283w | 2 | 0.000 | 88 |
| YOR194c | 5 | 0.400 | 306 | YOR238w | 1 | 0.000 | 0 | YOR284w | 8 | 0.286 | 613 |
| YOR195w | 4 | 0.167 | 244 | YOR239w | 3 | 0.000 | 43 | YOR285w | 10 | 0.267 | 736 |
| YOR196c | 2 | 0.000 | 47 | YOR241w | 2 | 1.000 | 0 | YOR287c | 4 | 0.333 | 110 |
| YOR197w | 3 | 0.333 | 289 | YOR242c | 2 | 1.000 | 0 | YOR288c | 6 | 0.333 | 500 |
| YOR198c | 5 | 0.600 | 113 | YOR243c | 2 | 1.000 | 0 | YOR289w | 8 | 0.071 | 1123 |
| YOR199w | 1 | 0.000 | 0 | YOR244w | 2 | 0.000 | 10 | YOR290c | 3 | 0.000 | 52 |
| YOR201c | 3 | 0.333 | 71 | YOR245c | 6 | 0.333 | 147 | YOR291w | 6 | 0.067 | 251 |
| YOR202w | 12 | 0.182 | 1137 | YOR246c | 12 | 0.348 | 493 | YOR292c | 11 | 0.345 | 382 |
| YOR203w | 5 | 0.300 | 140 | YOR247w | 17 | 0.301 | 1553 | YOR293w | 13 | 0.410 | 1080 |
| YOR204w | 5 | 0.100 | 429 | YOR248w | 9 | 0.278 | 573 | YOR294w | 5 | 0.300 | 82 |
| YOR205c | 4 | 0.000 | 426 | YOR249c | 2 | 1.000 | 0 | YOR295w | 1 | 0.000 | 0 |
| YOR206w | 12 | 0.136 | 1652 | YOR250c | 3 | 0.667 | 130 | YOR296w | 5 | 0.100 | 278 |
| YOR207c | 4 | 0.167 | 358 | YOR251c | 6 | 0.067 | 532 | YOR297c | 8 | 0.107 | 956 |
| YOR208w | 6 | 0.267 | 358 | YOR252w | 4 | 0.333 | 226 | YOR298c-a | 9 | 0.333 | 912 |
| YOR209c | 7 | 0.143 | 1552 | YOR253w | 2 | 0.000 | 47 | YOR298w | 7 | 0.238 | 257 |
| YOR210w | 5 | 0.300 | 182 | YOR254c | 4 | 0.167 | 278 | YOR299w | 8 | 0.321 | 361 |
| YOR211c | 1 | 0.000 | 0 | YOR255w | 6 | 0.133 | 551 | YOR300w | 2 | 0.000 | 22 |
| YOR212w | 3 | 0.000 | 21 | YOR256c | 2 | 0.000 | 11 | YOR301w | 12 | 0.394 | 589 |
| YOR213c | 1 | 0.000 | 0 | YOR257w | 4 | 0.167 | 77 | YOR302w | 21 | 0.171 | 2627 |
| YOR214c | 4 | 0.000 | 455 | YOR258w | 5 | 0.400 | 174 | YOR303w | 27 | 0.199 | 4348 |
| YOR215c | 5 | 0.200 | 353 | YOR259c | 5 | 0.800 | 100 | YOR304w | 7 | 0.000 | 489 |
| YOR216c | 3 | 0.000 | 138 | YOR260w | 4 | 0.333 | 288 | YOR305w | 1 | 0.000 | 0 |
| YOR217w | 2 | 0.000 | 6 | YOR261c | 4 | 0.667 | 310 | YOR306c | 15 | 0.390 | 1102 |
| YOR218c | 1 | 0.000 | 0 | YOR262w | 6 | 0.333 | 216 | YOR307c | 4 | 0.500 | 99 |
| YOR219c | 4 | 0.333 | 268 | YOR263c | 1 | 0.000 | 0 | YOR308c | 1 | 0.000 | 0 |
| YOR220w | 9 | 0.333 | 626 | YOR264w | 5 | 0.300 | 151 | YOR309c | 6 | 0.467 | 541 |
| YOR221c | 3 | 0.000 | 132 | YOR265w | 5 | 0.200 | 198 | YOR310c | 9 | 0.333 | 987 |
| YOR222w | 9 | 0.250 | 894 | YOR266w | 3 | 0.000 | 124 | YOR311c | 3 | 0.333 | 94 |
| YOR223w | 3 | 0.000 | 32 | YOR267c | 4 | 0.500 | 147 | YOR312c | 9 | 0.500 | 551 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YOR313c | 23 | 0.281 | 4379 | YOR352w | 1 | 0.000 | 0 | YOR396w | 2 | 0.000 | 7 |
| YOR314w | 14 | 0.242 | 1269 | YOR353c | 5 | 0.300 | 161 | YPL001w | 2 | 1.000 | 0 |
| YOR315w | 35 | 0.276 | 8609 | YOR354c | 14 | 0.242 | 1973 | YPL002c | 2 | 0.000 | 171 |
| YOR316c | 17 | 0.250 | 1284 | YOR355w | 13 | 0.231 | 1620 | YPL003w | 2 | 0.000 | 15 |
| YOR316c-a | 3 | 0.333 | 59 | YOR356w | 3 | 0.000 | 38 | YPL004c | 12 | 0.409 | 367 |
| YOR317w | 13 | 0.269 | 719 | YOR357c | 6 | 0.133 | 1148 | YPL005w | 7 | 0.238 | 518 |
| YOR318c | 16 | 0.217 | 2126 | YOR358w | 203 | 0.015 | 128658 | YPL006w | 3 | 0.333 | 23 |
| YOR319w | 23 | 0.269 | 3139 | YOR359w | 5 | 0.400 | 135 | YPL007c | 4 | 0.167 | 45 |
| YOR320c | 1 | 0.000 | 0 | YOR360c | 9 | 0.222 | 1195 | YPL008w | 3 | 0.333 | 200 |
| YOR321w | 2 | 1.000 | 0 | YOR361c | 5 | 0.500 | 214 | YPL009c | 3 | 0.333 | 54 |
| YOR322c | 4 | 0.333 | 387 | YOR362c | 4 | 0.667 | 65 | YPL010w | 3 | 0.000 | 288 |
| YOR323c | 5 | 0.400 | 140 | YOR363c | 152 | 0.023 | 88670 | YPL011c | 2 | 0.000 | 17 |
| YOR324c | 2 | 0.000 | 7 | YOR365c | 4 | 0.000 | 347 | YPL012w | 11 | 0.182 | 1082 |
| YOR325w | 4 | 0.167 | 102 | YOR366w | 3 | 0.333 | 218 | YPL013c | 4 | 0.167 | 382 |
| YOR326w | 6 | 0.267 | 601 | YOR367w | 5 | 0.100 | 674 | YPL014w | 10 | 0.244 | 828 |
| YOR327c | 7 | 0.333 | 278 | YOR368w | 6 | 0.267 | 477 | YPL015c | 8 | 0.143 | 807 |
| YOR328w | 14 | 0.220 | 1098 | YOR369c | 13 | 0.436 | 869 | YPL016w | 17 | 0.228 | 2308 |
| YOR329c | 3 | 0.333 | 32 | YOR370c | 3 | 1.000 | 0 | YPL017c | 16 | 0.275 | 1569 |
| YOR330c | 3 | 0.333 | 41 | YOR371c | 2 | 0.000 | 30 | YPL018w | 15 | 0.095 | 1394 |
| YOR332w | 6 | 0.133 | 394 | YOR372c | 376 | 0.008 | 411693 | YPL019c | 25 | 0.153 | 5483 |
| YOR333c | 3 | 0.000 | 46 | YOR373w | 5 | 0.200 | 190 | YPL020c | 2 | 0.000 | 4 |
| YOR334w | 1 | 0.000 | 0 | YOR374w | 24 | 0.250 | 2581 | YPL021w | 3 | 0.000 | 97 |
| YOR335c | 3 | 0.000 | 80 | YOR375c | 18 | 0.229 | 1970 | YPL022w | 2 | 0.000 | 37 |
| YOR336w | 7 | 0.095 | 603 | YOR376w | 5 | 0.000 | 284 | YPL023c | 2 | 1.000 | 0 |
| YOR337w | 4 | 0.500 | 108 | YOR376w-a | 3 | 1.000 | 0 | YPL024w | 17 | 0.353 | 913 |
| YOR338w | 12 | 0.242 | 2984 | YOR377w | 8 | 0.107 | 424 | YPL025c | 10 | 0.311 | 232 |
| YOR339c | 5 | 0.400 | 89 | YOR378w | 8 | 0.214 | 660 | YPL026c | 15 | 0.400 | 1083 |
| YOR340c | 8 | 0.179 | 442 | YOR380w | 12 | 0.348 | 619 | YPL027w | 3 | 0.667 | 16 |
| YOR341w | 10 | 0.222 | 746 | YOR381w | 7 | 0.286 | 262 | YPL028w | 6 | 0.200 | 407 |
| YOR342c | 13 | 0.385 | 958 | YOR381w-a | 1 | 0.000 | 0 | YPL029w | 3 | 0.000 | 132 |
| YOR343c | 6 | 0.467 | 205 | YOR382w | 30 | 0.237 | 5193 | YPL030w | 4 | 0.000 | 357 |
| YOR343c-a | 1 | 0.000 | 0 | YOR383c | 20 | 0.189 | 2321 | YPL031c | 6 | 0.000 | 494 |
| YOR343c-b | 1 | 0.000 | 0 | YOR384w | 6 | 0.333 | 159 | YPL032c | 4 | 0.167 | 171 |
| YOR343w-a | 3 | 0.667 | 13 | YOR385w | 7 | 0.333 | 298 | YPL033c | 4 | 0.000 | 79 |
| YOR343w-b | 2 | 0.000 | 13 | YOR386w | 9 | 0.083 | 430 | YPL034w | 15 | 0.181 | 3020 |
| YOR344c | 130 | 0.057 | 180916 | YOR387c | 10 | 0.222 | 1168 | YPL036w | 19 | 0.123 | 5863 |
| YOR345c | 1 | 0.000 | 0 | YOR388c | 18 | 0.216 | 2086 | YPL037c | 5 | 0.400 | 593 |
| YOR346w | 7 | 0.381 | 135 | YOR389w | 15 | 0.286 | 1146 | YPL038w | 121 | 0.010 | 32092 |
| YOR347c | 9 | 0.278 | 356 | YOR390w | 5 | 0.400 | 138 | YPL039w | 3 | 0.000 | 123 |
| YOR348c | 28 | 0.265 | 4009 | YOR391c | 26 | 0.135 | 4344 | YPL040c | 4 | 0.167 | 184 |
| YOR349w | 14 | 0.418 | 431 | YOR393w | 6 | 0.333 | 80 | YPL041c | 3 | 0.000 | 52 |
| YOR350c | 3 | 0.000 | 132 | YOR394c-a | 1 | 0.000 | 0 | YPL042c | 4 | 0.167 | 181 |
| YOR351c | 2 | 0.000 | 14 | YOR394w | 11 | 0.309 | 657 | YPL043w | 7 | 0.238 | 252 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YPL044c | 2 | 0.000 | 16 | YPL086c | 5 | 0.200 | 282 | YPL132w | 3 | 0.667 | 9 |
| YPL045w | 2 | 0.000 | 13 | YPL087w | 4 | 0.000 | 363 | YPL133c | 46 | 0.023 | 4985 |
| YPL046c | 1 | 0.000 | 0 | YPL088w | 14 | 0.352 | 993 | YPL134c | 5 | 0.300 | 123 |
| YPL047w | 1 | 0.000 | 0 | YPL089c | 211 | 0.021 | 131344 | YPL135w | 20 | 0.232 | 1758 |
| YPL048w | 6 | 0.867 | 32 | YPL090c | 11 | 0.400 | 644 | YPL137c | 11 | 0.291 | 499 |
| YPL049c | 93 | 0.037 | 72774 | YPL091w | 5 | 0.100 | 83 | YPL138c | 2 | 0.000 | 163 |
| YPL050c | 5 | 0.200 | 75 | YPL092w | 13 | 0.167 | 1340 | YPL139c | 9 | 0.139 | 1319 |
| YPL051w | 10 | 0.178 | 1599 | YPL093w | 11 | 0.291 | 660 | YPL140c | 1 | 0.000 | 0 |
| YPL052w | 4 | 0.500 | 100 | YPL094c | 6 | 0.400 | 294 | YPL141c | 5 | 0.400 | 115 |
| YPL053c | 2 | 1.000 | 0 | YPL095c | 9 | 0.167 | 562 | YPL142c | 2 | 0.000 | 23 |
| YPL054w | 12 | 0.106 | 922 | YPL096w | 3 | 0.667 | 22 | YPL143w | 12 | 0.394 | 820 |
| YPL055c | 2 | 1.000 | 0 | YPL097w | 3 | 0.333 | 121 | YPL144w | 7 | 0.429 | 201 |
| YPL056c | 17 | 0.228 | 2661 | YPL098c | 4 | 0.167 | 170 | YPL145c | 6 | 0.467 | 153 |
| YPL057c | 15 | 0.267 | 1236 | YPL100w | 2 | 1.000 | 0 | YPL146c | 4 | 0.333 | 229 |
| YPL058c | 14 | 0.330 | 746 | YPL101w | 3 | 0.667 | 14 | YPL147w | 8 | 0.214 | 380 |
| YPL059w | 7 | 0.143 | 455 | YPL102c | 1 | 0.000 | 0 | YPL148c | 5 | 0.400 | 91 |
| YPL060c-a | 2 | 0.000 | 6 | YPL103c | 1 | 0.000 | 0 | YPL149w | 4 | 0.333 | 129 |
| YPL060w | 3 | 0.000 | 18 | YPL106c | 8 | 0.393 | 783 | YPL150w | 3 | 0.000 | 25 |
| YPL061w | 23 | 0.261 | 2942 | YPL107w | 2 | 0.000 | 14 | YPL151c | 4 | 0.167 | 124 |
| YPL062w | 5 | 0.400 | 54 | YPL108w | 3 | 0.333 | 42 | YPL152w | 2 | 1.000 | 0 |
| YPL063w | 1 | 0.000 | 0 | YPL109c | 3 | 0.333 | 24 | YPL153c | 7 | 0.286 | 263 |
| YPL064c | 3 | 0.667 | 12 | YPL110c | 3 | 0.333 | 27 | YPL154c | 15 | 0.248 | 1043 |
| YPL065w | 1 | 0.000 | 0 | YPL111w | 18 | 0.196 | 3100 | YPL155c | 5 | 0.300 | 304 |
| YPL066w | 5 | 0.300 | 47 | YPL112c | 3 | 0.333 | 44 | YPL156c | 16 | 0.275 | 1303 |
| YPL067c | 7 | 0.429 | 283 | YPL113c | 11 | 0.345 | 572 | YPL157w | 7 | 0.381 | 295 |
| YPL068c | 9 | 0.333 | 457 | YPL114w | 4 | 0.167 | 99 | YPL158c | 6 | 0.333 | 144 |
| YPL069c | 1 | 0.000 | 0 | YPL115c | 1 | 0.000 | 0 | YPL159c | 5 | 0.400 | 275 |
| YPL070w | 6 | 0.200 | 161 | YPL116w | 5 | 0.200 | 208 | YPL160w | 8 | 0.286 | 791 |
| YPL071c | 8 | 0.179 | 480 | YPL117c | 7 | 0.238 | 398 | YPL161c | 5 | 0.200 | 159 |
| YPL072w | 1 | 0.000 | 0 | YPL118w | 1 | 0.000 | 0 | YPL162c | 2 | 0.000 | 12 |
| YPL073c | 2 | 1.000 | 0 | YPL119c | 5 | 0.400 | 167 | YPL163c | 13 | 0.282 | 957 |
| YPL074w | 4 | 0.500 | 5 | YPL120w | 3 | 0.333 | 35 | YPL164c | 4 | 0.167 | 70 |
| YPL075w | 288 | 0.013 | 292968 | YPL121c | 3 | 0.000 | 40 | YPL165c | 2 | 0.000 | 6 |
| YPL076w | 3 | 0.333 | 276 | YPL122c | 11 | 0.073 | 865 | YPL166w | 3 | 0.000 | 108 |
| YPL077c | 1 | 0.000 | 0 | YPL123c | 13 | 0.256 | 1117 | YPL167c | 2 | 1.000 | 0 |
| YPL078c | 7 | 0.238 | 133 | YPL124w | 6 | 0.067 | 366 | YPL168w | 3 | 0.667 | 16 |
| YPL079w | 10 | 0.422 | 716 | YPL125w | 4 | 0.167 | 111 | YPL169c | 1 | 0.000 | 0 |
| YPL080c | 4 | 0.500 | 41 | YPL126w | 8 | 0.321 | 289 | YPL170w | 11 | 0.291 | 1370 |
| YPL081w | 12 | 0.273 | 1301 | YPL127c | 5 | 0.400 | 68 | YPL171c | 34 | 0.205 | 6825 |
| YPL082c | 10 | 0.356 | 487 | YPL128c | 3 | 0.667 | 36 | YPL172c | 8 | 0.393 | 571 |
| YPL083c | 1 | 0.000 | 0 | YPL129w | 4 | 0.167 | 452 | YPL173w | 5 | 0.100 | 277 |
| YPL084w | 5 | 0.400 | 502 | YPL130w | 9 | 0.194 | 1138 | YPL174c | 2 | 0.000 | 19 |
| YPL085w | 6 | 0.267 | 342 | YPL131w | 11 | 0.382 | 1787 | YPL175w | 4 | 0.000 | 221 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YPL176c | 5 | 0.200 | 273 | YPL219w | 3 | 0.667 | 20 | YPL264c | 4 | 0.167 | 147 |
| YPL177c | 112 | 0.074 | 95575 | YPL220w | 6 | 0.800 | 53 | YPL265w | 20 | 0.279 | 1980 |
| YPL178w | 4 | 0.333 | 85 | YPL221w | 14 | 0.264 | 1552 | YPL266w | 8 | 0.179 | 700 |
| YPL179w | 2 | 1.000 | 0 | YPL222w | 9 | 0.250 | 917 | YPL267w | 6 | 0.467 | 331 |
| YPL180w | 7 | 0.095 | 1295 | YPL223c | 15 | 0.229 | 1366 | YPL268w | 11 | 0.218 | 944 |
| YPL181w | 6 | 0.333 | 273 | YPL224c | 1 | 0.000 | 0 | YPL269w | 5 | 0.200 | 220 |
| YPL182c | 3 | 0.000 | 152 | YPL226w | 7 | 0.286 | 488 | YPL270w | 5 | 0.000 | 41 |
| YPL183c | 3 | 0.333 | 42 | YPL227c | 4 | 0.167 | 224 | YPL271w | 9 | 0.250 | 146 |
| YPL183w-a | 3 | 0.667 | 13 | YPL228w | 2 | 0.000 | 53 | YPL272c | 5 | 0.400 | 60 |
| YPL184c | 1 | 0.000 | 0 | YPL229w | 4 | 0.333 | 390 | YPL273w | 7 | 0.286 | 331 |
| YPL185w | 1 | 0.000 | 0 | YPL230w | 63 | 0.055 | 76516 | YPL274w | 14 | 0.209 | 2230 |
| YPL186c | 8 | 0.536 | 169 | YPL231w | 9 | 0.278 | 904 | YPL275w | 7 | 0.143 | 897 |
| YPL187w | 21 | 0.186 | 4417 | YPL232w | 5 | 0.300 | 525 | YPL276w | 14 | 0.132 | 1320 |
| YPL188w | 8 | 0.000 | 646 | YPL233w | 2 | 0.000 | 141 | YPL277c | 17 | 0.309 | 2696 |
| YPL189c-a | 2 | 0.000 | 32 | YPL235w | 5 | 0.200 | 154 | YPL278c | 12 | 0.318 | 699 |
| YPL189w | 23 | 0.261 | 1773 | YPL236c | 4 | 0.167 | 143 | YPL279c | 3 | 0.333 | 30 |
| YPL190c | 5 | 0.200 | 250 | YPL237w | 1 | 0.000 | 0 | YPL280w | 19 | 0.228 | 1614 |
| YPL191c | 3 | 0.667 | 32 | YPL238c | 2 | 1.000 | 0 | YPL281c | 5 | 0.200 | 127 |
| YPL192c | 6 | 0.600 | 87 | YPL239w | 2 | 1.000 | 0 | YPL282c | 13 | 0.218 | 339 |
| YPL193w | 2 | 1.000 | 0 | YPL240c | 18 | 0.203 | 3927 | YPL283c | 22 | 0.277 | 1861 |
| YPL195w | 2 | 0.000 | 25 | YPL241c | 9 | 0.139 | 409 | YPR001w | 17 | 0.154 | 1160 |
| YPL196w | 3 | 0.000 | 40 | YPL242c | 12 | 0.227 | 1917 | YPR002c-a | 8 | 0.286 | 656 |
| YPL197c | 4 | 0.667 | 21 | YPL243w | 9 | 0.306 | 1218 | YPR002w | 12 | 0.242 | 827 |
| YPL198w | 17 | 0.265 | 3234 | YPL244c | 7 | 0.048 | 870 | YPR003c | 3 | 0.000 | 85 |
| YPL199c | 4 | 0.500 | 57 | YPL245w | 2 | 0.000 | 51 | YPR004c | 4 | 0.000 | 235 |
| YPL200w | 4 | 0.333 | 91 | YPL246c | 3 | 0.000 | 63 | YPR005c | 8 | 0.357 | 304 |
| YPL201c | 7 | 0.143 | 186 | YPL247c | 6 | 0.467 | 119 | YPR006c | 9 | 0.306 | 420 |
| YPL202c | 198 | 0.019 | 137677 | YPL248c | 165 | 0.011 | 139223 | YPR007c | 2 | 0.000 | 31 |
| YPL203w | 5 | 0.400 | 80 | YPL249c | 2 | 0.000 | 9 | YPR008w | 18 | 0.124 | 2639 |
| YPL204w | 5 | 0.200 | 135 | YPL249c-a | 13 | 0.218 | 2257 | YPR009w | 8 | 0.357 | 250 |
| YPL206c | 5 | 0.300 | 177 | YPL250c | 20 | 0.253 | 1930 | YPR010c | 10 | 0.378 | 633 |
| YPL207w | 8 | 0.000 | 179 | YPL251w | 18 | 0.111 | 2306 | YPR011c | 1 | 0.000 | 0 |
| YPL208w | 10 | 0.089 | 739 | YPL252c | 5 | 0.100 | 179 | YPR013c | 26 | 0.308 | 4659 |
| YPL209c | 6 | 0.200 | 144 | YPL253c | 23 | 0.138 | 4510 | YPR014c | 4 | 0.667 | 9 |
| YPL210c | 1 | 0.000 | 0 | YPL254w | 4 | 0.000 | 219 | YPR015c | 60 | 0.158 | 34950 |
| YPL211w | 7 | 0.429 | 595 | YPL255w | 6 | 0.400 | 183 | YPR016c | 5 | 0.600 | 37 |
| YPL212c | 7 | 0.429 | 269 | YPL256c | 11 | 0.255 | 715 | YPR017c | 2 | 0.000 | 103 |
| YPL213w | 5 | 0.000 | 284 | YPL257w | 4 | 0.333 | 70 | YPR018w | 3 | 0.333 | 241 |
| YPL214c | 5 | 0.200 | 267 | YPL258c | 7 | 0.333 | 321 | YPR019w | 6 | 0.333 | 594 |
| YPL215w | 4 | 0.167 | 393 | YPL260w | 1 | 0.000 | 0 | YPR020w | 9 | 0.167 | 115 |
| YPL216w | 7 | 0.238 | 170 | YPL261c | 1 | 0.000 | 0 | YPR021c | 4 | 0.333 | 157 |
| YPL217c | 7 | 0.190 | 339 | YPL262w | 8 | 0.179 | 291 | YPR022c | 2 | 1.000 | 0 |
| YPL218w | 4 | 0.333 | 129 | YPL263c | 4 | 0.333 | 118 | YPR024w | 4 | 0.333 | 122 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ | **ORF Name** | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YPR025c | 6 | 0.133 | 382 | YPR068c | 3 | 0.000 | 148 | YPR114w | 3 | 0.333 | 52 |
| YPR026w | 13 | 0.333 | 1192 | YPR069c | 5 | 0.500 | 460 | YPR115w | 3 | 0.333 | 47 |
| YPR027c | 10 | 0.244 | 839 | YPR070w | 2 | 0.000 | 99 | YPR116w | 4 | 0.333 | 191 |
| YPR028w | 7 | 0.143 | 473 | YPR071w | 3 | 0.000 | 137 | YPR117w | 1 | 0.000 | 0 |
| YPR029c | 5 | 0.300 | 315 | YPR072w | 8 | 0.107 | 2409 | YPR118w | 3 | 0.333 | 40 |
| YPR030w | 6 | 0.267 | 351 | YPR073c | 4 | 0.167 | 155 | YPR119w | 12 | 0.182 | 1010 |
| YPR031w | 1 | 0.000 | 0 | YPR074c | 13 | 0.333 | 1316 | YPR120c | 5 | 0.200 | 187 |
| YPR032w | 4 | 0.000 | 270 | YPR075c | 11 | 0.145 | 779 | YPR121w | 9 | 0.306 | 549 |
| YPR033c | 5 | 0.200 | 646 | YPR076w | 5 | 0.000 | 743 | YPR122w | 11 | 0.273 | 822 |
| YPR034w | 12 | 0.136 | 1979 | YPR077c | 1 | 0.000 | 0 | YPR123c | 2 | 0.000 | 119 |
| YPR035w | 18 | 0.248 | 3303 | YPR078c | 5 | 0.200 | 332 | YPR124w | 16 | 0.242 | 2312 |
| YPR036w | 15 | 0.295 | 1773 | YPR079w | 9 | 0.306 | 519 | YPR125w | 3 | 0.667 | 119 |
| YPR036w-a | 6 | 0.467 | 93 | YPR080w | 8 | 0.179 | 589 | YPR126c | 6 | 0.400 | 77 |
| YPR037c | 2 | 1.000 | 0 | YPR081c | 5 | 0.000 | 412 | YPR127w | 15 | 0.248 | 1170 |
| YPR038w | 6 | 0.333 | 218 | YPR082c | 2 | 0.000 | 22 | YPR128c | 6 | 0.333 | 420 |
| YPR039w | 6 | 0.333 | 218 | YPR083w | 2 | 0.000 | 22 | YPR129w | 3 | 0.000 | 367 |
| YPR040w | 8 | 0.321 | 479 | YPR084w | 2 | 0.000 | 18 | YPR130c | 1 | 0.000 | 0 |
| YPR041w | 2 | 0.000 | 130 | YPR085c | 3 | 0.000 | 57 | YPR131c | 5 | 0.300 | 59 |
| YPR042c | 2 | 0.000 | 31 | YPR086w | 3 | 0.333 | 47 | YPR132w | 10 | 0.422 | 702 |
| YPR043w | 9 | 0.444 | 2407 | YPR088c | 2 | 1.000 | 0 | YPR133c | 2 | 0.000 | 24 |
| YPR044c | 3 | 0.000 | 46 | YPR089w | 1 | 0.000 | 0 | YPR133w-a | 5 | 0.200 | 321 |
| YPR045c | 3 | 0.000 | 200 | YPR091c | 5 | 0.000 | 96 | YPR134w | 5 | 0.100 | 237 |
| YPR046w | 4 | 0.167 | 345 | YPR093c | 3 | 0.000 | 180 | YPR135w | 4 | 0.000 | 722 |
| YPR047w | 5 | 0.200 | 269 | YPR094w | 8 | 0.250 | 451 | YPR137w | 7 | 0.429 | 341 |
| YPR048w | 7 | 0.333 | 409 | YPR095c | 1 | 0.000 | 0 | YPR138c | 8 | 0.321 | 181 |
| YPR049c | 11 | 0.291 | 1115 | YPR097w | 1 | 0.000 | 0 | YPR139c | 7 | 0.048 | 621 |
| YPR051w | 3 | 0.333 | 107 | YPR098c | 1 | 0.000 | 0 | YPR140w | 6 | 0.067 | 486 |
| YPR052c | 3 | 0.000 | 80 | YPR099c | 4 | 0.833 | 7 | YPR141c | 6 | 0.533 | 131 |
| YPR053c | 2 | 0.000 | 7 | YPR100w | 2 | 1.000 | 0 | YPR142c | 2 | 0.000 | 27 |
| YPR054w | 4 | 0.167 | 500 | YPR101w | 6 | 0.600 | 101 | YPR143w | 5 | 0.400 | 80 |
| YPR055w | 6 | 0.267 | 391 | YPR102c | 13 | 0.346 | 1279 | YPR144c | 10 | 0.244 | 2571 |
| YPR056w | 5 | 0.200 | 314 | YPR103w | 8 | 0.286 | 577 | YPR145w | 20 | 0.189 | 5142 |
| YPR057w | 5 | 0.400 | 382 | YPR104c | 865 | 0.007 | 1540598 | YPR146c | 1 | 0.000 | 0 |
| YPR058w | 8 | 0.536 | 358 | YPR105c | 2 | 1.000 | 0 | YPR148c | 13 | 0.385 | 935 |
| YPR059c | 1 | 0.000 | 0 | YPR106w | 6 | 0.467 | 138 | YPR149w | 30 | 0.294 | 5067 |
| YPR060c | 5 | 0.400 | 363 | YPR107c | 12 | 0.197 | 1073 | YPR151c | 23 | 0.194 | 2168 |
| YPR061c | 8 | 0.321 | 237 | YPR108w | 16 | 0.142 | 2196 | YPR152c | 3 | 0.333 | 71 |
| YPR062w | 1 | 0.000 | 0 | YPR108w-a | 1 | 0.000 | 0 | YPR153w | 3 | 0.000 | 107 |
| YPR063c | 11 | 0.473 | 729 | YPR109w | 8 | 0.143 | 260 | YPR154w | 1 | 0.000 | 0 |
| YPR064w | 9 | 0.500 | 190 | YPR110c | 12 | 0.212 | 3168 | YPR155c | 5 | 0.200 | 103 |
| YPR065w | 419 | 0.021 | 397072 | YPR111w | 7 | 0.286 | 497 | YPR156c | 10 | 0.333 | 394 |
| YPR066w | 3 | 0.333 | 165 | YPR112c | 9 | 0.250 | 604 | YPR157w | 13 | 0.256 | 1687 |
| YPR067w | 6 | 0.400 | 426 | YPR113w | 8 | 0.214 | 415 | YPR158c-c | 5 | 0.200 | 88 |

Table A.1. Topological parameters of individual nodes of the yeast TRN (continued)

| ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ | ORF Name | $k_i$ | $C_i$ | $b_i$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| YPR158c-d | 4 | 0.167 | 42 | YPR173c | 1 | 0.000 | 0 | YPR191w | 11 | 0.218 | 339 |
| YPR158w | 12 | 0.212 | 2156 | YPR174c | 7 | 0.333 | 339 | YPR192w | 9 | 0.444 | 287 |
| YPR158w-a | 5 | 0.200 | 82 | YPR175w | 7 | 0.429 | 217 | YPR193c | 4 | 0.333 | 33 |
| YPR158w-b | 5 | 0.200 | 82 | YPR176c | 1 | 0.000 | 0 | YPR194c | 27 | 0.137 | 6204 |
| YPR159w | 10 | 0.289 | 837 | YPR177c | 1 | 0.000 | 0 | YPR195c | 8 | 0.143 | 534 |
| YPR160w | 27 | 0.234 | 4692 | YPR178w | 1 | 0.000 | 0 | YPR196w | 11 | 0.182 | 1328 |
| YPR161c | 4 | 0.000 | 170 | YPR179c | 5 | 0.300 | 149 | YPR197c | 2 | 0.000 | 14 |
| YPR162c | 2 | 1.000 | 0 | YPR180w | 3 | 1.000 | 0 | YPR198w | 13 | 0.154 | 898 |
| YPR163c | 7 | 0.429 | 269 | YPR181c | 5 | 0.400 | 102 | YPR199c | 744 | 0.004 | 1094498 |
| YPR164w | 4 | 0.167 | 243 | YPR182w | 4 | 0.167 | 74 | YPR200c | 11 | 0.309 | 866 |
| YPR165w | 2 | 1.000 | 0 | YPR183w | 4 | 0.833 | 9 | YPR201w | 17 | 0.257 | 2155 |
| YPR166c | 5 | 0.300 | 150 | YPR184w | 20 | 0.311 | 1997 | YPR202w | 14 | 0.363 | 928 |
| YPR167c | 15 | 0.333 | 1145 | YPR185w | 3 | 0.000 | 23 | YPR203w | 10 | 0.311 | 360 |
| YPR168w | 7 | 0.095 | 226 | YPR186c | 4 | 0.000 | 604 | YPR204w | 3 | 0.333 | 16 |
| YPR169w | 5 | 0.500 | 351 | YPR187w | 4 | 0.167 | 342 |  |  |  |  |
| YPR170c | 4 | 0.000 | 194 | YPR188c | 1 | 0.000 | 0 |  |  |  |  |
| YPR171w | 6 | 0.200 | 215 | YPR189w | 1 | 0.000 | 0 |  |  |  |  |
| YPR172w | 4 | 0.167 | 532 | YPR190c | 9 | 0.139 | 622 |  |  |  |  |

Table A.2. The frequency, f($k$), and the cumulative frequency of nodes, $n(k)$

| $k$ | f($k$) | $n(k)$ | $k$ | f($k$) | $n(k)$ | $k$ | f($k$) | $n(k)$ | $k$ | f($k$) | $n(k)$ |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 2188 | 1 | 1 | 315 | 1 | 45 | 134 | 1 | 100 | 46 | 2 | 155 |
| 1829 | 1 | 2 | 314 | 1 | 46 | 130 | 3 | 103 | 45 | 5 | 160 |
| 1375 | 1 | 3 | 301 | 1 | 47 | 129 | 1 | 104 | 43 | 2 | 162 |
| 1230 | 1 | 4 | 288 | 1 | 48 | 128 | 1 | 105 | 42 | 1 | 163 |
| 1156 | 1 | 5 | 277 | 1 | 49 | 122 | 1 | 106 | 40 | 2 | 165 |
| 1055 | 1 | 6 | 275 | 1 | 50 | 121 | 1 | 107 | 39 | 4 | 169 |
| 1033 | 1 | 7 | 269 | 1 | 51 | 120 | 1 | 108 | 36 | 1 | 170 |
| 916 | 1 | 8 | 266 | 1 | 52 | 118 | 1 | 109 | 35 | 7 | 177 |
| 865 | 1 | 9 | 264 | 1 | 53 | 116 | 1 | 110 | 34 | 5 | 182 |
| 756 | 1 | 10 | 254 | 1 | 54 | 112 | 2 | 112 | 33 | 4 | 186 |
| 744 | 1 | 11 | 247 | 3 | 57 | 111 | 2 | 114 | 32 | 10 | 196 |
| 688 | 1 | 12 | 242 | 1 | 58 | 106 | 1 | 115 | 31 | 9 | 205 |
| 666 | 1 | 13 | 240 | 2 | 60 | 104 | 1 | 116 | 30 | 17 | 222 |
| 637 | 1 | 14 | 238 | 1 | 61 | 102 | 1 | 117 | 29 | 12 | 234 |
| 594 | 1 | 15 | 236 | 1 | 62 | 100 | 1 | 118 | 28 | 18 | 252 |
| 585 | 1 | 16 | 223 | 2 | 64 | 99 | 1 | 119 | 27 | 15 | 267 |
| 577 | 1 | 17 | 222 | 1 | 65 | 98 | 1 | 120 | 26 | 13 | 280 |
| 552 | 1 | 18 | 218 | 1 | 66 | 97 | 2 | 122 | 25 | 25 | 305 |
| 547 | 1 | 19 | 215 | 1 | 67 | 96 | 1 | 123 | 24 | 29 | 334 |
| 534 | 1 | 20 | 211 | 1 | 68 | 93 | 1 | 124 | 23 | 27 | 361 |
| 522 | 1 | 21 | 210 | 1 | 69 | 90 | 1 | 125 | 22 | 27 | 388 |

Table A.2. The frequency, f(*k*), and the cumulative frequency of nodes, *n*(*k*) (continued)

| ***k*** | **f(*k*)** | ***n*(*k*)** | ***k*** | **f(*k*)** | ***n*(*k*)** | ***k*** | **f(*k*)** | ***n*(*k*)** | ***k*** | **f(*k*)** | ***n*(*k*)** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 510 | 1 | 22 | 203 | 1 | 70 | 85 | 2 | 127 | 21 | 39 | 427 |
| 506 | 1 | 23 | 201 | 2 | 72 | 84 | 1 | 128 | 20 | 40 | 467 |
| 504 | 1 | 24 | 200 | 1 | 73 | 80 | 2 | 130 | 19 | 53 | 520 |
| 492 | 1 | 25 | 199 | 2 | 75 | 78 | 1 | 131 | 18 | 65 | 585 |
| 482 | 1 | 26 | 198 | 2 | 77 | 77 | 1 | 132 | 17 | 77 | 662 |
| 459 | 1 | 27 | 194 | 1 | 78 | 76 | 1 | 133 | 16 | 73 | 735 |
| 458 | 1 | 28 | 191 | 1 | 79 | 69 | 1 | 134 | 15 | 82 | 817 |
| 448 | 1 | 29 | 189 | 1 | 80 | 68 | 1 | 135 | 14 | 123 | 940 |
| 425 | 1 | 30 | 188 | 2 | 82 | 67 | 1 | 136 | 13 | 126 | 1066 |
| 420 | 1 | 31 | 184 | 1 | 83 | 66 | 1 | 137 | 12 | 147 | 1213 |
| 419 | 1 | 32 | 170 | 2 | 85 | 65 | 1 | 138 | 11 | 174 | 1387 |
| 407 | 1 | 33 | 169 | 1 | 86 | 64 | 1 | 139 | 10 | 201 | 1588 |
| 377 | 1 | 34 | 168 | 1 | 87 | 63 | 3 | 142 | 9 | 287 | 1875 |
| 376 | 1 | 35 | 167 | 3 | 90 | 60 | 1 | 143 | 8 | 290 | 2165 |
| 358 | 1 | 36 | 166 | 1 | 91 | 59 | 1 | 144 | 7 | 362 | 2527 |
| 345 | 1 | 37 | 165 | 1 | 92 | 58 | 3 | 147 | 6 | 455 | 2982 |
| 343 | 1 | 38 | 162 | 1 | 93 | 57 | 1 | 148 | 5 | 590 | 3572 |
| 339 | 1 | 39 | 152 | 2 | 95 | 56 | 1 | 149 | 4 | 631 | 4203 |
| 334 | 1 | 40 | 150 | 1 | 96 | 53 | 1 | 150 | 3 | 735 | 4938 |
| 326 | 2 | 42 | 146 | 1 | 97 | 52 | 1 | 151 | 2 | 732 | 5670 |
| 324 | 1 | 43 | 144 | 1 | 98 | 50 | 1 | 152 | 1 | 686 | 6356 |
| 316 | 1 | 44 | 135 | 1 | 99 | 47 | 1 | 153 |  |  |  |

Table A.3. Average clustering coefficient and betweenness values for each degree

| **k** | ***C* (*k*)** | ***b* (*k*)** | **k** | ***C* (*k*)** | ***b* (*k*)** | **k** | ***C* (*k*)** | ***b* (*k*)** | **k** | ***C* (*k*)** | ***b* (*k*)** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 0.000 | 0 | 50 | 0.017 | 171958 | 144 | 0.026 | 115072 | 324 | 0.007 | 465973 |
| 2 | 1.000 | 114 | 52 | 0.010 | 33077 | 146 | 0.016 | 99176 | 326 | 0.023 | 519032 |
| 3 | 0.479 | 90 | 53 | 0.032 | 42977 | 150 | 0.048 | 81167 | 334 | 0.009 | 432706 |
| 4 | 0.340 | 205 | 56 | 0.209 | 16851 | 152 | 0.022 | 87564 | 339 | 0.018 | 226233 |
| 5 | 0.324 | 243 | 57 | 0.203 | 18951 | 162 | 0.009 | 226036 | 343 | 0.012 | 420044 |
| 6 | 0.298 | 337 | 58 | 0.056 | 58752 | 165 | 0.011 | 139223 | 345 | 0.008 | 467778 |
| 7 | 0.279 | 485 | 59 | 0.046 | 24449 | 166 | 0.049 | 134448 | 358 | 0.034 | 219573 |
| 8 | 0.291 | 559 | 60 | 0.158 | 34950 | 167 | 0.021 | 145470 | 376 | 0.008 | 411693 |
| 9 | 0.277 | 693 | 63 | 0.050 | 44491 | 168 | 0.021 | 77869 | 377 | 0.011 | 523332 |
| 10 | 0.280 | 831 | 64 | 0.021 | 54006 | 169 | 0.032 | 148567 | 407 | 0.009 | 345552 |
| 11 | 0.258 | 979 | 65 | 0.069 | 52553 | 170 | 0.016 | 178075 | 419 | 0.021 | 397072 |
| 12 | 0.268 | 1109 | 66 | 0.082 | 39033 | 184 | 0.023 | 136327 | 420 | 0.014 | 380453 |
| 13 | 0.255 | 1240 | 67 | 0.027 | 34011 | 188 | 0.013 | 95672 | 425 | 0.028 | 474296 |
| 14 | 0.277 | 1363 | 68 | 0.084 | 115913 | 189 | 0.013 | 78263 | 448 | 0.018 | 510855 |
| 15 | 0.260 | 1477 | 69 | 0.022 | 46596 | 191 | 0.011 | 115335 | 458 | 0.013 | 589228 |
| 16 | 0.267 | 1843 | 76 | 0.020 | 22083 | 194 | 0.022 | 76429 | 459 | 0.024 | 705126 |
| 17 | 0.274 | 1928 | 77 | 0.004 | 125739 | 198 | 0.028 | 149841 | 482 | 0.011 | 752603 |

Table A.3. Average clustering coefficient and betweenness values for each degree (continued)

| k | *C* (*k*) | *b* (*k*) | k | *C* (*k*) | *b* (*k*) | k | *C* (*k*) | *b* (*k*) | k | *C* (*k*) | *b* (*k*) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 18 | 0.259 | 2163 | 78 | 0.033 | 57802 | 199 | 0.017 | 122176 | 492 | 0.007 | 562971 |
| 19 | 0.259 | 2375 | 80 | 0.013 | 38767 | 200 | 0.012 | 79517 | 504 | 0.012 | 614058 |
| 20 | 0.255 | 2817 | 84 | 0.116 | 44305 | 201 | 0.032 | 84015 | 506 | 0.010 | 605184 |
| 21 | 0.246 | 2882 | 85 | 0.042 | 63098 | 203 | 0.015 | 128658 | 510 | 0.010 | 643610 |
| 22 | 0.257 | 3180 | 90 | 0.039 | 110053 | 210 | 0.015 | 363000 | 522 | 0.016 | 493176 |
| 23 | 0.244 | 4747 | 93 | 0.037 | 72774 | 211 | 0.021 | 131344 | 534 | 0.021 | 578631 |
| 24 | 0.213 | 3811 | 96 | 0.019 | 94209 | 215 | 0.018 | 151526 | 547 | 0.020 | 601548 |
| 25 | 0.224 | 4900 | 97 | 0.025 | 64579 | 218 | 0.027 | 146339 | 552 | 0.007 | 407305 |
| 26 | 0.229 | 4281 | 98 | 0.016 | 141988 | 222 | 0.014 | 134248 | 577 | 0.008 | 804470 |
| 27 | 0.207 | 5012 | 99 | 0.011 | 91373 | 223 | 0.012 | 242918 | 585 | 0.012 | 839314 |
| 28 | 0.214 | 4857 | 100 | 0.003 | 63988 | 236 | 0.040 | 104710 | 594 | 0.014 | 861633 |
| 29 | 0.213 | 5393 | 102 | 0.024 | 31538 | 238 | 0.012 | 200667 | 637 | 0.004 | 836047 |
| 30 | 0.230 | 5254 | 104 | 0.023 | 89297 | 240 | 0.021 | 383853 | 666 | 0.015 | 779413 |
| 31 | 0.192 | 9174 | 106 | 0.024 | 57111 | 242 | 0.010 | 199990 | 688 | 0.003 | 1544447 |
| 32 | 0.233 | 5824 | 111 | 0.021 | 126956 | 247 | 0.022 | 230509 | 744 | 0.004 | 1094498 |
| 33 | 0.157 | 9144 | 112 | 0.041 | 84939 | 254 | 0.003 | 248926 | 756 | 0.008 | 1414625 |
| 34 | 0.245 | 6444 | 116 | 0.027 | 142180 | 264 | 0.008 | 174707 | 865 | 0.007 | 1540598 |
| 35 | 0.193 | 7457 | 118 | 0.012 | 70076 | 266 | 0.015 | 339144 | 916 | 0.007 | 1230908 |
| 36 | 0.159 | 5881 | 120 | 0.028 | 48262 | 269 | 0.007 | 551939 | 1033 | 0.007 | 1949936 |
| 39 | 0.207 | 13235 | 121 | 0.010 | 32092 | 275 | 0.011 | 205404 | 1055 | 0.011 | 1491427 |
| 40 | 0.099 | 27470 | 122 | 0.033 | 125393 | 277 | 0.012 | 332117 | 1156 | 0.006 | 2489871 |
| 42 | 0.262 | 9463 | 128 | 0.029 | 117015 | 288 | 0.013 | 292968 | 1230 | 0.007 | 2988666 |
| 43 | 0.128 | 19086 | 129 | 0.024 | 135771 | 301 | 0.007 | 334676 | 1375 | 0.007 | 3379020 |
| 45 | 0.160 | 31364 | 130 | 0.032 | 111532 | 314 | 0.018 | 327148 | 1829 | 0.004 | 5162138 |
| 46 | 0.078 | 11218 | 134 | 0.015 | 49648 | 315 | 0.013 | 309200 | 2188 | 0.003 | 7721326 |
| 47 | 0.125 | 44124 | 135 | 0.037 | 15803 | 316 | 0.049 | 365525 | | | |

Table A.4. TFs in the constructed yeast TRN

| TF | ORF Name | TF | ORF Name | TF | ORF Name |
|---|---|---|---|---|---|
| Abf1p | YKL112w | Gat4p | YIR013c | Mal63p | MALR |
| Aca1p | YER045c | Gcn4p | YEL009c | Mata1p | A1 |
| Ace2p | YLR131c | Gcr1p | YPL075w | Matalpha1p | YCR040w |
| Ada2p | YDR448w | Gcr2p | YNL199c | Mbp1p | YDL056w |
| Adr1p | YDR216w | Gis1p | YDR096w | Mcm1p | YMR043w |
| Aft1p | YGL071w | Gis2p | YNL255c | Mdl2p | YPL270w |
| Aft2p | YPL202c | Gln3p | YER040w | Met28p | YIR017c |
| Arg80p | YMR042w | Gsm1p | YJL103c | Met31p | YPL038w |
| Arg81p | YML099c | Gts1p | YGL181w | Met32p | YDR253c |
| Aro80p | YDR421w | Gzf3p | YJL110c | Met4p | YNL103w |
| Arr1p | YPR199c | Haa1p | YPR008w | Mga1p | YGR249w |

Table A.4. TFs in the constructed yeast TRN (continued)

| TF | ORF Name | TF | ORF Name | TF | ORF Name |
|---|---|---|---|---|---|
| Ash1p | YKL185w | Hmlalpha2p | YCL067c | Phd1p | YKL043w |
| Azf1p | YOR113w | Hmra1p | YCR097w | Pho2p | YDL106c |
| Bas1p | YKR099w | Hmra2p | YCR096c | Pho4p | YFR034c |
| Bye1p | YKL005c | Hms1p | YOR032c | Pip2p | YOR363c |
| Cad1p | YDR423c | Hms2p | YJR147w | Plm2p | YDR501w |
| Cat8p | YMR280c | Hot1p | YMR172w | Pog1p | YIL122w |
| Cbf1p | YJR060w | Hpc2p | YBR215w | Ppr1p | YLR014c |
| Cdc14p | YFR028c | Hsf1p | YGL073w | Put3p | YKL015w |
| Cdc39p | YCR093w | Ifh1p | YLR223c | Rap1p | YNL216w |
| Cha4p | YLR098c | Ime1p | YJR094c | Rdr1p | YOR380w |
| Cin5p | YOR028c | Ime4p | YGL192w | Rds1p | YCR106w |
| Crz1p | YNL027w | Imp2'p | YIL154c | Rds2p | YPL133c |
| Cst6p | YIL036w | Ino2p | YDR123c | Rds3p | YPR094w |
| Cup2p | YGL166w | Ino4p | YOL108c | Reb1p | YBR049c |
| Cup9p | YPL177c | Ixr1p | YKL032c | Rfx1p | YLR176c |
| Dal80p | YKR034w | Kar4p | YCL055w | Rgm1p | YMR182c |
| Dal81p | YIR023w | Leu3p | YLR451w | Rgt1p | YKL038w |
| Dal82p | YNL314w | Lys14p | YDR034c | Rim101p | YHL027w |
| Dig1p | YPL049c | Mac1p | YMR021c | Rlm1p | YPL089c |
| Dig2p | YDR480w | Mal13p | YGR288w | Rme1p | YGR044c |
| Dot6p | YER088c | Mal33p | YBR297w | Rox1p | YPR065w |
| Ecm22p | YLR228c | Mga2p | YIR033w | Rph1p | YER169w |
| Elp6p | YMR312w | Mig1p | YGL035c | Rpn10p | YHR200w |
| Fhl1p | YPR104c | Mig2p | YGL209w | Rpn4p | YDL020c |
| Fkh1p | YIL131c | Mig3p | YER028c | Rsc30p | YHR056c |
| Fkh2p | YNL068c | Mot2p | YER068w | Rsf2p | YJR127c |
| Flo8p | YER109c | Mot3p | YMR070w | Rtg1p | YOL067c |
| Fzf1p | YGL254w | Msn1p | YOL116w | Rtg2p | YGL252c |
| Gal4p | YPL248c | Msn2p | YMR037c | Rtg3p | YBL103c |
| Gal80p | YML051w | Msn4p | YKL062w | Rts2p | YOR077w |
| Gat1p | YFL021w | Mss11p | YMR164c | Sfl1p | YOR140w |
| Gat3p | YLR013w | Mth1p | YDR277c | Sfp1p | YLR403w |
| Hac1p | YFL031w | Ndd1p | YOR372c | Sin3p | YOL004w |
| Hal9p | YOL089c | Ndt80p | YHR124w | Sip4p | YJL089w |
| Hap1p | YLR256w | Nrg1p | YDR043c | Skn7p | YHR206w |
| Hap2p | YGL237c | Nrg2p | YBR066c | Sko1p | YNL167c |
| Hap3p | YBL021c | Oaf1p | YAL051w | Smp1p | YBR182c |
| Hap4p | YKL109w | Opi1p | YHL020c | Sok2p | YMR016c |
| Hap5p | YOR358w | Otu1p | YFL044c | Sps18p | YNL204c |
| Hcm1p | YCR065w | Pdc2p | YDR081c | Spt2p | YER161c |
| Hir1p | YBL008w | Pdr1p | YGL013c | Spt23p | YKL020c |
| Hir2p | YOR038c | Pdr3p | YBL005w | Srd1p | YCR018c |
| Hmlalpha1p | YCL066w | Pdr8p | YLR266c | Stb1p | YNL309w |

Table A.4. TFs in the constructed yeast TRN (continued)

| TF | ORF Name | | TF | ORF Name | | TF | ORF Name |
|---|---|---|---|---|---|---|---|
| Stb5p | YHR178w | | Tec1p | YBR083w | | Yap1p | YML007w |
| Ste12p | YHR084w | | Thi2p | YBR240c | | Yap3p | YHL009c |
| Stp1p | YDR463w | | Tos4p | YLR183c | | Yap5p | YIR018w |
| Stp2p | YHR006w | | Tos8p | YGL096w | | Yap6p | YDR259c |
| Stp3p | YLR375w | | Tye7p | YOR344c | | Yap7p | YOL028c |
| Sum1p | YDR310c | | Uga3p | YDL170w | | Yhp1p | YDR451c |
| Sut1p | YGL162w | | Ume1p | YPL139c | | YJL206c | YJL206c |
| Swi1p | YPL016w | | Ume6p | YDR207c | | Yox1p | YML027w |
| Swi3p | YJL176c | | Upc2p | YDR213w | | YPR015c | YPR015c |
| Swi4p | YER111c | | Usv1p | YPL230w | | Yrm1p | YOR172w |
| Swi5p | YDR146c | | War1p | YML076c | | Yrr1p | YOR162c |
| Swi6p | YLR182w | | Xbp1p | YIL101c | | Zap1p | YJL056c |

# APPENDIX B: THE MATLAB CODE PERFORMING $Z_{\mathrm{corrected,TF}}$ CALCULATIONS

```
loadS;
loadTF;
loadZW1;

% ===========================================================
% Z-Score Calculations
% ===========================================================

ZT=zeros(size(TF));

for x=1:length(TF);
   a=TF(x);
   k=0;
   for y=1:length(S);
      if a==0;
         ZT(x)=0;
      else
         ZT(x)=ZT(x)+S(a,y)*ZW1(y);
         k=k+S(a,y);
      end
   end
   if a==0;
      ZT(x)=0;
   else
      if k==0
         k=100000000000;
      end
      ZT(x)=ZT(x)/k;
   end
```

```
end

% ==========================================================
% Normalization of Z-Scores
% ==========================================================

ZTN=zeros(length(TF),1000);

den=0;
for x=1:length(S)
    for y=1:length(S)
        den=den+S(x,y);
    end
end
den=den/(length(S)*length(S));

for j=1:1000
   j=j
   % Random Sparse Matrice Creation
   % -----------------------------------------------------------

   RND=sprand(length(S),length(S),den);
   for x=1:length(RND)
       x=x;
       for y=1:length(RND)
           if RND(x,y)>0
              RND(x,y)=1;
           end
       end
   end
   save RND RND;
   % z-score calculation for random matrice with the same sparcity
   % ------------------------------------------------------------
```

```
  for x=1:length(TF);
    a=TF(x);
    k=0;
    for y=1:length(RND);
      if a==0;
        ZTN(x,j)=0;
      else
        ZTN(x,j)=ZTN(x,j)+RND(a,y)*ZW1(y);
        k=k+RND(a,y);
      end
    end
    if a==0;
      ZTN(x,j)=0;
    else
        if k==0
        k=100000000000;
      end
      ZTN(x,j)=ZTN(x,j)/k;
    end
    save ZTN ZTN;
  end
end

% z-score normalization
% ------------------------------------------------------
ZCMN=zeros(length(TF),1);
ZCSD=zeros(length(TF),1);
for x=1:length(TF)
  for j=1:1000
    ZCMN(x)=ZCMN(x)+ZTN(x,j);
  end
  ZCMN(x)=ZCMN(x)/1000;
  for j=1:1000
```

```
      ZCSD(x)=ZCSD(x)+(ZTN(x,j)-ZCMN(x))^2;
   end
   ZCSD(x)=ZCSD(x)/1000;
   ZT(x)=(ZT(x)-ZCMN(x))/ZCSD(x);
 end
ZCSD
save ZT ZT;
```

# APPENDIX C: KEY TRANSCRIPTION FACTORS

Table C.1. Key TFs responsive to the deletion of *SNF1* gene

| **rank** | **$Z_{\mathrm{corrected,TF}}$** | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 8.0161 | 0.0000 | 3 | YBR215w | HPC2 |
| 2 | 5.1382 | 0.0000 | 15 | YPL016w | SWI1 |
| 3 | 4.7341 | 0.0000 | 9 | YJL176c | SWI3 |
| 4 | 4.1747 | 0.0000 | 7 | YMR312w | ELP6 |
| 5 | 4.0770 | 0.0000 | 16 | YDR081c | PDC2 |
| 6 | 3.9824 | 0.0000 | 24 | YLR266c | PDR8 |
| 7 | 3.9666 | 0.0000 | 8 | YPR094w | RDS3 |
| 8 | 3.6888 | 0.0001 | 9 | YGL252c | RTG2 |
| 9 | 3.5973 | 0.0002 | 29 | YGL166w | CUP2 |
| 10 | 3.2348 | 0.0006 | 187 | YDR096w | GIS1 |
| 11 | 3.1634 | 0.0008 | 26 | YER028c | MIG3 |
| 12 | 2.6040 | 0.0046 | 122 | YIR013c | GAT4 |
| 13 | 2.5991 | 0.0047 | 73 | YMR172w | HOT1 |
| 14 | 2.5640 | 0.0052 | 24 | YOR172w | YRM1 |
| 15 | 2.4608 | 0.0069 | 168 | YIL101c | XBP1 |
| 16 | 2.4290 | 0.0076 | 5 | YDR480w | DIG2 |
| 17 | 2.3150 | 0.0103 | 126 | YMR280c | CAT8 |
| 18 | 2.2530 | 0.0121 | 24 | YKL005c | BYE1 |
| 19 | 2.2472 | 0.0123 | 29 | YHL020c | OPI1 |
| 20 | 2.1611 | 0.0153 | 7 | YIL154c | IMP2' |
| 21 | 2.1158 | 0.0172 | 29 | YOR077w | RTS2 |
| 22 | 2.0723 | 0.0191 | 8 | YDR448w | ADA2 |
| 23 | 1.9656 | 0.0247 | 31 | YOL004w | SIN3 |
| 24 | 1.9175 | 0.0276 | 23 | YJL103c | GSM1 |
| 25 | 1.8321 | 0.0335 | 63 | YNL204c | SPS18 |
| 26 | 1.7450 | 0.0405 | 248 | YAL051w | OAF1 |
| 27 | 1.7147 | 0.0432 | 55 | YOR140w | SFL1 |
| 28 | 1.7147 | 0.0432 | 29 | YER045c | ACA1 |
| 29 | 1.6937 | 0.0452 | 187 | YIL036w | CST6 |
| 30 | 1.6914 | 0.0454 | 84 | YGL162w | SUT1 |
| 31 | 1.6685 | 0.0476 | 180 | YPL089c | RLM1 |
| 32 | 1.6676 | 0.0477 | 18 | YCL066w | HMLALPHA1 |
| 33 | 1.6645 | 0.0480 | 18 | YCR097w | HMRA1 |

Table C.2. Key TFs responsive to the deletion of *SNF4* gene

| **rank** | $Z_{\text{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 5.2109 | 0.0000 | 7 | YIL154c | IMP2' |
| 2 | 4.1936 | 0.0000 | 8 | YPR094w | RDS3 |
| 3 | 3.7235 | 0.0001 | 24 | YLR266c | PDR8 |
| 4 | 3.4286 | 0.0003 | 24 | YOR172w | YRM1 |
| 5 | 2.9887 | 0.0014 | 5 | YDR480w | DIG2 |
| 6 | 2.7043 | 0.0034 | 18 | YCL066w | HMLALPHA1 |
| 7 | 2.3051 | 0.0106 | 61 | YGL209w | MIG2 |
| 8 | 2.1167 | 0.0171 | 6 | YML051w | GAL80 |
| 9 | 1.8746 | 0.0304 | 18 | YPR008w | HAA1 |
| 10 | 1.8196 | 0.0344 | 38 | YHR124w | NDT80 |

Table C.3. Key TFs responsive to the deletion of *SNF1* and *SNF4* genes

| **rank** | $Z_{\text{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 6.1519 | 0.0000 | 9 | YCR093w | CDC39 |
| 2 | 3.2725 | 0.0005 | 8 | YPR094w | RDS3 |
| 3 | 3.2246 | 0.0006 | 9 | YGL252c | RTG2 |
| 4 | 3.1312 | 0.0009 | 12 | YDR034c | LYS14 |
| 5 | 3.1188 | 0.0009 | 3 | YBR215w | HPC2 |
| 6 | 3.0224 | 0.0013 | 18 | YPR008w | HAA1 |
| 7 | 2.5811 | 0.0049 | 63 | YNL204c | SPS18 |
| 8 | 2.4386 | 0.0074 | 187 | YDR096w | GIS1 |
| 9 | 2.3798 | 0.0087 | 29 | YGL166w | CUP2 |
| 10 | 2.3702 | 0.0089 | 122 | YIR013c | GAT4 |
| 11 | 2.1886 | 0.0143 | 73 | YMR172w | HOT1 |
| 12 | 2.1507 | 0.0157 | 8 | YDR448w | ADA2 |
| 13 | 2.0967 | 0.0180 | 7 | YMR312w | ELP6 |
| 14 | 2.0167 | 0.0219 | 187 | YIL036w | CST6 |
| 15 | 1.8408 | 0.0328 | 168 | YIL101c | XBP1 |
| 16 | 1.6782 | 0.0467 | 32 | YML076c | WAR1 |

Table C.4. Key TFs responsive to the deletion of *MIG1* gene

| **rank** | $Z_{\text{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 7.1489 | 0.0000 | 26 | YER028c | MIG3 |
| 2 | 6.7006 | 0.0000 | 8 | YIL154c | IMP2' |
| 3 | 6.3679 | 0.0000 | 5 | YDR480w | DIG2 |
| 4 | 5.4422 | 0.0000 | 61 | YGL209w | MIG2 |
| 5 | 4.823 | 0.0000 | 25 | YJL103c | GSM1 |
| 6 | 4.7076 | 0.0000 | 9 | YJL176c | SWI3 |
| 7 | 4.5571 | 0.0000 | 8 | YPR094w | RDS3 |
| 8 | 4.1502 | 0.0000 | 15 | YPL016w | SWI1 |
| 9 | 4.0021 | 0.0000 | 18 | YPR008w | HAA1 |

Table C.4. Key TFs responsive to the deletion of *MIG1* gene (continued)

| **rank** | $Z_{\mathbf{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 10 | 3.7811 | 0.0001 | 67 | YKL038w | RGT1 |
| 11 | 3.5519 | 0.0002 | 235 | YGL035c | MIG1 |
| 12 | 3.3388 | 0.0004 | 12 | YOR380w | RDR1 |
| 13 | 3.1162 | 0.0009 | 7 | YML051w | GAL80 |
| 14 | 2.9408 | 0.0016 | 28 | YLR375w | STP3 |
| 15 | 2.6248 | 0.0043 | 166 | YBR066c | NRG2 |
| 16 | 2.5953 | 0.0047 | 59 | YPR015c | YPR015c |
| 17 | 2.5914 | 0.0048 | 29 | YER045c | ACA1 |
| 18 | 2.1134 | 0.0173 | 35 | YIR033w | MGA2 |
| 19 | 1.9391 | 0.0262 | 7 | YPL270w | MDL2 |
| 20 | 1.9041 | 0.0284 | 45 | YPL133c | RDS2 |
| 21 | 1.8428 | 0.0327 | 129 | YIR013c | GAT4 |
| 22 | 1.8176 | 0.0346 | 24 | YKL005c | BYE1 |
| 23 | 1.8098 | 0.0352 | 84 | YGL162w | SUT1 |
| 24 | 1.6451 | 0.0500 | 8 | YDR448w | ADA2 |

Table C.5. Key TFs responsive to the deletion of *MIG2* gene

| **rank** | $Z_{\mathbf{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 10.363 | 0.0000 | 5 | YDR480w | DIG2 |
| 2 | 7.1447 | 0.0000 | 7 | YML051w | GAL80 |
| 3 | 4.6995 | 0.0000 | 8 | YDR448w | ADA2 |
| 4 | 2.8404 | 0.0023 | 26 | YER028c | MIG3 |
| 5 | 2.6282 | 0.0043 | 18 | YPR008w | HAA1 |
| 6 | 2.5415 | 0.0055 | 25 | YJL103c | GSM1 |
| 7 | 2.2851 | 0.0112 | 31 | YOL004w | SIN3 |
| 8 | 2.2459 | 0.0124 | 9 | YJL176c | SWI3 |
| 9 | 2.1419 | 0.0161 | 27 | YCR096c | HMRA2 |
| 10 | 2.0158 | 0.0219 | 15 | YPL016w | SWI1 |
| 11 | 1.9967 | 0.0229 | 20 | YCL066w | HMLALPHA1 |
| 12 | 1.7916 | 0.0366 | 67 | YKL038w | RGT1 |
| 13 | 1.7189 | 0.0428 | 57 | YKL020c | SPT23 |
| 14 | 1.714 | 0.0433 | 12 | YDR034c | LYS14 |

Table C.6. Key TFs responsive to the deletion of *MIG1* and *MIG2* genes

| **rank** | $Z_{\mathbf{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 5.2316 | 0.0000 | 26 | YER028c | MIG3 |
| 2 | 4.9745 | 0.0000 | 61 | YGL209w | MIG2 |
| 3 | 4.6398 | 0.0000 | 20 | YCL066w | HMLALPHA1 |
| 4 | 3.884 | 0.0001 | 15 | YPL016w | SWI1 |
| 5 | 3.8808 | 0.0001 | 8 | YIL154c | IMP2' |
| 6 | 3.6314 | 0.0001 | 9 | YJL176c | SWI3 |

Table C.6. Key TFs responsive to the deletion of *MIG1* and *MIG2* genes (continued)

| rank | $Z_{\text{corrected,TF}}$ | *p*-value | degree, *k* | ORF Name | Gene Name |
|---|---|---|---|---|---|
| 7 | 3.2742 | 0.0005 | 25 | YJL103c | GSM1 |
| 8 | 3.0904 | 0.0010 | 3 | YBR215w | HPC2 |
| 9 | 2.8607 | 0.0021 | 12 | YOR380w | RDR1 |
| 10 | 2.8331 | 0.0023 | 9 | YHR200w | RPN10 |
| 11 | 2.6297 | 0.0043 | 67 | YKL038w | RGT1 |
| 12 | 2.6013 | 0.0046 | 235 | YGL035c | MIG1 |
| 13 | 2.537 | 0.0056 | 129 | YIR013c | GAT4 |
| 14 | 2.5188 | 0.0059 | 8 | YPR094w | RDS3 |
| 15 | 2.4911 | 0.0064 | 8 | YDR448w | ADA2 |
| 16 | 2.2608 | 0.0119 | 7 | YML051w | GAL80 |
| 17 | 2.1894 | 0.0143 | 28 | YCL067c | HMLALPHA2 |
| 18 | 1.7096 | 0.0437 | 27 | YCR096c | HMRA2 |

Table C.7. Key TFs responsive to the deletion of *MIG3* gene

| rank | $Z_{\text{corrected,TF}}$ | *p*-value | degree, *k* | ORF Name | Gene Name |
|---|---|---|---|---|---|
| 1 | 10.252 | 0.0000 | 5 | YDR480w | DIG2 |
| 2 | 8.1369 | 0.0000 | 7 | YPL270w | MDL2 |
| 3 | 4.522 | 0.0000 | 29 | YER045c | ACA1 |
| 4 | 4.4773 | 0.0000 | 18 | YPR008w | HAA1 |
| 5 | 3.7234 | 0.0001 | 8 | YDR448w | ADA2 |
| 6 | 3.5799 | 0.0002 | 3 | YBR215w | HPC2 |
| 7 | 2.6916 | 0.0036 | 7 | YML051w | GAL80 |
| 8 | 2.221 | 0.0132 | 28 | YCL067c | HMLALPHA2 |
| 9 | 2.1896 | 0.0143 | 20 | YCL066w | HMLALPHA1 |
| 10 | 2.1635 | 0.0153 | 15 | YPL016w | SWI1 |
| 11 | 1.9957 | 0.0230 | 25 | YJL103c | GSM1 |
| 12 | 1.9105 | 0.0280 | 9 | YJL176c | SWI3 |
| 13 | 1.8609 | 0.0314 | 12 | YGR288w | MAL13 |
| 14 | 1.8249 | 0.0340 | 26 | YER028c | MIG3 |
| 15 | 1.8139 | 0.0348 | 20 | YCR097w | HMRA1 |

Table C.8. Key TFs responsive to the deletion of *MIG1, MIG2* and *MIG3* genes

| rank | $Z_{\text{corrected,TF}}$ | *p*-value | degree, *k* | ORF Name | Gene Name |
|---|---|---|---|---|---|
| 1 | 7.4385 | 0.0000 | 20 | YCL066w | HMLALPHA1 |
| 2 | 6.8346 | 0.0000 | 27 | YCR096c | HMRA2 |
| 3 | 5.9188 | 0.0000 | 26 | YER028c | MIG3 |
| 4 | 4.384 | 0.0000 | 61 | YGL209w | MIG2 |
| 5 | 4.1577 | 0.0000 | 8 | YIL154c | IMP2' |
| 6 | 3.8408 | 0.0001 | 25 | YJL103c | GSM1 |
| 7 | 3.6134 | 0.0002 | 3 | YBR215w | HPC2 |
| 8 | 3.3753 | 0.0004 | 7 | YML051w | GAL80 |

Table C.8. Key TFs responsive to the deletion of *MIG1, MIG2* and *MIG3* genes (continued)

| **rank** | **$Z_{\text{corrected,TF}}$** | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 9 | 3.3462 | 0.0004 | 9 | YHR200w | RPN10 |
| 10 | 2.8349 | 0.0023 | 9 | YGL252c | RTG2 |
| 11 | 2.7067 | 0.0034 | 18 | YPR008w | HAA1 |
| 12 | 2.6272 | 0.0043 | 12 | YGR288w | MAL13 |
| 13 | 2.5118 | 0.0060 | 67 | YKL038w | RGT1 |
| 14 | 2.5051 | 0.0061 | 28 | YCL067c | HMLALPHA2 |
| 15 | 2.4187 | 0.0078 | 9 | YJL176c | SWI3 |
| 16 | 2.4113 | 0.0079 | 235 | YGL035c | MIG1 |
| 17 | 2.3196 | 0.0102 | 129 | YIR013c | GAT4 |
| 18 | 2.3067 | 0.0105 | 15 | YPL016w | SWI1 |
| 19 | 2.1271 | 0.0167 | 47 | YCL055w | KAR4 |
| 20 | 1.9309 | 0.0267 | 8 | YDR448w | ADA2 |
| 21 | 1.8191 | 0.0344 | 35 | YIR033w | MGA2 |
| 22 | 1.7807 | 0.0375 | 99 | YDR253c | MET32 |

Table C.9. Key TFs responsive to oxygen availability under carbon limitation regime

| **rank** | **$Z_{\text{corrected,TF}}$** | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 1 | 7.7254 | 0.000 | 7 | YMR312w | ELP6 |
| 2 | 7.0418 | 0.000 | 8 | YDR448w | ADA2 |
| 3 | 6.4163 | 0.000 | 13 | YPL016w | SWI1 |
| 4 | 5.7943 | 0.000 | 8 | YJL176c | SWI3 |
| 5 | 4.1035 | 0.000 | 126 | YMR280c | CAT8 |
| 6 | 3.8557 | 0.000 | 131 | YOR363c | PIP2 |
| 7 | 3.7905 | 0.000 | 26 | YER045c | ACA1 |
| 8 | 3.6913 | 0.000 | 77 | YGL162w | SUT1 |
| 9 | 3.4546 | 0.000 | 168 | YIL101c | XBP1 |
| 10 | 3.3739 | 0.000 | 28 | YLR375w | STP3 |
| 11 | 3.2688 | 0.001 | 173 | YDR096w | GIS1 |
| 12 | 3.0767 | 0.001 | 156 | YBR066c | NRG2 |
| 13 | 3.065 | 0.001 | 237 | YAL051w | OAF1 |
| 14 | 3.0498 | 0.001 | 42 | YPL133c | RDS2 |
| 15 | 2.9718 | 0.001 | 177 | YIL036w | CST6 |
| 16 | 2.8665 | 0.002 | 58 | YNL204c | SPS18 |
| 17 | 2.8489 | 0.002 | 71 | YMR172w | HOT1 |
| 18 | 2.6323 | 0.004 | 9 | YGL252c | RTG2 |
| 19 | 2.3279 | 0.010 | 23 | YJL103c | GSM1 |
| 20 | 2.2971 | 0.011 | 176 | YLR256w | HAP1 |
| 21 | 2.2433 | 0.012 | 131 | YMR070w | MOT3 |
| 22 | 2.2432 | 0.012 | 30 | YHL020c | OPI1 |
| 23 | 2.2259 | 0.013 | 392 | YKL109w | HAP4 |

Table C.9. Key TFs responsive to oxygen availability under carbon limitation regime (continued)

| **rank** | $Z_{\text{corrected,TF}}$ | ***p*-value** | **degree, *k*** | **ORF Name** | **Gene Name** |
|---|---|---|---|---|---|
| 24 | 2.1986 | 0.014 | 23 | YKL005c | BYE1 |
| 25 | 2.1925 | 0.014 | 60 | YFR028c | CDC14 |
| 26 | 2.1569 | 0.016 | 353 | YDR043c | NRG1 |
| 27 | 2.1488 | 0.016 | 25 | YCR096c | HMRA2 |
| 28 | 2.1221 | 0.017 | 421 | YDR216w | ADR1 |
| 29 | 2.1046 | 0.018 | 55 | YPR015c | YPR015c |
| 30 | 2.0335 | 0.021 | 194 | YDR213w | UPC2 |
| 31 | 2.0329 | 0.021 | 204 | YGR044c | RME1 |
| 32 | 1.9108 | 0.028 | 182 | YOR358w | HAP5 |
| 33 | 1.9059 | 0.028 | 27 | YOL004w | SIN3 |
| 34 | 1.8781 | 0.030 | 227 | YDR207c | UME6 |
| 35 | 1.8574 | 0.032 | 104 | YJL089w | SIP4 |
| 36 | 1.8101 | 0.035 | 168 | YBL021c | HAP3 |
| 37 | 1.7892 | 0.037 | 216 | YGL035c | MIG1 |
| 38 | 1.7877 | 0.037 | 339 | YPR065w | ROX1 |
| 39 | 1.7753 | 0.038 | 9 | YOR380w | RDR1 |
| 40 | 1.7695 | 0.038 | 205 | YOR032c | HMS1 |
| 41 | 1.7594 | 0.039 | 395 | YOR028c | CIN5 |
| 42 | 1.7575 | 0.039 | 175 | YGL237c | HAP2 |
| 43 | 1.7117 | 0.043 | 92 | YMR021c | MAC1 |
| 44 | 1.6964 | 0.045 | 293 | YHR006w | STP2 |
| 45 | 1.6953 | 0.045 | 309 | YNL167c | SKO1 |
| 46 | 1.6842 | 0.046 | 23 | YOR172w | YRM1 |

# APPENDIX D: SIGNIFICANT SHARED GO BIOLOGICAL PROCESS TERMS OF KEY TRANSCRIPTION FACTORS

Table D.1. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| transcription | 25 out of 33 genes, 75.8 per cent | 1.69E-18 |
| transcription from RNA polymerase II promoter | 21 out of 33 genes, 63.6 per cent | 1.00E-16 |
| transcription, DNA-dependent | 23 out of 33 genes, 69.7 per cent | 3.57E-16 |
| RNA biosynthetic process | 23 out of 33 genes, 69.7 per cent | 3.86E-16 |
| regulation of transcription | 21 out of 33 genes, 63.6 per cent | 8.29E-16 |
| regulation of transcription from RNA polymerase II promoter | 18 out of 33 genes, 54.5 per cent | 2.03E-15 |
| regulation of transcription, DNA-dependent | 20 out of 33 genes, 60.6 per cent | 6.21E-15 |
| regulation of RNA metabolic process | 20 out of 33 genes, 60.6 per cent | 1.13E-14 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 21 out of 33 genes, 63.6 per cent | 1.62E-14 |
| regulation of nitrogen compound metabolic process | 21 out of 33 genes, 63.6 per cent | 1.76E-14 |
| regulation of gene expression | 21 out of 33 genes, 63.6 per cent | 3.29E-14 |
| regulation of macromolecule biosynthetic process | 21 out of 33 genes, 63.6 per cent | 5.19E-14 |
| regulation of cellular biosynthetic process | 21 out of 33 genes, 63.6 per cent | 1.01E-13 |
| regulation of biosynthetic process | 21 out of 33 genes, 63.6 per cent | 1.12E-13 |
| regulation of macromolecule metabolic process | 21 out of 33 genes, 63.6 per cent | 4.10E-13 |
| regulation of primary metabolic process | 21 out of 33 genes, 63.6 per cent | 1.24E-12 |
| regulation of cellular metabolic process | 21 out of 33 genes, 63.6 per cent | 2.72E-12 |
| regulation of metabolic process | 21 out of 33 genes, 63.6 per cent | 6.64E-12 |
| nucleic acid metabolic process | 27 out of 33 genes, 81.8 per cent | 9.58E-12 |
| nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 27 out of 33 genes, 81.8 per cent | 1.55E-10 |
| RNA metabolic process | 24 out of 33 genes, 72.7 per cent | 1.79E-10 |
| regulation of cellular process | 21 out of 33 genes, 63.6 per cent | 3.56E-09 |
| cellular nitrogen compound metabolic process | 27 out of 33 genes, 81.8 per cent | 3.81E-09 |
| nitrogen compound metabolic process | 27 out of 33 genes, 81.8 per cent | 5.49E-09 |
| cellular macromolecule biosynthetic process | 25 out of 33 genes, 75.8 per cent | 7.83E-09 |
| macromolecule biosynthetic process | 25 out of 33 genes, 75.8 per cent | 8.07E-09 |
| regulation of biological process | 21 out of 33 genes, 63.6 per cent | 9.86E-09 |
| positive regulation of macromolecule metabolic process | 12 out of 33 genes, 36.4 per cent | 9.91E-09 |
| positive regulation of transcription | 11 out of 33 genes, 33.3 per cent | 1.01E-08 |
| positive regulation of gene expression | 11 out of 33 genes, 33.3 per cent | 1.08E-08 |
| positive regulation of cellular metabolic process | 12 out of 33 genes, 36.4 per cent | 1.53E-08 |

Table D.1. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| positive regulation of metabolic process | 12 out of 33 genes, 36.4 per cent | 1.80E-08 |
| positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 11 out of 33 genes, 33.3 per cent | 2.51E-08 |
| positive regulation of nitrogen compound metabolic process | 11 out of 33 genes, 33.3 per cent | 2.51E-08 |
| gene expression | 26 out of 33 genes, 78.8 per cent | 2.68E-08 |
| positive regulation of macromolecule biosynthetic process | 11 out of 33 genes, 33.3 per cent | 4.87E-08 |
| positive regulation of cellular biosynthetic process | 11 out of 33 genes, 33.3 per cent | 7.27E-08 |
| positive regulation of biosynthetic process | 11 out of 33 genes, 33.3 per cent | 7.27E-08 |
| positive regulation of cellular process | 12 out of 33 genes, 36.4 per cent | 9.52E-08 |
| positive regulation of biological process | 12 out of 33 genes, 36.4 per cent | 1.24E-07 |
| positive regulation of transcription, DNA-dependent | 10 out of 33 genes, 30.3 per cent | 1.65E-07 |
| positive regulation of RNA metabolic process | 10 out of 33 genes, 30.3 per cent | 2.55E-07 |
| biological regulation | 21 out of 33 genes, 63.6 per cent | 4.22E-07 |
| cellular biosynthetic process | 25 out of 33 genes, 75.8 per cent | 1.77E-06 |
| biosynthetic process | 25 out of 33 genes, 75.8 per cent | 2.89E-06 |
| positive regulation of transcription from RNA polymerase II promoter | 8 out of 33 genes, 24.2 per cent | 4.54E-06 |
| cellular macromolecule metabolic process | 27 out of 33 genes, 81.8 per cent | 3.25E-05 |
| macromolecule metabolic process | 27 out of 33 genes, 81.8 per cent | 5.27E-05 |
| negative regulation of transcription from RNA polymerase II promoter | 5 out of 33 genes, 15.2 per cent | 0.00362 |
| negative regulation of transcription | 7 out of 33 genes, 21.2 per cent | 0.00368 |
| cellular metabolic process | 28 out of 33 genes, 84.8 per cent | 0.00377 |
| negative regulation of gene expression | 7 out of 33 genes, 21.2 per cent | 0.00407 |
| primary metabolic process | 27 out of 33 genes, 81.8 per cent | 0.00537 |
| chromatin organization | 7 out of 33 genes, 21.2 per cent | 0.00693 |
| metabolic process | 28 out of 33 genes, 84.8 per cent | 0.00695 |
| negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7 out of 33 genes, 21.2 per cent | 0.00736 |
| negative regulation of nitrogen compound metabolic process | 7 out of 33 genes, 21.2 per cent | 0.00736 |
| negative regulation of macromolecule biosynthetic process | 7 out of 33 genes, 21.2 per cent | 0.00781 |

Table D.2. Significant shared GO biological process terms of the key TFs identified for *ΔSNF4* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| transcription | 7 out of 10 genes, 70.0 per cent | 0.00024 |
| nucleic acid metabolic process | 9 out of 10 genes, 90.0 per cent | 0.00036 |
| regulation of transcription, DNA-dependent | 6 out of 10 genes, 60.0 per cent | 0.00048 |
| regulation of RNA metabolic process | 6 out of 10 genes, 60.0 per cent | 0.00058 |
| regulation of transcription | 6 out of 10 genes, 60.0 per cent | 0.0007 |

Table D.2. Significant shared GO biological process terms of the key TFs identified for *ΔSNF4* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 9 out of 10 genes, 90.0 per cent | 0.00095 |
| response to stimulus | 7 out of 10 genes, 70.0 per cent | 0.00105 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 6 out of 10 genes, 60.0 per cent | 0.0016 |
| regulation of nitrogen compound metabolic process | 6 out of 10 genes, 60.0 per cent | 0.00164 |
| regulation of gene expression | 6 out of 10 genes, 60.0 per cent | 0.00195 |
| regulation of macromolecule biosynthetic process | 6 out of 10 genes, 60.0 per cent | 0.00222 |
| response to chemical stimulus | 5 out of 10 genes, 50.0 per cent | 0.00255 |
| regulation of cellular biosynthetic process | 6 out of 10 genes, 60.0 per cent | 0.00268 |
| regulation of biosynthetic process | 6 out of 10 genes, 60.0 per cent | 0.00276 |
| cellular nitrogen compound metabolic process | 9 out of 10 genes, 90.0 per cent | 0.00285 |
| transcription, DNA-dependent | 6 out of 10 genes, 60.0 per cent | 0.00321 |
| nitrogen compound metabolic process | 9 out of 10 genes, 90.0 per cent | 0.00324 |
| RNA biosynthetic process | 6 out of 10 genes, 60.0 per cent | 0.00327 |
| regulation of macromolecule metabolic process | 6 out of 10 genes, 60.0 per cent | 0.00397 |
| regulation of primary metabolic process | 6 out of 10 genes, 60.0 per cent | 0.00543 |
| regulation of cellular metabolic process | 6 out of 10 genes, 60.0 per cent | 0.00676 |
| transcription from RNA polymerase II promoter | 5 out of 10 genes, 50.0 per cent | 0.00799 |
| regulation of metabolic process | 6 out of 10 genes, 60.0 per cent | 0.0087 |

Table D.3. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1ΔSNF4* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| transcription from RNA polymerase II promoter | 9 out of 16 genes, 56.2 per cent | 4.13E-06 |
| transcription | 10 out of 16 genes, 62.5 per cent | 1.03E-05 |
| transcription, DNA-dependent | 9 out of 16 genes, 56.2 per cent | 9.74E-05 |
| RNA biosynthetic process | 9 out of 16 genes, 56.2 per cent | 0.0001 |
| regulation of transcription, DNA-dependent | 7 out of 16 genes, 43.8 per cent | 0.00161 |
| regulation of transcription from RNA polymerase II promoter | 6 out of 16 genes, 37.5 per cent | 0.00182 |
| regulation of RNA metabolic process | 7 out of 16 genes, 43.8 per cent | 0.00197 |
| regulation of transcription | 7 out of 16 genes, 43.8 per cent | 0.00242 |
| nucleic acid metabolic process | 11 out of 16 genes, 68.8 per cent | 0.00398 |
| response to chemical stimulus | 6 out of 16 genes, 37.5 per cent | 0.004 |
| RNA metabolic process | 10 out of 16 genes, 62.5 per cent | 0.00443 |
| cellular nitrogen compound metabolic process | 12 out of 16 genes, 75.0 per cent | 0.00538 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 7 out of 16 genes, 43.8 per cent | 0.00618 |
| nitrogen compound metabolic process | 12 out of 16 genes, 75.0 per cent | 0.00628 |
| regulation of nitrogen compound metabolic process | 7 out of 16 genes, 43.8 per cent | 0.00633 |

Table D.3. Significant shared GO biological process terms of the key TFs identified for *ΔSNF1ΔSNF4* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of gene expression | 7 out of 16 genes, 43.8 per cent | 0.00771 |
| regulation of macromolecule biosynthetic process | 7 out of 16 genes, 43.8 per cent | 0.00889 |

Table D.4. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF1* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription | 13 out of 16 genes, 81.2 per cent | 9.10E-12 |
| transcription | 14 out of 16 genes, 87.5 per cent | 1.22E-11 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 13 out of 16 genes, 81.2 per cent | 5.90E-11 |
| regulation of nitrogen compound metabolic process | 13 out of 16 genes, 81.2 per cent | 6.20E-11 |
| regulation of gene expression | 13 out of 16 genes, 81.2 per cent | 9.21E-11 |
| regulation of macromolecule biosynthetic process | 13 out of 16 genes, 81.2 per cent | 1.22E-10 |
| regulation of cellular biosynthetic process | 13 out of 16 genes, 81.2 per cent | 1.87E-10 |
| regulation of biosynthetic process | 13 out of 16 genes, 81.2 per cent | 2.00E-10 |
| regulation of transcription, DNA-dependent | 12 out of 16 genes, 75.0 per cent | 2.19E-10 |
| transcription, DNA-dependent | 13 out of 16 genes, 81.2 per cent | 2.87E-10 |
| RNA biosynthetic process | 13 out of 16 genes, 81.2 per cent | 3.00E-10 |
| regulation of RNA metabolic process | 12 out of 16 genes, 75.0 per cent | 3.15E-10 |
| regulation of macromolecule metabolic process | 13 out of 16 genes, 81.2 per cent | 4.54E-10 |
| regulation of primary metabolic process | 13 out of 16 genes, 81.2 per cent | 9.20E-10 |
| regulation of cellular metabolic process | 13 out of 16 genes, 81.2 per cent | 1.51E-09 |
| regulation of metabolic process | 13 out of 16 genes, 81.2 per cent | 2.67E-09 |
| regulation of transcription from RNA polymerase II promoter | 10 out of 16 genes, 62.5 per cent | 4.46E-09 |
| transcription from RNA polymerase II promoter | 11 out of 16 genes, 68.8 per cent | 5.74E-09 |
| positive regulation of transcription | 8 out of 16 genes, 50.0 per cent | 6.41E-08 |
| positive regulation of gene expression | 8 out of 16 genes, 50.0 per cent | 6.74E-08 |
| positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 8 out of 16 genes, 50.0 per cent | 1.25E-07 |
| positive regulation of nitrogen compound metabolic process | 8 out of 16 genes, 50.0 per cent | 1.25E-07 |
| regulation of cellular process | 13 out of 16 genes, 81.2 per cent | 1.52E-07 |
| positive regulation of macromolecule biosynthetic process | 8 out of 16 genes, 50.0 per cent | 2.04E-07 |
| positive regulation of cellular biosynthetic process | 8 out of 16 genes, 50.0 per cent | 2.75E-07 |
| positive regulation of biosynthetic process | 8 out of 16 genes, 50.0 per cent | 2.75E-07 |
| regulation of biological process | 13 out of 16 genes, 81.2 per cent | 2.95E-07 |
| positive regulation of macromolecule metabolic process | 8 out of 16 genes, 50.0 per cent | 5.60E-07 |
| positive regulation of cellular metabolic process | 8 out of 16 genes, 50.0 per cent | 7.53E-07 |
| positive regulation of metabolic process | 8 out of 16 genes, 50.0 per cent | 8.39E-07 |
| nucleic acid metabolic process | 14 out of 16 genes, 87.5 per cent | 1.83E-06 |
| positive regulation of transcription, DNA-dependent | 7 out of 16 genes, 43.8 per cent | 2.10E-06 |
| RNA metabolic process | 13 out of 16 genes, 81.2 per cent | 2.36E-06 |
| positive regulation of cellular process | 8 out of 16 genes, 50.0 per cent | 2.59E-06 |
| positive regulation of RNA metabolic process | 7 out of 16 genes, 43.8 per cent | 2.86E-06 |
| positive regulation of biological process | 8 out of 16 genes, 50.0 per cent | 3.11E-06 |

Table D.4. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF1* mutant (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| biological regulation | 13 out of 16 genes, 81.2 per cent | 3.48E-06 |
| cellular macromolecule biosynthetic process | 14 out of 16 genes, 87.5 per cent | 4.19E-06 |
| macromolecule biosynthetic process | 14 out of 16 genes, 87.5 per cent | 4.27E-06 |
| nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 14 out of 16 genes, 87.5 per cent | 8.00E-06 |
| gene expression | 14 out of 16 genes, 87.5 per cent | 3.33E-05 |
| cellular nitrogen compound metabolic process | 14 out of 16 genes, 87.5 per cent | 4.37E-05 |
| negative regulation of transcription from RNA polymerase II promoter | 5 out of 16 genes, 31.2 per cent | 5.24E-05 |
| nitrogen compound metabolic process | 14 out of 16 genes, 87.5 per cent | 5.30E-05 |
| cellular biosynthetic process | 14 out of 16 genes, 87.5 per cent | 0.0001 |
| biosynthetic process | 14 out of 16 genes, 87.5 per cent | 0.00014 |
| negative regulation of transcription | 6 out of 16 genes, 37.5 per cent | 0.00026 |
| negative regulation of gene expression | 6 out of 16 genes, 37.5 per cent | 0.00028 |
| positive regulation of transcription from RNA polymerase II promoter | 5 out of 16 genes, 31.2 per cent | 0.00036 |
| negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 6 out of 16 genes, 37.5 per cent | 0.00049 |
| negative regulation of nitrogen compound metabolic process | 6 out of 16 genes, 37.5 per cent | 0.00049 |
| negative regulation of macromolecule biosynthetic process | 6 out of 16 genes, 37.5 per cent | 0.00051 |
| negative regulation of cellular biosynthetic process | 6 out of 16 genes, 37.5 per cent | 0.0007 |
| negative regulation of biosynthetic process | 6 out of 16 genes, 37.5 per cent | 0.0007 |
| negative regulation of macromolecule metabolic process | 6 out of 16 genes, 37.5 per cent | 0.00083 |
| negative regulation of cellular metabolic process | 6 out of 16 genes, 37.5 per cent | 0.00113 |
| negative regulation of metabolic process | 6 out of 16 genes, 37.5 per cent | 0.00124 |
| negative regulation of transcription, DNA-dependent | 5 out of 16 genes, 31.2 per cent | 0.00444 |
| negative regulation of RNA metabolic process | 5 out of 16 genes, 31.2 per cent | 0.00455 |
| negative regulation of cellular process | 6 out of 16 genes, 37.5 per cent | 0.00515 |
| cellular macromolecule metabolic process | 14 out of 16 genes, 87.5 per cent | 0.00569 |
| negative regulation of biological process | 6 out of 16 genes, 37.5 per cent | 0.00571 |
| macromolecule metabolic process | 14 out of 16 genes, 87.5 per cent | 0.0074 |

Table D.5. Significant shared GO biological process terms of the key TFs identified only for *ΔSNF4* mutant

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription by carbon catabolites | 2 out of 3 genes, 66.7 per cent | 0.00052 |
| cellular response to nutrient | 2 out of 3 genes, 66.7 per cent | 0.00087 |
| response to nutrient | 2 out of 3 genes, 66.7 per cent | 0.00109 |

Table D.6. Significant shared GO biological process terms of the key TFs identified for both *ΔSNF1* and *ΔSNF1ΔSNF4* mutants

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| transcription from RNA polymerase II promoter | 7 out of 12 genes, 58.3 per cent | 7.81E-05 |
| transcription | 8 out of 12 genes, 66.7 per cent | 7.85E-05 |
| transcription, DNA-dependent | 7 out of 12 genes, 58.3 per cent | 0.00092 |
| RNA biosynthetic process | 7 out of 12 genes, 58.3 per cent | 0.00094 |
| regulation of transcription from RNA polymerase II promoter | 5 out of 12 genes, 41.7 per cent | 0.00394 |
| nucleic acid metabolic process | 9 out of 12 genes, 75.0 per cent | 0.00551 |

Table D.7. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription | 6 out of 7 genes, 85.7 per cent | 3.05E-05 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 6 out of 7 genes, 85.7 per cent | 7.22E-05 |
| regulation of nitrogen compound metabolic process | 6 out of 7 genes, 85.7 per cent | 7.39E-05 |
| regulation of gene expression | 6 out of 7 genes, 85.7 per cent | 8.87E-05 |
| regulation of macromolecule biosynthetic process | 6 out of 7 genes, 85.7 per cent | 0.0001 |
| regulation of cellular biosynthetic process | 6 out of 7 genes, 85.7 per cent | 0.00012 |
| regulation of biosynthetic process | 6 out of 7 genes, 85.7 per cent | 0.00013 |
| regulation of macromolecule metabolic process | 6 out of 7 genes, 85.7 per cent | 0.00019 |
| transcription | 6 out of 7 genes, 85.7 per cent | 0.00021 |
| regulation of primary metabolic process | 6 out of 7 genes, 85.7 per cent | 0.00026 |
| regulation of cellular metabolic process | 6 out of 7 genes, 85.7 per cent | 0.00032 |
| regulation of metabolic process | 6 out of 7 genes, 85.7 per cent | 0.00042 |
| regulation of transcription, DNA-dependent | 5 out of 7 genes, 71.4 per cent | 0.00104 |
| regulation of RNA metabolic process | 5 out of 7 genes, 71.4 per cent | 0.00121 |
| positive regulation of macromolecule metabolic process | 4 out of 7 genes, 57.1 per cent | 0.00194 |
| positive regulation of cellular metabolic process | 4 out of 7 genes, 57.1 per cent | 0.00225 |
| positive regulation of metabolic process | 4 out of 7 genes, 57.1 per cent | 0.00238 |
| regulation of cellular process | 6 out of 7 genes, 85.7 per cent | 0.00274 |
| regulation of biological process | 6 out of 7 genes, 85.7 per cent | 0.00373 |
| positive regulation of cellular process | 4 out of 7 genes, 57.1 per cent | 0.00418 |
| positive regulation of biological process | 4 out of 7 genes, 57.1 per cent | 0.00458 |
| transcription, DNA-dependent | 5 out of 7 genes, 71.4 per cent | 0.00519 |
| RNA biosynthetic process | 5 out of 7 genes, 71.4 per cent | 0.00527 |

Table D.8. Significant shared GO biological process terms of the key TFs identified for both *ΔMIG1* and *ΔMIG1ΔMIG2* mutants excluding the key TFs identified for all three *ΔMIG1*, *ΔMIG2* and *ΔMIG1ΔMIG2* mutants

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| negative regulation of transcription from RNA polymerase II promoter by glucose | 2 out of 6 genes, 33.3 per cent | 0.00065 |
| negative regulation of transcription from RNA polymerase II promoter by carbon catabolites | 2 out of 6 genes, 33.3 per cent | 0.00065 |
| negative regulation of transcription by carbon catabolites | 2 out of 6 genes, 33.3 per cent | 0.00065 |
| negative regulation of transcription by glucose | 2 out of 6 genes, 33.3 per cent | 0.00065 |
| response to xenobiotic stimulus | 2 out of 6 genes, 33.3 per cent | 0.00065 |
| regulation of transcription from RNA polymerase II promoter by glucose | 2 out of 6 genes, 33.3 per cent | 0.00091 |
| regulation of transcription from RNA polymerase II promoter by carbon catabolites | 2 out of 6 genes, 33.3 per cent | 0.00121 |
| regulation of transcription by glucose | 2 out of 6 genes, 33.3 per cent | 0.00121 |
| response to chemical stimulus | 4 out of 6 genes, 66.7 per cent | 0.00389 |
| regulation of transcription by carbon catabolites | 2 out of 6 genes, 33.3 per cent | 0.00392 |
| response to stimulus | 5 out of 6 genes, 83.3 per cent | 0.00565 |
| cellular response to nutrient | 2 out of 6 genes, 33.3 per cent | 0.00657 |
| response to nutrient | 2 out of 6 genes, 33.3 per cent | 0.00816 |

Table D.9. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG1* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| response to xenobiotic stimulus | 3 out of 13 genes, 23.1 per cent | 8.36E-06 |
| negative regulation of transcription from RNA polymerase II promoter by glucose | 2 out of 13 genes, 15.4 per cent | 0.00408 |
| negative regulation of transcription from RNA polymerase II promoter by carbon catabolites | 2 out of 13 genes, 15.4 per cent | 0.00408 |
| negative regulation of transcription by carbon catabolites | 2 out of 13 genes, 15.4 per cent | 0.00408 |
| negative regulation of transcription by glucose | 2 out of 13 genes, 15.4 per cent | 0.00408 |
| regulation of transcription from RNA polymerase II promoter by glucose | 2 out of 13 genes, 15.4 per cent | 0.00571 |
| regulation of transcription from RNA polymerase II promoter | 5 out of 13 genes, 38.5 per cent | 0.00734 |
| regulation of transcription from RNA polymerase II promoter by carbon catabolites | 2 out of 13 genes, 15.4 per cent | 0.00761 |
| regulation of transcription by glucose | 2 out of 13 genes, 15.4 per cent | 0.00761 |

Table D.10. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG3* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription, mating-type specific | 2 out of 4 genes, 50.0 per cent | 0.00024 |
| regulation of transcription, DNA-dependent | 4 out of 4 genes, 100.0 per cent | 0.00055 |

Table D.10. Significant shared GO biological process terms of the key TFs identified only for *ΔMIG3* (comparing *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants) (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of RNA metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00062 |
| regulation of transcription | 4 out of 4 genes, 100.0 per cent | 0.0007 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00126 |
| regulation of nitrogen compound metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00128 |
| regulation of gene expression | 4 out of 4 genes, 100.0 per cent | 0.00144 |
| regulation of macromolecule biosynthetic process | 4 out of 4 genes, 100.0 per cent | 0.00158 |
| regulation of cellular biosynthetic process | 4 out of 4 genes, 100.0 per cent | 0.0018 |
| regulation of biosynthetic process | 4 out of 4 genes, 100.0 per cent | 0.00184 |
| transcription, DNA-dependent | 4 out of 4 genes, 100.0 per cent | 0.00205 |
| RNA biosynthetic process | 4 out of 4 genes, 100.0 per cent | 0.00208 |
| regulation of macromolecule metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00237 |
| transcription | 4 out of 4 genes, 100.0 per cent | 0.00261 |
| regulation of primary metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00295 |
| regulation of cellular metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00344 |
| cell fate commitment | 2 out of 4 genes, 50.0 per cent | 0.00363 |
| sex determination | 2 out of 4 genes, 50.0 per cent | 0.00363 |
| mating type determination | 2 out of 4 genes, 50.0 per cent | 0.00363 |
| regulation of metabolic process | 4 out of 4 genes, 100.0 per cent | 0.00412 |

Table D.11. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| regulation of transcription, DNA-dependent | 6 out of 8 genes, 75.0 per cent | 8.28E-05 |
| regulation of RNA metabolic process | 6 out of 8 genes, 75.0 per cent | 9.92E-05 |
| regulation of transcription | 6 out of 8 genes, 75.0 per cent | 0.00012 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 6 out of 8 genes, 75.0 per cent | 0.00028 |
| regulation of nitrogen compound metabolic process | 6 out of 8 genes, 75.0 per cent | 0.00029 |
| regulation of gene expression | 6 out of 8 genes, 75.0 per cent | 0.00034 |
| regulation of macromolecule biosynthetic process | 6 out of 8 genes, 75.0 per cent | 0.00039 |
| regulation of cellular biosynthetic process | 6 out of 8 genes, 75.0 per cent | 0.00048 |
| regulation of biosynthetic process | 6 out of 8 genes, 75.0 per cent | 0.00049 |
| transcription, DNA-dependent | 6 out of 8 genes, 75.0 per cent | 0.00058 |
| RNA biosynthetic process | 6 out of 8 genes, 75.0 per cent | 0.00059 |
| regulation of macromolecule metabolic process | 6 out of 8 genes, 75.0 per cent | 0.00071 |
| transcription | 6 out of 8 genes, 75.0 per cent | 0.00082 |
| regulation of primary metabolic process | 6 out of 8 genes, 75.0 per cent | 0.00098 |
| regulation of cellular metabolic process | 6 out of 8 genes, 75.0 per cent | 0.00123 |
| regulation of metabolic process | 6 out of 8 genes, 75.0 per cent | 0.0016 |

Table D.11. Significant shared GO biological process terms of the key TFs identified for *ΔMIG1*, *ΔMIG2* and *ΔMIG3* mutants (continued)

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| positive regulation of macromolecule metabolic process | 4 out of 8 genes, 50.0 per cent | 0.00393 |
| positive regulation of cellular metabolic process | 4 out of 8 genes, 50.0 per cent | 0.00455 |
| positive regulation of metabolic process | 4 out of 8 genes, 50.0 per cent | 0.00481 |
| positive regulation of cellular process | 4 out of 8 genes, 50.0 per cent | 0.00842 |
| positive regulation of biological process | 4 out of 8 genes, 50.0 per cent | 0.00922 |

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim)

| GO Term | Cluster frequency | *p*-value |
|---|---|---|
| transcription | 33 out of 46 genes, 71.7 per cent | 2.33E-23 |
| regulation of primary metabolic process | 32 out of 46 genes, 69.6 per cent | 1.69E-21 |
| regulation of metabolic process | 32 out of 46 genes, 69.6 per cent | 2.28E-20 |
| regulation of transcription from RNA polymerase II promoter | 24 out of 46 genes, 52.2 per cent | 3.43E-20 |
| regulation of transcription | 27 out of 46 genes, 58.7 per cent | 3.68E-19 |
| transcription from RNA polymerase II promoter | 26 out of 46 genes, 56.5 per cent | 5.92E-19 |
| regulation of cellular biosynthetic process | 28 out of 46 genes, 60.9 per cent | 9.49E-18 |
| regulation of biosynthetic process | 28 out of 46 genes, 60.9 per cent | 1.09E-17 |
| regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 27 out of 46 genes, 58.7 per cent | 1.66E-17 |
| regulation of nitrogen compound metabolic process | 27 out of 46 genes, 58.7 per cent | 1.84E-17 |
| regulation of transcription, DNA-dependent | 25 out of 46 genes, 54.3 per cent | 3.43E-17 |
| regulation of gene expression | 27 out of 46 genes, 58.7 per cent | 4.12E-17 |
| regulation of RNA metabolic process | 25 out of 46 genes, 54.3 per cent | 7.27E-17 |
| regulation of macromolecule biosynthetic process | 27 out of 46 genes, 58.7 per cent | 7.39E-17 |
| regulation of biological process | 33 out of 46 genes, 71.7 per cent | 1.22E-16 |
| biological regulation | 35 out of 46 genes, 76.1 per cent | 2.91E-16 |
| transcription, DNA-dependent | 27 out of 46 genes, 58.7 per cent | 3.93E-16 |
| RNA biosynthetic process | 27 out of 46 genes, 58.7 per cent | 4.30E-16 |
| regulation of cellular metabolic process | 28 out of 46 genes, 60.9 per cent | 7.62E-16 |
| regulation of macromolecule metabolic process | 27 out of 46 genes, 58.7 per cent | 1.03E-15 |
| regulation of cellular process | 29 out of 46 genes, 63.0 per cent | 8.73E-13 |
| nucleic acid metabolic process | 33 out of 46 genes, 71.7 per cent | 1.70E-11 |
| positive regulation of cellular metabolic process | 16 out of 46 genes, 34.8 per cent | 3.03E-11 |
| positive regulation of metabolic process | 16 out of 46 genes, 34.8 per cent | 3.75E-11 |
| positive regulation of cellular biosynthetic process | 15 out of 46 genes, 32.6 per cent | 8.30E-11 |
| positive regulation of biosynthetic process | 15 out of 46 genes, 32.6 per cent | 8.30E-11 |
| cellular macromolecule biosynthetic process | 33 out of 46 genes, 71.7 per cent | 1.04E-10 |
| macromolecule biosynthetic process | 33 out of 46 genes, 71.7 per cent | 1.08E-10 |
| positive regulation of cellular process | 16 out of 46 genes, 34.8 per cent | 2.26E-10 |

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim) (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| positive regulation of biological process | 16 out of 46 genes, 34.8 per cent | 3.48E-10 |
| nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 33 out of 46 genes, 71.7 per cent | 4.40E-10 |
| positive regulation of transcription | 13 out of 46 genes, 28.3 per cent | 2.49E-09 |
| positive regulation of gene expression | 13 out of 46 genes, 28.3 per cent | 2.70E-09 |
| biosynthetic process | 35 out of 46 genes, 76.1 per cent | 3.99E-09 |
| positive regulation of macromolecule metabolic process | 14 out of 46 genes, 30.4 per cent | 5.17E-09 |
| positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 13 out of 46 genes, 28.3 per cent | 7.28E-09 |
| positive regulation of nitrogen compound metabolic process | 13 out of 46 genes, 28.3 per cent | 7.28E-09 |
| gene expression | 33 out of 46 genes, 71.7 per cent | 9.86E-09 |
| regulation of carbohydrate metabolic process | 8 out of 46 genes, 17.4 per cent | 1.42E-08 |
| positive regulation of macromolecule biosynthetic process | 13 out of 46 genes, 28.3 per cent | 1.58E-08 |
| cellular biosynthetic process | 34 out of 46 genes, 73.9 per cent | 1.58E-08 |
| cellular nitrogen compound metabolic process | 33 out of 46 genes, 71.7 per cent | 1.77E-08 |
| RNA metabolic process | 27 out of 46 genes, 58.7 per cent | 2.02E-08 |
| nitrogen compound metabolic process | 33 out of 46 genes, 71.7 per cent | 2.69E-08 |
| negative regulation of transcription from RNA polymerase II promoter | 9 out of 46 genes, 19.6 per cent | 1.85E-07 |
| negative regulation of transcription | 12 out of 46 genes, 26.1 per cent | 4.23E-07 |
| negative regulation of gene expression | 12 out of 46 genes, 26.1 per cent | 5.04E-07 |
| positive regulation of transcription, DNA-dependent | 11 out of 46 genes, 23.9 per cent | 5.21E-07 |
| positive regulation of RNA metabolic process | 11 out of 46 genes, 23.9 per cent | 8.34E-07 |
| negative regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process | 12 out of 46 genes, 26.1 per cent | 1.44E-06 |
| negative regulation of nitrogen compound metabolic process | 12 out of 46 genes, 26.1 per cent | 1.44E-06 |
| negative regulation of macromolecule biosynthetic process | 12 out of 46 genes, 26.1 per cent | 1.60E-06 |
| negative regulation of cellular biosynthetic process | 12 out of 46 genes, 26.1 per cent | 2.93E-06 |
| negative regulation of biosynthetic process | 12 out of 46 genes, 26.1 per cent | 2.93E-06 |
| negative regulation of transcription, DNA-dependent | 11 out of 46 genes, 23.9 per cent | 3.78E-06 |
| negative regulation of RNA metabolic process | 11 out of 46 genes, 23.9 per cent | 4.00E-06 |
| negative regulation of macromolecule metabolic process | 12 out of 46 genes, 26.1 per cent | 4.11E-06 |
| positive regulation of transcription from RNA polymerase II promoter | 9 out of 46 genes, 19.6 per cent | 6.03E-06 |
| negative regulation of cellular metabolic process | 12 out of 46 genes, 26.1 per cent | 7.46E-06 |
| negative regulation of metabolic process | 12 out of 46 genes, 26.1 per cent | 8.91E-06 |
| cellular macromolecule metabolic process | 34 out of 46 genes, 73.9 per cent | 0.0001 |
| negative regulation of cellular process | 12 out of 46 genes, 26.1 per cent | 0.00013 |
| negative regulation of biological process | 12 out of 46 genes, 26.1 per cent | 0.00017 |
| macromolecule metabolic process | 34 out of 46 genes, 73.9 per cent | 0.00018 |
| positive regulation of gluconeogenesis | 3 out of 46 genes, 6.5 per cent | 0.00054 |
| primary metabolic process | 36 out of 46 genes, 78.3 per cent | 0.00232 |

Table D.12. Significant shared GO biological process terms of the key TFs responsive to oxygen availability (Clim) (continued)

| **GO Term** | **Cluster frequency** | ***p*-value** |
|---|---|---|
| positive regulation of cellular carbohydrate metabolic process | 3 out of 46 genes, 6.5 per cent | 0.00299 |
| positive regulation of glucose metabolic process | 3 out of 46 genes, 6.5 per cent | 0.00299 |
| positive regulation of carbohydrate metabolic process | 3 out of 46 genes, 6.5 per cent | 0.00299 |
| metabolic process | 37 out of 46 genes, 80.4 per cent | 0.006 |

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