Role of the cytoskeleton in signaling networks

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Summary

Intracellular signal transduction occurs through cascades of reactions involving dozens of proteins that transmit signals from the cell surface, through a crowded cellular environment filled with organelles and a filamentous cytoskeleton, to specific targets. Numerous signaling molecules are immobilized or transiently bound to the cytoskeleton, yet most models for signaling pathways have no specific role for this mesh, which is often presumed to function primarily as a scaffold that determines cell mechanics but not information flow. We combined analytical tools with several recently established large-scale protein-protein interaction maps for *Saccharomyces cerevisiae* to quantitatively address the role of the cytoskeleton in intracellular signaling. The results demonstrate that the network of signaling proteins is intimately linked to the cytoskeleton, suggesting that this interconnected filamentous structure plays a crucial and distinct functional role in signal transduction.

Supplemental data available online

Key words: Signal transduction, Cytoskeleton, Yeast, Protein interaction network

Introduction

The normal functioning of a cell requires constant interaction with its extracellular environment and with other cells, and these interactions lead to changes in cell physiology, cell shape and gene expression. Signals from neighboring cells and the extracellular matrix are perceived by membrane-bound receptors, resulting in changes in their biochemical or physical states that typically initiate a cascade of signaling events within the cell (Pawson, 1995; Rosales et al., 1995). Intracellular signal transduction might involve physical processes (such as diffusion), chemical changes (such as phosphorylation) of signaling intermediates or both. For most characterized signal transduction pathways, the initial signaling event and the end point are known, but intermediate events that transmit the signal are either partially or completely unknown. In order to fully understand intracellular signal transduction, it is essential to know the intermediate signaling molecules and to understand how information flows from one to the next. These issues are difficult to address experimentally because signaling molecules typically bind each other transiently and with relatively low affinities.

The cytoskeleton, an interconnected assembly of actin, intermediate filament and microtubule networks that extend throughout the entire cell, is involved in intracellular signal transduction (Rasmussen et al., 1990; Hameroff et al., 1992; Ingber, 1993a,b; Forgacs, 1995a,b; Burridge and Chrzanowska-Wodnicka, 1996; Janmey, 1998; Shafrir et al., 2000). Experimental evidence indicates that individual filaments of the cytoskeleton transmit mechanical perturbations, which can be used as tracks to move organelles within the cell, and provide transient docking sites for proteins and lipids (Mochly-Rosen, 1995; Isenberg and Niggli, 1998; Janmey, 1998). However, most of the evidence regarding the role of the cytoskeleton in signal transduction originates from experiments that employed destructive perturbations to the cytoskeleton, such as those caused by drugs that depolymerize filaments. These manipulations cause a complete loss of one or more cytoskeletal elements, leading to global changes that complicate the interpretation of experiments.

Recent progress in proteomics offers the possibility to quantitatively address the role of the cytoskeleton in intracellular signaling. Analysis of protein interactions on the scale of entire proteomes by yeast-two-hybrid screening and protein purification has generated a huge amount of information regarding protein networks within the cell. So far, these large scale experimental approaches have been applied most extensively to the budding yeast, *Saccharomyces cerevisiae* (Fields and Song, 1989; Gavin et al., 2002; Ho et al., 2002; Ito et al., 2001; Ito et al., 2000; Bader et al., 2001; Maslov and Sneppen, 2002; Mewes et al., 2002; Tong et al., 2002; Uetz et al., 2000; Xenarios et al., 2000; Jansen et al., 2003). In this study, we developed several independent, quantitative methods to probe for correlations of functionally defined protein classes. Specifically, we tested the hypothesis that the network of interacting cytoskeletal proteins and the network of signaling proteins are integrated to a higher degree than other functionally defined classes of proteins. We found that the correlation of signaling proteins with cytoskeletal

proteins is much stronger than with 15 other protein classes examined. These results strongly suggest that without the cytoskeleton, the intracellular signaling apparatus of the cell cannot properly function.

Materials and Methods

Interaction maps

Two independently performed, comprehensive two-hybrid assay screens were reported and interaction maps summarizing their results were extensively characterized (Ito et al., 2001; Uetz et al., 2000). These databases primarily contain information regarding pair-wise protein-protein interactions, although they also contain interactions mediated by intermediate bridging proteins. The database of interacting proteins (DIP) (http://dip.doe-mbi.ucla.edu/) (Xenarios et al., 2000) and the Munich Information Center for Protein Sequences (MIPS) (http://mips.gsf.de/) (Mewes et al., 2002) give information based on two-hybrid screens, biochemical purification, and genetically-derived interactions. Here, we present a quantitative analysis based on the two-hybrid screen of Uetz et al. (Uetz et al., 2000) (referred to as 'U database'), which contains 4480 interactions between 2115 proteins and is the smallest interaction network, and DIP (Xenarios et al., 2000) (referred to as 'D'), which contains 20,098 interactions among 5798 proteins and provides one of the largest networks. In the interaction maps analyzed in the present work, proteins are represented as nodes (small circles) and the interactions are represented as lines linking the nodes. Within these networks, a connected 'cluster' is defined as the set of proteins for which a path between any two nodes (through the links) exists. We performed our analysis on the largest connected cluster of each interaction network. For the U database, the largest such cluster contained 1458 nodes (approximately 24% of all yeast proteins), whereas the largest cluster for the DIP database contained 4198 nodes (approximately 68% of all yeast proteins). We note that, although strong disparities exist between the various datasets, all datasets led to similar results.

Quantitative analysis

To quantitatively study the clustering tendency of proteins in the various subclasses we employed several approaches. For global characterization of clustering we defined for each protein pair (i,j) in the interaction network the distance d_{ij} as the length of the shortest path connecting them, and analyzed the distance distribution $P(d_{ij})$ for all possible combinations of proteins. By this definition, the value of d_{AB} therefore is, d_{AB}=1 for proteins A and B that interact directly (i.e. are connected by one link) and d_{AB}=2 for proteins A and B that both interact directly with C, but not with each other (and thus d_{AC}=d_{CB}=1), etc. This metric describes the distribution of path lengths between all pairs of interacting proteins in a given cluster.

To characterize the local structure of interaction networks, we introduced the local clustering index $m_d(x/y)$, which counts all those proteins (denoted by y) that are at a distance d from a given protein (denoted by x). Here, x and y stand for the various protein classes: c, cytoskeletal protein; s, signaling protein; r, a protein that is not in class c or s. By its definition, $m_d(x/y)$ contains information about the number of those y-type proteins that are d steps away from a given protein x, or equivalently that can be reached from x by 3 links. The primary 'd=1-neighbors' or 'nearest neighbors' of a given protein x are those proteins that directly interact with protein x. The nearest-neighbor clustering index, $m_1(c^*/s)$ for a selected cytoskeletal protein c^* is then calculated as

$$m_1(c^*/s) = \frac{\text{number of those nearest neighbors of } c^* \text{ that are } s \text{ proteins}}{\text{total number of nearest neighbors of c*}}$$

For a given protein, this metric gives the proportion of interactions to other proteins in a given class. Analogously, $m_d(x/y)$ quantifies the composition of y-proteins at distance d from an x-protein. Thus, the analysis was carried out for pairs of proteins that directly interact (d=1), that interact via one bridging protein (d=2), and so on.

Results and Discussion

Definitions of signaling and cytoskeletal proteins

In order to construct the signaling (s) and cytoskeletal (c) protein sets, we categorized the gene products of *S. cerevisiae* as components of a signaling pathway, the cytoskeleton or neither of them (the random r set). The rules used to define these sets were based on experimentally determined, biochemical or genetic features of each protein, without a reference to the databases that constitute the available interaction maps. Because *S. cerevisiae* does not have intermediate filaments, the composition of the cytoskeleton was defined as actin, tubulin, proteins that bind actin or tubulin, proteins that bind a protein that binds actin or tubulin, and the septins, leading to the identification of 125 cytoskeletal proteins, which is 2.2% of the yeast proteome (see supplemental data for the entire list, http://jcs.biologists.org/supplemental/). This definition includes the filamentous septin, the actin and tubulin networks (including known cross-linkers, capping, severing, etc. proteins), and most proteins that localize to actin patches, which underlie the plasma membrane and are prominent components of the yeast cytoskeleton. The set of signaling proteins included all protein and lipid kinases, phosphatases, GTPases and their auxiliary factors, heterotrimeric G-protein-linked membrane receptors, nucleotide cyclases/phosphodiesterases, and biochemically or genetically characterized scaffolding proteins. This analysis identified 342 signaling proteins, 5.9% of the proteome (see supplemental data for the entire list). Twenty proteins were common to both sets. Importantly, the criteria used to define cytoskeletal and signaling proteins are conservative and independent of each other. Several metabolic kinases known to bind directly to the cytoskeleton (e.g. phosphofructokinase) were not included in the cytoskeleton protein set because they might obscure the more subtle interplay between the cytoskeleton and other signaling pathways. In addition, uncharacterized open reading frames with homology to known signal transduction proteins were excluded. These definitions, therefore, focused the analysis on proteins for which functional information is currently available.

Global clustering

In the currently available protein interaction databases, information was available for subsets of the proteins in the classes defined by us. In the database by Uetz et al. (Uetz et al., 2000) and in DIP (Xenarios et al., 2000), we identified 74 (U) and 92 (D) cytoskeletal proteins, and 141 (U) and 207 (D) signaling proteins in the largest interconnected clusters. Fifteen (U) and 18 (D) proteins were shared by the two classes in each database. Surprisingly, tubulin and tubulin-associated proteins were not present in the largest connected clusters for either the database by Uetz et al. or DIP; they formed separate connected clusters with a small number of proteins.

The largest connected cluster within the U database shows the c proteins in yellow, s proteins in green and proteins found in both classes in red (Fig. 1). Inspection of Fig. 1 qualitatively

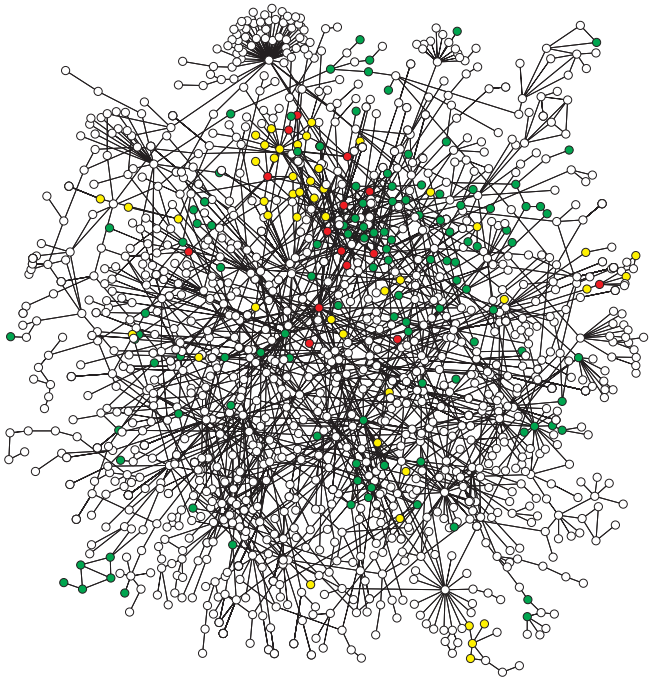

Fig. 1. The largest connected cluster of 1458 interacting proteins of the database by Uetz et al. (Uetz et al., 2000). In this cluster, yellow and green dots denote cytoskeletal and signaling proteins, respectively, as defined by our criteria. Proteins in red are shared by the two subclasses. The analogous cluster in the D network contains 4198 proteins. It is not shown here because the density of proteins was too high for visual examination.

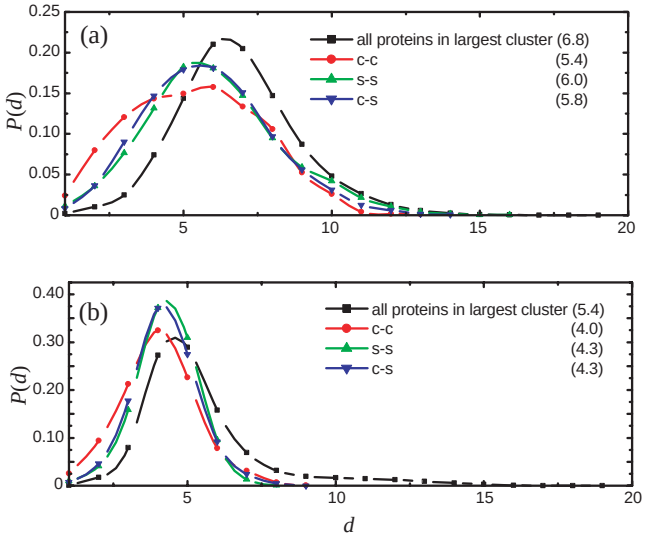

Fig. 2. Distance distribution $P(d)$ for proteins in the various classes. The notations in the figure are as follows: c-c, cytoskeleton-cytoskeleton; s-s, signaling-signaling; c-s, signaling-cytoskeleton. $P(d)$ for all proteins includes distances between any two proteins. Numbers in brackets give the average distances ($\langle d \rangle$) between indicated proteins. (a) Results based on the database of Uetz et al. (Uetz et al., 2000). (b) Results based on the DIP database. The larger number of proteins in the DIP dataset is manifest in a narrower distance distribution and higher peak values.

suggests correlations between cytoskeletal and signaling proteins because the majority of these two protein groups form relatively localized clusters within the network.

To quantify the clustering tendency of proteins in each class, we calculated the distance distribution $P(d)$ (see Materials and Methods) for all protein pairs in the largest interconnected clusters (Fig. 2). Because the distance between two proteins was defined as the number of links required to travel from one protein to another (see Materials and Methods), the function $P(d)$ for all proteins in a cluster reflects the degree to which the proteins within the cluster interact with each other. When calculated for the set of all proteins in the largest connected cluster in the database by Uetz et al., the peak of $P(d)$ was approximately at d=6.8. As expected, the peak of the distance distributions for the *c* and *s* proteins was shifted to lower values, 5.4 and 6.0, respectively, indicating that proteins within these groups preferentially interact with each other. The corresponding values for all proteins, cytoskeletal proteins and signaling proteins derived from the DIP data set are 5.4, 4.0 and 4.3, respectively. Notice that, due to our definition of the cytoskeletal protein class, the maximum value of d_{cc}, derived from an ideal interaction map, should be d_{cc}=4, because for each protein in this class (except for septins) the maximal distance from actin is two. (Although the distance between septins and actin is not constrained, only three septins appear in the largest interconnected U and D clusters so their effect on the maximum value of d_{cc} is negligible.) Not surprisingly, this (d_{cc}=4) is not reflected by the two datasets that were used, because our procedure to classify the yeast proteins is independent of these interaction maps. It is, however, consistent with the built-in enhanced clustering of cytoskeletal proteins in that $\langle d_{cc} \rangle$ is the smallest among the values listed in Fig. 2. Here, $\langle d \rangle$ denotes the average of d over the distribution $P(d)$. For the case of the DIP network map of cytoskeletal proteins, where $\langle d_{cc} \rangle$=4 (Fig. 2), the majority of *c*-*c* connections do indeed have d≈4. This observation suggests that $P(d)$ accurately describes interactions within the networks and, as more information is obtained regarding interactions of cellular proteins, the methods we have devised should be of general use.

Using distance distribution analysis, we also determined how closely signaling proteins are linked to cytoskeletal proteins. As can be seen from Fig. 2, the peak value of $P(d_{cs})$, the distance distribution for all pairs of *c* and *s* proteins, is also shifted to smaller d values, indicating that the two groups are more linked to each other within the network than it was expected for two random sets. Interestingly, the degree to which *s* proteins are linked to *c* proteins (as measured by $\langle d_{cs} \rangle$) was approximately the same as for *s* proteins alone (Fig. 2). This result suggests that signaling proteins are intimately linked to the cytoskeleton.

Local clustering

The distance distribution, $P(d)$ (Fig. 2), gives a global measure of clustering. To gain information about the local composition of the interaction networks, we calculated the local clustering index, $m_d(x/y)$ (see Materials and Methods). This metric characterizes the proportion of proteins at distance d from a given protein in the *x* class that are members of the protein class *y*. In Fig. 3 we plot the average clustering index

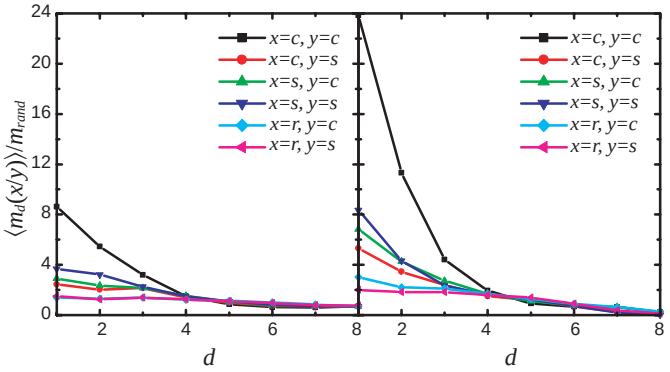

Fig. 3. Plot of the rescaled average local clustering index $\langle m_d\rangle/\langle m_{rand}\rangle$ using the database of Uetz et al. (Uetz et al., 2000) (left) and the DIP database (right).

$\langle m_d(x/y)\rangle = m_d(x/y)/N$ (with N being the total number of proteins in the network) for the various protein classes. This analysis indicates that, at short distances, signaling proteins and cytoskeletal proteins interact primarily with proteins of the same class. Notice that $\langle m_d(c/c)\rangle$ decays fast as a function of distance and at $d\approx4$ practically reaches its asymptotic value, indicating again that the networks derived from the U and D databases are consistent with our independent definition of the set of cytoskeletal proteins.

In the absence of any clustering tendency of proteins from two different classes (x and y) the local clustering index $\langle m_d(x/y)\rangle$ should be independent of distance and should be equal to the average density of the y proteins in the network $\langle m_{rand}(x/y)\rangle = N_y/N$, where N_y denotes the total number of proteins that belong to class y. By contrast, if proteins belonging to the x and y classes have a tendency to cluster, then $\langle m_{rand}(x/y)\rangle$ should be higher than N_y/N for small values of d, should decrease monotonically and converge to a value smaller (possibly zero) than N_y/N for large d values. These expectations are indeed supported by the plots in Fig. 3. For example, using the DIP dataset, the proportion of s proteins connected by a single link to a c protein (red curve at d=1) is almost three times greater than the same quantity evaluated by replacing the c protein by a randomly selected protein (magenta curve at d=1). Furthermore, this proportion is about six times higher than the proportion of s proteins linked to the cytoskeleton by six or more bonds (red curve at d=6). Similar relationships are seen for the proportion of c proteins that are linked to s proteins by few bonds compared to many bonds (green curve), whereas analysis of random protein sets shows the predicted flat distribution.

Notice that, because the protein classes c and s contain different number of proteins and the local clustering index is affected by the proportion of proteins in each class within the entire network, it was necessary to plot rescaled values of the clustering indices $\langle m_d(\mathrm{x/y})\rangle/m_{rand}$. The values of rescaled clustering indices are smaller than one already for d=8 (the largest distance is shown in Fig. 3), indicating that at large distances, there is no preferential interaction between proteins within the c and s classes.

To further address linkage between signaling and cytoskeletal proteins by using the local clustering index, we compared the nearest-neighbor clustering indexes $\langle m_1(x/y)\rangle$ that were calculated for all s and c proteins. To determine whether by this analysis s proteins are more closely linked to c proteins, it was necessary to compare m_1 of these groups to m_1 of randomly chosen proteins. The classes of randomly chosen proteins were termed the pseudo c and pseudo s classes and they contained as many randomly selected proteins as there are c and s proteins in the largest interconnected clusters of the employed protein interaction maps.

In Fig. 4 we summarize the results of this comparison. For the c proteins, $\langle m_1(c/c)\rangle$ is about an order of magnitude larger for the true cytoskeletal class than for its pseudo analogue, which might reflect our definition of the c class. However, the difference between the true and pseudo classes remains consistently large (around a factor of three) for all the other combinations of the x and y proteins, independently of the dataset used. These results indicate that, at least within the datasets used, the clustering tendency of the c and s proteins and the correlation of the two classes are inherent properties of these proteins.

The special role of the cytoskeleton in signaling networks

The results in Figs 2 to 4 suggest that the cytoskeleton and signaling networks are linked. However, this might fortuitously result from the limited nature of the interactions detected by the datasets used. To address this possibility, we studied the correlation between the class of signaling proteins and 15 other functional protein classes as defined by the MIP database (Mewes et al., 2002). We calculated local clustering indices for signaling proteins of each of the other 15 classes of proteins: $\langle m_d(s/i)\rangle/m_{rand}$ (i=0 to14), where i denotes the number of the

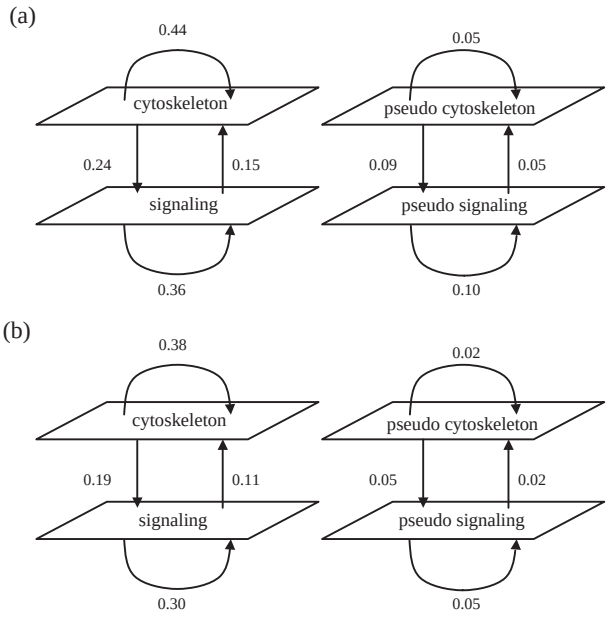

Fig. 4. The nearest-neighbor clustering index $\langle m_1(x/y)\rangle$. Arrows point from x to y. Left half in a and b U database and DIP database, respectively, summarize results from Fig. 3. Right half present results for pseudo protein classes that were constructed by randomly selecting 74 (U) and 92 (D) pseudo c class proteins, and 141(U) and 207 (D) pseudo s class proteins from the fully connected clusters.

functional protein class (specified in the legend to Fig. 5). As shown in Fig. 5, the nearest-neighbor clustering index (m_1) for *s* proteins to *c* proteins [2.83(U) and 6.68(D)] is almost twofold higher than to the next most closely linked class of proteins (class 2 in Fig. 5), that are involved in cell growth, cell division and DNA synthesis [1.54(U) and 3.9(D)]. These results confirm that the cytoskeleton plays a distinguished role in the organization of the signaling network of cells.

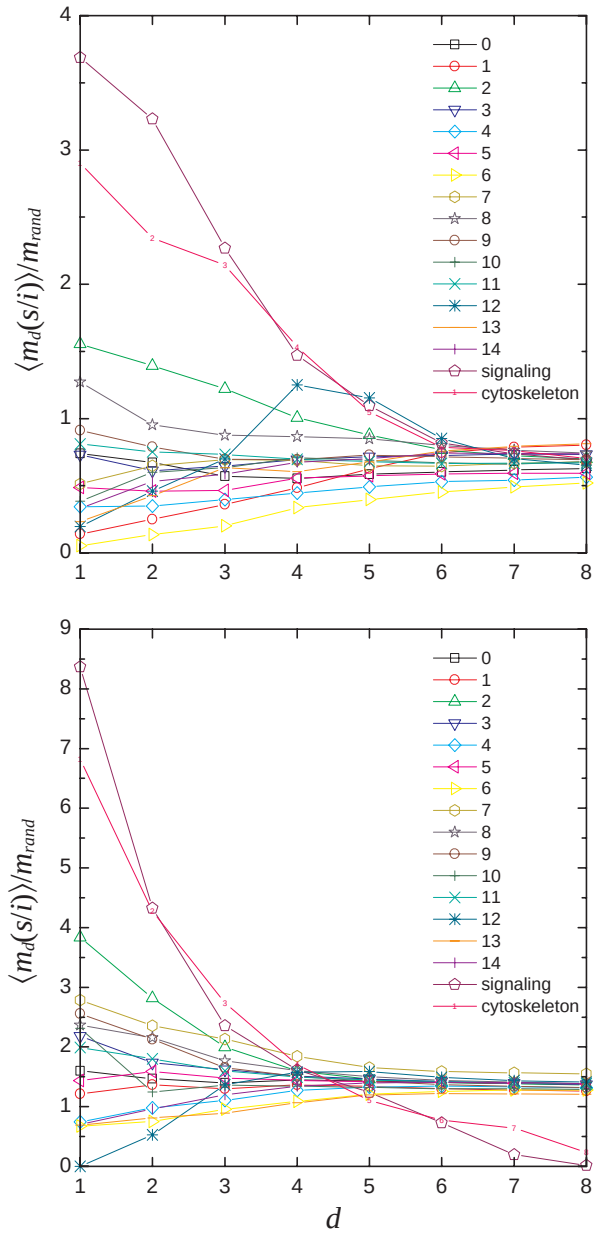

Fig. 5. $\langle m_d(s/i)\rangle/m_{rand}$ (i=0 to14) for fifteen functional protein classes in addition to the *s* and *c* classes. Plots are based on the database by Uetz et al. (Uetz et al., 2000) (top) and the DIP database (bottom). The 15 functional protein classes are: 0, metabolism; 1, energy; 2, cell growth, cell division and DNA synthesis; 3, transcription; 4, protein synthesis; 5, protein destination; 6, transport facilitation; 7, cellular transport and transport mechanisms; 8, cellular biogenesis; 9, cell rescue, defence, cell death and ageing; 10, ionic homeostasis; 11, cellular organization; 12, transposable elements; viral and plasmid proteins; 13, classification not yet clear cut; 14, unclassified proteins.

The cytoskeleton represents a global structure, spanning the entire cell. Thus, its association with various functional protein classes (in particular with the signaling network) could be expected. To see whether our analysis is consistent with this expectation, we repeated the above calculation for $\langle m_d(c/i)\rangle/m_{rand}$, the local clustering index of the cytoskeletal proteins, and plotted the results in Fig. 6. Indeed, as the comparison of Figs 5 and 6 reveals, the association of the *c* proteins with the 15 functional protein classes defined in the MIPS database is quite uniform, suggesting that signaling proteins have no special role in the organization of the cytoskeleton. This is particularly well reflected by the values of m_1. The nearest-neighbor clustering index for the *c* proteins to

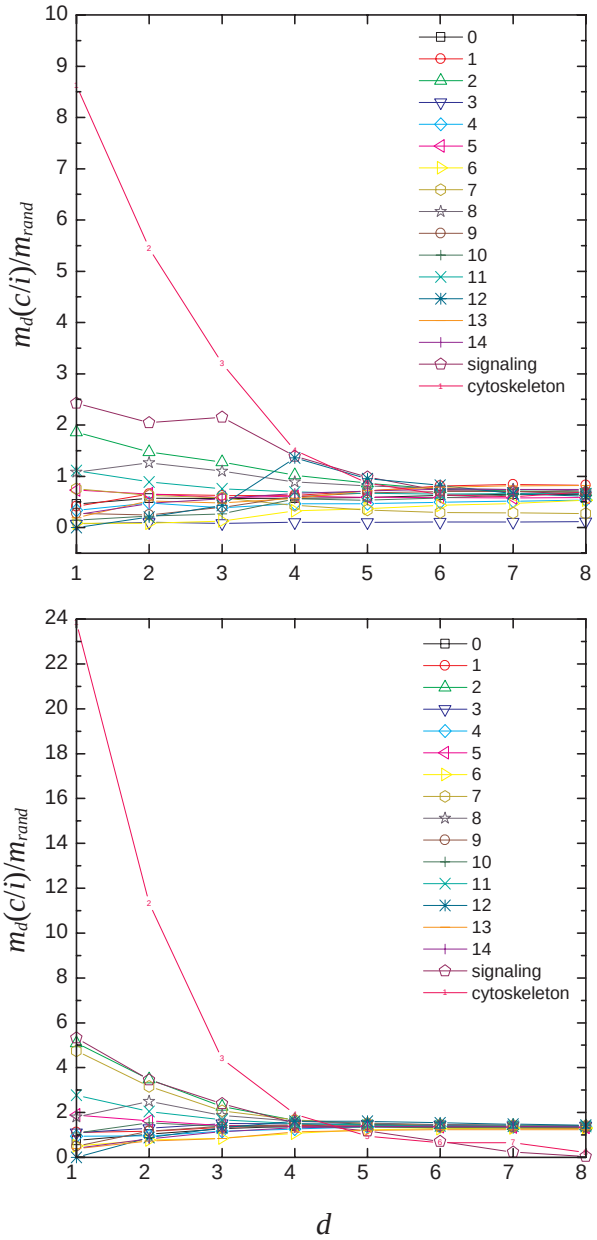

Fig. 6. $\langle m_d(c/i)\rangle/m_{rand}$ (i=0 to14) for 15 functional protein classes in addition to the *s* and *c* classes. Plots are based on the database by Uetz et al. (Uetz et al., 2000) (top) and the DIP database (bottom). The fifteen protein classes are the same as in Fig. 5.

the *s* proteins [$\langle m_1(c/s)\rangle$] is much closer to the analogous quantity of the *c* proteins to the proteins in class 2 [$\langle m_1(c/2)\rangle$], than the corresponding quantities with *c* replaced by *s*: $\langle m_1(c/s)\rangle/\langle m_1(c/2)\rangle$ is 44% (U) and 61% (D) smaller than $\langle m_1(s/c)\rangle/\langle m_1(s/2)\rangle$.

The quantitative analysis presented here, suggests that the topological properties of intracellular signaling pathways within the protein interaction network of *S. cerevisiae* are strongly dependent on the cytoskeleton. This linkage was even more evident when only those cytoskeletal and signaling proteins were analyzed, that are connected to each other exclusively through *c* or *s* proteins. The corresponding subnetwork derived from the U database is shown in Fig. 7. All proteins that directly connect the two classes are unusual in that they have the highest number of links (at least four). They are hubs and are distributed throughout the network, indicating that the cytoskeleton and the set of signaling molecules are linked in a global manner.

The protein interaction networks analyzed here are examples of scale-free networks (Barabasi and Albert, 1999; Jeong et al., 2001; Jeong et al., 2000) that are simultaneously tolerant to random errors and fragile against the removal of the most connected nodes or hubs (Albert et al., 2000). To investigate the significance of the hubs in the present context we removed all signaling proteins that link the signaling subnetwork to the cytoskeleton (23 of the 28 hubs). The resulting interaction map (with only those proteins shown that have at least one connection) is plotted in Fig. 8. The total collapse or fragmentation of the signaling network (as seen in Fig. 8) strongly suggests that without communication with the cytoskeleton the signaling apparatus of the cell cannot properly function.

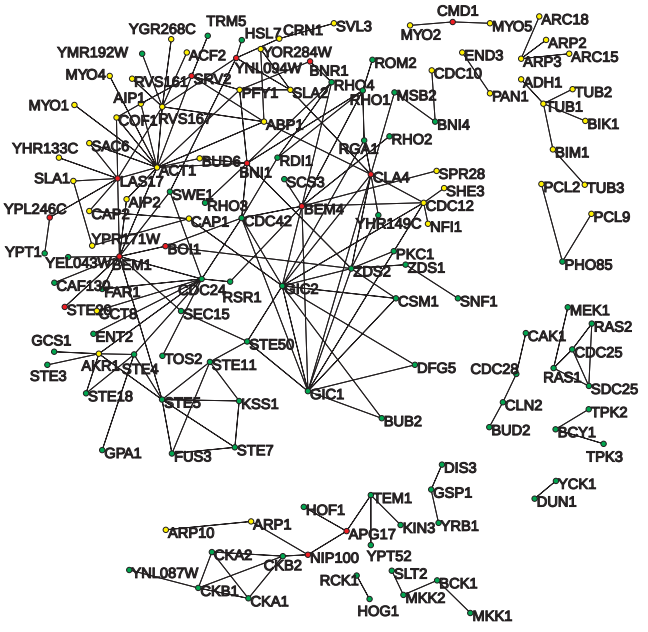

Fig. 7. Combined *c-s* signaling subnetwork, derived from the largest connected cluster in Fig. 1. Yellow and green dots denote signaling and cytoskeletal proteins, respectively, proteins in red are shared by the two subclasses. Only proteins with at least one connection are shown. [Results are only shown for the database by Uetz et al. (Uetz et al., 2000).]

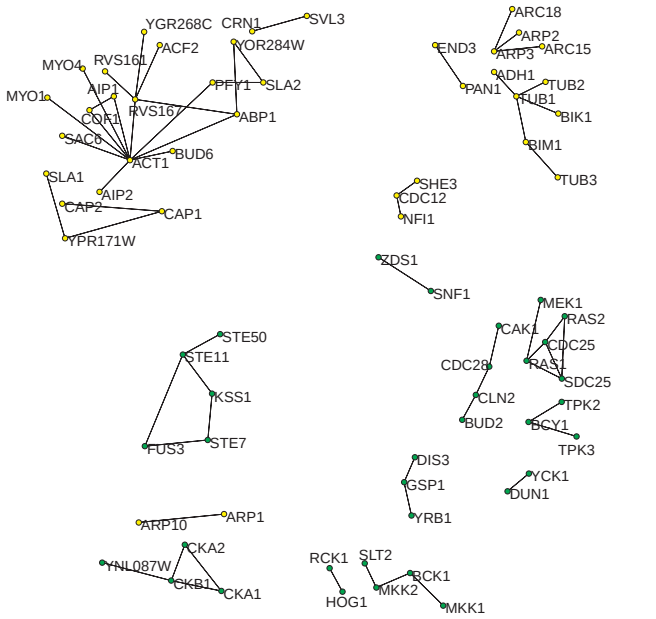

Fig. 8. The signaling subnetwork shown in Fig. 7, after the *s* proteins that connect to the cytoskeleton were taken out. [Results are only shown for the database by Uetz et al. (Uetz et al., 2000).]

It is perhaps not surprising that a large number of the most connected hubs in the subnetwork were identified as being members of both the cytoskeleton and the signaling subsets. Some of these proteins, such as the yeast WASP homolog Las17p and the yeast PAK1 kinase homolog Cla4p, are well-characterized regulators of the cytoskeleton and coordinate cytoskeletal dynamics with changes in cell growth, division, and mating. Other hubs provide crucial (possibly the only) connections between two parts of the signaling network. For example, Akr1p, an ankyrin repeat-containing cytoskeletal protein, provides a pathway in this network to transmit a signal from Gcs1p and Ste3p to other components of the mating pathway (Ste4p, Ste5p and Ste18p).

The analysis presented here provides quantitative evidence for the long-standing hypothesis that the cytoskeleton participates in an important way in intracellular signal transduction. How might the cytoskeleton be used in signal transduction pathways? The results of the network analysis suggest that the cytoskeleton is involved in at least two ways. First, individual proteins of the cytoskeleton might participate directly in signal transduction by linking two or more signaling proteins. One implication of this role is that the cytoskeleton might provide alternative signal transduction routes so that there are multiple pathways to transduce a signal. Second, the cytoskeleton might provide a macromolecular scaffold, which spatially organizes components of a signal transduction cascade (Park et al., 2003). This would be analogous to the role of molecular scaffolds, such as the yeast Ste5 protein, that tether multiple components of a pathway to promote signal transduction between them. The analysis presented here suggests that, during eukaryotic evolution, signaling pathways have incorporated components and features of the cytoskeleton as their integral parts and this might be a general feature of eukaryotic intracellular signal transduction networks.

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JCS01122 Role of the cytoskeleton in signaling networks
Supplemental data

Cytoskeletal proteins		
ORF Name	**Gene name**	**Brief characterization**
YAL020C	ATS1	alpha-tubulin suppressor
YAL029C	MYO4	myosin heavy chain, unconventional (class V) isoform
YBL007C	SLA1	cytoskeleton assembly control protein
YBL037W	APL3	AP-2 complex subunit, alpha-adaptin, 113 KD
YBL063W	KIP1	kinesin-related protein
YBL085W	BOI1	BEM1 protein-binding protein
YBR109C	CMD1	calmodulin
YBR130C	SHE3	required for mother cell-specific expression of HO, interacts with Cdc12p
YBR172C	SMY2	kinesin-related protein
YBR200W	BEM1	bud emergence mediator; scaffold protein
YBR234C	ARC40	Arp2/3 protein complex subunit, 40 kilodalton
YCL029C	BIK1	nuclear fusion protein
YCR002C	CDC10	septin; cell division control protein
YCR009C	RVS161	similarity to human amphiphysin and Rvs167p
YCR088W	ABP1	actin-binding protein
YDL022W	GPD1	glycerol-3-phosphate dehydrogenase (NAD+), cytoplasmic
YDL029W	ARP2	actin-like protein
YDL127W	PCL2	cyclin, G1/S-specific
YDL143W	CCT4	component of chaperonin-containing T-complex
YDL178W	AIP2	actin interacting protein 2
YDL179W	PCL9	cyclin like protein interacting with Pho85p
YDR106W	ARP10	similarity to Actin proteins
YDR129C	SAC6	actin filament bundling protein, fimbrin
YDR188W	CCT6	component of chaperonin-containing T-complex (zeta subunit)
YDR218C	SPR28	septin-related sporulation protein
YDR264C	AKR1	ankyrin repeat-containing protein
YDR388W	RVS167	reduced viability upon starvation actin binding protein
YDR424C	DYN2	dynein light chain 1, cytosolic
YDR488C	PAC11	required in the absence of Cin8p
YEL061C	CIN8	kinesin-related protein
YER007W	PAC2	involved in the stabilization of microtubles
YER016W	BIM1	binding to microtubules
YER081W	SER3	3-phosphoglycerate dehydrogenase
YER085C	not assigned	similarity to myosins

YER114C	BOI2	budding protein; binds BEM1
YFL037W	TUB2	beta-tubulin
YFL039C	ACT1	actin
YGL206C	CHC1	clathrin heavy chain
YGL216W	KIP3	kinesin-related protein required for nuclear migration
YGR015W	SPR3	septin, sporulation, binds Myo1p
YGR167W	CLC1	clathrin light chain
YGR241C	YAP1802	Yeast Adaptor Protein, member of AP180 protein family
YGR268C	HUA1	interacts with Sla1p, Rvs167p
YHL007C	STE20	ser/thr protein kinase of the pheromone pathway
YHR023W	MYO1	myosin-1 isoform (type II myosin) heavy chain
YHR107C	CDC12	septin
YHR129C	ARP1	centractin
YHR133C	NSG1	similarity to hypothetical protein YNL156c, interacts with WASP
YHR161C	YAP1801	Yeast Adaptor Protein, member of AP180 protein family
YIL034C	CAP2	F-actin capping protein, beta subunit
YIL062C	ARC15	subunit of the Arp2/3 complex
YIL138C	TPM2	tropomyosin, isoform 2
YIL142W	CCT2	chaperonin of the TCP1 ring complex, cytosolic
YIL149C	MLP2	involved in translocation of macromolecules between the
YIL155C	GUT2	glycerol-3-phosphate dehydrogenase, mitochondrial
YIL159W	BNR1	regulator of budding; has similarity to BNI1
YIR006C	PAN1	actin-cytoskeleton assembly protein
YJL008C	CCT8	component of chaperonin-containing T-complex
YJL014W	CCT3	chaperonin of the TCP1 ring complex, cytosolic
YJL042W	MHP1	microtubule-associated protein
YJL081C	ARP4	actin-related protein
YJL111W	CCT7	component of chaperonin-containing T-complex
YJR005W	APL1	AP-2 complex subunit, beta2-adaptin, 78 KD
YJR058C	APS2	AP-2 complex subunit, sigma2 subunit, 17 KD
YJR064W	CCT5	T-complex protein 1, epsilon subunit
YJR065C	ARP3	actin related protein
YJRO76C	CDC11	septin
YKL007W	CAP1	F-actin capping protein alpha subunit
YKL079W	SMY1	kinesin-related protein
YKL129C	MYO3	myosin type I
YKR054C	DYN1	dynein heavy chain, cytosolic
YLL021W	SPA2	involved in cell polarity and fusion
YLL050C	COF1	cofilin, actin binding and severing protein
YLR045C	STU2	suppressor of a cs tubulin mutation

YLR085C	ARP6	Actin-related protein
YLR144C	ACF2	necessary for cortical actin assembly
YLR212C	TUB4	gamma tubulin
YLR314C	CDC3	septin; cell division control protein
YLR319C	BUD6	bud site selection protein
YLR337C	VRP1	verprolin
YLR370C	ARC18	subunit of the Arp2/3 complex
YLR423c	APG17	protein involved in authophagy; binds Myo1p, Rho Tpases, exocyst
YLR429W	CRN1	a coronin, that binds actin and promotes its polymerization
YML085C	TUB1	alpha-1 tubulin
YML124C	TUB3	alpha-3 tubulin
YMR092C	AIP1	actin cytoskeleton component
YMR109W	MYO5	myosin I
YMR183C	SSO2	syntaxin, T-SNARE, interacts with YAP180, Pan1p
YNL020C	ARK1	Actin Regulating Kinase
YNL059C	ARP5	Actin-related protein
YNL079C	TPM1	tropomyosin 1
YNL084C	END3	required for endocytosis and cytoskeletal organization
YNL094W	APP1	similarity to S.pombe hypothetical protein, interacts with Rvs167p
YNL106C	INP52	phosphatidylinositol phosphate phosphatase
YNL138W	SRV2	adenylate cyclase-associated protein, 70kDa
YNL223W	AUT2	essential for autophagy
YNL243W	SLA2	cytoskeleton assembly control protein
YNL271C	BNI1	regulator of budding; interacts with Rho GTPases, profilin
YNL293W	MSB3	similarity to Mic1p and human transforming protein tre-2,
YNL298W	CLA4	ser/thr protein kinase
YOL062C	APM4	AP-2 complex subunit, mu2 subunit, 55 KD
YOL086C	ADH1	alcohol dehydrogenase I
YOL112W	MSB4	similarity to Mic1p and human transforming protein tre-2
YOR058C	ASE1	microtubule-associated protein (nonmotor)
YOR084W	not assigned	interacts with Cdc11p
YOR122C	PFY1	profilin
YOR141C	ARP8	Actin-related protein
YOR156C	NFI1	interacts with Cdc12p in 2-hybrid assay
YOR181W	LAS17	component of actin cortical patches; WASP homologue
YOR265W	RBL2	beta-tubulin binding protein
YOR284W	HUA2	interacts with Abp1, Rvs167, Sla2
YOR326W	MYO2	myosin heavy chain
YOR349W	CIN1	chromosome segregation protein
YPL032C	SVL3	strong similarity to Pam1p, interacts with coronin

YPL137C	not assigned	similarity to microtubule-interacting protein Mhp1p and to
YPL155C	KIP2	kinesin-related protein
YPL161C	BEM4	bud emergence protein; binds eptins, Rho GTPaes
YPL174C	NIP100	mitotic spindle positioning protein, component of the dynactin complex
YPL232W	SSO1	syntaxin-related protein, T-SNARE, interacts with YAP180, Pan1p
YPL239W	YAR1	ankyrin repeat-containing protein
YPL242C	IQG1	involved in cytokinesis, has similarity to mammalian IQGAP
YPL246C	RBD2	similarity to mouse proteinase activated receptor 2, interacts with Las17
YPR029C	APL4	AP-1 complex subunit, gamma-adaptin, 94 KD
YPR141C	KAR3	kinesin-related protein
YPR171W	BSP1	interacts with Cap1, Rvs167, Sla1

Signaling proteins		
ORF Name	**Gene name**	**Brief characterization**
YAL017W	FUN31	similarity to ser/thr protein kinases
YAL024C	LTE1	GDP/GTP exchange factor
YAL040C	CLN3	cyclin, G1/S-specific
YAL041W	CDC24	GTP/GDP exchange factor for Cdc42p
YAL048C	GON1	vesicle –mediated transport
YAR018C	KIN3	ser/thr protein kinase
YAR019C	CDC15	protein kinase of the MAP kinase kinase kinase family
YBL016W	FUS3	mitogen-activated protein kinase (MAP kinase)
YBL033C	RIB1	GTP cyclohydrolase II
YBL056W	PTC3	ser/thr protein phosphatase PP2C
YBL085W	BOI1	BEM1 protein-binding protein
YBL088C	TEL1	telomere length control protein
YBL105C	PKC1	ser/thr protein kinase
YBL106C	SRO77	Suppressor of defect in the small GTPase Rho3p
YBR036C	CSG2	calcium dependent regulatory protein
YBR059	AKL1	Ark-family Kinase-Like protein
YBR097W	VPS15	ser/thr protein kinase
YBR102C	EXO84	exocyst protein essential for secretion
YBR109C	CMD1	calmodulin
YBR125C	PTC4	serine/threonine protein phosphatases (PP2Cs)
YBR133C	HSL7	adapter in a regulatory pathway that relieves tyrosine
YBR136W	MEC1	cell cycle checkpoint protein
YBR140C	IRA1	inhibitory regulator protein of the ras-cyclic AMP pathway
YBR160W	CDC28	cyclin-dependent protein kinase
YBR164C	ARL1	ADP-ribosylation factor
YBR179C	FZO1	required for biogenesis of mitochondria
YBR200W	BEM1	bud emergence mediator
YBR228W	SLX1	similarity to hypothetical A.thaliana protein
YBR260C	RGD1	similarity to C.elegans GTPase-activating protein
YBR267W	not assigned	similarity to hypothetical protein YLR387c
YBR274W	CHK1	regulats inhibitory Cdk phosphorylation of Pds1
YBR275C	RIF1	RAP1-interacting factor 1
YCL004W	PGS1	phosphatidylglycerophosphate synthase
YCL024	KCC4	kinase coordinate cell cycle progression with the

YCL032W	STE50	pheromone response pathway protein
YCR008W	SAT4	serine/threonine-specific protein kinase
YCR027C	RSG1	rheb-like Gene involved in growth regulation
YCR038C	BUD5	GDP/GTP exchange factor for Rsr1p/Bud1p
YCR072C	not assigned	strong similarity to S. pombe trp-asp repeat containing
YCR073C	SSK22	MAP kinase kinase kinase
YCR086w	CSM1	involved in nuclear migration
YCR091W	KIN82	ser/thr protein kinase
YDL006W	PTC1	protein serine/threonine phosphatase 2c
YDL017W	CDC7	protein kinase
YDL025C	not assigned	similarity to probable protein kinase NPR1
YDL028C	MPS1	serine/threonine/tyrosine protein kinase
YDL047W	SIT4	ser/thr protein phosphatase
YDL077C	VPS39/VAM6	vacuolar carboxypeptidase Y
YDL079C	MRK1	ser/thr protein kinase
YDL101C	DUN1	protein kinase
YDL107W	MSS2	ser/thr protein kinase
YDL108W	KIN28	cyclin-dependent ser/thr protein kinase
YDL125C	HNT1	similarity to protein kinase C inhibitor-I
YDL127W	PCL2	cyclin, G1/S-specific
YDL132W	CDC53	controls G1/S transition
YDL135C	RDI1	rho GDP dissociation inhibitor with activity toward Rho1p
YDL137W	ARF2	GTP-binding protein of the ARF family
YDL159W	STE7	Serine/threonine/tyrosine protein kinase of the pheromone pathway
YDL192W	ARF1	small GTP-binding protein of the ARF family
YDL194W	SNF3	high-affinity glucose transporter/regulatory protein
YDL214C	PRR2	strong similarity to putative protein kinase NPR1
YDL226C	GCS1	ADP-ribosylation factor GTPase-activating protein (ARF-GAP)
YDL230W	PTP1	protein tyrosine phosphatase
YDL234C	GYP7	GTPase-activating protein for Ypt7p
YDL240W	LRG1	GTPase-activating protein of the rho/rac family
YDR002W	YRB1	ran-specific GTPase-activating protein
YDR054C	CDC34	E2 ubiquitin-conjugating enzyme
YDR103W	STE5	pheromone signal transduction pathway protein
YDR122W	KIN1	ser/thr protein kinase
YDR137W	RGP1	reduced growth phenotype protein
YDR226W	ADK1	adenylate kinase, cytosolic
YDR238C	SEC26	coatomer complex beta chain of secretory pathway vesicles
YDR247W	VHS1	protein serine/threonine kinase activity
YDR283C	GCN2	ser/thr protein kinase

YDR309C	GIC2	Cdc42 GTPase-binding protein
YDR373W	FRQ1	regulator of phosphatidylinositol-4-OH kinase protein
YDR379W	RGA2	similarity to Dbm1p and to the rat GAP-associated protein
YDR454C	GUK1	guanylate kinase
YDR466W	not assigned	protein kinase activity
YDR477W	SNF1	carbon catabolite derepressing ser/thr protein kinase
YDR490C	PKH1	ser/thr protein kinases
YDR507C	GIN4	ser/thr protein kinase
YDR523C	SPS1	ser/thr protein kinase
YDR524C	AGE1	similarity to ADP-ribosylation factor (ARF) GTPase
YEL022W	GEA2	GDP/GTP exchange factor for ARF
YEL043W	not assigned	weak similarity to Mad1p
YER031C	YPT31	GTP-binding protein of the rab family
YER075C	PTP3	protein tyrosine phosphatase
YER086W	ILV1	anabolic serine and threonine dehydratase precursor
YER096W	SHC1	sporulation specific protein
YER110C	KAP123	RAN-binding protein
YER114C	BOI2	budding protein
YER118C	SHO1	involved in the HOG1 high-osmolarity signal transduction
YER123W	YCK3	casein kinase, isoform 3
YER124C	DSE1	weak similarity to Dictyostelium WD40 repeat protein 2
YER129W	PAK1	DNA polymerase alpha suppressing protein kinase
YER136W	GDI1	GDP dissociation inhibitor
YER155C	BEM2	GTPase-activating protein
YER167W	BCK2	suppressor of mutations in protein kinase C pathway
YER170W	ADK2	adenylate kinase, mitochondrial
YER177W	BMH1	14-3-3 protein involved in rapamycin-sensitive signalling
YFL005W	SEC4	GTP-binding protein of the ras superfamily
YFL009W	CDC47	cell division control protein
YFL026W	STE2	pheromone alpha-factor receptor
YFL027C	GYP8	weak similarity to P.falciparum Pfmdr2 protein
YFL029C	CAK1	cdk-activating protein kinase
YFL031W	HAC1	transcription factor
YFL033C	RIM15	protein kinase involved in expression of meiotic genes
YFL038C	YPT1	GTP-binding protein of the rab family
YFL047W	RGD2	GTPase activating protein
YFR014C	CMK1	Ca2+/calmodulin-dependent ser/thr protein kinase type I
YFR019W	FAB1	phosphatidylinositol 3-phosphate 5-kinase
YFR028C	CDC14	dual specificity phosphatase
YGL006W	PMC1	calcium-transporting ATPase activity

YGL019W	CKB1	casein kinase II, beta subunit
YGL059W	not assigned	protein kinase activity
YGL097W	SRM1	GDP/GTP exchange factor for Gsp1p/Gsp2p
YGL099W	KRE35	similarity to putative human GTP-binding protein MMR1
YGL126W	SCS3	inositol phospholipid synthesis protein
YGL158W	RCK1	ser/thr protein kinase
YGL167C	PMR1	Ca2+-transporting P-type ATPase
YGL179C	TOS3	strong similarity to Pak1p, Elm1p and Kin82p
YGL180W	APG1	essential for autophagocytosis
YGL190C	CDC55	ser/thr phosphatase 2A regulatory subunit B
YGL227W	VID30	weak similarity to human RANBPM NP_005484.1
YGL233W	SEC15	vesicular traffic control protein
YGR014W	MSB2	multicopy suppressor of a cdc24 bud emergence defect
YGR040W	KSS1	ser/thr protein kinase of the MAP kinase family
YGR049W	SCM4	cdc4 suppressor
YGR052W	not assigned	similarity to ser/thr protein kinases
YGR070W	ROM1	GDP/GTP exchange protein for Rho1p
YGR080W	TWF1	twinfilin, an actin monomer sequestering protein
YGR092W	DBF2	ser/thr protein kinase related to Dbf20p
YGR100W	GYP2	GTPase activating protein
YGR134W	CAF130	hypothetical protein
YGR152C	RSR1	GTP-binding protein
YGR172C	YIP1	golgi membrane protein
YGR188C	BUB1	ser/thr protein kinase
YGR217W	CCH1	calcium channel protein
YGR221C	TOS2	similarity to hypothetical protein YHR149c
YGR262C	BUD32	weak similarity to protein kinases and M.jannaschii
YGR267C	FOL2	GTP cyclohydrolase I
YHL007C	STE20	ser/thr protein kinase of the pheromone pathway
YHR005C	GPA1	GTP-binding protein alpha subunit of the pheromone pathway
YHR022C	not assigned	weak similarity to ras-related protein
YHR030C	SLT2	ser/thr protein kinase of MAP kinase family
YHR061C	GIC1	Cdc42 GTPase-binding protein
YHR070W	TRM5	strong similarity to N.crassa met-10+ protein
YHR079C	IRE1	protein kinase
YHR082C	KSP1	ser/thr protein kinase
YHR102W	KIC1	ser/thr protein kinase that interacts with Cdc31p
YHR135C	YCK1	casein kinase I isoform
YHR149C	not assigned	similarity to hypothetical protein YGR221c
YHR205W	SCH9	serine/threonine protein kinase involved in stress response

YIL002C	INP51	phosphatidylinositol phosphate 5-phosphatase
YIL007C	NAS2	ubiquitin-dependent protein catabolism
YIL033C	BCY1	cAMP dependent protein kinase, regulatory subunit
YIL035C	CKA1	casein kinase II, catalytic alpha chain
YIL042C	not assigned	kinase activity
YIL068C	SEC6	exocyst complex
YIL095W	PRK1	serine/threonine protein kinase involved in regulation of
YIL118W	RHO3	GTP-binding protein of the rho family
YIL119C	RPI1	negative regulator of ras-cAMP pathway
YIL147C	SLN1	two-component signal transducer
YIL159W	BNR1	regulator of budding
YIR026C	YVH1	protein tyrosine phosphatase
YJL005W	CYR1	adenylate cyclase
YJL006C	CTK2	carboxy-terminal domain (CTD) kinase, beta subunit
YJL044C	GYP6	GTPase-activating protein
YJL085W	EXO70	70 kDa exocyst component protein
YJL089W	SIP4	interacts with SNF1 protein kinase
YJL095W	BCK1	ser/thr protein kinase of the MEKK family
YJL106W	IME2	ser/thr protein kinase
YJL128C	PBS2	tyrosine protein kinase of the MAP kinase kinase family
YJL141C	YAK1	ser/thr protein kinase
YJL157C	FAR1	cyclin-dependent kinase inhibitor (CKI)
YJL164C	TPK1	cAMP-dependent protein kinase 1, catalytic chain
YJL165C	HAL5	ser/thr protein kinase
YJL187C	SWE1	ser/tyr dual-specifity protein kinase
YJR031C	GEA1	GDP/GTP exchange factor for ARF
YJR059W	PTK2	involved in polyamine uptake
YJR061W	not assigned	similarity to Mnn4p
YJR066W	TOR1	phosphatidylinositol 3-kinase
YJR086W	STE18	GTP-binding protein gamma subunit of the pheromone pathway
YKL048C	ELM1	ser/thr-specific protein kinase
YKL067W	YNK1	nucleoside diphosphate kinase
YKL092C	BUD2	GTPase-activating protein for Bud1p/Rsr1p
YKL101W	HSL1	ser/thr protein kinase, coupling septin ring assembly to
YKL116C	PRR1	similarity to rat SNF1, Celegans unc-51, Dun1p and other
YKL126W	YPK1	ser/thr-specific protein kinase
YKL139W	CTK1	carboxy-terminal domain (CTD) kinase, alpha subunit
YKL161C	MLP1	strong similarity to ser/thr-specific protein kinase Slt2p
YKL166C	TPK3	cAMP-dependent protein kinase 3, catalytic chain
YKL168C	KKQ8	ser/thr protein kinase

YKL171W	not assigned	protein kinase activity
YKL178C	STE3	pheromone a-factor receptor
YKL190W	CNB1	calcineurin B, regulatory subunit
YKL198C	PTK1	polyamine transport enhancing protein
YKL203C	TOR2	phosphatidylinositol 3-kinase
YKR001C	VPS1	member of the dynamin family of GTPases
YKR014C	YPT52	GTP-binding protein of the rab family
YKR031C	SPO14	phospholipase D
YKR055W	RHO4	GTP-binding protein of the rho family
YKR240W	YKR2	protein kinase
YLL016W	SDC25	GDP/GTP exchange factor (GEF)
YLL019C	KNS1	ser/thr protein kinase
YLL021W	SPA2	involved in cell polarity
YLR006C	SSK1	two-component signal transducer
YLR039C	RIC1	involved in transcription of ribosomal proteins and
YLR063W	not assigned	ser/thr protein kinase
YLR096W	KIN2	ser/thr protein kinase
YLR113W	HOG1	ser/thr protein kinase of MAP kinase (MAPK) family
YLR178C	TFS1	cdc25-dependent nutrient- and ammonia-response cell-cycle
YLR206W	ENT2	clathrin binding protein, required for endocytosis
YLR229C	CDC42	GTP-binding protein of RAS superfamily
YLR240W	VPS34	phosphatidylinositol 3-kinase
YLR248W	RCK2	Ca/calmodulin-dependent ser/thr protein kinase
YLR262C	YPT6	GTP-binding protein of the rab family
YLR289W	GUF1	strong similarity to E. coli elongation factor-type
YLR293C	GSP1	GTP-binding protein of the ras superfamily
YLR305C	STT4	phosphatidylinositol-4-kinase
YLR310C	CDC25	GDP/GTP exchange factor for Ras1p and Ras2p
YLR362W	STE11	ser/thr protein kinase of the MEKK family
YLR371W	ROM2	GDP/GTP exchange factor for Rho1p
YLR423c	APG17	protein involved in authophagy
YLR433C	CNA1	calcineurin B, catalytic subunit
YLR452C	SST2	involved in desensitization to alpha-factor pheromone
YML001W	YPT7	GTP-binding protein of the RAB family
YML016C	PPZ1	ser/thr phosphatase required for normal osmoregulation
YML057W	CMP2	calcineurin B, catalytic subunit
YML059C	not assigned	hydrolase activity
YML064C	TEM1	GTP-binding protein of the RAS superfamily
YML097C	VPS9	vacuolar sorting protein
YML109W	ZDS2	multicopy suppressor of sin4

YML112W	CTK3	carboxy-terminal domain (CTD) kinase, gamma subunit
YML121W	GTR1	GTP-binding protein
YMR001C	CDC5	involved in regulation of DNA replication
YMR016C	SOK2	regulatory protein in the PKA signal transduction pathway
YMR028W	TAP42	component of the Tor signaling pathway
YMR032W	HOF1	involved in cytokinesis
YMR055C	BUB2	cell cycle arrest protein
YMR079W	SEC14	phosphatidylinositol(PI)/phosphatidylcholine(PC) transfer
YMR104C	YPK2	ser/thr protein kinase
YMR138W	CIN4	GTP-binding protein
YMR139W	RIM11	ser/thr protein kinase
YMR192W	APP2	similarity to mouse Tbc1 protein
YMR199W	CLN1	cyclin, G1/S-specific
YMR216C	SKY1	similarity to S.pombe dsk1, human SRPK1 and other protein
YMR235C	RNA1	GTPase activating protein
YMR238W	DFG5	required for filamentous growth, cell polarity, and cellular
YMR273C	ZDS1	involved in negative regulation of cell polarity
YMR291W	not assigned	protein kinase activity
YNL020C	ARK1	Actin Regulating Kinase
YNL053W	MSG5	dual-specifity protein phosphatase
YNL076W	MKS1	pleiotropic regulatory factor
YNL087W	not assigned	weak similarity to synaptogamins
YNL090W	RHO2	GTP-binding protein of the RHO subfamily of RAS-like
YNL093W	YPT53	GTP-binding protein of the RAB family (RAS superfamily)
YNL094W	APP1	similarity to S.pombe hypothetical protein
YNL098C	RAS2	GTP-binding protein
YNL106C	INP52	phosphatidylinositol phosphate phosphatase
YNL128W	TEP1	weak similarity to tensin and to the mammalian tumor
YNL138W	SRV2	adenylate cyclase-associated protein, 70kDa
YNL154C	YCK2	casein kinase I isoform
YNL161W	CBK1	strong similarity to U.maydis Ukc1p protein kinase
YNL169C	PSD1	phosphatidylserine decarboxylase 1
YNL173C	MDG1	GTP-binding protein of the pheromone-response pathway
YNL180C	RHO5	similarity to S.pombe Cdc42p and other GTP-binding proteins
YNL183C	NPR1	ser/thr protein kinase
YNL233W	BNI4	bud neck involved
YNL267W	PIK1	phosphatidylinositol 4-kinase
YNL271C	BNI1	regulator of budding
YNL272C	SEC2	GDP/GTP exchange factor
YNL293W	MSB3	similarity to Mic1p and human transforming protein tre-2,

YNL298W	CLA4	ser/thr protein kinase
YNL307C	MCK1	ser/thr/tyr protein kinase
YNR026C	SEC12	GDP/GTP exchange factor for Sar1p
YNR031C	SSK2	MAP kinase kinase kinase of the high osmolarity signal
YNR047W	not assigned	similarity to ser/thr protein kinases
YOL016C	CMK2	Ca2+/calmodulin-dependent ser/thr protein kinase, type II
YOL021C	DIS3	3'->5' exoribonuclease required for 3' end formation of 5.8S
YOL045W	not assigned	similarity to ser/thr protein kinase
YOL081W	IRA2	GTPase-activating protein for RAS proteins
YOL100W	PKH2	similarity to ser/thr protein kinases
YOL110W	SHR5	RAS suppressor
YOL112W	MSB4	similarity to Mic1p and human transforming protein tre-2
YOL113W	SKM1	Ste20/PAK-like protein kinase
YOL128C	YGK3	Yeast homologue of mammalian Glycogen Synthase Kinase 3
YOR039W	CKB2	casein kinase II beta' chain
YOR061W	CKA2	casein kinase II alpha' chain
YOR070C	GYP1	GTPase activating protein for Ypt1p and Sec4p
YOR089C	VPS21	GTP-binding protein
YOR094W	ARF3	ADP-ribosylation factor 3
YOR101W	RAS1	GTP-binding protein
YOR107W	RGS2	negative regulator of glucose-induced cAMP signaling pathway
YOR109W	INP53	phosphatidylinositol phosphate phosphatase
YOR127W	RGA1	RHO-type GTPase-activating protein for Cdc42p
YOR134W	BAG7	structural homolog of Sac7p
YOR149C	SMP3	protein kinase C pathway protein
YOR181W	LAS17	component of actin cortical patches
YOR185C	GSP2	GTP-binding protein of the RAS superfamily
YOR188W	MSB1	morphogenesis-related protein
YOR208W	PTP2	protein-tyrosine-phosphatase
YOR211C	MGM1	dynamin-like protein
YOR212W	STE4	GTP-binding protein beta subunit of the pheromone pathway
YOR231W	MKK1	ser/thr protein kinase
YOR233W	KIN4	ser/thr protein kinase
YOR267C	HRK1	Hygromycin Resistance Kinase
YOR287C	not assigned	weak similarity to PITSLRE protein kinase isoforms
YOR351C	MEK1	ser/thr protein kinase
YPL016W	SWI1	component of SWI/SNF global transcription activator complex
YPL026C	SKS1	suppressor kinase of snf3
YPL031C	PHO85	cyclin-dependent protein kinase
YPL042C	SSN3	cyclin-dependent CTD kinase

YPL051W	ARL3	ADP-ribosylation factor-like protein, member of the arf-sar
YPL115C	BEM3	GTPase-activating protein for Cdc42p and Rho1p
YPL140C	MKK2	protein kinase of the map kinase kinase (MEK) family
YPL141C	not assigned	strong similarity to protein kinase Kin4p
YPL150W	not assigned	similarity to ser/thr protein kinases
YPL153C	RAD53	ser/thr/tyr protein kinase
YPL161C	BEM4	bud emergence protein
YPL174C	NIP100	component of the dynactin complex
YPL203W	TPK2	cAMP-dependent protein kinase 2, catalytic chain
YPL204W	HRR25	casein kinase I, ser/thr/tyr protein kinase
YPL209C	IPL1	ser/thr protein kinase
YPL218W	SAR1	GTP-binding protein of the ARF family
YPL236C	not assigned	similarity to Prk1p, and serine/threonine protein kinase
YPL246C	RBD2	rhomboid protease
YPL249C	GYP5	GTPase activating protein
YPL256C	CLN2	cyclin, G1/S-specific
YPL268W	PLC1	1-phosphatidylinositol-4,5-bisphosphate phosphodiesterase
YPR017C	DSS4	GDP/GTP exchange factor for Sec4p
YPR048W	TAH18	similarity to M.domestica NADPH-ferrihemoprotein reductase
YPR055W	SEC8	protein transport protein
YPR073C	LTP1	protein-tyrosine-phosphatase
YPR106W	ISR1	protein kinase
YPR111W	DBF20	cell cycle protein kinase related to Dbf2p
YPR161C	SGV1	ser/thr protein kinase
YPR165W	RHO1	GTP-binding protein of the rho subfamily of ras-like
YPT10	YPT10	similarity to GTP-binding proteins
YPT11	YPT32	small GTP-binding protein essential for Golgi function
YPT32	YPT32	small GTP-binding protein essential for Golgi function