7-1-2013

# Identification of genes required for differentiation of quiescent and nonquiescent cells in stationary phase cultures of Saccharomyces cerevisiae

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# IDENTIFICATION OF GENES REQUIRED FOR DIFFERENTIATION OF QUIESCENT AND NONQUIESCENT CELLS IN STATIONARY PHASE CULTURES OF SACCHAROMYCES CEREVISIAE

**by**

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**B.S. BIOLOGICAL SCIENCE**

THESIS

Submitted in Partial Fulfillment of the
Requirements for the Degree of

**Master of Science, Biomedical Science**

The University of New Mexico
Albuquerque, New Mexico

**July, 2013**

**ACKNOWLEDGEMENTS**

I hereby acknowledge and give thanks to my thesis advisor, Dr. Margaret Werner-Washburne for her guidance and support. I also thank Melissa Wilson and Ignacio Ortiz for their constant support and help in every aspect of this work.

In addition, I thank my committee members, Dr. Todd Thompson and Dr. Donald Natvig for encouraging me and going the extra mile to help me to finish this thesis.

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# List of Abbreviations

| | |
|---|---|
| SP | Stationary phase |
| YPD | Yeast peptone dextrose growth media |
| EP | Exponential phase |
| DS | Diauxic shift |
| mRNA | Messenger RNA |
| NQ | Nonquiescent |
| Q | Quiescent |
| TCA | Tricarboxylic acid cycle |
| SGA | Synthetic genetic analysis |
| GFP | Green fluorescent protein |
| SIR2 | Silent information regulator 2 |
| SIRT1 | Sirtuin (silent mating type information regulation 2 homolog) |
| GO | Gene ontology |

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## CHAPTER 1. Introduction

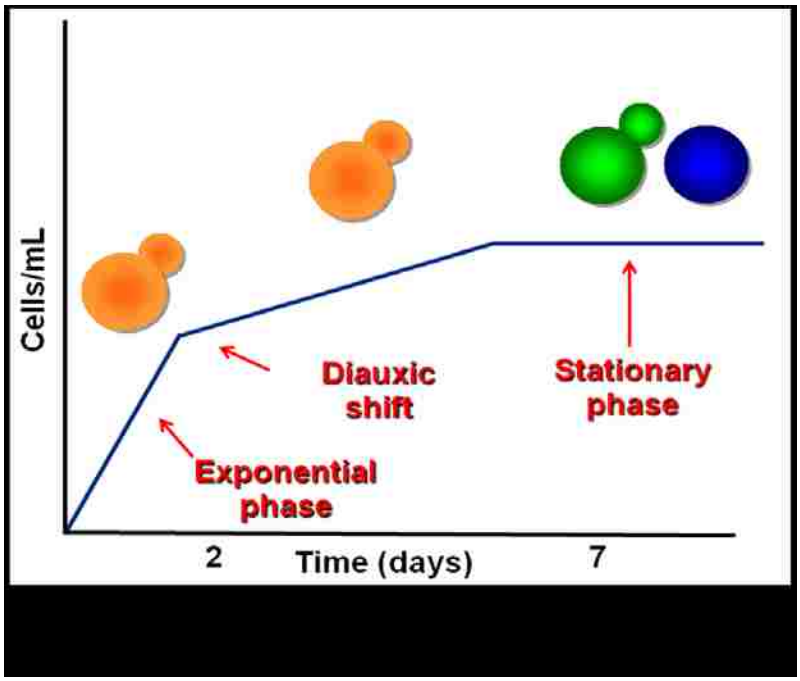
The yeast, *Saccharomyces cerevisiae*, is well-suited for studies involving basic cellular processes and, as such, was one of the first organisms considered to be a "model" organism for eukaryotic investigations (Botstein *et al.*, 1997). Using yeast, researchers were able to identify human cell cycle genes and study the eukaryotic cell cycle at a level not possible in other organisms leading to two Nobel prizes in the 1970's (2001). Since then, an additional Nobel prize was awarded for research using yeast that highlighted the importance of telomeres in understanding the cellular aging process. (Blackburn, 2005)

Yeast has been successful as a tool for important discoveries relating to eukaryotic cellular processes, in part, because it is easy to grow, easy to study biochemically, and, most importantly, it was possible to carry out gene replacement through homologous recombination. Yeast was also the first eukaryote to have its genome sequenced (Goffeau *et al.*, 1996). Interestingly, approximately 42% of the yeast genome, or more than 2400 yeast genes have human orthologs, confirming the value of yeast as a model for understanding cellular process in humans.

Quiescence is a ubiquitous but poorly understood cellular phase and is defined as an inactive, dormant or resting state. Most microbes and a majority of eukaryotic cells exist in this quiescent or $G_0$ phase of the cell cycle (Lewis and Gattie, 1991). It had been thought that yeast stationary phase (SP) cultures were homogeneous and predominantly consisted of cells in this quiescent state (Werner-Washburne *et al.*, 1993a). However, yeast SP cells do retain the ability to re-grow under the appropriate conditions (Gray *et al.*, 2004).

## Yeast Growth Phases

When yeast cultures are grown to SP in rich, glucose-based medium (YPD), they exhibit three phases of growth (Figure 1). The first phase, called exponential phase (EP), occurs in the presence of an abundance of nutrients, such as glucose. As cultures exhaust glucose they enter the second phase of growth, the diauxic shift (DS). The third phase, post-diauxic and post-glucose exhaustion, is SP. This third and final phase is typically reached 5-7 days after inoculation and is characterized by a growth pattern in which there is no net change in cell number within the culture meaning that cells die and divide at the same rate.

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In EP, the cells grow rapidly and fermentation is used for growth via ATP production (Werner-Washburne *et al.*, 1996). To date, most laboratory research using yeast has focused on EP cultures, specifically, cultures within the range of 0.6 and 1 OD

($2x10^7$ cells/ml). EP cultures contain both virgin daughter cells, those that have not reproduced and a population of mother cells which have reproduced multiple times.

In DS, cells undergo a temporary arrest and begin the physiological shift from fermentation to respiration. This is a very complex point in the growth cycle and not well understood. In fact, recent work suggestions that cell density prior to DS may induce high affinity glucose translocators that cause the culture to exhaust glucose. Nevertheless, during the post-diauxic phase, cultures do have non-fermentable carbon sources, such as acetate and ethanol, available to fuel growth.

In SP, all carbon sources are exhausted (Pringle and Hartwell, 1981). Yeast cultures in SP exhibit no net change in cell number. While it was previously thought that cells in SP cultures were homogeneous in a dead, dying or quiescent state, research from our laboratory and others has shown that many of the cells in the culture are not only alive but also viable and able to reproduce thereby providing for the cell number in a culture to remain constant. (Allen *et al.*, 2006a; Li *et al.*, 2009).

**Characterization of Stationary Phase Cultures**

These phase-specific phenotypes lead to questions about basic cellular processes, such as differentiation, mitochondrial function and aging. What processes and genes are involved in the differentiation of stationary phase cultures into quiescent and non-quiescent fractions? Are any of the genes involved in this differentiation significant to other basic cellular processes such as aging, reproduction and respiration? How do processes such as autophagy, apoptosis, metabolism and protein turnover contribute to the differentiation process?

Stationary phase-specific mRNAs were first identified by a time-course study of the wild-type yeast cultures entering and exiting SP, it was found that after re-feeding the SP cultures over 1000 mRNAs were present at or above a 2-fold level when compared to pre-DS cultures (Werner-Washburne *et al.*, 1993b). These mRNAs are involved in processes including aerobic respiration, metabolism and ribosome biogenesis. In addition, several of the genes that were found to be essential for SP survival were involved in mitochondrial function and apoptosis. These are interesting results for cultures that had previously been thought to contain cells that were essentially dead (Martinez *et al.*, 2004b). The survival of cells requires an efficiency in preparation and maintenance of structures and cellular processes. The rapid and sizable increase in mRNAs involved with respiration and metabolism suggests that cells in SP cultures are quiescent, in a resting state, yet also poised to respond quickly and specifically to the introduction of nutrients by "awakening" from the quiescent state with the processing of essential mRNAs.

Surprisingly, cells in SP cultures were also found to contain extraction-resistant or "sequestered" mRNAs that are rapidly solubilized in response to different stresses (Aragon *et al.*, 2008a). The presence of mRNAs in SP cultures was further highlighted in microarray experiments where it was found that 2000 transcripts were present in SP cells after the cultures were exposed to stress-inducing factors. Specifically, the mRNAs identified encode proteins that are involved in DNA repair, ribosome assembly and processing and response to oxidative stress. We suggested these mRNAs poise the cells for synchronous entry into the cell cycle as nutrients are reintroduced into the culture.

The differences in the categories of transcripts between these two experiments show that not only are SP cultures not senescent or dead but also they are responsive both to re-feeding of nutrients and to stress-inducing factors (Martinez *et al.*, 2004a). These findings pointed to the notion that there were multiple populations of cells present in SP cultures. The natural question that arose asked, "What are the mechanisms and genes involved in the maintenance and differentiation of SP cultures?"

Transcriptome data suggests that SP yeast cells are poised to respond to stress and reintroduction of nutrients by releasing extraction-resistant mRNAs for survival (Martinez *et al.*, 2004a). However, it is well known that the presence of mRNAs, while suggestive, does not always indicate translation or protein abundance. In order to investigate our hypothesis about the significance of mRNA presence, an in vivo high-throughput analysis using a yeast GFP-fusion library found that approximately 5% of the 25,000 experimental strains showed a greater than 2-fold difference in protein abundance when comparing EP and SP cultures (Davidson *et al.*, 2011). In addition, the processes the strains are involved in are different. EP strains were involved with biosynthetic processes and SP strains were involved in mitochondrial function.

In order to answer this question we performed experiments using density gradient centrifugation with a Percoll gradient (Davidson *et al.*; Allen *et al.*, 2006a; Aragon *et al.*, 2006). With this method, we discovered that, in fact, SP cultures are not homogeneous but heterogeneous. The culture separated into two distinct and predominant populations of cells in SP cultures (Figure 2). The populations were characterized in a variety of ways and we have labeled these two populations nonquiescent (NQ) and quiescent (Q).


The NQ fraction, which is less dense, consists of mother and daughter cells, many of which are budded. NQ cells are almost 100% viable at 7 days in YPD but only about 50% are able to divide. Of the NQ cells that are able to divide, approximately 40% exhibit mitochondrial defects, identified by petite colonies (Allen *et al.*, 2006a). NQ cells have also been demonstrated to an abundance of mRNAs that encode proteins involved with Ty-element transposition and DNA recombination and repair which may be instrumental in the high percentage of NQ cells with mitochondrial defects (Aragon *et al.*, 2008b). These findings are consistent with our hypothesis that genetic changes are occurring in NQ cells.

At day 7, approximately 50% of the NQ fraction also exhibits high levels of reactive oxygen species (ROS) and those cells that have high ROS are viable but have lost the ability to reproduce (Allen *et al.*, 2006b). In addition, 50% of NQ cells become apoptotic at 14 days.

The Q fraction consists of 91% virgin daughter cells that do not divide (Allen *et al.*, 2006b). Reactive oxygen species are not present at detectable levels in Q cells. Apoptosis and mitochondrial defects are not present in this fraction. Q cells are dense, refractile and stable. The cells in the Q fraction contain thousands of mRNAs in P-bodies or RNA granules that were released by protease treatment (Aragon *et al.*, 2008b). These mRNAs were found to be significantly involved with vesicle-related processes as well as oxidative stress and metabolism processes. This finding leads us to question why cultures lacking in readily available nutrients would expend valuable energy in generating mRNAs and storing them.

**Identification of Q/NQ by Flow Cytometry**

We examined GFP expression using the GFP-fusion set of strains grown to SP and analyzed by flow cytometry (Davidson *et al.*, 2011). Analysis of the results revealed that strains that differentiated into Q and NQ fractions exhibited two peaks of fluorescence. Thereafter, it was found that 38 individual strains exhibiting two peaks of fluorescence by flow cytometry had differentiated into Q and NQ fractions. In the case of CIT1, a gene that is the first enzyme in the tricarboxylic acid cycle (TCA and a strain that consistently differentiates into Q and NQ fractions, this differentiation begins to occur at approximately 14-20 hours post DS. This finding supports the hypothesis that this differentiation is programmed and highly genetically regulated.

Of the strains having two peaks, almost 60% were tagged proteins involved in mitochondrial function. Consistent with the importance of mitochondrial function, after separation of SP cultures, it was found that the Q fraction exhibited a greater than 6-fold

increase in respiration when compared with the NQ fraction (Davidson *et al.*). While it is known that the NQ cells produce a high percentage of slow-growing colonies due to mitochondrial defects (petite colonies), the finding that the Q fraction does not exhibit petite colonies but respire at a significantly higher rate than NQ cells, further points to genes involved in mitochondrial function being important for Q cell survival.

Subsequently, several genes involving autophagy were found to be significant in the NQ fraction and sequestering of thousands of sequestered mRNAs was abundant in the Q fraction (Allen *et al.*, 2006a; Aragon *et al.*, 2006). These features have also been observed in a study that involved a genome-wide screen of the yeast genome focused on chronological life span in SP cultures (Fabrizio and Longo, 2008). These data suggest that genes involved in these processes will be found to be involved in the differentiation of SP cultures into Q and NQ fractions.

Specific Aims:

1. To identify genes involved in differentiation of SP cultures into Q and NQ fractions.
2. To analyze identified genes with respect to GO process, determine overlap with other genome-scale lists of genes involved in aging, stress, etc.
3. To determine phenotypes associated with genes involved in the differentiation process.

## Genome-enabled Methods

Yeast is an extremely tractable organism in the laboratory and, in the post-genomic era, several important sets of strains have been developed. The yeast GFP-tagged gene set (Huh *et al.*, 2003) consisting of 4,159 clones and the yeast deletion sets (Winzeler *et al.*, 1999) are two powerful tools that have broadened our understanding of cellular structure and function, conserved processes, and even environmental responses. The availability of these tools provides for uniquely rich methods of studying biology at a genome-wide scale.

The yeast GFP-tagged library was developed to take advantage of the visualization properties of green fluorescent protein (GFP) that is derived from a species of jellyfish (Chalfie *et al.*, 1994). In this library, 4,159 of the genes in the yeast genome have been modified by attaching the sequence for GFP at the 3' end of the coding sequence for one gene in the genome (Huh *et al.*, 2003). This construct provides for the GFP protein to be transcribed as an attachment to the protein for which that gene encodes. Thus, localization of the protein can be visualized using fluorescence microscopy as well as a powerful tool when combined with flow cytometry.

The yeast deletion sets are comprised of strains in which one gene has been deleted and replaced with a cassette consisting of a Kanamycin-resistant marker flanked by unique barcodes (Smith *et al.*, 2009) (Figure 3). These sets are available as haploid or diploid and provide a way to identify cells present in yeast cultures that carry individual gene deletions. The presence of the unique barcodes on each deletion strain is well-

suited to yeast competitive assays providing a way to determine genes that are important for cell growth and survival.

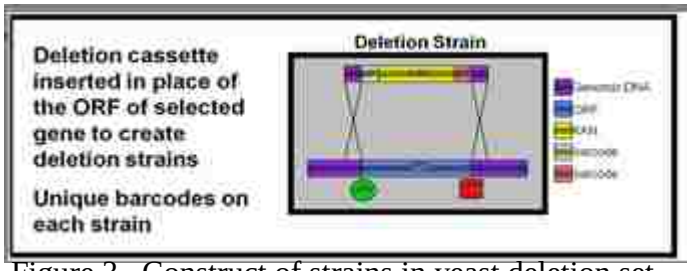


Figure 3. Construct of strains in yeast deletion set.

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The power of the yeast deletion sets lies in the ability to design experiments that determine the presence and abundance of strains grown in mixed populations by identifying the unique barcodes on each strain. The mixed population environment provides for a better understanding of the interaction of the genes by addressing issues of fitness and response to stress within a culture as well as functional information about the yeast genome. The deletion sets allow us to tease out the intricacies of cellular processes by growing cells in pools and gathering results that broaden our understanding of the potential combinatorial and/or coordinated nature of genes involved in those processes.

Various approaches have been used to unravel cellular processes in yeast using the deletion sets. An SGA reporter-based assay focused on understanding regulators and modifying factors with respect to SIR2, a yeast gene known to be important for stress response and homologous to SIRT1 in humans, utilized the haploid deletion set. Twenty loci were found to be important for regulation of this gene, specifically, negative regulation of chromatin and DNA metabolism (Raisner and Madhani, 2008).

The unique barcodes which flank the deletion cassette in each strain make this tool perfectly suited for microarray-based experimentation. The method of growing the complete deletion set consisting of over 4500 mutant strains in a pool, revealed the significance of genes involved with autophagy and *de novo* purine biosynthesis in the extension of chronological lifespan (Matecic *et al.*; Powers *et al.*, 2006; Fabrizio and Longo, 2008). In addition, experiments seeking to understand the aging process have utilized the deletion sets to collect data that shows pathways involving autophagy, apoptosis, mitochondrial processes, purine biosynthesis and the TOR growth pathway are important for cellular lifespan and aging .

A genomic approach to experimentation, of necessity, addresses more than one gene or pathway. Rather, genomics is focused on the possible interactions of several genes and pathways. The approach used in this study addresses broad hypotheses encompassing the complete genome as an investigatory tool towards understanding cellular processes at a higher level. The whole genome approach is valuable and lays the framework for focusing in on specific, smaller sets of genes and processes in future work.

## CHAPTER 2. METHODS

### Pooled Strains Used in this Study

Homozygous, heterozygous and DAmP deletion pools (YSC1063, Open Biosystems, YKO Mata his3D1 leu2D0 lys2D0 ura3D0) were a generous gift of the Nislow lab at the University of Toronto, Canada. They were prepared as outlined in Pierce, et. al., (Pierce *et al.*, 2007), delivered to our lab and placed in a -80 freezer until use.

**Preparation of Samples for Microarray Analysis**

To grow cells, 50 ul of approximately 10 OD frozen DAmP, heterozygous deletion, and homozygous deletion set pools were plated on YPD in triplicate and grown for 2 days at 30ºC and 250 rpm. Cells were harvested from plates, cell counts were obtained and $10^7$ cells were inoculated into 5 flasks per pool with 100ml of YPD plus 500 ul ampicillin.

Approximately 20 hours after inoculation (directly prior to DS), glucose tests were performed and cell counts were used to determine DS. Samples of all pools were collected. The same cultures were allowed to grow to SP, 7 days post-inoculation. Samples of SP cultures were collected and Q and NQ cells were obtained from these cultures by density gradient centrifugation (Allen *et al.*, 2006a). Three technical replicates were obtained from biological replicate 1, resulting in 3 technical and 3 biological replicates for each sample. All samples were pelleted at a concentration of $10^7$/ml and sent on dry ice via overnight delivery to the Nislow laboratory for microarray analysis (Affymetrix).

The original datasets comprising the homozygous, heterozygous and DaMP deletion pools contained 13,929 strains with measurements for all replicates of DS, SP, NQ, and Q. (Table 1) The data for each of the ORFs with both uptags and downtags were averaged together. This

**Table 1**. Summary of Strains Used for Analysis

| Strains | Total | Above background |
|---|---|---|
| Homozygous deletion | 4594 | 3849 (84%) |
| Heterozygous deletion | 1270 | 1111 (87%) |
| DAmP | 1004 | 800 (80%) |
| Total | 6868 | 5760 (84%) |

averaging resulted in a measurement for each strain.

Homozygous strains that had measurements above the background measurement of 200 in the DS set were considered in these experiments. Fold comparisons among all samples were performed and strains which exhibited a 2-fold or higher change were selected as the criteria for further analysis.

**Library Preparation**

The core set of 411 deletion strains that were found to be abundant in all samples when compared to the Q sample, were streaked from the deletion master set onto YPD plates treated with 500ul G418. Strains were grown for 2 days and cells were harvested into 1 ml aliquots with a final concentration of 20% glycerol for storage at -80˚C as permanent stocks. Four of the 411 strains did not grow and were not included in the master set. In preparation for phenotypic assays, a master set was prepared by placing 200 ul of each deletion strain from the permanent stocks into 96-well plates, resulting in five 96-well plates containing the 400 deletion strains to be further analyzed.

**Strain Preparation and Growth for Phenotypic Assays**

For phenotypic assays, three sets of 96-well plates containing 200ul of YPD and 500ul/100 ml G418 were inoculated from the library using a pin apparatus. The plates were sealed with Breathe-Easy membranes (Sigma Aldrich, St. Louis, MO, #380059). The plates were then grown for 7 days with shaking at 30°C.

## Viability Assay

Viability of deletion strains was determined using the LIVE/DEAD® FungaLight™ Yeast Viability Assay (Invitrogen). The assay contained 0.033 mM propidium iodide, 0.006 mM Syto9 in PBS. Samples were prepared by pipetting 50 ul of each strain into 96-well plates to which was added 150 ul of working solution. Samples were incubated in a water bath at 30°C for 30 minutes. Samples were then analyzed with an Accuri C6 flow cytometer using 480/500 nm emission/excitation for live samples in the FL1 detector and using 490/635 nm emission/excitation for dead samples in the FL-3 detector.

## Cell separation and harvest

To separate Q and NQ cells, Percoll (GE Healthcare, Piscataway, NJ) density gradients were made using a solution of one part 1.5 M NaCl to eight parts Percoll (vol/vol) (Allen *et al.*, 2006a) (Allen *et al.*, 2006). The gradients were formed using 10-ml of the Percoll solution in 15-ml Corex tubes. The tubes were centrifuged at 24,700 × *g* for 15 min at 4ºC in a Beckman Coulter (Fullerton, CA) JA-17 rotor. For separations, 5-ml samples of SP cultures were first pelleted by centrifugation for 3 min at 3270 × *g* in a room-temperature Beckman Allegra tabletop centrifuge, resuspended in 500 µl 50 mM Tris-HCl buffer (pH 7.5), and overlaid onto the gradients, which were then centrifuged at 400 × *g* for 60 min at 25ºC in a tabletop centrifuge with a swinging bucket rotor (Allegra X12-R, Beckman Coulter). After density-gradient centrifugation, the Q (dense) and NQ (less-dense) fractions were collected by pipette and pelleted by centrifugation in a microfuge, and each fraction was washed in 13 ml Tris buffer. The cell pellets were resuspended in 1 ml Tris buffer, concentration/pH and cells/ml were determined using a

Z2 Coulter Counter (Beckman Coulter). The cells were again pelleted and then suspended in 100 µl of their own filter-sterilized, conditioned media.

## CHAPTER 3. RESULTS

To identify genes that are involved in the differentiation process of yeast cultures into quiescent (Q) and non-quiescent (NQ) fractions, pools of the genome-scale, yeast bar-code deletion set (Invitrogen) were grown from exponential to stationary phase, harvested, and analyzed. This deletion set consists of strains that have one gene removed and replaced with a cassette constructed with a Kanamycin-resistance marker flanked by unique barcodes per strain.

When analyzing results using the deletion sets, it is important to recognize that the strains being used are surviving despite the lack of the individual gene that has been deleted. Therefore, when abundance levels are high for a particular strain, the hypothesis is that the deleted gene is not necessary for survival of the strain. Low abundance levels indicate that the gene is necessary, either solely or in association with other genes, for strain survival.

### Reproducibility of Experimental Method in Analysis of Yeast Homozygous Deletion Set by Microarray

To address the questions of efficacy of experimental design, technical and biological reproducibility was determined by comparing results from the same and different samples taken at the same time point. While this study compiled data using the homozygous, heterozygous and DamP deletion sets, all results presented here are focused solely on the homozygous datasets. Based on scatter plot analysis both technical and biological replicates were found to be highly reproducible ($R^2$ for biological replicates of

0.975 and 0.978 for technical replicates) (Figure 4 and Supplemental Material). These results provided confidence that any differences seen between samples represented actual biological differences.

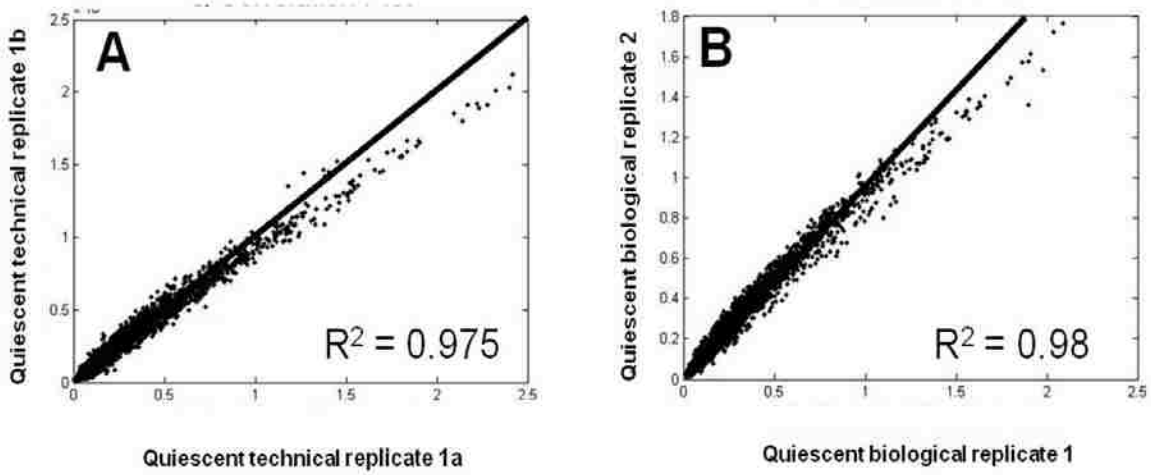


**Figure 4. Scatter plot of microarray results of yeast culture biological and technical grown in pools consisting of 3852 bar-coded deletion strains.** Cultures were harvested at specified timepoints and microarray analysis of the pools was performed. All strains that exhibited a relative abundance measurement over the average of the diauxic shift pool sample (3852 strains) were normalized to the average relative abundance measurement for all combined measurements on the sample microarray. A) Comparison of the relative abundance measurements of two technical replicates in the quiescent sample reveals a correlation coefficient of 0.975; B) Comparison of the relative abundance measurements of two biological replicates in the Quiescent sample reveals a correlation coefficient of 0.98.

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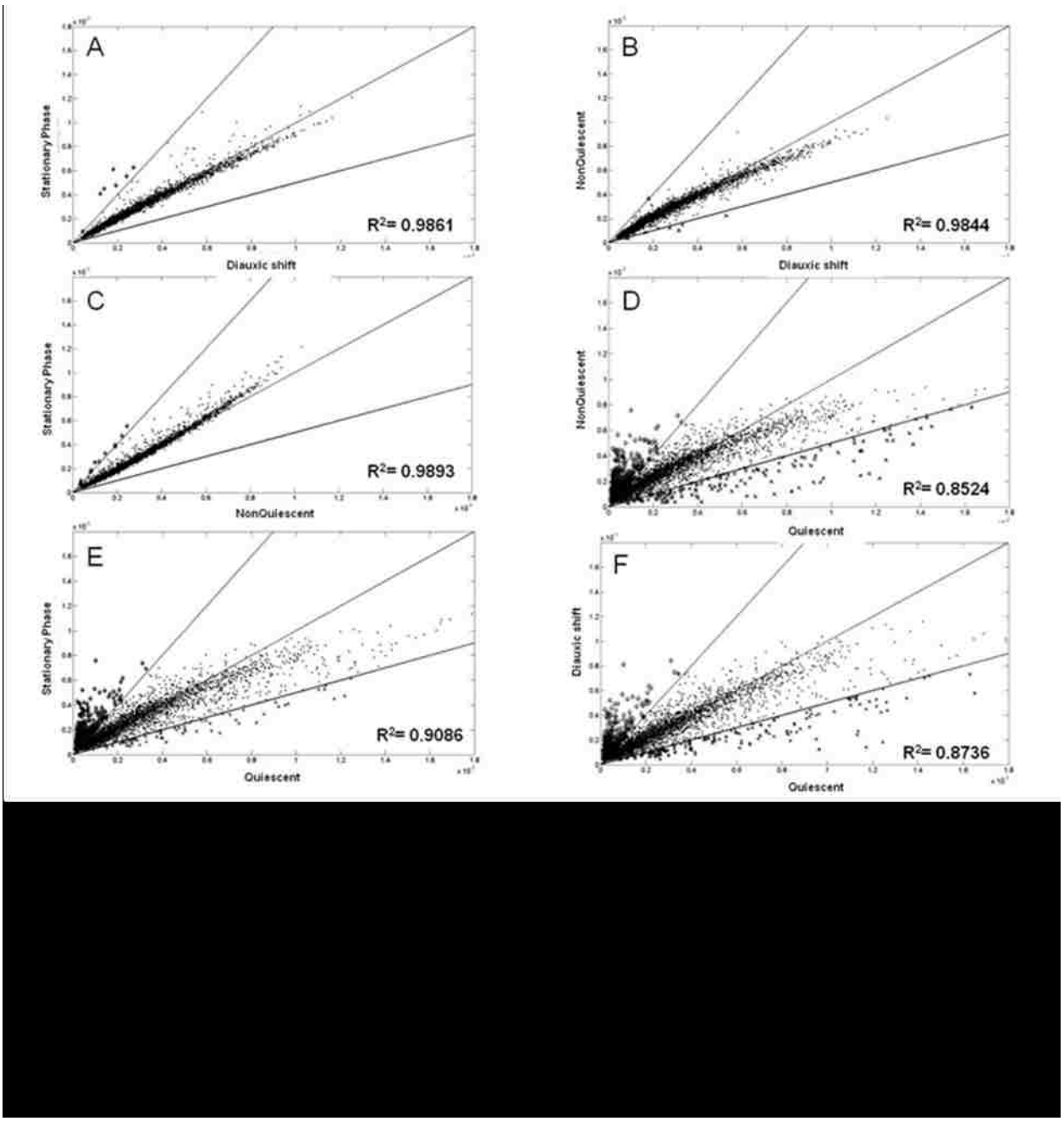
## Scatterplots of pairwise comparisons of distribution and clustering of strains ≥ 2 fold between samples

To identify strains that were involved in differentiation of SP cultures, results from the microarray experiment on the pooled samples of the homozygous deletion set were statistically analyzed. After removing strains with measurements below the experimental background noise (average of 200 fluorescence units in the diauxic shift (DS) samples), a total of 3,849 strain remained. Biological replicate measurements for these 3,849 strains were normalized and percentages were calculated for each strain and

plotted on scatter plots. Superimposed on the scatter plot are lines indicating the boundaries of +/- 2 fold differences in abundance as well as the middle line that represents a correlation coefficient of 1. Those strains that occur on the middle line showed no difference in abundance for the two samples. These scatter plots reveal the distribution and clustering of the individual strains within the pool samples. (Figure 5A-F)

Figures 5A, B and C show that a majority of the strains compared had no difference in abundance. However, there were a few strains, specifically, 1, 13 and 10 strains, respectively, in the remaining sample comparisons that were ≥ +/- 2 fold. Correlation coefficients for these plots were 0.9861, 0.9844 and 0.9893 respectively.

Figures 5D-F were quite different. These plots reveal that while many of the strains fell within the range that indicated no significant difference in abundance, there were many strains that were significant. In figures 5D, E and F there were 666, 508 and 562 strains exhibiting a broad range of abundance by fold within the ≥ +/-2 fold criteria, respectively. Correlation coefficients were also significant for these plots as in 5A-C, being 0.8524 for 3D, 09086 for 5E and 0.8736 for 5F. These three figures (Figures 3D, 3E and 3F) represent comparisons between DS, NQ and SP against the Q samples.




**Fold Comparison of Strains between Samples Reveals Significant Number of Genes Important for Quiescent Fraction Formation**

To determine whether there was a pattern within the abundant genes revealed by the scatter plots for sample comparisons (Figure 5A-F), pairwise fold calculations were

performed comparing abundance of individual deletion strains between samples. Overall, 86.4% of the 3849 strains had less than 2-fold differences. The remaining 13.6% of the 3849 strains had fold differences between the various samples ranging from 0 to 23.5.

The comparison of fold change between the samples revealed that highest number of strains, highest % of all strains and highest fold changes occurred when the NQ, DS and SP samples were compared to the Q sample (Table 2). The number of strains ≥ 2 fold in these comparisons totaled 1,410 strains that are possibly important for the level of abundance in the Q sample.

TABLE 2. Comparison of Strains Between Datasets

| Datasets Compared | # Strains ≥ 2 Fold | % of 3849 Strains | Highest Fold Change |
|---|---|---|---|
| **NQ/Q** | **522** | **13.6** | **23.5** |
| **SP/Q** | **440** | **11.4** | **22.0** |
| **DS/Q** | **448** | **11.6** | **22.9** |
| Q/DS | 114 | 3.0 | 8.3 |
| Q/NQ | 144 | 3.7 | 10.8 |
| Q/SP | 68 | 3.8 | 4.2 |
| NQ/DS | 1 | 0 | 2 |
| NQ/SP | 0 | 0 | -- |
| SP/DS | 1 | 0 | 3.4 |
| SP/NQ | 13 | 0.3 | 2.6 |
| DS/SP | 0 | 0 | -- |
| DS/NQ | 9 | 0.2 | 3.2 |

The second most significant set of comparisons can also be seen in Table 2, which is the converse relationship of the Q sample to the other samples in the experiment. In these comparisons, the number of genes, percent of total strains and fold changes were less great but still potentially important. There were a total of 326 genes representing a high of 3.8% of the 3849 genes analyzed and exhibiting a fold change of 10.8. All other comparisons revealed a minimal total number of 15 strains. (Table 2)

## Analysis of genes found to be important for abundance in the Q sample reveals a core set of strains

To further analyze the significance of the high numbers of abundant strains in the samples, a comparison of the lists of strains revealed a common core set of 411 strains that were important for Q sample abundance. In Figure 6A, the Q sample showed reduced abundance when compared to the other samples. The fact that these are deletion strains points to the potential importance of the presence these 411 genes in order to form the Q sample.

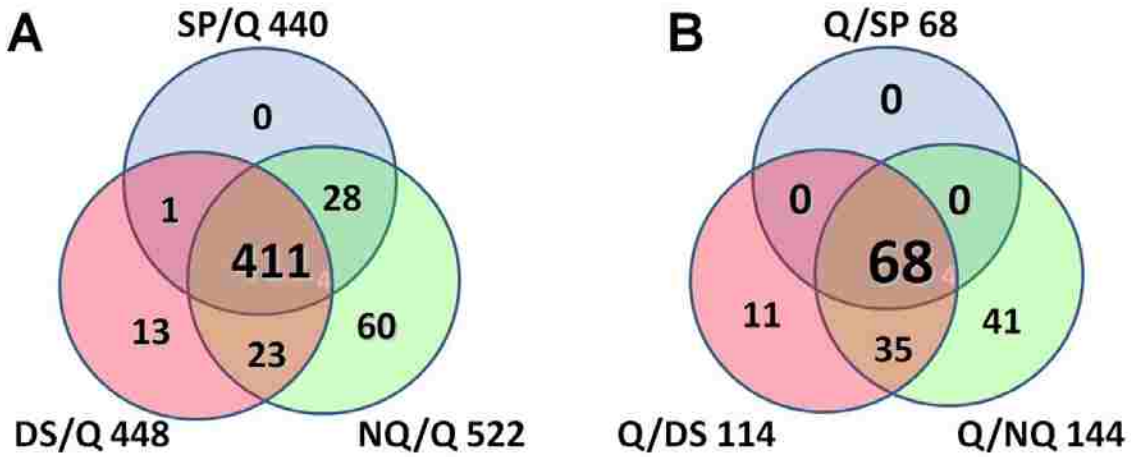



**Figure 6. Venn Diagram Representing Overlap of Strains Important for Q Cell Formation.** A) A representation of the numbers of strains ≥ 2 fold where abundance is greater in the Q sample when compared to all other samples; B) A representation of the numbers of strains ≥ 2 fold where abundance is greater in all samples than in the Q sample.

Figure 6B represents the inverse fold analysis of the sample comparisons. A common core set of 68 strains was found to be important for Q sample abundance. However, in this analysis the abundance of the Q sample was greater than the compared samples. This indicates that the deletion of these strains is not important for formation of the Q sample.

## Gene Ontology Analysis of Core Gene Sets Reveals Significant Processes Involved in Differentiation of SP Cultures into Q and NQ

To further characterize the 411 core set of genes found in the comparison of all samples against the Q sample, an analysis of the processes these genes are involved in was performed using GO Termfinder from the Saccharomyces Genome Database (www.sgd.org). Using this tool, the annotated yeast genome information was queried using our list of 411 genes and the processes associated with these genes were identified. This GO tool analyzes the query list of genes by gathering the known processes each gene is related to and reports not only the process categories but also the number of genes and percents of genes found in those process categories. The experimental frequency is the percentage of genes in our sample of 411 that are involved in each process. The background frequency is the percentage genes in the entire yeast genome that are involved in each process. The p-value represents the statistical comparison of our dataset of 411 genes to the yeast genome. (Figure 7).

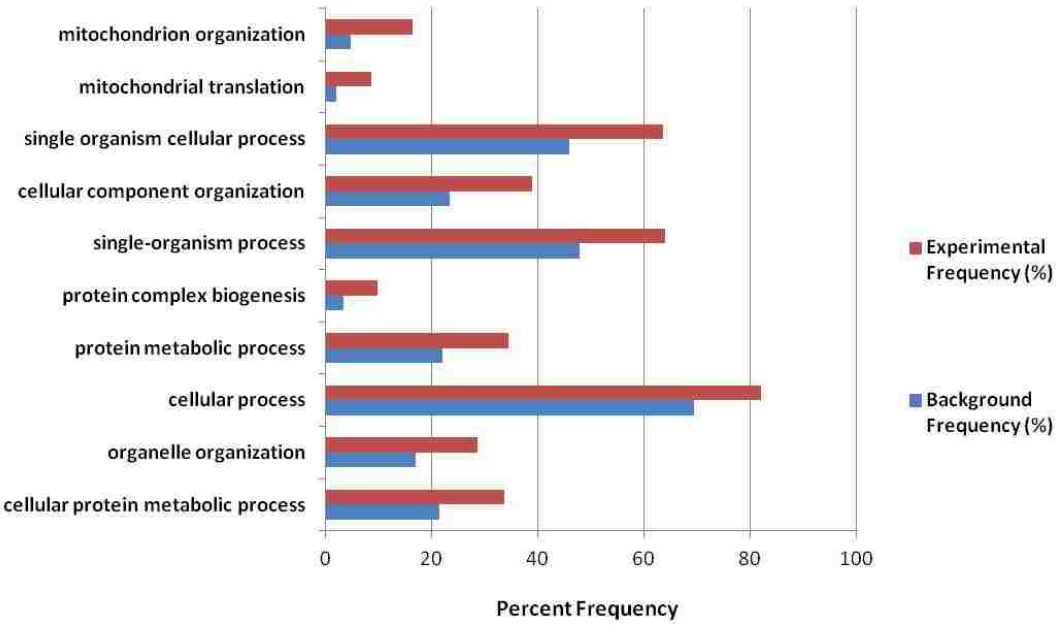



**Figure 7. Gene Ontology of Significant Processes in Core Set of 411 Genes**. Analysis of the 411 core genes involved in the differentiation of SP cultures into Q and NQ was performed using GO Term Finder at the Saccharomyces Genome Database (SGD). The most significant categories are presented on the Y axis.

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The most significant categories revealed by this analysis of the 411 genes were mitochondrial and protein-related processes. The statistical p-values for these processes ranged from $10^{-17}$ to $10^{-06}$. Six additional process categories were statistically significant (data not shown, see Appendices A and B). These categories also reflected mitochondrial and protein-related processes.

## Analysis of 411 Core Genes Reveals Importance of Vacuolar Processes for Viability

To determine the viability of the 411 core set of genes, a fluorescence assay (Fungalight) was performed which measured abundance of live cells within a culture. In previous studies using wild-type yeast cells, nearly 100% of Q and NQ cells were found

to be viable (Allen *et al.*, 2006a). In order to determine whether the deletions represented by the 411 core genes which resulted in decreased Q formation had any effect on these previous results, a library containing 407 of the 411 strains was prepared in 96 well plates and each strain was inoculated into an individual well for growth to SP. Six of the 411 strains were excluded from this study due to our inability to culture the strains to SP. Quantification of the fluorescence was achieved by flow cytometry using a wild-type yeast strain (BY4741) as a control.

Fold calculations were performed for each strain against the plate average. A total of 43 strains (10.5% of 407) showed a viability measurement by fluorescence at 2 fold or higher (Figure 8).

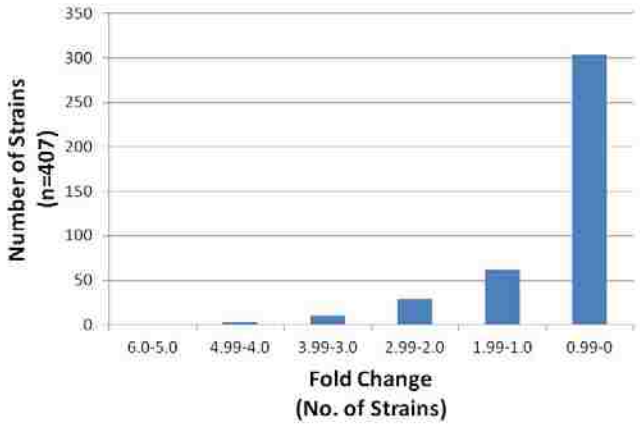


**Figure 8. Results of viability assay.** The viability assay (Fungalight) determines the number of live strains within a sample using two stains. Syto®9 labels all yeast cells within a culture and propidium iodine labels cells with damaged cell walls. The presence of both stains is verified and quantified by flow cytometry and the quantification of live cells is ascertained by calculating the difference between the two stain measurements.

To determine the processes that these 43 genes are involved in, the Saccharomyces Genome Database was again queried. Twenty-one processes were revealed as significant with statistical p-values ranging from $10^{-08}$ to $10^{-05}$ (see Appendices C and D for complete list of processes and genes). The six most significant categories shown here were all associated with processes related to the vacuole, such as protein targeting and localization to the vacuole and vacuolar transport (Figure 9).

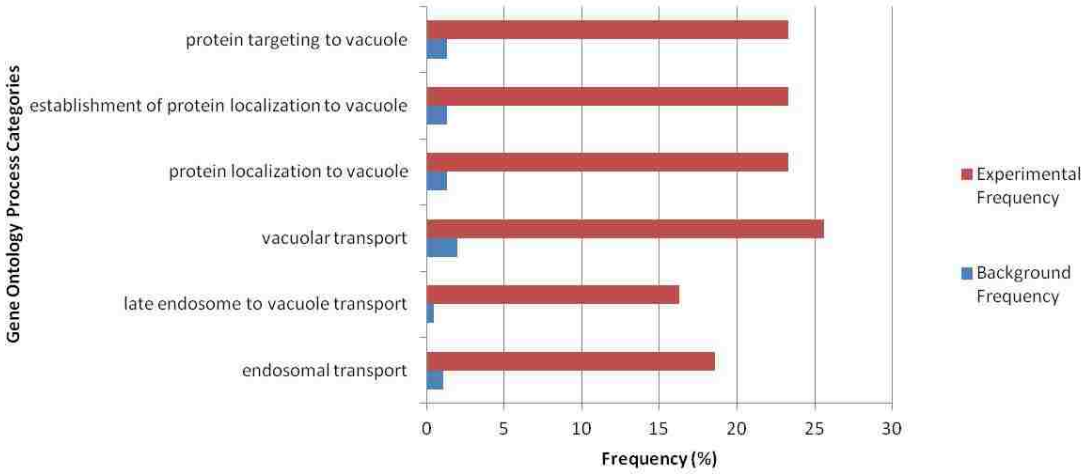


**Figure 9. Gene Ontology for Strains 2 fold or greater in viability assay.** Bar graph representing in percents the most frequent gene process categories for genes with viability measurements ≥ 2 fold . Experimental frequency represents the % likelihood that "x" number of genes would be present in the list of 43 total genes. Genomic frequency represents the % likelihood that "x" number of genes would be present in the list of 43 when compared to the total number of genes in the whole genome within that process category.

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## CHAPTER 4. Discussion

Cellular differentiation is an important process for the development and maintenance of an organism. Determining the genes necessary for this complex process will lead to a better understanding of basic cellular function and important areas of study about human health such as stem cell and cancer cell behavior. This genome-wide study identified over 400 genes which are important for differentiation of stationary phase yeast

cultures. This result address the genomic hypothesis of this study that a core set of genes is important for differentiation of yeast SP cultures. These genes are predominantly involved in mitochondrial function thereby supporting our hypothesis that mitochondrial function is integral to the differentiation process (Allen *et al.*, 2006a).

Our understanding of the differentiation of SP cultures into Q and NQ fractions was further informed by the result that the fate of Q and NQ differentiation is, at least in part, determined by the identification of distinct genes, genetic patterns and processes. Many of the core set of genes necessary for Q cell formation are involved with mitochondrial processes. This fits with our previous findings about NQ and Q phenotypes (Allen *et al.*, 2006a). NQ cells exhibit mitochondrial defects and their metabolism is distinct from Q cell metabolism. Q cells do not exhibit mitochondrial defects. It is, therefore, not surprising that the deletion of these 411 core genes that are mainly involved in mitochondrial processes resulted in a decreased abundance in the Q fraction in our samples. Further, the 68 gene deletions that resulted in an abundance of Q cells over all other samples were not involved with mitochondrial processes but, rather, transcriptional, translational and organelle and cell structure-related processes.

A study using the yeast homozygous deletion set focused on identifying genes essential for mitochondrial stability. A dataset including hundreds of genes required for mitochondrial DNA maintenance, respiratory growth and protein synthesis (Merz and Westermann, 2009). Many of the genes found to be important for these important mitochondrial processes were also found in this study to be important for differentiation of SP cultures. The core set of 411 deletion genes found in this study resulted in reduced Q abundance. The correlation of genes found between these two studies focuses our

understanding of the differentiation of SP cultures on stability of mitochondria. Q cells are known to have stable mitochondria. The deletion of genes necessary for mitochondrial stability contributed to the lack of Q abundance in the core set of genes revealed in our data. In effect, these deletions destabilized cells programmed to become Q cells and resulted in an abundance of NQ cells with destabilized mitochondria.

Our experimentation about viability elucidated previous results from research in mixed SP cultures. While previous work in the Werner-Washburne laboratory found that almost all cells in SP cultures were viable, this work using mixed, unseparated SP samples, showed that the deletion of over 40 genes found to be important for formation of Q and NQ fractions affected viability of these deletion strains. These results lead us to ask why are vacuolar processes so important to the viability of SP cultures? Future experimentation is required to isolate whether the viability of both the Q and NQ fractions is affected by these gene deletions or whether these results reflect the impact of these gene deletions on one of these phenotypically distinct cell types.

The purpose of the vacuole and its related processes are important to the homeostasis and function of the cell. Storage of waste materials as part of the autophagic pathway and transport of these items outside of the cell are essential for the cell. Accumulation of polyphosphate in the vacuole has been shown to affect viability in SP cultures where Ppn1 and Ppx1, genes involved with polyphosphate degradation, were deleted (De Virgilio, 2012). While these genes strains with these specific gene deletions were not significant in this study, it is possible associated genes either up or downstream of the process would merit further investigation.

Autophagy is a process that is a known phenotype associated with NQ cells. The vacuole is an essential element for autophagic processes in the cell. A genome-wide screen using the yeast deletion set identified vacuolar sorting proteins as being important for lifespan (Fabrizio *et al.*, 2010). The connection between the previous finding that 50% of NQ cells exhibit increased levels of autophagy over Q cells and the finding that vacuolar processes this study are highly significant to the viability of SP cultures merits further investigation into the importance of the process of autophagy to differentiation of SP cultures.

In conclusion, it is clear that mitochondria and protein-related processes are important to differentiation of SP yeast cultures. These results lead to further questions about the differentiation process. What part do mitochondria play in this differentiation? What are the signals or pathways being induced to promote differentiation? And, finally, and more broadly, can the answers to these questions lead to control or manipulation of that differentiation?

# List of Appendices

| Appendix A. Significant Term Finder Gene Ontology by Process for 411 Genes | | | | |
|---|---|---|---|---|
| **GOID** | **GO_term** | **Cluster frequency** | **Background frequency** | **P-value** |
| 7005 | mitochondrion organization | 67 out of 411 genes, 16.3% | 338 out of 7168 background genes, 4.7% | 2.64E-17 |
| 32543 | mitochondrial translation | 35 out of 411 genes, 8.5% | 137 out of 7168 background genes, 1.9% | 1.87E-11 |
| 44763 | single-organism cellular process | 261 out of 411 genes, 63.5% | 3282 out of 7168 background genes, 45.8% | 7.62E-11 |
| 16043 | cellular component organization | 160 out of 411 genes, 38.9% | 1676 out of 7168 background genes, 23.4% | 2.62E-10 |
| 44699 | single-organism process | 263 out of 411 genes, 64.0% | 3423 out of 7168 background genes, 47.8% | 6.49E-09 |
| 70271 | protein complex biogenesis | 40 out of 411 genes, 9.7% | 233 out of 7168 background genes, 3.3% | 2.17E-07 |
| 19538 | protein metabolic process | 142 out of 411 genes, 34.5% | 1569 out of 7168 background genes, 21.9% | 8.13E-07 |
| 9987 | cellular process | 337 out of 411 genes, 82.0% | 4967 out of 7168 background genes, 69.3% | 1.21E-06 |
| 6996 | organelle organization | 117 out of 411 genes, 28.5% | 1217 out of 7168 background genes, 17.0% | 1.45E-06 |
| 44267 | cellular protein metabolic process | 138 out of 411 genes, 33.6% | 1536 out of 7168 background genes, 21.4% | 2.75E-06 |
| 97034 | mitochondrial respiratory chain complex IV biogenesis | 12 out of 411 genes, 2.9% | 26 out of 7168 background genes, 0.4% | 4.74E-06 |
| 71840 | cellular component organization or biogenesis | 168 out of 411 genes, 40.9% | 2025 out of 7168 background genes, 28.3% | 9.40E-06 |
| 6623 | protein targeting to vacuole | 21 out of 411 genes, 5.1% | 94 out of 7168 background genes, 1.3% | 4.71E-05 |
| 72666 | establishment of protein localization to vacuole | 21 out of 411 genes, 5.1% | 94 out of 7168 background genes, 1.3% | 4.71E-05 |

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| 33365 | protein localization to organelle | 43 out of 411 genes, 10.5% | 313 out of 7168 background genes, 4.4% | 5.12E-05 |
| 72665 | protein localization to vacuole | 21 out of 411 genes, 5.1% | 95 out of 7168 background genes, 1.3% | 5.73E-05 |

| Appendix B. Gene List for Significant GO Term Finder Process Categories | | |
|---|---|---|
| **GOID** | **GO_term** | Gene(s) annotated to the term |
| 7005 | mitochondrion organization | CBP6/YBR120C:MRPL32/YCR003W:SLM5/YCR024C:RIM1/YCR028C-A:SLM3/YDL033C:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:MRPL1/YDR116C:CBS2/YDR197W:MRPL28/YDR462W:MZM1/YDR493W:EMI1/YDR512C:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:OXA1/YER154W:MRP13/YGR084C:SHY1/YGR112W:CCM1/YGR150C:PET54/YGR222W:MSR1/YHR091C:PTH1/YHR189W:RSM25/YIL093C:COX16/YJL003W:YJR120W:CMC1/YKL137W:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:MRPL13/YKR006C:COX17/YLL009C:PET309/YLR067C:MSS51/YLR203C:COA4/YLR218C:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:ARC18/YLR370C:ATP10/YLR393W:ATP18/YML081C-A:ABF2/YMR072W:MRPS17/YMR188C:COA6/YMR244C-A:PET111/YMR257C:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:MRPL22/YNL177C:RRG9/YNL213C:MRPL17/YNL252C:ATP23/YNR020C:RSM19/YNR037C:MDM38/YOL027C:MSE1/YOL033W:HMI1/YOL095C:MRPL23/YOR150W:PET123/YOR158W:PNT1/YOR266W:TIM18/YOR297C:MIP1/YOR330C:MRPS16/YPL013C:MSY1/YPL097W:RTC6/YPL183W-A:MDM36/YPR083W:MRPL51/YPR100W:MRP2/YPR166C |
| 32543 | mitochondrial translation | CBP6/YBR120C:MRPL32/YCR003W:SLM5/YCR024C:CBS1/YDL069C:MRPL1/YDR116C:CBS2/YDR197W:MRPL28/YDR462W:RSM18/YER050C:MRP13/YGR084C:PET54/YGR222W:MSR1/YHR091C:PTH1/YHR189W:RSM25/YIL093C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:MRPL13/YKR006C:PET309/YLR067C:MSS51/YLR203C:MRPL15/YLR312W-A:MRPS17/YMR188C:PET111/YMR257C:SWS2/YNL081C:MRPL22/YNL177C:MRPL17/YNL252C:RSM19/YNR037C:MDM38/YOL027C:MSE1/YOL033W:MRPL23/YOR150W:PET123/YOR158W:MRPS16/YPL013C:MSY1/YPL097W:RTC6/YPL183W-A:MRPL51/YPR100W:MRP2/YPR166C |
| 44763 | single-organism cellular process | SHE1/YBL031W:PSY4/YBL046W:PIN4/YBL051C:SAS3/YBL052C:PTC3/YBL056W:ATG8/YBL078C:UGA2/YBR006W:HHF1/YBR009C:GAL1/YBR020W:ATP3/YBR039W:ECM33/YBR078W:CBP6/YBR120C:HSL7/YBR133C:DPB3/YBR278W:BSD2/YBR290W:MAL31/YBR298C:SGF29/YCL010C:STE50/YCL032W:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:PTC6/YCR079W:CDC50/YCR094W:GIT1/ |

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| | | YCR098C:SLM3/YDL033C:MBP1/YDL056W:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:SNF3/YDL194W:ACK1/YDL203C:SOK1/YDR006C:VMS1/YDR049W:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:STB3/YDR169C:CBS2/YDR197W:MSC2/YDR205W:PMP3/YDR276C:HIM1/YDR317W:PEX3/YDR329C:MSN5/YDR335W:VPS74/YDR372C:RVS167/YDR388W:SPT3/YDR392W:SXM1/YDR395W:ERD1/YDR414C:MRPL28/YDR462W:KRE2/YDR483W:VPS52/YDR484W:VPS60/YDR486C:MZM1/YDR493W:RSM28/YDR494W:GIN4/YDR507C:EMI1/YDR512C:NPR2/YEL062W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:KAP123/YER110C:UBP3/YER151C:OXA1/YER154W:BCK2/YER167W:ATG18/YFR021W:ERV14/YGL054C:SGF73/YGL066W:SNF4/YGL115W:PEX14/YGL153W:MTL1/YGR023W:YGR054W:ENV11/YGR071C:MRP13/YGR084C:SHY1/YGR112W:CCM1/YGR150C:MVB12/YGR206W:PET54/YGR222W:SMI1/YGR229C:YTA7/YGR270W:HSE1/YHL002W:NPR3/YHL023C:ARD1/YHR013C:SLT2/YHR030C:SMF2/YHR050W:KSP1/YHR082C:MSR1/YHR091C:GRE3/YHR104W:UBA4/YHR111W:ATG7/YHR171W:PTH1/YHR189W:SKN7/YHR206W:SET5/YHR207C:RSM25/YIL093C:RPI1/YIL119C:COX16/YJL003W:PEP8/YJL053W:JEM1/YJL073W:PBS2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:PFD1/YJL179W:SOP4/YJL192C:POL32/YJR043C:UTR1/YJR049C:KCH1/YJR054W:LIA1/YJR070C:MOG1/YJR074W:HOC1/YJR075W:YJR120W:MGM101/YJR144W:DID4/YKL002W:VPS24/YKL041W:MNR2/YKL064W:HAP4/YKL109W:CMC1/YKL137W:DBR1/YKL149C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:DOA1/YKL213C:MRPL13/YKR006C:DID2/YKR035W-A:COX17/YLL009C:UBI4/YLL039C:VPS13/YLL040C:SSK1/YLR006C:FRE8/YLR047C:SPT8/YLR055C:PET309/YLR067C:GIS3/YLR094C:HOG1/YLR113W:SRN2/YLR119W:NHA1/YLR138W:MSS51/YLR203C:COA4/YLR218C:SEC72/YLR292C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:YLR391W:ATP10/YLR393W:TUS1/YLR425W:ATG23/YLR431C:ATP18/YML081C-A:MSC1/YML128C:MVP1/YMR004W:RIM9/YMR063W:ABF2/YMR072W:GID8/YMR135C:YIM1/YMR152W:MRPS17/YMR188C:COA6/YMR244C-A:PET111/YMR257C:SAP30/YMR263W:CUE1/YMR264W:HER2/YMR293C:JNM1/YMR294W:GLC8/YMR311C:TGL3/YMR313C:SSN8/YNL025C:COG6/YNL041C:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:YNL296W:DAL82/YNL314W:VPS27/YNR006W:ATG3/YNR007C:ATP2 |

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|---|---|---|
| | | 3/YNR020C:SSK2/YNR031C:RSM19/YNR037C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:IRA2/YOL081W:HMI1/YOL095C:SHR5/YOL110W:MDY2/YOL111C:RPS19A/YOL121C:VPS68/YOL129W:SHE4/YOR035C:ETT1/YOR051C:VAM10/YOR068C:VPS5/YOR069W:MRPL23/YOR150W:PET123/YOR158W:NPT1/YOR209C:RUD3/YOR216C:HNT3/YOR258W:PNT1/YOR266W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:VMA4/YOR332W:MRS2/YOR334W:MSC6/YOR354C:PDE2/YOR360C:GPB1/YOR371C:MRPS16/YPL013C:LGE1/YPL055C:MFM1/YPL060W:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:UME1/YPL139C:ATG5/YPL149W:TRE1/YPL176C:CTI6/YPL181W:RTC6/YPL183W-A:NEW1/YPL226W:KAR9/YPL269W:NTO1/YPR031W:TIP41/YPR040W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 16043 | cellular component organization | PIM1/YBL022C:SHE1/YBL031W:SAS3/YBL052C:ATG8/YBL078C:HHF1/YBR009C:ECM33/YBR078W:CBP6/YBR120C:DPB3/YBR278W:SGF29/YCL010C:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:CDC50/YCR094W:SLM3/YDL033C:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:ACK1/YDL203C:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:CBS2/YDR197W:PEX3/YDR329C:RVS167/YDR388W:SPT3/YDR392W:PPM1/YDR435C:MRPL28/YDR462W:MZM1/YDR493W:GIN4/YDR507C:EMI1/YDR512C:GIM4/YEL003W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:KAP123/YER110C:OXA1/YER154W:ATG18/YFR021W:SGF73/YGL066W:SNF4/YGL115W:PEX14/YGL153W:MTL1/YGR023W:ENV11/YGR071C:PAC10/YGR078C:MRP13/YGR084C:VOA1/YGR106C:SHY1/YGR112W:PRE9/YGR135W:CCM1/YGR150C:MVB12/YGR206W:PET54/YGR222W:ARD1/YHR013C:SLT2/YHR030C:KSP1/YHR082C:MSR1/YHR091C:UBA4/YHR111W:ATG7/YHR171W:PTH1/YHR189W:SKN7/YHR206W:SET5/YHR207C:RSM25/YIL093C:COX16/YJL003W:JEM1/YJL073W:PBS2/YJL128C:ATG27/YJL178C:PFD1/YJL179W:LIA1/YJR070C:YJR120W:IBA57/YJR122W:DID4/YKL002W:VPS24/YKL041W:MUD2/YKL074C:CYT2/YKL087C:CMC1/YKL137W:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:CBT1/YKL208W:MRPL13/YKR006C:COX17/YLL009C:VPS13/YLL040C:SPT8/YLR055C:PET309/YLR067C:MSS51/YLR203C:COA4/YLR218C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:YLR391W:ATP10/YLR393W:TUS1/YLR425W:ATP18/YML081C-A:GIM5/YML094W:ABF2/YMR072W:CIN4/YMR138W:MRPS17/YMR188C:COA6/YMR244C- |

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|---|---|---|
| | | A:PET111/YMR257C:CUE1/YMR264W:HER2/YMR293C:JNM1/YMR294W:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:HMI1/YOL095C:MDY2/YOL111C:SHE4/YOR035C:ETT1/YOR051C:VAM10/YOR068C:MRPL23/YOR150W:PET123/YOR158W:PNT1/YOR266W:CAF20/YOR276W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:MRPS16/YPL013C:LGE1/YPL055C:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:COX11/YPL132W:POC4/YPL144W:ATG5/YPL149W:RTC6/YPL183W-A:KAR9/YPL269W:NTO1/YPR031W:ISA2/YPR067W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 44699 | single-organism process | SHE1/YBL031W:PSY4/YBL046W:PIN4/YBL051C:SAS3/YBL052C:PTC3/YBL056W:ATG8/YBL078C:UGA2/YBR006W:HHF1/YBR009C:GAL1/YBR020W:ATP3/YBR039W:ECM33/YBR078W:CBP6/YBR120C:HSL7/YBR133C:DPB3/YBR278W:BSD2/YBR290W:MAL31/YBR298C:SGF29/YCL010C:STE50/YCL032W:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:PTC6/YCR079W:CDC50/YCR094W:GIT1/YCR098C:SLM3/YDL033C:MBP1/YDL056W:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:SNF3/YDL194W:ACK1/YDL203C:SOK1/YDR006C:VMS1/YDR049W:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:STB3/YDR169C:CBS2/YDR197W:MSC2/YDR205W:PMP3/YDR276C:HIM1/YDR317W:PEX3/YDR329C:MSN5/YDR335W:VPS74/YDR372C:RVS167/YDR388W:SPT3/YDR392W:SXM1/YDR395W:ERD1/YDR414C:MRPL28/YDR462W:KRE2/YDR483W:VPS52/YDR484W:VPS60/YDR486C:MZM1/YDR493W:RSM28/YDR494W:GIN4/YDR507C:EMI1/YDR512C:NPR2/YEL062W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:KAP123/YER110C:UBP3/YER151C:OXA1/YER154W:BCK2/YER167W:ATG18/YFR021W:ERV14/YGL054C:SGF73/YGL066W:SNF4/YGL115W:PEX14/YGL153W:MTL1/YGR023W:YGR054W:ENV11/YGR071C:MRP13/YGR084C:SHY1/YGR112W:CCM1/YGR150C:MVB12/YGR206W:PET54/YGR222W:SMI1/YGR229C:YTA7/YGR270W:HSE1/YHL002W:NPR3/YHL023C:ARD1/YHR013C:SLT2/YHR030C:SMF2/YHR050W:KSP1/YHR082C:MSR1/YHR091C:GRE3/YHR104W:UBA4/YHR111W:ATG7/YHR171W:PTH1/YHR189W:SKN7/YHR206W:SET5/YHR207C:RSM25/YIL093C:RPI1/YIL119C:COX16/YJL003W:PEP8/YJL053W:JEM1/YJL073W:KHA1/YJL094C:PBS |

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|---|---|---|
| | | 2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:PFD1/YJL179W:SOP4/YJL192C:POL32/YJR043C:UTR1/YJR049C:KCH1/YJR054W:LIA1/YJR070C:MOG1/YJR074W:HOC1/YJR075W:YJR120W:MGM101/YJR144W:DID4/YKL002W:VPS24/YKL041W:MNR2/YKL064W:HAP4/YKL109W:CMC1/YKL137W:DBR1/YKL149C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:DOA1/YKL213C:MRPL13/YKR006C:DID2/YKR035W-A:COX17/YLL009C:UBI4/YLL039C:VPS13/YLL040C:SSK1/YLR006C:FRE8/YLR047C:SPT8/YLR055C:PET309/YLR067C:GIS3/YLR094C:HOG1/YLR113W:SRN2/YLR119W:NHA1/YLR138W:MSS51/YLR203C:COA4/YLR218C:SEC72/YLR292C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:YLR391W:ATP10/YLR393W:TUS1/YLR425W:ATG23/YLR431C:ATP18/YML081C-A:MSC1/YML128C:MVP1/YMR004W:RIM9/YMR063W:ABF2/YMR072W:GID8/YMR135C:YIM1/YMR152W:MRPS17/YMR188C:COA6/YMR244C-A:PET111/YMR257C:SAP30/YMR263W:CUE1/YMR264W:HER2/YMR293C:JNM1/YMR294W:GLC8/YMR311C:TGL3/YMR313C:SSN8/YNL025C:COG6/YNL041C:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:YNL296W:DAL82/YNL314W:VPS27/YNR006W:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:ZRG17/YNR039C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:IRA2/YOL081W:HMI1/YOL095C:SHR5/YOL110W:MDY2/YOL111C:RPS19A/YOL121C:VPS68/YOL129W:SHE4/YOR035C:ETT1/YOR051C:VAM10/YOR068C:VPS5/YOR069W:MRPL23/YOR150W:PET123/YOR158W:NPT1/YOR209C:RUD3/YOR216C:HNT3/YOR258W:PNT1/YOR266W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:VMA4/YOR332W:MRS2/YOR334W:MSC6/YOR354C:PDE2/YOR360C:GPB1/YOR371C:MRPS16/YPL013C:LGE1/YPL055C:MFM1/YPL060W:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:UME1/YPL139C:ATG5/YPL149W:TRE1/YPL176C:CTI6/YPL181W:RTC6/YPL183W-A:NEW1/YPL226W:KAR9/YPL269W:NTO1/YPR031W:TIP41/YPR040W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 70271 | protein complex biogenesis | PIM1/YBL022C:CBP6/YBR120C:CDC10/YCR002C:CBS1/YDL069C:CBS2/YDR197W:PPM1/YDR435C:MZM1/YDR493W:GIN4/YDR507C:EMI1/YDR512C:GIM4/YEL003W:AFG3/YER017C:PET117/YER058W:OXA1/YER154W:SGF73/YGL066W:PEX14/YGL153W:PAC10/YGR078C:VOA1/YGR106C:SHY1/YGR11 |

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|---|---|---|
| | | 2W:PRE9/YGR135W:MVB12/YGR206W:PET54/YGR222W:COX16/YJL003W:CYT2/YKL087C:CMC1/YKL137W:CBT1/YKL208W:COX17/YLL009C:PET309/YLR067C:MSS51/YLR203C:COA4/YLR218C:ATP10/YLR393W:ATP18/YML081C-A:GIM5/YML094W:CIN4/YMR138W:COA6/YMR244C-A:PET111/YMR257C:BNI1/YNL271C:ATP23/YNR020C:MDM38/YOL027C:COX11/YPL132W:POC4/YPL144W |
| 19538 | protein metabolic process | FMT1/YBL013W:PIM1/YBL022C:PSY4/YBL046W:SAS3/YBL052C:PTC3/YBL056W:HHF1/YBR009C:MNN2/YBR015C:CBP6/YBR120C:BSD2/YBR290W:SGF29/YCL010C:GID7/YCL039W:MRPL32/YCR003W:CWH43/YCR017C:SLM5/YCR024C:YIH1/YCR059C:PTC6/YCR079W:NAT1/YDL040C:RPS29B/YDL061C:CBS1/YDL069C:RPP1B/YDL130W:VMS1/YDR049W:YOS9/YDR057W:DOA4/YDR069C:MRPL1/YDR116C:CBS2/YDR197W:RMD5/YDR255C:SPT3/YDR392W:ERD1/YDR414C:PPM1/YDR435C:MRPL28/YDR462W:KRE2/YDR483W:RSM28/YDR494W:RPL37B/YDR500C:GIN4/YDR507C:EUG1/YDR518W:UBC8/YEL012W:GDA1/YEL042W:MNN1/YER001W:YND1/YER005W:AFG3/YER017C:RSM18/YER050C:ICP55/YER078C:YCK3/YER123W:UBP3/YER151C:ATG18/YFR021W:SGF73/YGL066W:SNF4/YGL115W:RPL9A/YGL147C:YGR054W:ENV11/YGR071C:MRP13/YGR084C:PRE9/YGR135W:MRPL9/YGR220C:PET54/YGR222W:ARD1/YHR013C:SLT2/YHR030C:KSP1/YHR082C:MSR1/YHR091C:UBA4/YHR111W:ECM14/YHR132C:MTG2/YHR168W:ATG7/YHR171W:PTH1/YHR189W:MNL1/YHR204W:SET5/YHR207C:NOT3/YIL038C:RSM25/YIL093C:RPL40A/YIL148W:AIM22/YJL046W:JEM1/YJL073W:MEF2/YJL102W:PBS2/YJL128C:PFD1/YJL179W:MNN11/YJL183W:LIA1/YJR070C:HOC1/YJR075W:DID4/YKL002W:VPS24/YKL041W:CYT2/YKL087C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:DOA1/YKL213C:MRPL13/YKR006C:UBI4/YLL039C:SSK1/YLR006C:SPT8/YLR055C:PET309/YLR067C:HOG1/YLR113W:SRN2/YLR119W:MSS51/YLR203C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:AEP1/YMR064W:RPL15B/YMR121C:GID8/YMR135C:CIN4/YMR138W:MRPS17/YMR188C:SCJ1/YMR214W:PET111/YMR257C:CUE1/YMR264W:RCE1/YMR274C:SWS2/YNL081C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:ALG9/YNL219C:MRPL17/YNL252C:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:MPD2/YOL088C:SHR5/YOL110W:RPS19A/YOL121C:ALG6/YOR002W:ETT1/YOR051C:ALG8/YOR067C:TMA46/YOR091W:MRPL23/YOR150W:PET123/YOR158W:LIP5/YOR196C:CAF20/YOR276W:GPB1/YOR371C:MRPS16/YPL013C:EGD1/YPL037C:LGE1/YPL055C:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:PPT2/YPL148C:ATG5/YPL149W:TRE1/YPL176C:RTC6/YPL183W-A:ALG5/YPL227C:NTO1/YPR031W:MRPL51/YPR100W:CLB2/ |

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|---|---|---|
| | | YPR119W:MRP2/YPR166C |
| 9987 | cellular process | FMT1/YBL013W:PIM1/YBL022C:SHE1/YBL031W:PSY4/YBL046W:PIN4/YBL051C:SAS3/YBL052C:PTC3/YBL056W:ATG8/YBL078C:COQ1/YBR003W:UGA2/YBR006W:HHF1/YBR009C:MNN2/YBR015C:GAL1/YBR020W:ATP3/YBR039W:MUM2/YBR057C:ECM33/YBR078W:MIS1/YBR084W:CBP6/YBR120C:HSL7/YBR133C:PDB1/YBR221C:DPB3/YBR278W:BSD2/YBR290W:MAL31/YBR298C:SGF29/YCL010C:STE50/YCL032W:GID7/YCL039W:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:YIH1/YCR059C:PTC6/YCR079W:CDC50/YCR094W:GIT1/YCR098C:SLM3/YDL033C:NAT1/YDL040C:MBP1/YDL056W:RPS29B/YDL061C:CBS1/YDL069C:RXT3/YDL076C:QRI7/YDL104C:RPP1B/YDL130W:CRD1/YDL142C:SNF3/YDL194W:ACK1/YDL203C:SOK1/YDR006C:VMS1/YDR049W:YOS9/YDR057W:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:ARO1/YDR127W:STB3/YDR169C:CBS2/YDR197W:MSC2/YDR205W:RMD5/YDR255C:PMP3/YDR276C:HIM1/YDR317W:PEX3/YDR329C:MSN5/YDR335W:VPS74/YDR372C:RVS167/YDR388W:SPT3/YDR392W:SXM1/YDR395W:ERD1/YDR414C:PPM1/YDR435C:MRPL28/YDR462W:KRE2/YDR483W:VPS52/YDR484W:VPS60/YDR486C:MZM1/YDR493W:RSM28/YDR494W:RPL37B/YDR500C:GIN4/YDR507C:EMI1/YDR512C:EUG1/YDR518W:UBC8/YEL012W:GDA1/YEL042W:NPR2/YEL062W:MNN1/YER001W:YND1/YER005W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:CEM1/YER061C:KAP123/YER110C:YCK3/YER123W:UBP3/YER151C:OXA1/YER154W:BCK2/YER167W:PDA1/YER178W:LPD1/YFL018C:ATG18/YFR021W:QCR6/YFR033C:ERV14/YGL054C:SGF73/YGL066W:SNF4/YGL115W:RPL9A/YGL147C:ARO2/YGL148W:PEX14/YGL153W:TAN1/YGL232W:MTL1/YGR023W:YGR054W:ENV11/YGR071C:MRP13/YGR084C:SHY1/YGR112W:PRE9/YGR135W:CCM1/YGR150C:MVB12/YGR206W:MRPL9/YGR220C:PET54/YGR222W:SMI1/YGR229C:YTA7/YGR270W:HSE1/YHL002W:NPR3/YHL023C:CBP2/YHL038C:ARD1/YHR013C:SLT2/YHR030C:SMF2/YHR050W:COX6/YHR051W:HTD2/YHR067W:KSP1/YHR082C:MSR1/YHR091C:GRE3/YHR104W:UBA4/YHR111W:MTG2/YHR168W:ATG7/YHR171W:PTH1/YHR189W:MNL1/YHR204W:SKN7/YHR206W:SET5/YHR207C:NOT3/YIL038C:RSM25/YIL093C:RPI1/YIL119C:RPL40A/YIL148W:MRS1/YIR021W:COX16/YJL003W:AIM22/YJL046W:TDH1/YJL052W:PEP8/YJL053W:JEM1/YJL073W:MEF2/YJL102W:LSM1/YJL124C:PBS2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:PFD1/YJL179W:MNN11/YJL183W:SOP4/YJL192C:POL32/YJR043C:UTR1/YJR049C:KCH1/YJR054W:LIA1/YJR070C:OPI3/YJR073C:MOG1/YJR074W:HOC1/YJR075W:YJR120W:MGM101/YJR144W:DID4/YKL002W:MAE1/YKL029C:VPS24/ |

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|---|---|---|
| | | YKL041W:OAR1/YKL055C:MNR2/YKL064W:MUD2/YKL074C:CYT2/YKL087C:HAP4/YKL109W:PGM1/YKL127W:CMC1/YKL137W:DBR1/YKL149C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:CBT1/YKL208W:DOA1/YKL213C:MRPL13/YKR006C:DID2/YKR035W-A:COX17/YLL009C:UBI4/YLL039C:VPS13/YLL040C:SSK1/YLR006C:PPR1/YLR014C:FRE8/YLR047C:SPT8/YLR055C:PET309/YLR067C:GIS3/YLR094C:HOG1/YLR113W:SRN2/YLR119W:NHA1/YLR138W:COQ9/YLR201C:MSS51/YLR203C:QRI5/YLR204W:COA4/YLR218C:SEC72/YLR292C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:VAC14/YLR386W:YLR391W:ATP10/YLR393W:COX8/YLR395C:TUS1/YLR425W:ATG23/YLR431C:ATP18/YML081C-A:DAT1/YML113W:MSC1/YML128C:MVP1/YMR004W:RIM9/YMR063W:AEP1/YMR064W:ABF2/YMR072W:RPL15B/YMR121C:GID8/YMR135C:CIN4/YMR138W:YIM1/YMR152W:MRPS17/YMR188C:HFA1/YMR207C:SCJ1/YMR214W:COA6/YMR244C-A:PET111/YMR257C:SAP30/YMR263W:CUE1/YMR264W:RCE1/YMR274C:DSS1/YMR287C:HER2/YMR293C:JNM1/YMR294W:GLC8/YMR311C:TGL3/YMR313C:SSN8/YNL025C:COG6/YNL041C:COX5A/YNL052W:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ALG9/YNL219C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:YNL296W:DAL82/YNL314W:FIG4/YNL325C:VPS27/YNR006W:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:IRA2/YOL081W:MPD2/YOL088C:HMI1/YOL095C:SHR5/YOL110W:MDY2/YOL111C:RPS19A/YOL121C:VPS68/YOL129W:ALG6/YOR002W:SHE4/YOR035C:ETT1/YOR051C:CYT1/YOR065W:ALG8/YOR067C:VAM10/YOR068C:VPS5/YOR069W:TMA46/YOR091W:MRPL23/YOR150W:PET123/YOR158W:LIP5/YOR196C:NPT1/YOR209C:RUD3/YOR216C:MCT1/YOR221C:HNT3/YOR258W:PNT1/YOR266W:MOD5/YOR274W:CAF20/YOR276W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:VMA4/YOR332W:MRS2/YOR334W:MNE1/YOR350C:MSC6/YOR354C:PDE2/YOR360C:GPB1/YOR371C:MRPS16/YPL013C:EGD1/YPL037C:LGE1/YPL055C:MFM1/YPL060W:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:COX11/YPL132W:UME1/YPL139C:PPT2/YPL148C:ATG5/YPL149W:PET20/YPL159C:TRE1/YPL176C:CTI6/YPL181W:RTC6/YPL183W-A:NEW1/YPL226W:ALG5/YPL227C:KAR9/YPL269W:NTO1/YPR031W:TIP41/YPR040W:ISA2/YPR067W:MED1/YPR070W: |

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|---|---|---|
| | | MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C:QCR2/YPR191W |
| 6996 | organelle organization | SHE1/YBL031W:PSY4/YBL046W:PIN4/YBL051C:SAS3/YBL052C:PTC3/YBL056W:ATG8/YBL078C:UGA2/YBR006W:HHF1/YBR009C:GAL1/YBR020W:ATP3/YBR039W:ECM33/YBR078W:CBP6/YBR120C:HSL7/YBR133C:DPB3/YBR278W:BSD2/YBR290W:MAL31/YBR298C:SGF29/YCL010C:STE50/YCL032W:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:PTC6/YCR079W:CDC50/YCR094W:GIT1/YCR098C:SLM3/YDL033C:MBP1/YDL056W:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:SNF3/YDL194W:ACK1/YDL203C:SOK1/YDR006C:VMS1/YDR049W:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:STB3/YDR169C:CBS2/YDR197W:MSC2/YDR205W:PMP3/YDR276C:HIM1/YDR317W:PEX3/YDR329C:MSN5/YDR335W:VPS74/YDR372C:RVS167/YDR388W:SPT3/YDR392W:SXM1/YDR395W:ERD1/YDR414C:MRPL28/YDR462W:KRE2/YDR483W:VPS52/YDR484W:VPS60/YDR486C:MZM1/YDR493W:RSM28/YDR494W:GIN4/YDR507C:EMI1/YDR512C:NPR2/YEL062W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:KAP123/YER110C:UBP3/YER151C:OXA1/YER154W:BCK2/YER167W:ATG18/YFR021W:ERV14/YGL054C:SGF73/YGL066W:SNF4/YGL115W:PEX14/YGL153W:MTL1/YGR023W:YGR054W:ENV11/YGR071C:MRP13/YGR084C:SHY1/YGR112W:CCM1/YGR150C:MVB12/YGR206W:PET54/YGR222W:SMI1/YGR229C:YTA7/YGR270W:HSE1/YHL002W:NPR3/YHL023C:ARD1/YHR013C:SLT2/YHR030C:SMF2/YHR050W:KSP1/YHR082C:MSR1/YHR091C:GRE3/YHR104W:UBA4/YHR111W:ATG7/YHR171W:PTH1/YHR189W:SKN7/YHR206W:SET5/YHR207C:RSM25/YIL093C:RPI1/YIL119C:COX16/YJL003W:PEP8/YJL053W:JEM1/YJL073W:KHA1/YJL094C:PBS2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:PFD1/YJL179W:SOP4/YJL192C:POL32/YJR043C:UTR1/YJR049C:KCH1/YJR054W:LIA1/YJR070C:MOG1/YJR074W:HOC1/YJR075W:YJR120W:MGM101/YJR144W:DID4/YKL002W:VPS24/YKL041W:MNR2/YKL064W:HAP4/YKL109W:CMC1/YKL137W:DBR1/YKL149C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:DOA1/YKL213C:MRPL13/YKR006C:DID2/YKR035W-A:COX17/YLL009C:UBI4/YLL039C:VPS13/YLL040C:SSK1/YLR006C:FRE8/YLR047C:SPT8/YLR055C:PET309/YLR067C:GIS3/YLR094C:HOG1/YLR113W:SRN2/YLR119W:NHA1/YLR138W:MSS51/YLR203C:COA4/YLR218C:SEC72/YLR292C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:YLR391W:ATP10/YLR393W:TUS1/YLR425W:ATG23/YLR431C:ATP18/YML081C- |

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|---|---|---|
| | | A:MSC1/YML128C:MVP1/YMR004W:RIM9/YMR063W:ABF2/YMR072W:GID8/YMR135C:YIM1/YMR152W:MRPS17/YMR188C:COA6/YMR244C-A:PET111/YMR257C:SAP30/YMR263W:CUE1/YMR264W:HER2/YMR293C:JNM1/YMR294W:GLC8/YMR311C:TGL3/YMR313C:SSN8/YNL025C:COG6/YNL041C:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:YNL296W:DAL82/YNL314W:VPS27/YNR006W:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:ZRG17/YNR039C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:IRA2/YOL081W:HMI1/YOL095C:SHR5/YOL110W:MDY2/YOL111C:RPS19A/YOL121C:VPS68/YOL129W:SHE4/YOR035C:ETT1/YOR051C:VAM10/YOR068C:VPS5/YOR069W:MRPL23/YOR150W:PET123/YOR158W:NPT1/YOR209C:RUD3/YOR216C:HNT3/YOR258W:PNT1/YOR266W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:VMA4/YOR332W:MRS2/YOR334W:MSC6/YOR354C:PDE2/YOR360C:GPB1/YOR371C:MRPS16/YPL013C:LGE1/YPL055C:MFM1/YPL060W:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:UME1/YPL139C:ATG5/YPL149W:TRE1/YPL176C:CTI6/YPL181W:RTC6/YPL183W-A:NEW1/YPL226W:KAR9/YPL269W:NTO1/YPR031W:TIP41/YPR040W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 44267 | cellular protein metabolic process | FMT1/YBL013W:PIM1/YBL022C:PSY4/YBL046W:SAS3/YBL052C:PTC3/YBL056W:HHF1/YBR009C:MNN2/YBR015C:CBP6/YBR120C:BSD2/YBR290W:SGF29/YCL010C:GID7/YCL039W:MRPL32/YCR003W:CWH43/YCR017C:SLM5/YCR024C:YIH1/YCR059C:PTC6/YCR079W:NAT1/YDL040C:RPS29B/YDL061C:CBS1/YDL069C:RPP1B/YDL130W:VMS1/YDR049W:YOS9/YDR057W:DOA4/YDR069C:MRPL1/YDR116C:CBS2/YDR197W:RMD5/YDR255C:SPT3/YDR392W:ERD1/YDR414C:PPM1/YDR435C:MRPL28/YDR462W:KRE2/YDR483W:RSM28/YDR494W:RPL37B/YDR500C:GIN4/YDR507C:EUG1/YDR518W:UBC8/YEL012W:GDA1/YEL042W:MNN1/YER001W:YND1/YER005W:AFG3/YER017C:RSM18/YER050C:YCK3/YER123W:UBP3/YER151C:ATG18/YFR021W:SGF73/YGL066W:SNF4/YGL115W:RPL9A/YGL147C:YGR054W:ENV11/YGR071C:MRP13/YGR084C:PRE9/YGR135W:MRPL9/YGR220C:PET54/YGR222W:ARD1/YHR013C:SLT2/YHR030C:KSP1/YHR082C:MSR1/YHR091C:UBA4/YHR111W:MTG2/YHR168W:ATG7/YHR171W:PTH1/YHR189W:MNL1/YHR204W:SET5/YHR207C:NOT3/YIL038C:RSM25/YIL093C:RPL40A/YIL148W:AIM22/YJL046W:JEM1/YJL073W:MEF2/YJL102W:PBS2/YJL128C:PFD1/YJL179W:MNN11/YJL183W:LIA1/YJR070C:DID4/YKL002W:VPS24/YKL041W |

| | | |
|---|---|---|
| | | :CYT2/YKL087C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:DOA1/YKL213C:MRPL13/YKR006C:UBI4/YLL039C:SSK1/YLR006C:SPT8/YLR055C:PET309/YLR067C:HOG1/YLR113W:SRN2/YLR119W:MSS51/YLR203C:MRPL15/YLR312W-A:MDM30/YLR368W:AEP1/YMR064W:RPL15B/YMR121C:GID8/YMR135C:CIN4/YMR138W:MRPS17/YMR188C:SCJ1/YMR214W:PET111/YMR257C:CUE1/YMR264W:RCE1/YMR274C:SWS2/YNL081C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:ALG9/YNL219C:MRPL17/YNL252C:ATG3/YNR007C:SSK2/YNR031C:RSM19/YNR037C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:MPD2/YOL088C:SHR5/YOL110W:RPS19A/YOL121C:ALG6/YOR002W:ETT1/YOR051C:ALG8/YOR067C:TMA46/YOR091W:MRPL23/YOR150W:PET123/YOR158W:LIP5/YOR196C:CAF20/YOR276W:GPB1/YOR371C:MRPS16/YPL013C:EGD1/YPL037C:LGE1/YPL055C:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:PPT2/YPL148C:ATG5/YPL149W:TRE1/YPL176C:RTC6/YPL183W-A:ALG5/YPL227C:NTO1/YPR031W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 97034 | mitochondrial respiratory chain complex IV biogenesis | PET117/YER058W:SHY1/YGR112W:PET54/YGR222W:COX16/YJL003W:CMC1/YKL137W:COX17/YLL009C:PET309/YLR067C:MSS51/YLR203C:COA4/YLR218C:COA6/YMR244C-A:PET111/YMR257C:MDM38/YOL027C |
| 71840 | cellular component organization or biogenesis | PIM1/YBL022C:SHE1/YBL031W:SAS3/YBL052C:ATG8/YBL078C:HHF1/YBR009C:ECM33/YBR078W:CBP6/YBR120C:DPB3/YBR278W:SGF29/YCL010C:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:CDC50/YCR094W:SLM3/YDL033C:CBS1/YDL069C:QRI7/YDL104C:CRD1/YDL142C:ACK1/YDL203C:NOP6/YDL213C:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:CBS2/YDR197W:PEX3/YDR329C:RVS167/YDR388W:SPT3/YDR392W:PPM1/YDR435C:MRPL28/YDR462W:KRE2/YDR483W:MZM1/YDR493W:GIN4/YDR507C:EMI1/YDR512C:GIM4/YEL003W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:KAP123/YER110C:OXA1/YER154W:ATG18/YFR021W:SGF73/YGL066W:SNF4/YGL115W:PEX14/YGL153W:MTL1/YGR023W:ENV11/YGR071C:PAC10/YGR078C:MRP13/YGR084C:VOA1/YGR106C:SHY1/YGR112W:PRE9/YGR135W:CCM1/YGR150C:MVB12/YGR206W:PET54/YGR222W:SMI1/YGR229C:ARD1/YHR013C:SLT2/YHR030C:KSP1/YHR082C:MSR1/YHR091C:UBA4/YHR111W:ATG7/YHR171W:PTH1/YHR189W:SKN7/YHR206W:SET5/YHR207C:RSM25/YIL093C:RPI1/YIL119C:RPL40A/YIL148W:COX16/YJL003W:JEM1/YJL073W:PBS2/YJL128C:ATG27/YJL178C:PFD1/YJL179W:LIA1/YJR070C:HOC1/YJR075W:YJR120W:IBA57/YJR122W:DID4/YKL002W:VPS24/YKL041W:MUD2/YKL074C:CYT2/YKL087C:CMC1/YKL137W:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/Y |

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|---|---|---|
| | | KL197C:CBT1/YKL208W:MRPL13/YKR006C:COX17/YLL009C:VPS13/YLL040C:SPT8/YLR055C:PET309/YLR067C:MSS51/YLR203C:COA4/YLR218C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:YLR391W:ATP10/YLR393W:TUS1/YLR425W:ATP18/YML081C-A:GIM5/YML094W:ABF2/YMR072W:CIN4/YMR138W:MRPS17/YMR188C:COA6/YMR244C-A:PET111/YMR257C:CUE1/YMR264W:HER2/YMR293C:JNM1/YMR294W:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:HMI1/YOL095C:MDY2/YOL111C:RPS19A/YOL121C:SHE4/YOR035C:ETT1/YOR051C:VAM10/YOR068C:MRPL23/YOR150W:PET123/YOR158W:PNT1/YOR266W:CAF20/YOR276W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:MRPS16/YPL013C:LGE1/YPL055C:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:COX11/YPL132W:POC4/YPL144W:ATG5/YPL149W:RTC6/YPL183W-A:NEW1/YPL226W:KAR9/YPL269W:NTO1/YPR031W:ISA2/YPR067W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C |
| 6623 | protein targeting to vacuole | FMT1/YBL013W:PIM1/YBL022C:SHE1/YBL031W:PSY4/YBL046W:PIN4/YBL051C:SAS3/YBL052C:PTC3/YBL056W:ATG8/YBL078C:COQ1/YBR003W:UGA2/YBR006W:HHF1/YBR009C:MNN2/YBR015C:GAL1/YBR020W:ATP3/YBR039W:MUM2/YBR057C:ECM33/YBR078W:MIS1/YBR084W:CBP6/YBR120C:HSL7/YBR133C:PDB1/YBR221C:DPB3/YBR278W:BSD2/YBR290W:MAL31/YBR298C:SGF29/YCL010C:STE50/YCL032W:GID7/YCL039W:LRE1/YCL051W:KAR4/YCL055W:CDC10/YCR002C:MRPL32/YCR003W:RVS161/YCR009C:CWH43/YCR017C:SLM5/YCR024C:RIM1/YCR028C-A:RRT12/YCR045C:YIH1/YCR059C:PTC6/YCR079W:CDC50/YCR094W:GIT1/YCR098C:SLM3/YDL033C:NAT1/YDL040C:MBP1/YDL056W:RPS29B/YDL061C:CBS1/YDL069C:RXT3/YDL076C:QRI7/YDL104C:RPP1B/YDL130W:CRD1/YDL142C:SNF3/YDL194W:ACK1/YDL203C:SOK1/YDR006C:VMS1/YDR049W:YOS9/YDR057W:DOA4/YDR069C:PAA1/YDR071C:MRPL1/YDR116C:ARO1/YDR127W:STB3/YDR169C:CBS2/YDR197W:MSC2/YDR205W:RMD5/YDR255C:PMP3/YDR276C:HIM1/YDR317W:PEX3/YDR329C:MSN5/YDR335W:VPS74/YDR372C:RVS167/YDR388W:SPT3/YDR392W:SXM1/YDR395W:ERD1/YDR414C:PPM1/YDR435C:MRPL28/YDR462W:KRE2/YDR483W:VPS52/YDR484W:VPS60/YDR486C:MZM1/YDR493W:RSM2 |

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|---|---|---|
| | | 8/YDR494W:RPL37B/YDR500C:GIN4/YDR507C:EMI1/YDR512C:EUG1/YDR518W:UBC8/YEL012W:GDA1/YEL042W:NPR2/YEL062W:MNN1/YER001W:YND1/YER005W:AFG3/YER017C:RSM18/YER050C:PET117/YER058W:CEM1/YER061C:KAP123/YER110C:YCK3/YER123W:UBP3/YER151C:OXA1/YER154W:BCK2/YER167W:PDA1/YER178W:LPD1/YFL018C:ATG18/YFR021W:QCR6/YFR033C:ERV14/YGL054C:SGF73/YGL066W:SNF4/YGL115W:RPL9A/YGL147C:ARO2/YGL148W:PEX14/YGL153W:TAN1/YGL232W:MTL1/YGR023W:YGR054W:ENV11/YGR071C:MRP13/YGR084C:SHY1/YGR112W:PRE9/YGR135W:CCM1/YGR150C:MVB12/YGR206W:MRPL9/YGR220C:PET54/YGR222W:SMI1/YGR229C:YTA7/YGR270W:HSE1/YHL002W:NPR3/YHL023C:CBP2/YHL038C:ARD1/YHR013C:SLT2/YHR030C:SMF2/YHR050W:COX6/YHR051W:HTD2/YHR067W:KSP1/YHR082C:MSR1/YHR091C:GRE3/YHR104W:UBA4/YHR111W:MTG2/YHR168W:ATG7/YHR171W:PTH1/YHR189W:MNL1/YHR204W:SKN7/YHR206W:SET5/YHR207C:NOT3/YIL038C:RSM25/YIL093C:RPI1/YIL119C:RPL40A/YIL148W:MRS1/YIR021W:COX16/YJL003W:AIM22/YJL046W:TDH1/YJL052W:PEP8/YJL053W:JEM1/YJL073W:MEF2/YJL102W:LSM1/YJL124C:PBS2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:PFD1/YJL179W:MNN11/YJL183W:SOP4/YJL192C:POL32/YJR043C:UTR1/YJR049C:KCH1/YJR054W:LIA1/YJR070C:OPI3/YJR073C:MOG1/YJR074W:HOC1/YJR075W:YJR120W:MGM101/YJR144W:DID4/YKL002W:MAE1/YKL029C:VPS24/YKL041W:OAR1/YKL055C:MNR2/YKL064W:MUD2/YKL074C:CYT2/YKL087C:HAP4/YKL109W:PGM1/YKL127W:CMC1/YKL137W:DBR1/YKL149C:RSM22/YKL155C:MRP49/YKL167C:MRPL38/YKL170W:PEX1/YKL197C:CBT1/YKL208W:DOA1/YKL213C:MRPL13/YKR006C:DID2/YKR035W-A:COX17/YLL009C:UBI4/YLL039C:VPS13/YLL040C:SSK1/YLR006C:PPR1/YLR014C:FRE8/YLR047C:SPT8/YLR055C:PET309/YLR067C:GIS3/YLR094C:HOG1/YLR113W:SRN2/YLR119W:NHA1/YLR138W:COQ9/YLR201C:MSS51/YLR203C:QRI5/YLR204W:COA4/YLR218C:SEC72/YLR292C:EXG1/YLR300W:ACO1/YLR304C:MRPL15/YLR312W-A:MDM30/YLR368W:SSQ1/YLR369W:ARC18/YLR370C:ROM2/YLR371W:VAC14/YLR386W:YLR391W:ATP10/YLR393W:COX8/YLR395C:TUS1/YLR425W:ATG23/YLR431C:ATP18/YML081C-A:DAT1/YML113W:MSC1/YML128C:MVP1/YMR004W:RIM9/YMR063W:AEP1/YMR064W:ABF2/YMR072W:RPL15B/YMR121C:GID8/YMR135C:CIN4/YMR138W:YIM1/YMR152W:MRPS17/YMR188C:HFA1/YMR207C:SCJ1/YMR214W:COA6/YMR244C-A:PET111/YMR257C:SAP30/YMR263W:CUE1/YMR264W:RCE1/YMR274C:DSS1/YMR287C:HER2/YMR293C:JNM1/YMR294W:GLC8/YMR311C:TGL3/YMR313C:SSN8/YNL025C:COG6 |

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|---|---|---|
| | | /YNL041C:COX5A/YNL052W:POR1/YNL055C:TPM1/YNL079C:SWS2/YNL081C:RHO2/YNL090W:APP1/YNL094W:PHO23/YNL097C:NCS2/YNL119W:FPR1/YNL135C:MRPL22/YNL177C:WHI3/YNL197C:RRG9/YNL213C:ALG9/YNL219C:ATG2/YNL242W:MRPL17/YNL252C:BNI1/YNL271C:WSC2/YNL283C:YNL296W:DAL82/YNL314W:FIG4/YNL325C:VPS27/YNR006W:ATG3/YNR007C:ATP23/YNR020C:SSK2/YNR031C:RSM19/YNR037C:BRE5/YNR051C:MDM38/YOL027C:MSE1/YOL033W:PEX15/YOL044W:IRA2/YOL081W:MPD2/YOL088C:HMI1/YOL095C:SHR5/YOL110W:MDY2/YOL111C:RPS19A/YOL121C:VPS68/YOL129W:ALG6/YOR002W:SHE4/YOR035C:ETT1/YOR051C:CYT1/YOR065W:ALG8/YOR067C:VAM10/YOR068C:VPS5/YOR069W:TMA46/YOR091W:MRPL23/YOR150W:PET123/YOR158W:LIP5/YOR196C:NPT1/YOR209C:RUD3/YOR216C:MCT1/YOR221C:HNT3/YOR258W:PNT1/YOR266W:MOD5/YOR274W:CAF20/YOR276W:SNF2/YOR290C:TIM18/YOR297C:MIP1/YOR330C:VMA4/YOR332W:MRS2/YOR334W:MNE1/YOR350C:MSC6/YOR354C:PDE2/YOR360C:GPB1/YOR371C:MRPS16/YPL013C:EGD1/YPL037C:LGE1/YPL055C:MFM1/YPL060W:BRO1/YPL084W:MSY1/YPL097W:VPS30/YPL120W:RNY1/YPL123C:COX11/YPL132W:UME1/YPL139C:PPT2/YPL148C:ATG5/YPL149W:PET20/YPL159C:TRE1/YPL176C:CTI6/YPL181W:RTC6/YPL183W-A:NEW1/YPL226W:ALG5/YPL227C:KAR9/YPL269W:NTO1/YPR031W:TIP41/YPR040W:ISA2/YPR067W:MED1/YPR070W:MDM36/YPR083W:MRPL51/YPR100W:CLB2/YPR119W:MRP2/YPR166C:QCR2/YPR191W |
| 72666 | establishment of protein localization to vacuole | ATG8/YBL078C:BSD2/YBR290W:ATG18/YFR021W:MVB12/YGR206W:HSE1/YHL002W:ATG7/YHR171W:ATG27/YJL178C:DID2/YKR035W-A:VPS13/YLL040C:SRN2/YLR119W:ATG23/YLR431C:MVP1/YMR004W:COG6/YNL041C:ATG2/YNL242W:VPS27/YNR006W:ATG3/YNR007C:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:ATG5/YPL149W:TRE1/YPL176C |
| 33365 | protein localization to organelle | ATG8/YBL078C:BSD2/YBR290W:PEX3/YDR329C:VPS74/YDR372C:ERD1/YDR414C:AFG3/YER017C:KAP123/YER110C:OXA1/YER154W:ATG18/YFR021W:PEX14/YGL153W:MVB12/YGR206W:HSE1/YHL002W:SLT2/YHR030C:ATG7/YHR171W:PEP8/YJL053W:PBS2/YJL128C:VPS35/YJL154C:FAR1/YJL157C:ATG27/YJL178C:MOG1/YJR074W:DID4/YKL002W:PEX1/YKL197C:DID2/YKR035W-A:VPS13/YLL040C:SRN2/YLR119W:SEC72/YLR292C:ATG23/YLR431C:MVP1/YMR004W:COG6/YNL041C:ATG2/YNL242W:VPS27/YNR006W:ATG3/YNR007C:MDM38/YOL027C:PEX15/YOL044W:MDY2/YOL111C:VPS68/YOL129W:VPS5/YOR069W:PNT1/YOR266W:TIM18/YOR297C:BRO1/YPL084W:VPS30/YPL120W:ATG5/YPL149W:TRE1/YPL176C |
| 72665 | protein localization to | ATG8/YBL078C:BSD2/YBR290W:ATG18/YFR021W:MVB12/Y |

| | | |
|---|---|---|
| | vacuole | GR206W:HSE1/YHL002W:ATG7/YHR171W:ATG27/YJL178C:DID2/YKR035W-A:VPS13/YLL040C:SRN2/YLR119W:ATG23/YLR431C:MVP1/YMR004W:COG6/YNL041C:ATG2/YNL242W:VPS27/YNR006W:ATG3/YNR007C:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:ATG5/YPL149W:TRE1/YPL176C |

| **Appendix C. Significant GO Term Finder Categories from Viability Assay** | | | | |
|---|---|---|---|---|
| **GOID** | **GO_term** | **Cluster frequency** | **Background frequency** | **P-value** |
| 6623 | protein targeting to vacuole | 10 out of 43 genes, 23.3% | 94 out of 7168 background genes, 1.3% | 2.79E-08 |
| 72666 | establishment of protein localization to vacuole | 10 out of 43 genes, 23.3% | 94 out of 7168 background genes, 1.3% | 2.79E-08 |
| 72665 | protein localization to vacuole | 10 out of 43 genes, 23.3% | 95 out of 7168 background genes, 1.3% | 3.10E-08 |
| 7034 | vacuolar transport | 11 out of 43 genes, 25.6% | 146 out of 7168 background genes, 2.0% | 1.26E-07 |
| 45324 | late endosome to vacuole transport | 7 out of 43 genes, 16.3% | 36 out of 7168 background genes, 0.5% | 2.76E-07 |
| 16197 | endosomal transport | 8 out of 43 genes, 18.6% | 79 out of 7168 background genes, 1.1% | 3.62E-06 |
| 19941 | modification-dependent protein catabolic process | 10 out of 43 genes, 23.3% | 176 out of 7168 background genes, 2.5% | 1.31E-05 |
| 6511 | ubiquitin-dependent protein catabolic process | 10 out of 43 genes, 23.3% | 176 out of 7168 background genes, 2.5% | 1.31E-05 |
| 70727 | cellular macromolecule localization | 14 out of 43 genes, 32.6% | 431 out of 7168 background genes, 6.0% | 2.30E-05 |
| 51603 | proteolysis involved in cellular protein catabolic process | 10 out of 43 genes, 23.3% | 190 out of 7168 background genes, 2.7% | 2.72E-05 |
| 43162 | ubiquitin-dependent protein catabolic process via the multivesicular body sorting pathway | 5 out of 43 genes, 11.6% | 22 out of 7168 background genes, 0.3% | 3.35E-05 |
| 43632 | modification-dependent macromolecule catabolic process | 10 out of 43 genes, 23.3% | 195 out of 7168 background genes, 2.7% | 3.48E-05 |

| | | | | |
|---|---|---|---|---|
| 6886 | intracellular protein transport | 12 out of 43 genes, 27.9% | 311 out of 7168 background genes, 4.3% | 3.70E-05 |
| 44257 | cellular protein catabolic process | 10 out of 43 genes, 23.3% | 203 out of 7168 background genes, 2.8% | 5.07E-05 |
| 15031 | protein transport | 12 out of 43 genes, 27.9% | 324 out of 7168 background genes, 4.5% | 5.78E-05 |
| 6508 | proteolysis | 10 out of 43 genes, 23.3% | 208 out of 7168 background genes, 2.9% | 6.37E-05 |
| 6605 | protein targeting | 11 out of 43 genes, 25.6% | 265 out of 7168 background genes, 3.7% | 6.47E-05 |
| 44265 | cellular macromolecule catabolic process | 12 out of 43 genes, 27.9% | 330 out of 7168 background genes, 4.6% | 7.05E-05 |
| 30163 | protein catabolic process | 10 out of 43 genes, 23.3% | 212 out of 7168 background genes, 3.0% | 7.61E-05 |
| 72594 | establishment of protein localization to organelle | 10 out of 43 genes, 23.3% | 217 out of 7168 background genes, 3.0% | 9.45E-05 |
| 34613 | cellular protein localization | 13 out of 43 genes, 30.2% | 410 out of 7168 background genes, 5.7% | 9.88E-05 |

| **Appendix D. Gene List for Signficant Term Finder Process Categories for Process** | | |
|---|---|---|
| **GOID** | **GO_term** | **Gene(s) annotated to the term** |
| 6623 | protein targeting to vacuole | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 72666 | establishment of protein localization to vacuole | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 72665 | protein localization to vacuole | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 7034 | vacuolar transport | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:VPS24/YKL041W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 45324 | late endosome to vacuole transport | HSE1/YHL002W:VPS24/YKL041W:DID2/YKR035W-A:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 16197 | endosomal transport | HSE1/YHL002W:VPS24/YKL041W:DID2/YKR035W-A:VPS68/YOL129W:VPS5/YOR069W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 19941 | modification-dependent protein catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 6511 | ubiquitin-dependent protein catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 70727 | cellular macromolecule | BSD2/YBR290W:MSN5/YDR335W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:SHR5/YOL110W:VPS68/YOL129 |

| | | |
|---|---|---|
| | localization | W:SHE4/YOR035C:VPS5/YOR069W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 51603 | proteolysis involved in cellular protein catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 43162 | ubiquitin-dependent protein catabolic process via the multivesicular body sorting pathway | DOA4/YDR069C:VPS24/YKL041W:SRN2/YLR119W:BRO1/YPL084W:TRE1/YPL176C |
| 43632 | modification-dependent macromolecule catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 6886 | intracellular protein transport | BSD2/YBR290W:MSN5/YDR335W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:SHR5/YOL110W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 44257 | cellular protein catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 15031 | protein transport | BSD2/YBR290W:MSN5/YDR335W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:SHR5/YOL110W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 6508 | proteolysis | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 6605 | protein targeting | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:SHR5/YOL110W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |

| | | |
|---|---|---|
| 44265 | cellular macromolecule catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:NOT3/YIL038C:LSM1/YJL124C:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 30163 | protein catabolic process | BSD2/YBR290W:DOA4/YDR069C:PRE9/YGR135W:VPS24/YKL041W:DOA1/YKL213C:SRN2/YLR119W:GID8/YMR135C:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 72594 | establishment of protein localization to organelle | BSD2/YBR290W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:VPS68/YOL129W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |
| 34613 | cellular protein localization | BSD2/YBR290W:MSN5/YDR335W:HSE1/YHL002W:ATG7/YHR171W:DID2/YKR035W-A:SRN2/YLR119W:MVP1/YMR004W:SHR5/YOL110W:VPS68/YOL129W:VPS5/YOR069W:BRO1/YPL084W:VPS30/YPL120W:TRE1/YPL176C |

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