# Phenotypic Investigation of Biofilm <br> Formation and Transcriptional Analysis of Invasive Growth of Commercial Wine Saccharomyces cerevisiae 

Ee Lin Tek

A thesis submitted for the degree of Doctor of Philosophy


## THE UNIVERSITY of ADELAIDE

Department of Wine and Food Science
Faculty of Science
The University of Adelaide
September 2017

## Contents

Abstract ..... viii
Declaration statement ..... x
Acknowledgements ..... xi
Thesis overview and structure ..... xii
1 Literature review ..... 1
1.1 Commercial wine yeast in the vineyard and winery ..... 2
1.2 Yeast's lifestyle as multicellular communities ..... 3
1.3 Biofilm formation of $S$. cerevisiae ..... 4
1.4 Biofilm-related phenotypes in $S$. cerevisiae ..... 7
1.5 Mat formation in response to nutrient availability ..... 9
1.6 Regulation of mat formation, filamentous growth and invasive growth ..... 10
1.7 Cell-cell communication in morphological transitions ..... 11
1.8 Quorum sensing in yeast ..... 11
1.9 Hydrogen sulfide is a potential cell-cell signalling molecule in $S$. cerevisiae ..... 13
1.10 Research questions and objectives ..... 14
2 Wine yeast biofilms ..... 15
Contextual statement ..... 15
Statement of Authorship ..... 16
Manuscript: Evaluation of the ability of commercial wine yeasts to form biofilms (mats) and adhere to plastic: implications for the microbiota of the winery environment ..... 18
2.1 Abstract ..... 19
2.2 Keywords ..... 19
2.3 Introduction ..... 19
2.4 Materials and Methods ..... 21
2.4.1 Yeast strains and media ..... 21
2.4.2 Mat formation assays ..... 23
2.4.3 Vitality and nuclear staining ..... 24
2.4.4 DNA preparation and PCR conditions ..... 24
2.4.5 Mat culture harvest and total RNA extraction ..... 25
2.4.6 Quantitative real-time PCR ..... 25
2.4.7 Plastic adhesion assays ..... 26
2.4.8 Winery hose adhesion assays ..... 27
2.5 Results ..... 27
2.5.1 Prototrophic diploid $\Sigma 1278$ b as a laboratory reference ..... 27
2.5.2 Wine yeasts display diverse mat architectures ..... 31
2.5.3 Cell morphologies in the mat rim and mat body reveal distinct lifestyles ..... 31
2.5.4 Some wine strains grow invasively at the start of mat formation ..... 31
2.5.5 Wine strain L2056 forms mats with a more rapidly expanding sector ..... 34
2.5.6 Plastic adhesion ..... 36
2.5.7 Wine yeast grow invasively and conduct fermentation on grape pulp soft agar ..... 37
2.5.8 Wine strain L2056 forms initial attachment on winery hose soft plastic ..... 38
2.6 Discussion ..... 39
2.7 Funding ..... 41
2.8 Acknowledgements ..... 42
2.9 Supplementary Data ..... 42
2.9.1 Methods ..... 42
2.9.2 Figures ..... 43
3 Mat formation in a low nitrogen medium ..... 49
Contextual statement ..... 49
Statement of Authorship ..... 50
Manuscript: Factors influencing filamentous and invasive growth of yeast cells in mat formation in a low nitrogen environment ..... 52
3.1 Abstract ..... 53
3.2 Keywords ..... 53
3.3 Introduction ..... 53
3.4 Materials and Methods ..... 54
3.4.1 Yeast strains and media ..... 54
3.4.2 SLAD mat assays ..... 56
3.4.3 Microscopy imaging and image processing ..... 56
3.4.4 Conditioned medium mat assays ..... 56
3.4.5 Nitrogen and glucose measurement ..... 57
3.5 Results ..... 57
3.5.1 Nitrogen limitation induces filamentous and invasive growth in mats ..... 57
3.5.2 Mat size and biomass increases with increasing ammonium sulfate ..... 60
3.5.3 Filamentous growth is inhibited by a neighbouring mat ..... 60
3.5.4 Conditioned medium affects cell elongation in liquid culture but not invasive growth ..... 61
3.5.5 Effect of aromatic alcohols, ethanol, hydrogen sulfide and sulfite on yeast growing on SLAD mat assays ..... 62
3.6 Discussion ..... 66
3.7 Funding ..... 69
3.8 Acknowledgements ..... 69
3.9 Supplementary Data ..... 69
3.9.1 Methods ..... 69
4 Understanding wine yeast invasive growth through transcriptional analysis ..... 72
Contextual statement ..... 72
Statement of Authorship ..... 73
Manuscript: Transcriptional analysis of invasively growing wine strains of Saccharomyces cerevisiae ..... 75
4.1 Keywords ..... 76
4.2 Summary ..... 76
4.3 Introduction ..... 76
4.4 Results and Discussion ..... 78
4.4.1 Global change in gene expression between surface and invasively growing cells ..... 78
4.4.2 Glucose import ..... 80
4.4.3 Carbohydrate metabolism / fungal-type cell wall organisation ..... 80
4.4.4 Medium-chain fatty acid biosynthesis pathway ..... 81
4.4.5 Genetic interaction network analysis predicts genes modulating invasive growth ..... 82
4.4.6 Protein interaction network analysis suggests Ssa 2 p as the major determinant of invasive growth ..... 84
4.4.7 Expression levels of transcription factor genes do not correlate with their previously reported involvement in invasive growth ..... 86
4.4.8 Cellular water homeostasis: aquaglyceroporin gene FPS1 is required for invasive growth ..... 88
4.5 Conclusions ..... 89
4.6 Experimental Procedures ..... 90
4.6.1 Yeast strains ..... 90
4.6.2 Genomic DNA preparation and PCR conditions ..... 90
4.6.3 Low nitrogen invasive growth assays ..... 91
4.6.4 Sample harvest and RNA extraction ..... 91
4.6.5 RNA sequencing and analysis ..... 92
4.6.6 Network analysis ..... 92
4.7 Acknowledgements ..... 93
4.8 Supporting Information ..... 93
4.8.1 Tables ..... 93
4.8.2 Figures ..... 97
5 Conclusions ..... 99
5.1 Summary of findings ..... 99
5.2 Contribution to knowledge ..... 100
5.3 Limitations and future directions ..... 102
Appendix A Method development for mat formation and plastic adhesion assays ..... 104
A. 1 Mat formation assays ..... 104
A.1.1 Reproduction of results by Reynolds and Fink (2001) and test mat formation ability of commercial wine yeast strains ..... 104
A.1.2 Evaluation of medium preparation methods for mat assays ..... 105
A.1.3 Evaluation of mat inoculation with cells at exponential growth phase107
A. 2 Plastic adhesion assays ..... 108
A.2.1 Refinement of staining and washing methods ..... 108
A.2.2 Determination of the maximum absorption of Crystal Violet ..... 109
Appendix B Method development for mat formation assays in a low nitrogen medium (SLAD) ..... 111
B.0.1 Determination of inoculation rate ..... 111
B.0.2 Preliminary study on the effect of sulfide on mat formation in SLAD 116
Appendix C Attempt to construct $\Delta$ aqy1 in AWRI796 ..... 119
C.0.1 Transformation with homologous recombination ..... 119
C.0.2 Construction of KanMX gene replacement cassette from a plasmid. ..... 120
Appendix D Supporting information for Chapter 4 ..... 121
Bibliography ..... 146

## Nomenclature

## Term

Biofilm

Mat Thin layer of yeast biomass on low-density agar that resembles a film

Filamentous growth Interchangeable with pseudohyphal growth, a form of growth as a colony that has a filamentous shape, usually contains chains of elongated cells

Filamentous mat
Invasive growth A form of growth that penetrates agar
'Hub and spokes' mat A flat mat that has raised cables radiating from the hub

NB Filamentous growth and invasive growth are not ploidy-specific unless specified.

## Abstract

This study investigated the morphological properties, environmental effects on and gene expression of biofilms, more specifically referred to as mats, formed by laboratory and commercial wine strains of Saccharomyces cerevisiae. Two morphological assays were conducted: mat formation and plastic adhesion. Mat features varied between strains and included various architectures, cellular morphologies, and incidence of invasive growth. One commercial strain, L2056, formed mats where a sector produced a distinctive mat morphology, which was retained when subcultured. In considering the role of biofilms in winery conditions, mat formation assays were also performed with grape pulp and adhesion to the soft plastic of common winery hoses. All strains grew invasively on all agar media and appeared to conduct fermentation on the grape-pulp mat assay. Some strains also had the ability to adhere to winery hose plastic. When only limited nitrogen was available, both laboratory and commercial wine strains formed mats with a subpopulation of cells that switched to filamentous and invasive growth. Such invasive growth was influenced by nitrogen concentration, the presence of a neighbouring mat, and by the addition of yeast metabolites. Ethanol and hydrogen sulfide were found to enhance invasive growth of cells within mats exposed to low levels of nitrogen whereas tryptophol and 2-phenylethanol suppressed this enhancement. Sulfite was found to delay overall mat growth. In an effort to understand the cellular decision to switch morphology, changes in the transcriptome of invasively growing cells were studied. In this analysis, 272 genes were identified to be upregulated and 84 genes were downregulated in invasively growing cells. Of the ten largest differentially expressed genes, four were genes encoding hexose transporters (HXT3, HXT4, HXT6 and HXT7) which had an increase in transcript abundance up to 13 -fold. One hypothetical gene (AWRI796_5153) with a 6-fold increase in transcript abundance, has translation sequence homologous to an amidase domain. Following differential expression and Gene Ontology analysis, five GO categories represented the 37 significantly enriched GO terms in the upregulated gene set of invasively growing cells, these being glucose import, carbohydrate metabolic process, fungal-type cell wall organisation, medium-chain fatty acid biosynthetic process and cellular water homeostasis. Since cellular water homeostasis has not previously been associated with invasive growth, and four out of five genes in this group were found to be significantly upregulated in the invasively growing cells, further analysis of deletion mutants of each of these confirmed that FPS1, encoding the glycerol export protein, is required for invasive growth of yeast mats in low nitrogen conditions. In summary, this work reports the phenotypic properties of commercial wine yeast biofilms in
environments of both rich nutrient and low nitrogen, either in typical laboratory type agar media or in conditions simulating that of a grape or wine hose. The ability of these yeasts to form complex morphologies, grow invasively into grape solids and attach to winery hose plastic may confer their residency and survival in the vineyard and winery. The influence of different yeast metabolites and transcriptional changes in invasively growing cells provide further understanding of this morphogenetic program.

## Declaration statement

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

I give consent to this copy of my thesis, when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library Search and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

## En Lin Tek

$1 /$

## Acknowledgements

I would like to thank my supervisors, Prof Vladimir Jiranek, Dr Joanna Sundstrom and Dr Jennie Gardner, for their mentoring, guidance and encouragement throughout my candidature. Thanks to my independent advisor, Prof Steve Oliver, for the conceptual input and critiques for this project and the opportunity for me to undertake research at the University of Cambridge for 11 weeks. RNA-sequencing work would not be possible without Dr Andy Hesketh.

I wish to acknowledge the support from The University of Adelaide; scholarships and operating funds, these being the Adelaide Graduate Research Scholarship, the Research Abroad Scholarship, and the DR Stranks Travelling Fellowship provided by The University of Adelaide, and a Supplementary PhD Scholarship by Wine Australia. I would also like to acknowledge Dr Charles Boone (University of Toronto, Canada) for donating yeast strains in the $\Sigma 1278$ b background.

I am grateful to be part of the Wine Microbiology and Microbial Biotechnology research group where the staff and students offered generous assistance. Particularly, I would like to mention Nick, for solving many technical issues; Michelle, for providing yeast strain I1 and sharing knowledge on yeast metabolism; Tommaso, for helping to acquire winery hoses; and Jin, for giving advice on molecular biology techniques. I also thank Louise, Max, former students, Gang and Danfeng, former visitors, Marine, Sydney, and Helene for their companionship during my study.

Special thanks to Jess and Lisa for listening and sharing life journey and experiences, Alfredo for inspiring me to keep going when I was losing determination, Henry and Neesha for all the laughs, Christoph for the excitements, Thomas and Lenna for their moral support, friends and fellow dancers for keeping my life balance.

Finally, great appreciations to my beloved family for their support, respect, and love.

## Thesis overview and structure

Purposefully inoculated fermentations using commercial wine yeast are broadly implemented due to their success in completing fermentation efficiently and producing quality wine. Many commercial wine strains, usually Saccharomyces cerevisiae, were originally isolated from indigenous microflora of successful fermentations. These strains are now produced commercially and are widely available. Evidence suggests that the use of commercial strains leads to their presence and survival in the vineyard and winery. This could potentially lead to an alteration in native microflora in must and subsequently influence the regional character of wine. The mechanism of how these commercial yeasts remain in the winery environment is barely understood.

Biofilm formation is considered a survival strategy for many fungi and bacteria under harsh conditions. S. cerevisiae has been reported to be able to form biofilms, evidenced by the ability to grow into a mat and to adhere to plastic. These abilities have been investigated in not only laboratory strains, but also some clinical yeasts and yeasts isolated from wine grapes and must. It is likely that commercial wine yeasts also possess the ability to form biofilms which could drive their residency in the wine making environment. Current knowledge on yeast biofilms has focussed on the laboratory strain $\Sigma 1278$ b which is not directly applicable to the understanding of wine yeast biofilms since they are substantially genetically different. The study of biofilm formation by commercial wine yeast and their characteristics is therefore warranted.

Given that biofilms are a multicellular growth form, and nitrogen is known to be essential for yeast proliferation, biofilm formation could be affected by nitrogen availability. Lack of nitrogen has been shown to induce a pseudohyphal (filamentous) and invasive growth response in yeast. Filamentous mats can be formed when cells are starved for glucose but the mat formation response to low nitrogen has not been reported. Filamentous and invasive growth responses can be manipulated by other environmental triggers and putative signalling molecules such as temperature, pH , atmosphere, preservatives and fusel alcohols. Studies have shown that cell-cell communication can occur in biofilm formation, but the involvement of this system in yeast, especially $S$. cerevisiae biofilms is poorly understood.

In a quest to understand wine yeast biofilms in greater details, the present study has three aims:

1. Investigation of commercial wine yeast biofilm-forming ability and characteristics;
2. Exploration of mat formation in low nitrogen conditions and the influence of putative quorum sensing or signalling molecules; and
3. Study the genetic regulation of wine yeast biofilms or related phenotypes.

This dissertation has been organised in several chapters to present background information, reports of studies to answer each of the aims, and a conclusion. Chapter 1 establishes the field of knowledge and summarises critical gaps for the present study. Areas of discussion include yeast biofilms and related morphological phenotypes, influence of nitrogen availability, and potential signalling molecules. Chapter 2 presents mat characteristics and plastic adhesion properties of commercial wine yeast strains which addresses Aim 1. Chapter 3 addresses Aim 2 where data involving mat formation of commercial wine yeast strains in a low nitrogen environment and the response to potential signalling molecules is presented. Based on the findings from Chapter 3 that describe invasive growth as the primary observation in low-nitrogen, Chapter 4 presents the investigation of transcriptional changes of invasively growing wine yeast. Chapter 5 is a summary of the main findings including how this work contributes to current knowledge, limitations and future directions of the work.

Chapters 2-4 are presented as unsubmitted work prepared in manuscript style. For consistency, the typing, format, and referencing styles have been adjusted. Numbering of figures and tables has also been modified according to the order in the dissertation. References from all chapters can be found in the Bibliography.

## Chapter 1

## Literature review

## Contextual statement

This literature review was mostly written within the first six months of candidature and only covers the literature up to August 2014. The purpose of this literature review was to provide the background information and establish a theoretical framework for this PhD project. For a more updated literature, please refer to the introduction section in Chapters 2 to 4.

### 1.1 Commercial wine yeast in the vineyard and winery

Traditional wine production takes advantage of indigenous yeasts in grape must and on winery equipment to carry out fermentation, i.e. uninoculated or indigenous fermentation as opposed to the relatively modern practice of purposeful inoculation with commercial wine yeast strains. The surface of intact grapes is predominantly colonised with species of Kloeckera, Hanseniaspora, Candida, Cryptococcus, Rhodotorula, Pichia, Kluyveromyces, and Hansenula, which usually dominate the early stage of alcoholic fermentation (Fleet and Heard, 1993). The composition of microflora on grapes fluctuates depending on climatic influences, soil and viticulture practices, grape variety, the incidence of physical damage of grapes, and potential insect vectors (Mortimer and Polsinelli, 1999; Pretorius et al., 1999; Stefanini et al., 2012). The yeast flora of must is further influenced by harvest method, transport time, grape temperature, and must treatment (Pretorius et al., 1999). Yeasts resident on winery equipment are likely introduced through contact with grapes, use of commercial starter cultures, and use of oak barrels with the source varying depending on the surface nature of equipment and cleaning and sanitisation practices (Martini, 1993; Ciani et al., 2004; Goddard et al., 2010). As the fermentation progresses, conditions usually favour the growth of Saccharomyces cerevisiae, which often becomes predominant at the later stage of the process. Due to a variety of factors that influence the microflora in must, the microbial composition of an uninoculated fermentation is highly variable between fermentations, vintages and subsequently is unpredictable.

The capacity to control and predict fermentation aids winemakers to produce quality products. This has led to the common use of commercial starter culture preparations. A large selection of wine yeast is manufactured in an active dry form and is available to inoculate grape must. For large-scale wineries, this method is beneficial since the use of commercial cultures is more likely to produce consistent, reliable and predictable outcomes. In addition to ethanol and nutrient stress tolerance, commercial wine yeast are also selected based on organoleptic properties such as desirable concentrations of organic acids and volatile thiols and little to no production of compounds generally considered as faults, such as hydrogen sulfide.

The use of commercial wine yeast for inoculation has become common practice since the second half of the twentieth century, however, there are some wineries that continue to use the traditional uninoculated method. This is mainly a result of the belief that the regional character will be retained in the wine, due to the presence of indigenous microbes from the region specific to the grapes (rather than inoculation with a purchased commercial yeast). An alternative that some winemakers choose is to use a reduced amount of a single culture or perform mixed culture inoculation with non-Saccharomyces species. Some studies report benefits of this practice, such as enhancing wine quality and complexity (Comitini et al., 2011; Azzolini et al., 2012; Gobbi et al., 2013). More specifically, the
mixed culture fermentation of Lachancea thermotolerans and $S$. cerevisiae reduced pH and enhanced the production of 2-phenylethanol and glycerol, and the differences were also detected in sensory analysis (Gobbi et al., 2013). Also, the combination of Metschnikowia pulcherrima and $S$. cerevisiae enhanced medium-chain fatty acid, 2-phenylethanol and isoamyl acetate production and increased polysaccharide content in wine (Comitini et al., 2011). Furthermore, the use of Torulaspora delbrueckii with $S$. cerevisiae enhanced the aroma of Amarone wine by affecting alcohol, fermentative ester, fatty acid and lactone content (Azzolini et al., 2012).

The frequent use of commercial wine yeast in wineries may result in survival of residual yeast on winemaking equipment, or in wine lees (which is often disposed of in close proximity) even after sanitation. The impact of these yeast in the winery and vineyard ecosystem remains unknown. There is evidence that traces of commercial wine yeast are found in proximal vineyards. Three out of 13 such sites recovered commercial yeasts isolated from vineyards in the coastal regions of Western Cape, South Africa (Van der Westhuizen et al., 2000). A three-year study of Portuguese and French vineyards found that dissemination of commercial yeast was primarily restricted to short distances, with $94 \%$ of recovered commercial yeasts at 10 to 200 m from the winery (Valero et al., 2005). However, the population varied from year to year. Historical use of commercial yeast can also affect yeast microflora in uninoculated fermentation. For instance, a study spanning seven years of uninoculated fermentations in a winery that had routinely used commercial strains to inoculate fermentations reported that eight out of ten of the dominant yeasts isolated were commercial strains that had previously been used in the winery (Blanco et al., 2011). Furthermore, S. cerevisiae, the common commercial wine yeast, has been found inhabiting the winery surfaces prior to harvest (Bokulich et al., 2013). Residual commercial yeast can therefore survive in a winery or vineyard, and may consequently affect wine styles relying on fermentation with indigenous microflora. Information on how these yeast behave in a winery environment and mechanisms supporting their survival is limited.

### 1.2 Yeast's lifestyle as multicellular communities

Yeast cells experience many and varied nutritional challenges in both nature and industry where competition for nutrients leads to the selection of fitter individuals. For example, during alcoholic fermentation, nutrients are utilised and some, such as assimilable nitrogen, become limiting especially in high sugar and low nitrogen content grape juices. In other cases, yeast cells encounter physical or chemical stresses, such as high osmolarity, low pH and the presence of toxins (Bauer and Pretorius, 2000). In response to these environmental challenges, yeast often undergo morphological changes and develop diverse structured multicellular communities (Brückner and Mösch, 2012). The advantages of being in such a community are:
(a) having better protection from a harmful environment,
(b) having enhanced survival due to differentiation into specialised cell types, and
(c) the provision of nutrients to the surviving cells in the community when supplies are limited (Palková and Váchová, 2006).

The architecture of multicellular communities can be influenced by their environment. For example, some industrial yeast cells flocculate after completing alcoholic fermentation and they can either form a sediment as flocs or float on the liquid surface as flors (Martínez et al., 1997; Verstrepen et al., 2003). Yeast can also form biofilms, which can be defined as a structured cell aggregate that is attached to a solid or semisolid surface and is encased by an extracellular matrix (Ramage et al., 2005; Zara et al., 2005). Previous investigations of yeast biofilms focussed on clinical implications, such as biofilms of Candida spp., due to their association with virulence, pathogenesis and impact on human infections. S. cerevisiae also possesses common features of yeast and bacterial biofilms (Parsek and Singh, 2003; Hasan et al., 2009; Bojsen et al., 2012). Since S. cerevisiae is both a key industrial organism and one of the standard models of eukaryotic cellular biology, due to its genomic tractability, it is the preferred model to study mechanisms underlying yeast biofilm formation.

### 1.3 Biofilm formation of $S$. cerevisiae

Biofilms are communities of microorganisms attached to a surface, surrounded by selfproduced extracellular matrix, with the formation involving cell-surface and cell-cell interactions (O'Toole et al., 2000). The cycle of biofilm development consists of initial surface attachment, colonisation, biofilm maturation and cell detachment (Fig. 1.1; O'Toole et al., 2000).


Figure 1.1: Model of biofilm development cycle. Figure adapted from O'Toole et al. (2000).

Biofilm forming ability of $S$. cerevisiae was first reported by Reynolds and Fink (2001) where they demonstrated that $S$. cerevisiae was able to form a flat mat with 'hub and spokes' structure covering a large area across the surface of a YPD low-density agar medium (Fig. 1.2; Reynolds and Fink, 2001).


Figure 1.2: A mat formed by a haploid $S$. cerevisiae $\Sigma 1278$ b strain on a $0.3 \%$ agar YPD plate after 13 days at $25^{\circ} \mathrm{C}$. Figure adapted from Reynolds and Fink (2001).

The group also showed that $S$. cerevisiae was able to adhere to plastic and adhesion was enhanced when cells were grown in low glucose conditions, indicating a nutrient-mediated response (Reynolds and Fink, 2001). Adhesion is an indication of the first step in biofilm development in pathogenic yeast and bacteria (O’Toole et al., 2000). Mat formation is thought to be similar to the ability to 'slide' on a low-density agar medium observed in non-flagellated Mycobacterium spp. which has a close connection with biofilm formation (Martínez et al., 1999; Recht et al., 2000). This form of translocation requires cell surface glycopeptidolipids. Similarly, both structured mat formation and plastic adhesion require Flo11p, a yeast adhesion-related cell surface glycoprotein. When FLO11 was deleted, yeast cells adhered poorly to plastic and formed a poorly spreading mass of cells without complex structure (Reynolds and Fink, 2001). In this report, the term "biofilm" will be used to describe all forms of surface-attached multicellular communities with extracellular matrix and any related biofilm-forming ability tests such as adhesion, whereas "mat" refers specifically to the thin layer of yeast biomass that resembles a film on low-density agar.

Following the discovery of S. cerevisiae's ability to form biofilms, many studies have investigated genes affecting mat formation and the regulatory pathways involved. Numerous signalling pathways have been identified that regulate the expression of $F L O 11$ (Fig. 1.3; Brückner and Mösch, 2012). Briefly, these include the mitogen-activated protein kinase (MAPK) pathway, the cAMP-PKA pathway, the SNF pathway, and the RIM pathway. A handful of FLO11-independent pathways have also been reported, such as the multivesicular body protein sorting pathway, the cell wall integrity pathway that is not via MAPK cascade, and the molecular chaperone of 70 kDa heat shock proteins (Martineau et al., 2007; Sarode et al., 2011, 2014).


Figure 1.3: Regulation of $F L O 11$ expression. Arrows indicate positive regulation and inhibition is shown by bars. Figure adapted from Brückner and Mösch (2012).

So far, these $S$. cerevisiae biofilm studies have mainly been investigated in common laboratory strains. Wine strains of $S$. cerevisiae are known to be genetically different compared to laboratory strains, and this can affect their phenotypes (Borneman et al., 2008, 2011). The ability to form biofilms seems to be an inherent property for most microbes to survive in natural challenging environments (Costerton et al., 1995). Wine yeast are the dominant yeasts historically found in fermenting grape musts and where they have undergone natural selection driven by the conditions in grape juice fermentation (Querol et al., 1994). This may include the ability to form biofilms. Casalone and colleagues (2005) reported the ability of nine wine yeast isolates from grape and must to form mats that varied in size. S. cerevisiae has also been isolated from a mixed population biofilm developed on the rotating biological contactor disc in winery wastewater systems (Malandra et al., 2003). During the wastewater treatment process, industrial yeasts including $S$. cerevisiae adapted to the aerobic conditions in wastewater, combined with bacteria forming mixed population biofilms on the surface of the disc while degrading organic compounds (Malandra et al., 2003). This formation is beneficial because it can reduce the chemical oxygen demand of wastewater and bulking problems (Andreottola et al., 2005). The mechanism of this development is not completely understood. Therefore, an investigation of wine yeast biofilm formation is important within the context of the wine industry.

Biofilm formation might also serve as a model of survival to contribute to the understanding of how wine yeast respond to nutritional status such as during the course of fermentation. Even though $S$. cerevisiae is the principal organism for alcoholic fermentation, it is not usually prevalent on healthy intact grape berries, instead, it is commonly found on damaged grape berries and in the winery (Mortimer and Polsinelli, 1999; Bokulich et al., 2013). Damaged berries allow wine yeast to access rich nutrients from the semisolid grape interior, and hence encourage colonisation. An understanding of the successful yeast colonisation and behaviour on grapes would also be of great interest. More importantly,
the understanding of biofilm formation of commercial wine yeast could serve as the possible mechanisms for their residency and survival in the vineyard and winery.

### 1.4 Biofilm-related phenotypes in $S$. cerevisiae

In $S$. cerevisiae, the cell surface glycoprotein, Flo11p, required for mat formation and plastic adhesion, is also required for other phenotypes, such as invasive and filamentous growth (Lambrechts and Bauer, 1996; Lo and Dranginis, 1998). Invasive growth involves growing cells penetrating an agar medium. Haploid yeast cells have been shown to grow invasively in response to glucose depletion, which is termed haploid invasive growth (Cullen and Sprague, 2000). The authors also observed a filamentous morphology containing elongated cells that had a unipolar budding pattern associated with invasive growth (Fig. 1.4; Cullen and Sprague, 2000, 2002). Palecek and colleagues (2000) further showed that unipolar budding with or without cell elongation was sufficient to promote invasive growth.


Figure 1.4: (A) Microcolonies forming from single cells of $\Sigma 1278$ b on Synthetic Complete medium lacking glucose after 24 h visualised by light microscopy at $200 \times$ magnification. Inset image represents an example of a microcolony formed in the presence of glucose. (B) A microcolony grown on SC medium lacking glucose visualised perpendicular to the plane of agar invasion by light microscopy. All images are at the same scale, with scale bar in (A) representing $40 \mu \mathrm{~m}$. Figure adapted from Cullen and Sprague (2000).

Diploid cells have been shown to respond to nitrogen depletion, by growing into colonies with filamentous form where the filamentous regions contained chains of elongated cells growing away from the colony (Fig. 1.5; Gimeno et al., 1992). This morphology is similar to the hyphae formed by filamentous fungi, and therefore has been termed diploid pseudohyphal growth. The authors also reported that cells of diploid pseudohyphal growth can invade into agar.


Figure 1.5: (A) Filamentous colonies formed by diploid cells of CGX19, a strain congenic to the $\Sigma 1278$ b genetic background, on a low nitrogen medium after 11 days of incubation. Scale bar, 0.2 mm . (B) A high magnification view of a filamentous colony of the same strain on a low nitrogen medium after 2 days of incubation. Scale bar, $30 \mu \mathrm{~m}$. Figure adapted from Gimeno et al. (1992).

Filamentous growth (pseudohyphal growth) is a complex morphogenetic differentiation program that is tightly controlled with cell polarity, cell cycle and cell adhesion (Cullen and Sprague, 2012). At the start of a new cell cycle, $G_{1}$, cell polarity is determined by bud-site-selection proteins, which will direct bud growth (Park and Bi, 2007). Haploid cells bud in an axial pattern whereas diploid cells bud in a bipolar pattern (Chant and Pringle, 1995). When a cue to switch to filamentous growth is encountered, cells of both ploidy switch to a distal-unipolar budding pattern through Bud8p localisation (Gimeno et al., 1992; Harkins et al., 2001; Cullen and Sprague, 2002). When a bud emerges, actin cables extend into the bud and the bud grows apically (Pruyne and Bretscher, 2000). When nutrition is limiting, apical growth is prolonged at $G_{2}$ phase, resulting in elongated cells (Kron et al., 1994). At the end of the cell cycle, cell adhesion proteins, such as Flo11p, enable cells to remain attached (Guo et al., 2000; Halme et al., 2004). Given that this differentiation occurs in response to nutrient limitation, it is widely believed that this represents a nutrient foraging response. Since nutrient fluctuation occurs in the winery environment, filamentous growth may also be employed for persistence and nutrient search.

Another biofilm-related phenotype is complex colony morphology or structured morphology from fluffy colonies, which also requires Flo11p (Granek and Magwene, 2010; Šťovíček et al., 2010). Fluffy colonies are raised but not smooth and have an aerial morphology. Colonies of such type produced a protective extracellular matrix, were more agar-adhesive, and may contain pseudohyphae and agar invasion ability (Šťovíček et al., 2010; Váchová et al., 2011). The extracellular matrix contained a glycoprotein of molecular weight $>200 \mathrm{kDa}$ that is not related to flocculins (Kuthan et al., 2003). A genome-wide transcriptome analysis showed that the fluffy formation involved cell wall remodelling, secretion and modification of cell wall/membrane proteins, amino acid metabolism and nutrient transport (Š̌̌ovíček et al., 2014). This formation that harbours multiple transcriptomic and phenotypic modulations is seen as a protective mechanism to survive in the wild environment. Similar traits may be part of biofilm formation to support colonisation.

### 1.5 Mat formation in response to nutrient availability

Most mat formation studies of $S$. cerevisiae have been conducted in rich media. However, regulation of the key gene in mat formation, FLO11, involves pathways that are dependent on nutritional signals including glucose and nitrogen (Fig. 1.3). The impact of glucose on mat formation has been reported. For instance, formation of the 'hub and spokes' structure on mats was delayed if glucose concentration was increased (Reynolds et al., 2008). In contrast, S. cerevisiae formed a filamentous mat, a mat that has filamentous periphery, on a glucose-limiting medium (Fig. 1.6; Karunanithi et al., 2012). It appeared that both 'hub and spokes' structure on mats and filamentous growth are impacted by glucose availability. It is unclear if filamentous growth contributed to the 'hub and spokes' formation.


Figure 1.6: (A) Mats formed by $\Sigma 1278$ b on $0.3 \%$ agar YEPD media (top panel; containing glucose) and $0.3 \%$ agar YEP media (bottom panel; lacking glucose). Photographs were taken after 4 days (YEPD) and 15 days (YEP) of incubation. Scare bar, 1 cm . (B) Microscopic examination of mat perimeters in (A). Scale bar, $100 \mu \mathrm{~m}$. Figure adapted from Karunanithi et al. (2012).

Nitrogen is well known to be essential for yeast growth, and therefore required for wine yeast to function efficiently for alcoholic fermentation (Bell and Henschke, 2005). Inadequate nitrogen in the second half of oenological fermentations is common and often results in stuck or sluggish fermentation. Yeast readily utilise all available nitrogen in a must fermentation, and thus they would be commonly exposed to a nitrogen-depleted environment. Since a mat is formed by expansion through the continuous cell division from the mat edge, nitrogen, or lack thereof may be an important factor for this expansion. This nutrient has not been thoroughly investigated for its influence on mat formation, although a few studies demonstrated that nitrogen limitation induced filamentous and invasive growth (Gimeno et al., 1992; Casalone et al., 2005; Chen and Fink, 2006). Filamentous and invasive growth can be affected by other metabolites or environmental factors. For example, fusel
alcohols, by-products of amino acid catabolism via the Ehrlich pathway, have been shown to stimulate hyphal-like elongated cells, which could lead to multicellular filamentation (Dickinson, 1994, 1996). Other environmental factors that have been reported to affect invasive growth included salt, preservatives, pH , temperature, and modified atmosphere (Zupan and Raspor, 2010). This wide variety of stimulators suggest that there are many factors and biological pathways affecting this mode of growth and these may be synergetic or antagonistic in the presence of multiple stimulators.

### 1.6 Regulation of mat formation, filamentous growth and invasive growth

Although mat formation, filamentous growth and invasive growth require Flo11p and some shared core signalling pathways, large-scale studies have found specific genes regulating each phenotype (Jin et al., 2008; Ryan et al., 2012; Shively et al., 2013). To identify genes necessary for filamentous growth induced by butanol in $S$. cerevisiae, Jin and colleagues (2008) screened a library of 3,627 transposon insertion gene disruption constructs and 2,043 overexpression constructs in a haploid version of filamentous strain $\Sigma 1278$ b. Of 487 genes identified as being necessary for filamentous growth, 243 were also necessary for haploid invasive growth. To study genes required for mat formation, filamentous growth as well as invasive growth, Ryan and colleagues (2012) screened both haploid and homozygous diploid $\Sigma 1278$ b gene deletion libraries. The group identified 688, 600 and 577 genes required for mat formation in rich nutrient low-density agar medium, diploid pseudohyphal growth in nitrogen-limited medium, and haploid invasive growth in rich medium, respectively. Haploid invasive growth and mat formation were found to be significantly correlated, with 300 genes common to both phenotypes. Sixty-one core genes required for all three phenotypes, included FLO11 and a number of genes encoding proteins involving in the regulation of $F L O 11$ gene expression. These were components of the Rpd3L histone deacetylase complex, members of the Rim101 signalling pathway, and transcription factors for FLO11, Mit1p, Tec1p, Flo8p, and Mss11p. In contrast, Shively and colleagues (2013) found 551 genes that when overexpressed exaggerated diploid invasive growth in sufficient nitrogen and highlighted the potential role of nuclear Hog1p in repressing invasive growth. The findings from these studies suggest that each of these growth transitions have unique regulatory networks and these may be different for haploid and diploid cells.

### 1.7 Cell-cell communication in morphological transitions

Cell-cell communication via signals could lead to morphological changes and contribute to yeast community organisation (Honigberg, 2011). Intercellular communication such as quorum sensing (QS) is responsible for group motility, biofilm formation and maintenance, and production of virulence factors in bacteria (Miller and Bassler, 2001; Sperandio et al., 2002). This is similar to the communication system that controls physiological functions in multicellular organisms.

Cell-cell communication involves a chemical signalling molecule, secreted by one cell and sensed by another to trigger diverse behaviours (Youk and Lim, 2014). A wellstudied example is the yeast mating system (Cottier and Mühlschlegel, 2011). Pheromones are peptides, namely a-factor produced by MATa cells and $\alpha$-factor produced by $\alpha$ cells. Haploid cells of each mating type sense and respond to the opposite factor, triggering a morphological response, forming a structure called a 'shmoo', resulting in directional growth towards the other cell. When shmoos touch, mating occurs and diploid cells are formed.

A QS system, on the other hand, relies on a particular cell density to be reached before a function is triggered. The concentration of a signalling molecule increases as cell numbers increase. When the 'quorum' threshold is reached, the molecule induces intracellular signalling pathway(s), altering gene expression, and resulting in a population response. This is widely used and well researched in bacterial populations, and to some extent in yeast populations (Henke and Bassler, 2004; Albuquerque and Casadevall, 2012).

### 1.8 Quorum sensing in yeast

The QS phenomenon was not described in eukaryotes until the $21^{\text {st }}$ century when farnesol was identified as a cell-density-dependent signalling molecule in Candida albicans (Hornby et al., 2001). Farnesol inhibits, while tyrosol initiates, the switch from yeast-form cells to hyphae formation at a threshold concentration (Hornby et al., 2001; Chen et al., 2004). However, there are conflicting reports on the molecular pathway acted on by farnesol to prevent this morphological switch. Davis-Hanna and colleagues (2008) and Hall and colleagues (2011) showed that farnesol inhibited genes involved in the Ras-cAMP pathway that leads to hyphal formation but Sato and colleagues (2004) showed no effect from farnesol on this pathway.

Quorum sensing in $S$. cerevisiae has more recently been proposed. Tryptophol and 2-phenylethanol have been described as QS molecules as their production and action is cell-density-dependent (Chen and Fink, 2006). These aromatic alcohols are generated
from their corresponding amino acids, tryptophan and phenylalanine, via the Ehrlich pathway (Hazelwood et al., 2008). Similar to other fusel alcohols, they were shown to induce S. cerevisiae pseudohyphal formation (Dickinson, 1996; Chen and Fink, 2006). The effect was enhanced when nitrogen was scarce. For example, pseudohyphal formation was present on Synthetic Low Ammonium Dextrose agar which contained $50 \mu \mathrm{M}$ ammonium sulfate, but not on Synthetic Minimal Dextrose agar which contained 37 mM ammonium sulfate (Chen and Fink, 2006). The production of these aromatic alcohols was also greatly reduced when cells were grown in a medium containing greater than $500 \mu \mathrm{M}$ ammonium sulfate. Therefore, the production of tryptophol and 2-phenylethanol is regulated by both population density and the nutritional state of the environment independently.

Aromatic alcohols are important in wine production as they contribute to the complexity of wine aroma profiles (Francis and Newton, 2005). They are produced by yeast during fermentation in three enzymatic reactions comprising transamination, decarboxylation and dehydrogenation (Hazelwood et al., 2008). Two of the enzymes used in the transamination and decarboxylation steps, encoded by ARO9 and ARO10, are regulated by the transcription factor Aro80p (Iraqui et al., 1999). Tryptophol can upregulate ARO9 and ARO10 expression via Aro80p, resulting in a positive feedback loop to further stimulate aromatic alcohol synthesis (Chen and Fink, 2006). Likewise, high cell density also induces production via the same feedback regulation. On the contrary, ARO9 and ARO10 expression is repressed in high nitrogen conditions, consistent with the observation of low aromatic alcohol production when large amounts of ammonium sulfate are available (Chen and Fink, 2006).

Although the biosynthesis of tryptophol and 2-phenylethanol is understood, how these putative QS molecules induce the morphological transition from yeast-form to filamentous form is unclear. There are four signalling pathways known to regulate filamentous transition: the cAMP-PKA, MAPK, SNF and TOR pathways, which all target FLO11, the same genes required for mat formation, adhesion between cells, cell-to-surface adhesion, pseudohyphae formation and agar invasion (Sengupta et al., 2007; Cullen and Sprague, 2012). Both cAMP-PKA and MAPK pathways activate FLO11 while the SNF pathway regulates repressors of the FLO11 promoter (Kuchin et al., 2002; Braus et al., 2003). The FLO11 transcription factor regulated by the TOR pathway requires further investigation. Chen and Fink (2006) showed that tryptophol and 2-phenylethanol induced FLO11 expression and filamentation through Tpk2p, and its downstream Flo8p. Tpk2p is a subunit of PKA whereas Flo8p is the transcription factor of FLO11. The upstream elements of Tpk2p in the cAMP-PKA pathway were not required, neither were the elements of the MAPK pathway. Besides that, two transcription factors, Cat8p and Mig1p, were predicted to be responsible for regulating genes that were differentially expressed in response to the proposed QS aromatic alcohols (Wuster and Babu, 2010).

### 1.9 Hydrogen sulfide is a potential cell-cell signalling molecule in $S$. cerevisiae

Although work to fully describe a QS system is still underway for $S$. cerevisiae, there are molecules excreted by $S$. cerevisiae that result in a cell-cell signalling phenomenon and coordination, such as ammonia. Ammonia is produced by yeast colonies and is perceived as a signal by neighbouring colonies, resulting in growth inhibition towards the ammonium-producing neighbouring colonies (Palková et al., 1997). Another potential signalling molecule is hydrogen sulfide $\left(\mathrm{H}_{2} \mathrm{~S}\right)$. This molecule is released during fermentation when nitrogen is deficient (Jiranek et al., 1995; Gardner et al., 2002; Wang et al., 2003). Stuck fermentations caused by insufficient nitrogen are often difficult to restart, even when additional nitrogen is supplied thereafter. Reports suggested that this is due to inactivation of glucose transporters (Busturia and Lagunas, 1986). The presence of signalling compounds, such as $\mathrm{H}_{2} \mathrm{~S}$, may prevent the re-activation of the glucose transport system but this requires further investigation.

The production of $\mathrm{H}_{2} \mathrm{~S}$ is part of the sulfate assimilation pathway that leads to the biosynthesis of sulfur-containing amino acids, cysteine, methionine and glutathione (Thomas and Surdin-Kerjan, 1997). Hydrogen sulfide is an undesirable product in wine due to its rotten egg aroma. However, intracellular $\mathrm{H}_{2} \mathrm{~S}$ is thought to be responsible for metabolic synchronisation in a yeast population (Murray et al., 2003). When pulses of $\mathrm{Na}_{2} \mathrm{~S}$ were added, the respiratory cycle of the whole population spontaneously reset, suggesting that $\mathrm{H}_{2} \mathrm{~S}$ may act as a microbial cell-cell signalling molecule (Murray et al., 2003; Lloyd, 2006). Hydrogen sulfide signalling is recognised in animal systems to maintain oxygen homeostasis and mediate the response to nutritional status (Iranon and Miller, 2012).

In mammals, nitrogen restriction, particularly cysteine and methionine, delivers health benefits and longevity (Miller et al., 2005; Plaisance et al., 2011; Elshorbagy et al., 2013; Lees et al., 2014). Exposure of mice to $\mathrm{H}_{2} \mathrm{~S}$ resulted in the same health benefits as nitrogen restriction and offered protection against oxygen deprivation (Blackstone and Roth, 2007; Hine and Mitchell, 2015). Hydrogen sulfide also increased thermotolerance and lifespan in the nematode Caenorhabditis elegans (Miller and Roth, 2007). Similarly, $\mathrm{H}_{2} \mathrm{~S}$-mediated biological benefits have also been reported in yeast. The deletion of MET17 leads to $\mathrm{H}_{2} \mathrm{~S}$ accumulation and increased $\mathrm{H}_{2} \mathrm{~S}$ production on both BiGGY agar (containing bismuth salt and sulfite to be reduced to bismuth and sulfide forming brown to black precipitate) and synthetic grape juice medium (Linderholm et al., 2008). This mutant has an extended chronological lifespan when grown in minimal medium (Johnson and Johnson, 2014). Other benefits include increased resistance to heat shock, oxidative and heavy metal stresses, and metal chelate toxicity (Singh and Sherman, 1974; Brown et al., 2006; Hwang et al., 2007; Johnson et al., 2014). A microarray experiment has shown that there is significant overlap of gene expression in the presence of $\mathrm{H}_{2} \mathrm{~S}$ and a stress
response (Jia et al., 2011). Since the formation of $\mathrm{H}_{2} \mathrm{~S}$ integrates with a number of stress responses, including nitrogen restriction, $\mathrm{H}_{2} \mathrm{~S}$ could potentially be a signalling molecule that influences other nitrogen-deficient responses such as filamentous and invasive growth. Further work is required for this to be confirmed.

### 1.10 Research questions and objectives

S. cerevisiae is the common commercial wine yeast used in inoculated fermentations. The persistence of this species in the vineyard and winery is an important question, especially as this would affect winemaking that pursuits geographical characteristics from the native microflora. $S$. cerevisiae has been shown to be capable of forming biofilms in both environmental (wine and medical) and laboratory strains. These properties have however not been fully evaluated in commercial wine yeast strains. It is not clear whether the biofilm-related phenotypes such as filamentous and invasive growth co-existed with wine yeast biofilms. The relatedness of biofilm assays to the winemaking context is also lacking. The first part of this study is to investigate biofilm traits of commercial wine yeast on the standard assays - mat formation on a rich medium and plastic adhesion in a low glucose medium. The investigation is extended to mat formation on grape pulp and adhesion to winery hose plastic. This knowledge will contribute to determining if and how the yeast colonise and survive in a winery/vineyard environment.

Yeast are frequently exposed to nutrient fluctuation including nitrogen depletion. Filamentous colonies are formed on nitrogen-limited solid agar and can be enhanced by the putative $S$. cerevisiae quorum sensing molecules, tryptophol and 2-phenylethanol (Chen and Fink, 2006). However, mat formation response (on semisolid agar) to low nitrogen conditions has not been investigated. The second part of this study will contribute to this knowledge and determine if quorum sensing and signalling molecules have a synergetic or antagonistic effect on mat formation in a low nitrogen environment.

Biofilm formation by laboratory S. cerevisiae requires Flo11p (Reynolds and Fink, 2001). There are several signalling pathways leading to the expression of FLO11. It is unknown if biofilms formed by commercial wine yeast also require Flo11p and whether it is regulated in a similar way. The final part of this study aims to understand the biological processes of commercial wine yeast biofilms or associated phenotypes using RNA-sequencing.

## Chapter 2

## Wine yeast biofilms

## Contextual statement

The manuscript in this chapter addresses the first aim; to investigate the biofilm-forming ability of commercial wine yeasts. The study was conducted based on methods described by Reynolds and colleagues (2001) in the first $S$. cerevisiae biofilm publication. During attempts to reproduce mat and adhesion assays as per published methods, it became evident that further optimisation of these methods was required. Therefore, preliminary studies were conducted to finalise the methodology used in this manuscript and are outlined in Appendix A.

## Statement of Authorship

| Title of Paper | Evaluation of the ability of commercial wine yeasts to form biofilms (mats) and adhere to plastic: impact on microbiota in the winery environment |
| :---: | :---: |
| Publication Status | Г Published Г Accepted for Publication <br> $\Gamma$ Submitted for Publication F Unpublished and Unsubmitted work written in <br> manuscript style  |
| Publication Details | Written in manuscript style for FEMS Microbiology Ecology |

Principal Author

| Name of Principal Author (Candidate) | Ee Lin Tek |  |  |  |  |
| :--- | :--- | :---: | :---: | :---: | :---: |
| Contribution to the Paper | Performed all experiments and data analysis, interpreted data, and wrote manuscript. |  |  |  |  |
| Overall percentage (\%) | $70 \%$ |  |  |  |  |
| Certification: | This paper reports on original research I conducted during the period of my Higher Degree by <br> Research candidature and is not subject to any obligations or contractual agreements with a <br> third party that would constrain its inclusion in this thesis. I am the primary author of this paper. |  |  |  |  |
| Signature | $\quad$ Date |  |  |  | $04-09 / 17$ |

## Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:
i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to $100 \%$ less the candidate's stated contribution.

| Name of Co-Author | Joanna F. Sundstrom |  |
| :--- | :--- | :--- |
| Contribution to the Paper | Construction of FLO11 deletion in prototrophic $\Sigma 1278 \mathrm{~b}$, L2056 and AWRI796, supervised <br> development of work, helped in data interpretation and editing of the manuscript. |  |
| Signature |  | Date |


| Name of Co-Author | Jennie M. Gardner |  |  |
| :--- | :--- | :--- | :--- |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |  |
|  |  |  | Date |
| Signature |  |  |  |
| Name of Co-Author | Stephen G. Oliver |  |  |


| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |
| :--- | :--- | :--- |
| Signature |  | Date |


| Name of Co-Author | Vladimir Jiranek |  |  |
| :--- | :--- | :--- | :--- |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |  |
|  |  |  |  |
| Signature |  | Date | 4.9 .17 |

Please cut and paste additional co-author panels here/as required.

# Evaluation of the ability of commercial wine yeasts to form biofilms (mats) and adhere to plastic: implications for the microbiota of the winery environment 

Ee Lin Tek ${ }^{1}$, Joanna F. Sundstrom ${ }^{1}$, Jennie M. Gardner ${ }^{1}$, Stephen G. Oliver ${ }^{2}$, Vladimir Jiranek ${ }^{1,3 *}$<br>${ }^{1}$ Department of Wine and Food Science, University of Adelaide, Waite Campus, South Australia 5064, Australia.<br>${ }^{2}$ Department of Biochemistry \& Cambridge System Biology Centre, University of Cambridge, United Kingdom.<br>${ }^{3}$ Australian Research Council Training Centre for Innovative Wine Production.<br>*Corresponding author: PMB 1, Glen Osmond, South Australia 5064, Australia. Tel: 618-8313-6651; E-mail: vladimir.jiranek@adelaide.edu.au

### 2.1 Abstract

Commercially available active dried wine yeasts are regularly used by winemakers worldwide to achieve reliable fermentations and obtain quality wine. This practice has led to increased evidence of traces of commercial wine yeast in the vineyard, winery and uninoculated musts. The mechanism(s) that enables commercial wine yeast to persist in the winery environment and the impact on native microbial communities by this persistence is poorly understood. This study has investigated the ability of commercial wine yeasts to form biofilms and adhere to plastic. The results indicate that the biofilms formed by commercial yeasts consist of cells with a combination of different lifestyles (replicative and non-replicative) and growth modes including invasive growth, bud elongation, sporulation and a mat sectoring-like phenotype. Invasive growth was greatly enhanced on grape pulp regardless of strain, while adhesion on plastic varied between strains. The findings suggest a possible mechanism that allows commercial yeast to colonise and survive in the winery environment, which may have implications for the indigenous microbiota profile as well as the population profile in uninoculated fermentations if their dissemination is not controlled.

### 2.2 Keywords

Saccharomyces cerevisiae; wine yeast; biofilms; mats; plastic adhesion; invasive growth

### 2.3 Introduction

The fermentation of must with deliberately inoculated commercial strains of Saccharomyces cerevisiae is a common practice in winemaking throughout the world. This practice ensures consistent and reliable fermentations that achieve specific sensory outcomes. The alternative, the use of uninoculated musts in which 'wild' yeast species from the grapes and winery undertake the fermentation, is believed to bring out the regional character of wines since the indigenous yeast population will vary in different geographical locations (Gayevskiy and Goddard, 2012; Bokulich et al., 2014; Knight et al., 2015; Pinto et al., 2015). There is increased interest in using both methods in individual wineries, as well as using mixed starter cultures, to impart a regional character to the product of fermentations predominantly carried out by commercial yeast strains (Ciani et al., 2010). However, the frequent use of commercial strains without containment, prompts the question as to whether such practices could have an important impact on shaping the microbial ecology of the vineyard or the winery.

The country of New Zealand represents an island group that has only been inhabited by humans in comparatively recent time (800-1000 BP; Hurles et al., 2003).

Nevertheless, some $S$. cerevisiae isolates from uninoculated fermentation were found to be genotypically similar to isolates from a French oak barrel, suggesting that human activity has a role in affecting the endogenous yeast population and the resulting fermentations (Goddard et al., 2010). Reports show the prevalence and survival of commercial yeast strains in the winery, and in the vineyard at up to 700 m from the winery. While this suggests that the dissemination of such commercial strains to the environment has already occurred, their incidence was inconsistent from vintage to vintage (Valero et al., 2005, 2007; Cordero-Bueso et al., 2011; Martiniuk et al., 2016). Within a single vintage, the microbial communities residing winery surfaces at the University of California, Davis fluctuated during harvest (Bokulich et al., 2013). However, S. cerevisiae, one of the common inoculum in that winery, appeared to colonise the winery surfaces. A seven-year study of uninoculated fermentations in a winery that had routinely used commercial strains prior to this to inoculate fermentations, found that eight out of ten of the dominant yeasts isolated were commercial strains that had previously been used in the winery (Blanco et al., 2011). Whilst there is increasing evidence from different parts of the world to suggest commercial yeast remain in the winemaking environment, there is limited information on how such residual commercial yeasts behave and survive in this environment, and the properties that permit these yeasts to become members of the vineyard and/or winery microbiota remain unclear.

It is known that surface attachment and different modes of growth, such as biofilms, enable the long-term survival of fungi and bacteria in diverse ecological niches. The yeast $S$. cerevisiae is able to form biofilms as evidenced by two tests: mat formation on low density agar and adhesion to plastic (Reynolds and Fink, 2001). Both mat formation and plastic adhesion require the cell surface protein Flo11p. S. cerevisiae can also undergo nutrient-regulated filamentous and invasive growth, which are believed to be mechanisms used to forage for nutrients (Cullen and Sprague, 2000, 2012). These properties are not found in the universal laboratory reference strain S288C, due to a mutation in the FLO8 gene, whose product is required for FLO11 transcription (Liu et al., 1996; Rupp et al., 1999). In contrast, the laboratory strain $\Sigma 1278$ b, like many wild yeasts, displays biofilm-forming ability, filamentation and invasive growth (Hope and Dunham, 2014). It has been suggested that the loss of biofilm-like characteristics was due to domestication in the laboratory where yeast are grown routinely in rich media (Kuthan et al., 2003). This suggests that biofilms, surface adhesion and filamentous/invasive growth may confer on wild $S$. cerevisiae strains the ability to invade and thrive in unfavourable nutrient environments.

Many wild S. cerevisiae isolates, from a variety of geographical niches including those from wine grapes and must, have been shown to form mats exhibiting a range of shapes and sizes (Hope and Dunham, 2014; Sidari et al., 2014). This is different to the commonly studied laboratory strain $\Sigma 1278$ b that forms a large mat consisting of a central hub and spokes. This result challenges our understanding of the genetic basis and phenotypic roles of yeast biofilms in ecological contexts, since most studies that characterise
yeast mats have been based on $\Sigma 1278$ b (Reynolds, 2006; Martineau et al., 2007, 2010; Sarode et al., 2011, 2014; Chen et al., 2014).

Currently, limited information exists for the biofilm-forming ability of commercial wine yeast strains, which could be the mechanism enabling them to persist in the vineyard and winery (Zara et al., 2005; Rodriguez et al., 2014). To date, no research has addressed the details of mat formation for commercial wine yeast strains (such as cell and mat morphology, filamentation and invasive growth). Additionally, most biofilm studies on $S$. cerevisiae have been focused on mat formation of cells grown on the rich Yeast Extract Peptone Dextrose (YPD) medium and on adhesion to hard plastics. Little is known about how these yeast biofilm test results translate to survival in winery conditions. Sidari and colleagues (2014) investigated the biofilm formation of wild S. cerevisiae strains using deficient media for carbon and nitrogen such as SLAD and low glucose YPD to simulate fermentation conditions. The present study was undertaken to assess the mat-forming ability of commercial wine yeast strains as well as to investigate features of their mats, including structure, cellular morphology and any incidence of filamentous and invasive growth. Mats were grown on low-density ( $0.3 \%$ ) agar to approximate the density of grape pulp. This study demonstrated how mat features change in response to grape pulp and the ability of commercial wine yeasts to adhere to the soft plastics of which hoses in the winery are made. We believe the results of this study provide a functional perspective on the role of commercial wine yeast biofilms in the wine ecosystem.

### 2.4 Materials and Methods

### 2.4.1 Yeast strains and media

Yeast strains used in this study are listed in Table 2.1. Five wine yeasts and a derivative were selected from preliminary experiments in this laboratory suggesting diverse mat phenotypes. Yeast Peptone Dextrose broth (YPD, $1 \%$ yeast extract, $2 \%$ bacto peptone, $2 \%$ glucose) or YPD-agar (YPD with 0.3 or $2 \%$ agar) was used to grow yeast strains. Deletion of FLO11 in prototrophic $\Sigma 1278$ b, L2056 and AWRI796 strains was achieved by transformation (Gietz and Schiestl, 2007) with a KanMX gene replacement cassette (Wach et al., 1994) generated by PCR using FLO11_A and FLO11_D primers (Table 2.2) and genomic DNA of the BY4741 $\Delta$ flo11 strain (Winzeler et al., 1999). Positive transformants were selected using YPD-agar $(2 \%)+0.02 \%$ G418-sulfate (Astral, NSW, Australia). Homozygous diploid deletants were then isolated by sporulation using the PRE5 and SPO2 media (Codon et al., 1995), dissection and re-diploidisation, and verified by PCR amplification and sequencing using the primers FLO11_783bpup_F and FLO11_506bpdown_R (Table 2.2). Strain I1 was generated by transformation of the KanMX cassette (generated with PCR using primers SUL1_A and SUL1_D, Table 2.2, and genomic DNA of the BY4741 $\Delta$ sul1 strain; Winzeler et al., 1999) into the commercial wine yeast 'Distinction', followed
by sporulation, dissection and isolation of the re-diploidised wild type progeny.

Table 2.1: Yeast strains used in this study.

| Yeast strain | Genotype and comments | Reference |
| :---: | :---: | :---: |
| L2056 | Commercial wine yeast strain; diploid | Lallemand Australia |
| EC1118 | Commercial wine yeast strain; diploid | Lallemand Australia |
| AWRI796 | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| PDM | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| Distinction | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| I1 | Diploid derivative of Distinction | This study |
| Prototrophic इ1278b | Wild type laboratory strain; diploid | Ryan et al. (2012) |
| Auxotrophic 51278 b | $\begin{aligned} & \text { Y12958; MATa/ } \alpha \\ & \text { can1D:STE2pr-Sp-his5/CAN1 } \\ & \text { lyp1D::STE3pr-LEU2/LYP1 } \\ & \text { his3::his3G/his3::his3G leu2A/leu2D } \\ & \text { ura3D/ura3D } \end{aligned}$ | Dowell et al. (2010) |
| $\begin{aligned} & \mathrm{P} \Sigma 1278 \mathrm{~b} \\ & \Delta \text { flo11 / } \Delta \text { flo } 11 \end{aligned}$ |  | This study |
| $\begin{aligned} & \mathrm{A} \Sigma 1278 \mathrm{~b} \\ & \Delta \text { flo } 11 / \Delta \text { flo11 } \end{aligned}$ | $\begin{aligned} & \text { Y12958; } \\ & \text { flo11s::KanMX/flo11s::KanMX } \end{aligned}$ | Ryan et al. (2012) |
| $\begin{aligned} & \text { L2056 } \\ & \Delta \text { flo11 / } \Delta \text { flo11 } \end{aligned}$ | flo11వ::KanMX/flo11昂:KanMX | This study |
| AWRI796 $\Delta$ flo11 / $\Delta$ flo11 | flo11వ::KanMX/flo11景::KanMX | This study |
| $\begin{aligned} & \text { BY4741 } \\ & \text { Dfo11 } \end{aligned}$ | MATa his3 $\Delta 1$ leu2 $\Delta 0$ met15 00 ura3 $\Delta 0$ flo11D::KanMX | Thermo Fisher Scientific Australia |
| BY4741 | MATa his3 1 leu2 0 met15 0 ura3 ${ }^{\text {a }}$ | Thermo Fisher |
| $\Delta$ sul1 | sul1 $\Delta:: K a n M X$ | Scientific Australia |

Table 2.2: Primers for amplification and expected product sizes.

| Primer name | Sequence (5' to 3') | Product size <br> of BY4741 <br> $(\mathbf{b p})$ |
| :--- | :--- | :--- |
| FLO11_A | AATGTCCGTGTTCGAATTAAATAAA | $4666\left(\mathrm{WT}^{1}\right) ;$ |
| FLO11_D | CCAATACTACCGGTACTTGTTCTTG | $2146\left(\mathrm{del}^{2}\right)$ |
| FLO11_783bpup_F | TGTTGTCTTTTTAACGGTCGTACTG | $5394(\mathrm{WT}) ;$ |
| FLO11_506bpdown_R | CCTGGTCGAAGATTATTAGTTGTGC | $2876(\mathrm{del})$ |
| SUL_A | TCGAACACTGTCATTTGAAATTATG | $3104(\mathrm{WT}) ;$ |
| SUL_D | GGACATTTGTAGAAAATAGGCTCAA | $2108(\mathrm{del})$ |
| ${ }^{1}$ wild type |  |  |

### 2.4.2 Mat formation assays

YPD-agar ( $0.3 \%$ ) was prepared by mixing an equal volume of autoclaved $0.6 \% \mathrm{w} / \mathrm{v}$ bacteriological agar (Amyl Media; Cat No. RM250) and filter sterilised $2 \times$ YPD. 25 mL of medium was aliquoted per 90 mm plate, and then used within 24 h .

Exponential-phase cultures were prepared by inoculation of YPD broth with an overnight culture at $1.25 \times 10^{6}$ cells $\mathrm{mL}^{-1}$ and incubating for $5-7 \mathrm{~h}$. The culture was diluted in Phosphate Buffered Saline (PBS; $137 \mathrm{mM} \mathrm{NaCl}, 2.7 \mathrm{mM} \mathrm{KCl}, 10 \mathrm{mM} \mathrm{Na} \mathrm{NPO}_{4}$, $1.8 \mathrm{mM} \mathrm{KH} \mathrm{HO}_{4}, \mathrm{pH} 7.4$ ) to $1 \times 10^{6}$ cells $\mathrm{mL}^{-1}$ and an aliquot of $5 \mu \mathrm{~L}$ was spotted at the centre of a 90 mm YPD-agar ( $0.3 \%$ ) plate. At least six replicate mats of each strain were prepared. The plates were wrapped in cling film and incubated with yeast inoculum side up at $25^{\circ} \mathrm{C}$ for 13 days, unless otherwise indicated. To determine whether auxotrophy reduced spoke formation merely by reducing growth, $0.029 \%$ histidine, $0.117 \%$ leucine and $0.029 \%$ uracil were supplemented into YPD-agar ( $0.3 \%$ ).

L2056 mats with a sectoring-like phenotype were subcultured to determine if each sector formed the same distinct mat structure. For direct subculturing, cells were picked up with a $1 \mu \mathrm{~L}$ inoculation loop and transferred to a fresh YPD-agar ( $0.3 \%$ ) plate. To remove any temporary stress-induced phenotypes, cells were subcultured after re-growing in YPD. For this method, cells were grown in YPD broth to stationary phase before being used to prepare exponential-phase cultures and plating as described above.

Where indicated, mats were washed off the plate with a gentle stream of water to reveal invasive growth specific to mat formation on $0.3 \%$ agar. Plates were first incubated at $4{ }^{\circ} \mathrm{C}$ for 30 min before washing as this prevented the agar from being removed during washing. Where indicated, to confirm adherence to agar, cells were also subjected to rubbing with a gloved finger. Invasive growth was confirmed by needing to break the agar to reach those cells.

Mats were photographed using either a Samsung Galaxy S3 camera, S5 camera or ProtoCOL 3 (Synbiosis). Mat areas were measured from ProtoCOL 3 images using Fiji software (Schindelin et al., 2012). Detailed steps for processing and measuring are in the Supplementary Data.

The morphology of cells obtained from mats mounted in PBS were observed and imaged at $400 \times$ and $1000 \times$ magnification using a Nikon Eclipse 50i microscope and an attached Digital Sight DS-2MBWc camera with NIS-Elements F3.0 imaging software (Nikon).

For the grape-pulp assay, organic table grapes were surface sterilised with $70 \%$ v/v ethanol before skinning. Pulp was homogenised with a stick blender. Grape pulp agar ( $0.3 \% \mathrm{w} / \mathrm{v}$ agar) was prepared by mixing homogenised pulp and autoclaved agar in a $3: 1$ ratio. 25 mL of medium was aliquoted per 90 mm plate, and then used within 24 h . Yeast
were inoculated at the centre of the agar using a toothpickwith cells cultured on YPD-agar $(2 \%)$. Plates were wrapped and incubated at $25^{\circ} \mathrm{C}$ as described above. Negative controls with no inoculum resulted in no contamination. Mat images were taken using a Nikon SMZ1270 stereomicroscope and an attached DS-Fi3 camera with the NIS-Elements F4.60 software. Mats were washed off as described above. Cross-section samples were prepared by slicing the agar with a scalpel blade and placed on a glass slide with the cut side facing up.

High-sugar YPD-agar ( $5 \%$ glucose, $5 \%$ fructose, $1 \%$ yeast extract, $2 \%$ bacto peptone, $0.3 \%$ agar) was prepared as described for YPD-agar ( $0.3 \%$ ). Yeast were inoculated using a toothpick for this assay. Images were taken on Day 3 using the ProtoCOL 3.

### 2.4.3 Vitality and nuclear staining

Cells with elongated buds were stained for vitality and nuclear DNA to visualise the physiological state. For vitality staining, yeast cells were resuspended in $20 \mu \mathrm{~L}$ of $1 \times \mathrm{PBS}$ containing $6.5 \mu \mathrm{~g} \mathrm{~mL}{ }^{-1}$ propidium iodide (PI; Life Technologies, formerly Invitrogen; Cat No. P3566) and $4.75 \mu \mathrm{~g} \mathrm{~mL}{ }^{-1}$ bis-(1,3-dibarbituric acid)-trimethine oxonol (DiBAC4(3); Sigma-Aldrich; Cat No. D8189) on a glass slide. The slide was incubated for 5 min in a black humid chamber. DAPI (Sigma-Aldrich; Cat No. D9542) staining was performed according to Meluh's Protocol (John Hopkins School of Medicine, 1999) for staining of the nucleus. Stained cells were observed using a Nikon Eclipse 50i microscope with an attached Nikon Intensilight C-HGFI illuminator and a suitable filter set. Filter sets used included G2-A (excitation 510-560, barrier 590) for PI, GFP-B (excitation 460-500, barrier 510-560) for DiBAC4(3) and UV-2A (excitation 330-380, barrier 420) for DAPI. Black and white fluorescence images were obtained. Fluorescence colours were then applied using the Fiji software (Schindelin et al., 2012).

### 2.4.4 DNA preparation and PCR conditions

Genomic DNA was extracted as described in Adams et al. (1998). Other DNA preparations for PCR amplification were carried out according to the Chelex-based procedure described by Antonangelo et al. (2013) with the heating step substituted with boiling for 10 min . $25 \mu \mathrm{~L}$ PCR reactions consisted of $1 \times$ Hi-Fi Buffer, 1 mM dNTP Mix (Bioline; Cat No. BIO-39028), $0.2 \mu \mathrm{M}$ primer, 0.5 units polymerase (Bioline Velocity DNA Polymerase; Cat No. BIO-21098) and $2 \mu \mathrm{~L}$ of the Chelex-extracted DNA. The thermocycling program was $98^{\circ} \mathrm{C}$ for 2 min , followed by 30 cycles of 30 s at $98^{\circ} \mathrm{C}, 30 \mathrm{~s}$ at $58^{\circ} \mathrm{C}$ and 1.5 min at $72^{\circ} \mathrm{C}$, followed by 5 min at $72^{\circ} \mathrm{C}$. Primers used and the expected product sizes are listed in Table 2.2. PCR products were separated on a $0.8-1 \% \mathrm{w} / \mathrm{v}$ TAE-agarose gel containing GelRed nucleic acid stain (Biotin; Cat No. 41003). DNA fragments of deletion products were excised from the gel and purified using the Wizard SV Gel and PCR Clean-Up System

### 2.4.5 Mat culture harvest and total RNA extraction

Spoked and non-spoked mats of L2056 were harvested by using a cover slip with forceps to pick up cells across all regions from rim to centre. An inoculation loop was used to transfer and resuspend cells in 1 mL Trizol reagent (Life Technologies; Cat No. 15596-018). The sample was snap frozen in liquid nitrogen for 20 s . RNA extraction was performed using a combination of Trizol reagent and a Qiagen RNeasy Mini kit (Cat No. 74104). Samples were thawed on ice. Glass beads were added up to the halfway mark of the meniscus. Six cycles of 45 s of vortexing and 45 s of rest on ice were used to disrupt cells. Tubes were incubated at $65^{\circ} \mathrm{C}$ for 3 min and $200 \mu \mathrm{~L}$ of chloroform was added, followed by vortexing for 15 s before leaving at room temperature for 5 min . Tubes were centrifuged at $20,817 \times g$ for 10 min at $4^{\circ} \mathrm{C}$. Supernatant was recovered to a fresh tube and an equal volume of $70 \% \mathrm{v} / \mathrm{v}$ ethanol was added, mixed by pipetting, before continuing according to the Qiagen RNeasy Mini kit manufacturer's instructions. RNA quality and quantity were checked using a NanoDrop ND-1000 UV-visible light spectrophotometer (Thermo Fisher Scientific) and on $1 \%$ TAE-agarose gel. The absence of genomic DNA contamination in RNA preparations was confirmed using RNA as a template in real-time PCR assays.

### 2.4.6 Quantitative real-time PCR

Quantitative real-time PCR was performed to compare the two L2056 mat structures that resulted from subculturing and determine whether this was associated with differential gene expression of FLO11. Primers for reference genes and the gene of interest (Table 2.3) used in real-time PCR were as published in Teste et al. (2009) and Van Mulders et al. (2009). Two micrograms of total RNA was reverse-transcribed into cDNA using an iScript cDNA synthesis kit (Bio-Rad; Cat No. 1708891) in a $40 \mu \mathrm{~L}$ reaction mixture. The RT-PCR reaction mix ( $10 \mu \mathrm{~L}$ total volume) consisted of $5 \mu \mathrm{~L}$ SsoFast EvaGreen Supermix (Bio-Rad; Cat No. 1725203), $0.2 \mu \mathrm{M}$ of each primer, $2 \mu \mathrm{~L}$ water and $2 \mu \mathrm{~L}$ of a 1:10 dilution of the cDNA preparation. Each reaction was done in triplicate. Triplicates of no template control were included for each primer pair run. The thermocycling program was $95^{\circ} \mathrm{C}$ for 30 s , followed by 40 cycles of 5 s at $95^{\circ} \mathrm{C}$ and 5 s at $60^{\circ} \mathrm{C}$, followed by a hold at $65^{\circ} \mathrm{C}$ for 5 s before an end at $95^{\circ} \mathrm{C}$. The melt curve data was checked to confirm primer specificity and contamination.

Table 2.3: Primer sequences for qRT-PCR.

| Target | Sequence |
| :--- | :--- |
| Reference gene | F: CACGGATAGTGGCTTTGGTGAACAATTAC |
| ALG9 | R: TATGATTATCTGGCAGCAGGAAAGAACTTGGG |
| TAF10 | F: ATATTCCAGGATCAGGTCTTCCGTAGC |
|  | R: GTAGTCTTCTCATTCTGTTGATGTTGTTGTTG |
|  | F: GATACTTGGAATCCTGGCTGGTCTGTCTC |
| Gene of interest | R: AAAGGGTCTTCTGTTTCATCACCTGTATTTGC |
| FLO11 | F: GTTCAACCAGTCCAAGCGAAA |
| gDNA |  |
| contamination <br> verification <br> ACT1 |  |
|  | R: GTAGTTACAGGTGTGGTAGGTGAAGTG |
|  | F: ATTATATGTTTAGAGGTTGCTGCTTTGG |
|  | R: CAATTCGTTGTAGAAGGTATGATGCC |

A standard curve was used to determine the PCR reaction efficiency for each primer pair. Quantitative PCR was performed on a ten-fold serial dilution of cDNA samples over six points. Each concentration was done in triplicate. The standard curve for all primer pairs used in the study had $90-110 \%$ reaction efficiency and an $r^{2}$ value $>0.980$.

Three reference genes, ALG9, TAF10 and UBC6, were used for normalisation as suggested by Teste et al. (2009). Analysis of qRT-PCR reactions with qBase ${ }^{P L U S}$ (Biogazelle) using all reference genes returned an M value below 1 , an acceptable range of stable expression for heterogeneous sample according to Taylor et al. (2015) and Vandesompele et al. (2002). Results were imported to GraphPad Prism version 7.02 software for a two-way analysis of variance (ANOVA) with a Sidak multiple comparisons test.

### 2.4.7 Plastic adhesion assays

Plastic adhesion was performed for auxotrophic $\Sigma 1278$ b, prototrophic $\Sigma 1278$ b, L2056, AWRI796 and prototrophic $\Sigma 1278$ b $\Delta$ flo11/ $\Delta$ flo11 as described by Reynolds and Fink (2001) with slight modifications. Cells were grown in Synthetic Complete medium (SC; $0.17 \%$ Yeast Nitrogen Base without amino acids and ammonium sulfate, $0.079 \%$ Complete Supplement Mixture, $0.5 \%$ ammonium sulfate) with $2 \%$ glucose overnight, washed with sterile ultrapure water, resuspended in 10 mL sterile ultrapure water and split into two 50 mL tubes. The cells were harvested and resuspended in SC with either $0.1 \%$ or $2 \%$ glucose to an $\mathrm{OD}_{600}$ of 1.0 . Six replicates of $100 \mu \mathrm{~L}$ aliquots were transferred to 96 -well non-treated polystyrene plates (Corning; Manufacturing No. 3370). The plates were incubated for $0,1,3$ or 6 h at $28^{\circ} \mathrm{C}$. An equal volume of $1 \% \mathrm{v} / \mathrm{v}$ Crystal Violet solution
(Sigma-Aldrich; Cat No. HT90132) was added to each well and removed after 15 min . This step was repeated before washing with $100 \mu \mathrm{~L}$ once and $200 \mu \mathrm{~L}$ twice with Reverse Osmosis water. $100 \mu \mathrm{~L}$ of $10 \%$ sodium dodecyl sulfate (SDS) was added to each well to solubilise Crystal Violet for 30 min . Absorbance at 590 nm was measured after mixing with $100 \mu \mathrm{~L}$ sterile ultrapure water. $\Sigma 1278 \mathrm{~b} \Delta$ flo $11 / \Delta$ flo 11 was excluded in $2 \%$ glucose due to poor growth and therefore insufficient overnight culture for both conditions.

### 2.4.8 Winery hose adhesion assays

This assay is a modified version of the plastic adhesion assay. A new winery hose (Red Heliflex composed of polyvinyl chloride, the most commonly used hose for wine transfer) was cut into half-circle strips and sterilised by dipping into $70 \% \mathrm{v} / \mathrm{v}$ ethanol. Four sterile hose strips were placed in a 90 mm plate. 10 mL Synthetic Low Ammonium Dextrose (SLAD; $0.17 \%$ Yeast Nitrogen Base without amino acids and ammonium sulfate, $2 \%$ glucose, $50 \mu \mathrm{M}$ ammonium sulfate) cultures of two overnights were harvested and resuspended in 25 mL of fresh SLAD before being added to the plate. Plate were incubated at $30^{\circ} \mathrm{C}$ for seven days. Sterile forceps were used to pick up strips and dip them in water to rinse off unattached cells. The strips were then observed with a light microscope for attached cells. Negative control with a blank medium showed no cells attached.

For the assay incorporating shaking, winery hose was cut into quarter strips and sterilised with $70 \% \mathrm{v} / \mathrm{v}$ ethanol. A strip was added to a 50 mL tube containing 10 mL SLAD after inoculation of yeast. Cultures were incubated at $30^{\circ} \mathrm{C}$ with shaking at 130 rpm for four days. Cell attachment on strips was observed as above. Cells were imaged at $400 \times$ magnification using the Nikon Eclipse 50i microscope with the attached camera and NIS-Elements F4.60 software.

### 2.5 Results

### 2.5.1 Prototrophic diploid $\Sigma 1278$ b as a laboratory reference

$\Sigma 1278$ b is the most commonly used strain in mat studies since, unlike S288C, it has a functional FLO8 gene and is considered to have wild type adhesion and filamentation phenotypes. Since the wine yeast strains in this study were diploid, diploid $\Sigma 1278$ b was selected as the reference strain. Furthermore, auxotrophic and prototrophic diploid strains produced different mats. Auxotrophic $\Sigma 1278$ b formed a smaller mat (Fig. 2.1A and B; YPD) with fewer spokes, defined as raised cables radiating from the hub (Fig. 2.1C), compared to the prototrophic $\Sigma 1278$ b mat. Deletion of FLO11 in either background abolished spokes (Fig. 2.1A). Since auxotrophic $\Sigma 1278$ b has been reported to form a spoked mat, the incubation time was extended to check for spoke formation. More spokes arose as
the mats aged. Ten percent of the mats developed spokes by Day 16 compared to none on Day 11 (Fig. 2.1C), thus confirming the ability of auxotrophic $\Sigma 1278$ b to form mats with spokes. However, the average number of spokes per mat was markedly less for auxotrophic than for prototrophic $\Sigma 1278$ b (ca. 0.16 vs 5.74 after 16 days). Supplementation with histidine, leucine and uracil improved growth, as evidenced by increased mat areas (Fig. 2.1B) and indeed restored spoked mat features (Fig. 2.1D). Accordingly, in order to avoid the potential complication of exogenous amino acid supplementation on mat formation and given the similarity of its mat formation to that previously published, prototrophic $\Sigma 1278$ b was selected as the laboratory strain reference in this study of wine yeast mat morphology.


Figure 2.1: Mat features of $\Sigma 1278$ b. (A) Mats formed by prototrophic and auxotrophic $\Sigma 1278$ b on YPD-agar ( $0.3 \%$ ) and YPD-agar ( $0.3 \%$ ) supplemented with $0.029 \%$ histidine, $0.117 \%$ leucine and $0.029 \%$ uracil. Last column shows mats of prototrophic and auxotrophic $\Sigma 1278$ b $\Delta$ flo11 / $\Delta$ flo11 on YPD-agar ( $0.3 \%$ ). Images were taken on Day 9. (B) Boxplot showing mat areas $\left(\mathrm{cm}^{2}\right)$ of auxotrophic (black) and prototrophic (white) $\Sigma 1278$ b growing on YPD-agar ( $0.3 \%$ ) and supplemented YPD-agar ( $0.3 \%$ ). Please refer to next page for (C) and (D).


Figure 2.1: (C) Number of spokes formed by 37 auxotrophic (black) and 38 prototrophic (white) $\Sigma 1278$ b mats on YPD-agar ( $0.3 \%$ ) on Day 11 and 16. (D) Number of spokes formed by auxotrophic (black) and prototrophic (white) $\Sigma 1278$ b mats grown on YPD-agar ( $0.3 \%$ ) (Day 12 for prototrophic and Day 21 for auxotrophic to normalise mat size) and supplemented YPD-agar (0.3\%) (Day 12).

### 2.5.2 Wine yeasts display diverse mat architectures

Commercial wine yeast strains L2056, AWRI796, EC1118 and PDM formed similar sized mats to those of prototrophic $\Sigma 1278$ b when they matured (Fig. 2.2A). Both L2056 and AWRI796 grew into circular mats and relatively smooth surfaces but those of L2056 had crinkled edges. In contrast, the mats formed by EC1118 and PDM had a petal-like shape, with curved spokes. 'Distinction', a commercial strain derived from PDM via ethyl methanesulfonate (EMS) mutagenesis (strain 22.1 in Cordente et al., 2009), formed a smaller petal-like mat, but without distinct spokes. I1, the product of a re-diploidised spore of 'Distinction', formed a round, smooth-surfaced mat similar to that of AWRI796 but smaller in size.

### 2.5.3 Cell morphologies in the mat rim and mat body reveal distinct lifestyles

The morphology of cells from different regions of each yeast mat, including the rim, centre, body and spokes (if present) was examined. In most cases, cells from the mat rim had a uniform, actively-dividing population (Fig. 2.2B, Fig. S1A). The cells from the mat body, centre or spokes each formed a non-uniform population made up of cells of various sizes and morphology; for example, cells with enlarged vacuoles, elongated buds and cells undergoing sporulation. The wine strains L2056 (arrows in Fig. 2.2B), EC1118 and Distinction had more sporulation events compared to other strains tested. In addition, cell-cell adhesion observed in PBS mount slides was more prevalent in the mat body compared to the mat rim (data not shown). Elongated buds of cells taken from mats were most likely non-viable as both vitality stains ( $\mathrm{DiBAC} 4(3)$ and PI ) were readily taken up, DAPI staining also revealed that these contained no nuclear DNA (Fig. 2.2C).

### 2.5.4 Some wine strains grow invasively at the start of mat formation

Mats of $\Sigma 1278$ b and the commercial wine strains tested were washed off with water to observe agar invasion events. All strains (as represented by $\Sigma 1278$ b and 'Distinction' in Fig. 2.2D), except the strain I1, were able to grow invasively from 2 days after inoculation, indicating that agar invasion occurred at or soon after inoculation in the early stage of mat formation. Invasive growth was confirmed by needing to break the agar to reach those cells. Invasive growth only developed at the centre of the mat where the inoculum had been applied (boxes in Fig. 2.2D; plate). No correlation between mat size and agar invasion was observed. The invasive growth structures were similar between strains (Fig. 2.2D; micrograph). No filamentous cells were observed on the edge of the invasive structures.

(B)


Figure 2.2: Features of yeast mats on YPD-agar (0.3\%), prototrophic $\Sigma 1278$ b at Day 8, wine yeast at Day 13. Representative images were chosen to display the range of morphological features observed. (A) Images of mats typical of prototrophic $\Sigma 1278 \mathrm{~b}$ and each wine yeast strain. (B) Morphologies of cells from mat rim and mat body of $\Sigma 1278$ b and L2056. Arrows indicate sporulation. Please refer to next two pages for (C), (D) and (E).
(C)


Brightfield


DAPI



MICROGRAPH


Figure 2.2: (C) Fluorescence micrographs of prototrophic $\Sigma 1278$ b cells with elongated buds stained with a combination of DiBAC4(3) (green) and PI (red) or L2056 cells with DAPI. Co-staining with both $\operatorname{DiBAC4}(3)$ and PI is visualised by an orange fluorescence. (D) Plate and micrograph images of invasively growing cells from washed yeast mats, with and without rubbing. Please refer to next page for (E).


Figure 2.2: (E) Mats formed by L2056 $\Delta$ flo11 / $\Delta$ flo11 and AWRI796 $\Delta$ flo11 / $\Delta$ flo11 (Day 13).

Compared to the mats formed by wine yeasts, the $\Delta$ flo11/ $\Delta$ flo11 strains had reduced mat size (compare images in Fig. 2.2E with those in Fig. 2.2A; the plate size and incubation time (13 days) were the same in both cases). The L2056 mutant had more petal structures than the AWRI796 mutant.

### 2.5.5 Wine strain L2056 forms mats with a more rapidly expanding sector

Some L2056 mats developed a sector that expanded across the agar more quickly than the rest of the mat. Of 38 biological replicates, $55 \%$ developed a sector with such growth (Fig. $2.3 \mathrm{~A})$. Cells were subcultured from the typical part of the mat and the expanding sector to fresh plates (primary direct subculturing) to compare mat morphologies. Cells from the expanding sector formed a $\Sigma 1278$ b-like spoked mat, whilst cells from the standard part of the mat produced a smooth mat similar to the original L2056 mat (Fig. 2.3A). The spoked and smooth mat phenotypes, respectively, persisted when cells were subcultured from the primary direct subculture to fresh plates (secondary direct subculturing; Fig. 2.3A). This was independent of whether the inoculum came from the rim, body, spokes or centre (data not shown). After overnight growth of cells from the original L2056 mat in YPD broth, aimed to remove any temporary stress-induced phenotypes, the differences were still evident. However, when the inoculum came from the secondary direct subculture, the difference was minimal: here the expanding sector had more structured surfaces compared to the standard sector, which formed smooth surfaces. No distinct differences on cellular morphology between the two types of mats were observed (Fig. S1B).


Figure 2.3: Mat morphology of an L2056 'sectoring' mat and its subcultures on YPD-agar ( $0.3 \%$ ). (A) An example of an original L2056 mat with a more rapidly expanding sector. Expanding and standard sectors from the original L2056 mat were subcultured directly onto YPD-agar ( $0.3 \%$; primary direct subculture; $\mathrm{n}=2$ ). Cells from the rim, body, spokes (if any) and centre of the primary subculture mats were subcultured (secondary direct subculture, $n=4$ for each mat section). Expanding and standard sectors from the original mat were also grown in YPD broth prior to plating on a fresh YPD-agar $(0.3 \% ; \mathrm{n}=5)$, as were cells from the mat body of the secondary subcultures $(\mathrm{n}=4)$. (B) FLO11 PCR products from genomic DNA isolated from L2056 mats, amplified with FLO11_A and FLO11_D primers. $\mathrm{E}=$ expanding sector; $\mathrm{S}=$ standard sector. (C) Relative fold change in FLO11 gene expression between non-spoked and spoked mats produced by cells in the expanding and standard sector of an L2056 mat ( $\mathrm{n}=4$ ). Each replicate is indicated by an enclosed circle. The long horizontal lines represent the mean and the error bars represent standard deviation. The difference is not statistically significant.

FLO11 is well known to affect cell adhesion and filamentation, and various gene sizes have been reported to affect biofilm-forming ability (Zara et al., 2009). Previous work in this laboratory had shown that PCR amplification of FLO11 from L2056 yields two amplicons. FLO11 was PCR amplified from cells within expanding and standard sectors of the original, primary and secondary subcultured mats to determine if these two amplicons were lost due to a meiotic event. Two products of expected sizes were amplified in each case (Fig. 2.3B), suggesting this had not occurred. FLO11 gene expression level was then compared between spoked and non-spoked mats produced by cells in the expanding sector and standard sector, respectively. Two out of four spoked mats showed increased FLO11 gene expression by two- and three-fold compared to non-spoked mats (Fig. 2.3C).

### 2.5.6 Plastic adhesion

Auxotrophic $\Sigma 1278$ b showed the most adhesion to plastic in both low and sufficient glucose conditions (Fig. 2.4). Prototrophic $\Sigma 1278$ b and L2056 displayed a modest increase in plastic adhesion ability in $0.1 \%$ glucose compared to that in $2 \%$ glucose, while AWRI796 was not affected by this nutrient change and showed less adhesion compared to $\Sigma 1278$ b $\Delta$ flo $11 / \Delta$ flo11 after 3 and 6 h in $0.1 \%$ glucose.


Figure 2.4: Plastic adhesion of laboratory and wine strains grown in SC medium with either 0.1 or $2 \%$ glucose. Absorbance at 590 nm was measured after $0,1,3$ and 6 h of incubation. Each data point represents the mean of six samples: ( $\square$ ) auxotrophic $\Sigma 1278$ b, (o) prototrophic $\Sigma 1278$ b, ( $\triangle$ ) L2056, ( $\bullet$ ) AWRI796, ( $\mathbf{(})$ prototrophic $\Sigma 1278$ b $\Delta$ flo11/ $\Delta$ flo11, (■) no cells (control). The error bars represent standard deviation and are included for all time points.

### 2.5.7 Wine yeast grow invasively and conduct fermentation on grape pulp soft agar

$\Sigma 1278$ b and several commercial wine yeast strains were plated onto grape pulp agar for mat assays. Instead of forming a large mat, grape pulp induced fermentation. Bubble-forming mats were observed on Day 3. There was no structured morphology observed on the culture surfaces (Fig. 2.5A). On Day 9, gas was observed trapped underneath the agar (Fig. 2.5B) which raised the agar, resulting in some surface culture (e.g. $\Sigma 1278 \mathrm{~b}$ ) coming into contact with the plate lid (Fig. 2.5A). Occurrence of cell adhesion and invasive growth can be seen after gently washing with water. Compared to the YPD mat assay, where the invasive growth only occurred in a few patches (Fig. 2.2D), the invasive growth in grape pulp agar was extensive (Fig. 2.5B; post-wash, cross-section).

The Brix of grape pulp was $17^{\circ}$, which means $75 \%$ pulp agar would have approximately $12.75^{\circ}$ ( $12.7 \%$ sugar). To investigate whether the fermentation phenotype was solely induced by the high sugar concentration in grape pulp, YPD containing $10 \%$ total sugar (equimolar glucose and fructose) was prepared for mat assays. The high-sugar YPD-agar, however, did not induce the fermentation phenotype observed on grape pulp (Fig. 2.5C). Flat mats instead of bubble-forming mats were observed.


Figure 2.5: Grape-pulp mat assay. (A) Mat images of $\Sigma 1278 \mathrm{~b}$ and a representative wine strain, EC1118, on grape pulp agar (0.3\%) at Day 9. (B) Images of EC1118 from the underside of the agar, post-wash and cross-section. Black arrows indicate invasively growing cells; white arrow indicates the grape pulp agar. (C) Day 3 image of EC1118 on high-sugar (10\%) YPD-agar (0.3\%).

### 2.5.8 Wine strain L2056 forms initial attachment on winery hose soft plastic

To begin to provide some insight into the potential significance of adhesion in a winemaking context, two assays were performed to investigate whether wine yeast are able to adhere to the soft plastics of commonly used winery hose. The first assay was modified from that used above to monitor plastic adhesion. All four strains tested, $\Sigma 1278$ b, L2056, AWRI796 and prototrophic $\Sigma 1278 \mathrm{~b} \Delta$ flo11/ $\Delta$ flo11 showed no adhesion. The second assay was performed in a 50 mL tube with shaking to imitate juice flowing through a winery hose. $\Sigma 1278$ b and L2056 were observed to have initial attachment to the hose plastic, but this was not true for AWRI796 and prototrophic $\Sigma 1278$ b $\Delta$ flo11/ $\Delta$ flo11 (Fig. 2.6). This matches the plastic adhesion result in plates, that AWRI796 did not adhere well, $\Sigma 1278$ b had the most adhesion followed by L2056 (Fig. 2.4).


Figure 2.6: Cell adhesion on plastic of a common winery hose, Red Heliflex. Images of plastic after four days of incubation in SLAD culture with shaking and after rinsing with water to remove unbound cells.

### 2.6 Discussion

Similar to the wild $S$. cerevisiae strains isolated from wine grapes and must (Sidari et al., 2014), commercial wine yeast strains were found to form varied mat sizes with structured architecture that differed from those formed by the laboratory yeast, $\Sigma 1278$ b. This may be explained by the genome differences between wine strains (Borneman et al., 2008, 2011, 2016). In this study, EC1118, PDM, Distinction and I1 are closely related whereas L2056 and AWRI796 are different from each other and from the others. Other wild yeasts have also been shown to produce mats with morphologies that did not conform with the standard 'hub and spokes' structure. For example, the mats formed by wild flor strains, V80, V23 and M23 (Zara et al., 2009), did not fully cover the agar plate and had no spoke formation, similar to 'Distinction' and I1 in this study, but differing in rim shape. The baking yeast YS2 (Hope and Dunham, 2014) formed a relatively larger, smooth surface mat, like AWRI796. Highly complex mats, which were formed by soil yeast YPS128 and bee yeast UWOPS05-227.2 (Hope and Dunham, 2014) were distinct from each other as well as from any of the strains in this study. Deletion of the FLO11 gene in two wine strains, L2056 and AWRI796, resulted in smaller sized mats, confirming that FLO11 is also required for a full-sized wine yeast mat formation.

The ability to form mats by a panel of commercial wine yeast strains suggests the ability to adhere to surfaces in the wine environment, which could include equipment, grapevine and grape berries. It could also help these yeast to form associations with other microbes. The results in grape-pulp mat assay suggest that commercial wine yeast could adhere and even invade grapes for colonisation. The winery hose adhesion trial also provides an indication of an initial attachment to soft plastic by wine yeast. In addition to the ability to co-flocculate with other wine-associated yeast strains (Rossouw et al., 2015), the adhesion and invasion properties shown in this study could drive the microbial population resident in the vineyard and winery, and subsequently affecting the population in fermentations. This may explain the previous reports that commercial strains contribute to the yeast population in uninoculated fermentations (Hall et al., 2011; Martiniuk et al., 2016; Scholl et al., 2016).

Mat formation can be considered as an expansion of colony formation. Analysis of the cellular morphologies between the mat rim and body reveals distinct lifestyles between these populations. The replicative phase is characterised by many actively dividing cells and these were present in the mat rim of all yeast mats examined. The non-replicative phase as observed in mat body is when cells are no longer proliferating, similar to colonies growing on rich medium. Yeast biofilm colonies described by Váchová et al. (2011) also have distinct cell types on different parts of the structure: non-dividing cells on the surface of the aerial region and dividing cells inside the colonies. However, unlike biofilm colonies, mats are thin and have no aerial regions. The cell type differences were more distinct between mat body and rim. Cells of the mat body were heterogenous. They included
cells that were sporulating, had elongated buds or enlarged vacuoles. This heterogeneous population has been described in aging yeast colonies, which consist of upper and lower regions with different stress resistances (Palková et al., 2014). The diversity of stress tolerance within a community arises from metabolic specialisation and cooperation between cells (Campbell et al., 2016). This mixture of differentiated cells within the mat body may contribute to supporting the survival of cells in the expanding edge i.e. mat rim.

An interesting cell type was found through microscopic observation in the mat body. Cells with an elongated bud were visualised with nuclear staining, the results suggesting the cell cycle arrested before nuclear migration (no nuclear DNA in elongated buds shown in Fig. 2.2C). Gladfelter and colleagues (2005) have shown that elongated bud morphology occurs due to Swe1p-mediated $G_{2}$ arrest. Whilst other studies (Gladfelter et al., 2004; Homoto and Izawa, 2016) have shown this morphology is often associated with septin mislocalisation, Gladfelter and colleagues (2005) also showed $G_{2}$ arrest could aggravate the effect of septin disorganisation. Ethanol has been shown to increase Swe1p expression, which inhibits Cdc28p kinase activity and subsequently causes $G_{2}$ arrest cell cycle delay (Booher et al., 1993; Kubota et al., 2004). There may be environmental signals other than ethanol causing either $G_{2}$ arrest or septin mislocalisation during mat formation, which requires further investigation.

Similar to the report by Rodriguez et al. (2014), L2056 formed crinkled-edge mats. In addition, this study also reports, for the first time, that mats formed by L2056 can be sectored (Fig. 2.3A). When the original L2056 mat was subcultured, cells from the expanding growth sector formed a typical $\Sigma 1278$ b 'hub and spokes' mat whereas the standard growth sector formed a non-spoked mat, similar to the original L2056 mat. Sectoring colonies have been observed in other fungi. For example, it is an indication of phenotypic switching in haploid Candida tropicalis (Porman et al., 2011), where the opaque sector shows more mating-competence. The fungus Metarhizium anisopliae forms a sector that has lost sporulation capacity, activity of certain enzymes, and changes in secondary metabolite profiles (Ryan et al., 2002). Sectoring can also occur when a fungus mutates and adapts to become drug resistance (He et al., 2014). In this study, two types of mats were formed persistently after two cycles of direct subculturing as well as subculturing after re-growing in rich medium. Since Flo11p is known to be important for forming 'hub and spokes' in $\Sigma 1278$ b mats and the gene length is related to the biofilm-forming ability in flor strains (Zara et al., 2009), the length of FLO11 genes in cells of the two types of mats was studied. No difference in FLO11 allele sizes of either sectors in the original L2056 mat, primary or secondary subcultures was seen (Fig. 2.3B), suggesting no meiotic events had occurred. FLO11 expression levels were then compared between the two types of mats. Two out of four spoked mats showed an increase in expression compared to non-spoked mats (Fig. 2.3C), which suggests FLO11 may be involved in mat expansion and/or spoke formation through differential expression, similar to the model suggested by Regenberg et al. (2016). Differential expression of FLO11 in $\Sigma 1278$ b was shown to generate Flo11+ and Flo11 ${ }^{-}$cells, containing adhesive and non-adhesive cells, in
mat formation (Regenberg et al., 2016). The differentiated mat had a spoked structure and was larger than the undifferentiated Flo11- mat. This may explain the formation of the rapidly expanding sector in the original L2056 mat, being due to the differentiated state. This differentiated state was carried on to the subcultures and resulted in spoked mats (Fig. 2.3A). Since L2056 has two unequal sized FLO11 alleles, it is also possible that the differential expression involves switching of the expression of either allele.

While most mat studies use auxotrophic $\Sigma 1278$ b strains, in this study auxotrophic $\Sigma 1278$ b did not form mat structures as widely reported. However, the 'hub and spokes' structure was formed with extended incubation or nutrient supplementation (Fig. 2.1C and D). There have been cases when supplementation did not compensate for auxotrophies (Corbacho et al., 2011). The particular amino acids used for supplementation may also influence physiological regulation because some amino acid biosynthesis pathways are connected (Niederberger et al., 1981). In the plastic adhesion experiment, adhesion ability was affected by auxotrophies - the auxotrophic $\Sigma 1278$ b was shown to be more adhesive than prototrophic $\Sigma 1278$ b (Fig. 2.4). Changes in metabolic flux induced by auxotrophic vs prototrophic states, may interfere with system-wide regulatory processes (Grüning et al., 2010). Therefore, it is suggested that prototrophic strains are more representative of the natural state and should be used in future studies.

It is noticeable that the number of spokes formed by $\Sigma 1278$ b in this study was less than those reported previously (Reynolds and Fink, 2001). This was probably due to the size of the inoculum. Toothpick inoculation (widely used in other mat publications) generated $>10$ spokes while inoculation of 800 and 50 cells yielded almost none (Fig. S2). In order to control initial cell numbers, an inoculum size of 5,000 cells was chosen, which produced representative spokes.

Despite showing a variety of mat structures by commercial wine yeast, this study also demonstrated broad responses accompanied with mat features by visualising cell morphologies and growth modes. The findings contribute to a better understanding of commercial yeast lifestyle on biofilms and adhesion with respect to wine environments. The observations may provide an explanation for the survival of commercial strains which might influence the natural microflora in the vineyard and winery in the long-term.

### 2.7 Funding

This work was supported by Wine Australia [GWR Ph1305] awarded to ELT and Australian Research Council [DP 20111529] awarded to VJ and SGO, which also supported JFS and JMG. ELT was supported by a University of Adelaide Graduate Research Scholarship.

Conflict of interest: None declared.

### 2.8 Acknowledgements

Prototrophic $\Sigma 1278$ b, auxotrophic $\Sigma 1278$ b and A $\Sigma 1278$ b $\Delta$ flo $11 / \Delta$ flo11 were kindly donated by Dr Charles Boone (University of Toronto). The authors thank the Australian Wine Research Institute for providing the Red Heliflex hose and access to ProtoCOL 3, and Dr Michelle Walker (University of Adelaide) for generating strain I1.

### 2.9 Supplementary Data

### 2.9.1 Methods

## Mat area measurement from ProtoCOL 3 images

1. Capture images as described in ProtoCOL 3 manual. Exposure was set at 60 ms .
2. Download and install Fiji from http://imagej.net/Fiji/Downloads.
3. Open the application.
4. Open an image that needs to be measured.
5. Click Analyze from the menu, select Set Scale. Enter 583 pixels $=9 \mathrm{~cm}$, check Global and press OK. Now the image and the following images opened within this session have been calibrated.
6. To convert into a black and white image, click Image from the menu, choose Adjust and select Threshold. Change the Threshold colour to $\mathbf{B} \& \mathbf{W}$, press Close.
7. Click Wand (tracing) tools from the icon menu, move cursor to anywhere in the mat (black area), click on the mat. This will select the thresholded object - mat.
8. Click Analyze from the menu, select Set Measurement. Check Area and press OK.
9. To measure, click Analyze from the menu, select Measure. A result table with the area measurement will pop up. Save the results for future use and close all the boxes.
10. To measure subsequent images in the same session, open a new image, Image $>$ Adjust $>$ Threshold $>$ Close, click on the mat, Analyze $>$ Measure

### 2.9.2 Figures

Figure S1: Cellular morphology from yeast mats grown on YPD-agar (0.3\%). (A) Prototrophic $\Sigma 1278$ b and wine strains (B) L2056 subcultures. Scale bars, $50 \mu \mathrm{~m}$. N/A $=$ not applicable.




Body - thick region


Rim


그


Centre


Body - thin region


## Centre



Body - thin region




Figure S2: Mat formation of prototrophic $\Sigma 1278$ b on YPD-agar ( $0.3 \%$ ) with inocula from either a toothpick with cells or cell suspensions ( 800 or 50 cells per $5 \mu \mathrm{~L}$ ).


## Chapter 3

# Mat formation in a low nitrogen medium 

## Contextual statement

Chapter 2 illustrated a variety of mat features for several commercial wine yeast strains. The manuscript in this chapter evaluated the response of wine yeast during mat formation under limiting nitrogen conditions and several factors that could affect the response, which corresponds to the second aim (p. xiii) of this project. Wine yeast assimilate nitrogen since it is an essential nutrient enabling growth. Fermenting wine musts commonly utilise all available nitrogen, often before all sugars are catabolised, the depletion of nitrogen from rotting grapes on the vine is expected to be similar. Thus, whether it be a fermenting must in a winery or grapes in the vineyard, exposure of yeast to an environment with significantly depleted nitrogen is common. Previous studies with a filamentation focus have used solid medium ( $2 \%$ agar) with very low nitrogen as it stimulates diploid cells to undergo pseudohyphal growth. The availability of nitrogen could also be an important factor in mat formation on less dense media ( $0.3 \%$ agar). Preliminary studies were performed to refine methodology used in this section of work, including optimal inoculation rate and the effect of a putative cell signalling compound (Appendix B), in order to establish the scope of work undertaken.

## Statement of Authorship

| Title of Paper | Factors influencing filamentous and invasive growth of yeast cells in mat formation in a low <br> nitrogen environment |
| :--- | :--- |
| Publication Status | 「 Published $\quad$ T Accepted for Publication |
| 「 Submitted for Publication $\quad$ Unpublished and Unsubmitted work written in |  |
| manuscript style |  |

Principal Author

| Name of Principal Author (Candidate) | Ee Lin Tek |  |
| :---: | :---: | :---: |
| Contribution to the Paper | Performed all experiments and data analysis, interpreted data, and wrote manuscript. |  |
| Overall percentage (\%) | 80\% |  |
| Certification: | This paper reports on original research I conducted during the period of my Higher Degree by Research candidature and is not subject to any obligations or contractual agreements with a third party that would constrain its inclusion in this thesis. I am the primary author of this paper. |  |
| Signature | Date | 04/09/17 |

## Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:
i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to $100 \%$ less the candidate's stated contribution.

| Name of Co-Author | Jennie M. Gardner |  |
| :--- | :--- | :--- |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |
| Signature |  | Date |



| Contribution to the Paper | Supervised development of work and helped in data interpretation. |  |
| :--- | :--- | :--- |
| Signature |  | Date |


| Name of Co-Author | Vladimir Jiranek |  |  |
| :--- | :--- | :--- | :--- |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |  |
|  |  | Date | 4.9 .9 |
| Signature |  |  |  |

Please cut and paste additional co-author panels here ás required.
()

# Factors influencing filamentous and invasive growth of yeast cells in mat formation in a low nitrogen environment 

Ee Lin Tek ${ }^{1}$, Jennie M. Gardner ${ }^{1}$, Joanna F. Sundstrom ${ }^{1}$, Stephen G. Oliver ${ }^{2}$, Vladimir Jiranek ${ }^{1,3 *}$<br>${ }^{1}$ Department of Wine and Food Science, University of Adelaide, Waite Campus, South Australia 5064, Australia.<br>${ }^{2}$ Department of Biochemistry \& Cambridge System Biology Centre, University of Cambridge, United Kingdom.<br>${ }^{3}$ Australian Research Council Training Centre for Innovative Wine Production.

*Corresponding author: PMB 1, Glen Osmond, South Australia 5064, Australia. Tel: 618-8313-6651; E-mail: vladimir.jiranek@adelaide.edu.au

### 3.1 Abstract

Saccharomyces cerevisiae forms complex mat structures on low agar YPD. In response to nutrient limitation, budding yeast can become adherent, switch to a filamentous form and grow invasively. Accordingly, mat structure is affected i.e. a filamentous mat is formed on a glucose-limited medium. In this study, a proportion of yeast in a mat switched to filamentous and invasive growth on a nitrogen-limited medium. Also, increasing nitrogen content increased cellular growth and mat size. The formation of filamentous and invasive foci within a mat was enhanced by ethanol and hydrogen sulfide but was inhibited by aromatic alcohols and sulfite. As previously reported, filamentous growth was also affected by neighbouring mats. This growth transition to filamentation and invasion, in low nitrogen low-density agar, may be a response adapted to the environmental niche typical of yeast, rotting fruit, which has low density and decreasing nutrients.

### 3.2 Keywords

Filamentous growth; invasive growth; low nitrogen; mats; aromatic alcohols; sulfide and sulfite

### 3.3 Introduction

Saccharomyces cerevisiae forms mats on a low-density agar (0.3\%) medium (Reynolds and Fink, 2001). Mat structures are complex and diverse and depend on the strain background (Hope and Dunham, 2014). The laboratory yeast strain $\Sigma 1278$ b generates a mat with characteristics of a central hub and radiating spokes. Hub and spoke formation can be delayed if glucose concentration is increased (Reynolds et al., 2008). Conversely, a filamentous mat is formed if glucose is removed (Karunanithi et al., 2012). The direction of filamentous growth has also been shown to be affected by the presence of a neighbouring mat (Karunanithi et al., 2012).

Yeast also undergo filamentous and invasive growth on medium-density agar $(2 \%)$ when nitrogen is limited (Gimeno et al., 1992). Hyphal-like elongated cells can be stimulated by a number of fusel alcohols, which are by-products from catabolism of some amino acids (Dickinson, 1994, 1996). Conditioned medium from a $\Sigma 1278$ b stationary-phase culture was reported to stimulate filamentous and invasive growth (Chen and Fink, 2006). The group demonstrated that tryptophol and 2-phenylethanol were acting as quorum sensing molecules that enhanced the filamentous and invasive phenotype on low nitrogen agar.

Hydrogen sulfide $\left(\mathrm{H}_{2} \mathrm{~S}\right)$ is associated with nitrogen deficiency during fermentation
(Jiranek et al., 1995). Nitrogen deficiency can cause a stuck fermentation. This is often difficult to restart even when additional nitrogen is supplied. Many reports have suggested that this is largely based on delayed nitrogen ameliorations being ineffective due to reduced hexose transporter activity. However, there is evidence that $\mathrm{H}_{2} \mathrm{~S}$ may also act as a cell-cell signalling molecule (Lloyd, 2006). Its presence has been postulated to alter the metabolic clock of the yeast population (Sohn et al., 2000). Microarrays have shown significant overlap of gene expression in the presence of $\mathrm{H}_{2} \mathrm{~S}$ and a stress response (Jia et al., 2011). It is possible that the presence of by-products such as $\mathrm{H}_{2} \mathrm{~S}$ could inhibit yeast cell metabolism resulting in reduced fermentation of residual sugars. Like tryptophol and 2-phenylethanol, $\mathrm{H}_{2} \mathrm{~S}$ could potentially be a signalling molecule that affects other nitrogen-deficient responses such as filamentous and invasive growth. Interestingly, within the sulfate assimilation pathway, the precursor of sulfide is sulfite, which has been shown to block invasive growth (Zupan and Raspor, 2010). Several mechanisms have been proposed how sulfite inhibits growth (see review in Divol et al., 2012). Briefly, these include the reduction of intracellular ATP by activating ATPase, inhibition of key metabolic enzymes such as GAPDH, binding to co-enzymes, co-factors and to a number of metabolites including acetaldehyde (Schimz and Holzer, 1979; Schimz, 1980; Hinze and Holzer, 1986; Carmack et al., 1950; Rankine and Pocock, 1969). These could lead to cell death as energy metabolism is negatively impacted.

Since yeast cells are able to produce filamentous and invasive mats on glucoselimited low-density ( $0.3 \%$ ) agar and limited nitrogen can induce this form of growth on medium-density (2\%) agar, a hypothesis is made that filamentous and invasive mats would form when nitrogen is scarce on low-density agar. Agar of a lower density has similar consistency to the material where yeast are commonly found in nature; fruit, e.g. grape pulp, and thus is relevant when considering this microorganism's environmental niche. Yeast growing on grapes would deplete nutrients in their immediate vicinity and may switch to filamentous and invasive growth modes to enhance survival. With this in mind, this study investigated mat formation in a low nitrogen environment by $S$. cerevisiae including $\Sigma 1278$ b and several wine yeast strains to see if the response is widespread for different genetic backgrounds. The addition of compounds or factors known or hypothesised to influence filamentous and invasive growth such as the presence of a neighbouring mat, tryptophol, 2-phenylethanol, $\mathrm{H}_{2} \mathrm{~S}$ and sulfite was also evaluated.

### 3.4 Materials and Methods

### 3.4.1 Yeast strains and media

Yeast strains used in this study are listed in Table 3.1. Strain I1 was generated by transformation (Gietz and Schiestl, 2007) of a KanMX cassette (generated with PCR using primers $5^{\prime}$-TCGAACACTGTCATTTGAAATTATG- $3^{\prime}$ and $5^{\prime}$-GGACATTTGTAGAAAA

TAGGCTCAA-3', and genomic DNA of the BY4741 $\Delta$ sul1 strain; Wach et al., 1994; Winzeler et al., 1999) into the commercial wine yeast 'Distinction', followed by sporulation, dissection and isolation of the re-diploidised wild type progeny.

Table 3.1: Yeast strains used in this study.

| Yeast strain | Genotype and comments | Reference |
| :--- | :--- | :--- |
| Prototrophic $\Sigma 1278$ b | Wild type laboratory strain; diploid | Ryan et al. (2012) |
| L2056 | Commercial wine yeast strain; diploid | Lallemand Australia |
| EC1118 | Commercial wine yeast strain; diploid | Lallemand Australia |
| AWRI796 | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| PDM | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| Distinction | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| I1 | Diploid derivative of Distinction | This study |
| BY4741 $\Delta$ sul1 | MATa his3 $\Delta 1$ leu2 0 met15 00 | Thermo Fisher |
|  | ura3 $\Delta 0$ sul1 $\Delta:$ :KanMX | Scientific Australia |

Synthetic Low Ammonium Dextrose (SLAD; 0.17\% Yeast Nitrogen Base without amino acids and ammonium sulfate (Beckton Dickinson; Cat No. 233520), 2\% glucose and $50 \mu \mathrm{M}$ ammonium sulfate) was filter sterilised as a $10 \times$ stock and diluted as required with sterile ultrapure water. Bacto agar (BD; Cat No. 260001) was washed twice in 800 mL ultrapure water in a 1 L Schott bottle, swirled to mix and rested for 15 min before decanting, followed by autoclaving. SLAD low-density agar ( $0.3 \%$ ) used in mat assays was prepared by mixing equal volumes of $2 \times$ SLAD and $0.6 \%$ molten Bacto agar, and where indicated, the addition of one or more of the following chemicals: $0.05 \% \mathrm{v} / \mathrm{v}$ ethanol, $50 \mu \mathrm{M}$ tryptophol, $50 \mu \mathrm{M}$ 2-phenylethanol, $0.4 \mathrm{mg} \mathrm{L}^{-1}$ sodium sulfide $\left(\mathrm{Na}_{2} \mathrm{~S} .9 \mathrm{H}_{2} \mathrm{O}\right)$ and/or $0.01 \%$ w/v sodium metabisulfite $\left(\mathrm{Na}_{2} \mathrm{~S}_{2} \mathrm{O}_{5}\right)$. Tryptophol and 2-phenylethanol stock solutions (50 mM ) were prepared in 50 mL of $25 \% \mathrm{v} / \mathrm{v}$ ethanol making the final concentration of ethanol in SLAD agar containing aromatic alcohols $0.05 \%$. All chemicals were sourced in ultrapure form from Sigma Aldrich. Aliquots of 10 mL were poured onto 60 mm polystyrene Petri dishes (Techno Plas; Cat No. S6014S10). Media were only made and poured one day prior to plating.

Conditioned medium (CM) was prepared as follows. Yeast were inoculated from glycerol stocks and cultured in 25 mL SLAD in two separate Erlenmeyer flasks for 48 h at $28{ }^{\circ} \mathrm{C}$ with agitation. Cultures were mixed and centrifuged at $20,817 \times g$ for 10 min to collect the supernatant. Supernatant was tested for nitrogen (ammonia) and glucose content using enzymatic assays (see below). The supernatant was supplemented up to the original nitrogen ( $50 \mu \mathrm{M}$ ammonium sulfate) and glucose ( $2 \%$ ) content in SLAD and filter sterilised.

### 3.4.2 SLAD mat assays

Yeast were inoculated from glycerol stocks into 10 mL SLAD and incubated for 48 h at $28{ }^{\circ} \mathrm{C}$ with agitation. Cells were subsequently inoculated into 25 mL of fresh SLAD at $1 \times 10^{4}$ cells $\mathrm{mL}^{-1}$ and incubated for $16-18 \mathrm{~h}$ to obtain an exponential-phase culture.

The exponential-phase culture was diluted in Phosphate Buffered Saline (PBS; $\left.137 \mathrm{mM} \mathrm{NaCl}, 2.7 \mathrm{mM} \mathrm{KCl}, 10 \mathrm{mM} \mathrm{Na} 2 \mathrm{HPO}_{4}, 1.8 \mathrm{mM} \mathrm{KH}_{2} \mathrm{PO}_{4}, \mathrm{pH} 7.4\right)$ to $2 \times 10^{5}$ cells $\mathrm{mL}^{-1}$. An aliquot of $5 \mu \mathrm{~L}$ diluted culture was spotted at the centre of each plate (four to nine replicates per strain, per medium). Plates were incubated at $25^{\circ} \mathrm{C}$, yeast inoculum side up. Images of each mat were taken after 3, 6 and 9 days of incubation. To observe invasive growth structures, mats were washed with a gentle stream of water from a laboratory squeeze bottle after being kept at $4^{\circ} \mathrm{C}$ for half an hour.

For paired SLAD mat assays, two diluted cultures were inoculated approximately 1 mm apart on SLAD agar.

### 3.4.3 Microscopy imaging and image processing

Mats were observed and imaged at $40 \times$ magnification from the underside of the plates (with lid on) using a Nikon Eclipse 50i microscope and an attached Digital Sight DS-2MBWc camera with NIS-Elements F3.0 imaging software (Nikon). Four to six images were taken for each mat to capture all sectors. The sector images were stitched (Preibisch et al., 2009; Thévenaz and Unser, 2007) using Fiji software (Schindelin et al., 2012) to reconstruct a complete single mat image. The stitched image size of each mat was standardised using the stacking function in the same software. Detailed steps for image stitching and stacking are in the Supplementary Data.

### 3.4.4 Conditioned medium mat assays

Yeast were cultured in 50 mL SLAD for 48 h . Cultures were washed twice with PBS before being inoculated into 20 mL of fresh SLAD or CM at $1 \times 10^{4}$ cells $\mathrm{mL}^{-1}$ and incubated for 16 h . Following incubation, cell images were taken at $400 \times$ magnification using the microscope and camera described above. Images were processed and cell elongation ratio (ratio of major to minor axis) was measured using Fiji software (Schindelin et al., 2012). Steps are described in the Supplementary Data. Cultures were also plated as described in SLAD mat assays.

Statistical analysis was performed with a Welch's T-test using GraphPad Prism version 7.02 software for Windows.

### 3.4.5 Nitrogen and glucose measurement

Residual nitrogen and glucose were analysed spectrophotometrically with enzymatic methods. Nitrogen was analysed with a Megazyme Ammonia Assay Kit (Rapid; Cat No. K-AMIAR), according to the manufacturer's instructions. Glucose was measured according to the method of Mannheim (1989). For both assays, $1 \times$ SLAD was used to generate a calibration curve.

### 3.5 Results

### 3.5.1 Nitrogen limitation induces filamentous and invasive growth in mats

Several commercial wine yeast strains and laboratory strain prototrophic $\Sigma 1278$ b were tested for mat formation in SLAD to stimulate nitrogen limitation. Maximum mat size was approximately $4-5 \mathrm{~mm}$ in diameter, and this was often observed at the first time point analysed (3 days). In comparison, the maximum size of a colony grown from the same strains on SLAD with $2 \%$ agar reaches 1 mm (Joanna Sundstrom, pers. comm.). As the maximum mat size is at least 4 -fold wider than colonies formed on SLAD with $2 \%$ agar, and cell growth occurs as a thin layer across the surface, these have been defined as mats rather than colonies. Mat expansion also extends beyond the boundary of the inoculum drop. This can be visualised in Appendix B, Figure B.1A, where growth of the mat inoculated with a single cell doubles in size between 3 and 9 days. The mats had no complex structures, but a subset of yeast cells grew filamentously and invaded the agar in all strains except I1 (Fig. 3.1A). The number of invasive foci varied between strains. Wine yeast had large, round invasive growth structures in comparison to $\Sigma 1278$ b which were more filamentous (Fig. 3.1B). These structures can only be reached by breaking the agar, and thus were classified as invasive. The progression of filamentous, invasive mat formation for $\Sigma 1278$ b, AWRI796 and EC1118 after 3, 6 and 9 days can be seen in Figure 3.1C. Interestingly, the size of the mat has limited changes, cells on the mat rim did not grow along the surface, yet the invasively growing cells continued to grow over time. Invasively growing cells at the mat rim grew much quicker than those inside the mat as shown by the different sizes of the structure.


Figure 3.1: SLAD mat assays on SLAD low-density agar (0.3\%). (A) SLAD mat morphologies of $\Sigma 1278$ b and selected wine yeast strains. Approximately 1000 cells were spotted on the plate. Four to six images were taken for each mat after 9 days and stitched to generate a single mat image. A typical representative image of each strain is shown. Scale bar, 1 mm . (B) Micrographs of mats post-wash showing invasive growth structures of $\Sigma 1278$ b and the wine strain AWRI796. Please refer to next page for (C).
(C)

| DAY |  |  |  |
| :---: | :---: | :---: | :---: |
| 3 | 6 | 9 |  |



Figure 3.1: (C) Stitched mat images of $\Sigma 1278 \mathrm{~b}$ and the wine strains, AWRI796 and EC1118, after 3, 6 and 9 days. Note the same mat for each strain is imaged over the time series. Scale bar, 1 mm .

### 3.5.2 Mat size and biomass increases with increasing ammonium sulfate

Since nitrogen is a limiting growth factor and mat size on SLAD is reduced significantly compared to mats reported in rich medium, this section investigated whether there were any structural or size changes to mats as the amount of nitrogen increased. The filamentous invasive structures of $\Sigma 1278$ b changed to a more rounded invasive structure when ten times more ammonium sulfate ( $500 \mu \mathrm{M}$ ) was included in the medium (Fig. 3.2). The structures were still observed underneath the agar surface. The overall mat biomass and size increased with increasing ammonium sulfate for both $\Sigma 1278$ b and AWRI796. With 100 times more ammonium sulfate ( 5 mM ), the invasive structures of both strains were similar.


Figure 3.2: SLAD mat morphologies of $\Sigma 1278$ b and AWRI796 after 3 days on SLAD low-density agar ( $0.3 \%$ ) with $50 \mu \mathrm{M}, 500 \mu \mathrm{M}$ and 5 mM ammonium sulfate. The invasive structures of cells grown on $500 \mu \mathrm{M}$ and 5 mM ammonium sulfate could not be shown in the original brightness due to increased biomass. Therefore, brightness was increased to reveal the invasive structures.

### 3.5.3 Filamentous growth is inhibited by a neighbouring mat

In order to test whether filamentous growth can be enhanced or inhibited by a neighbouring filamentous mat, paired SLAD mat assays were performed with cells inoculated at a distance of approximately 1 mm on the same plate. Filamentous growth was inhibited by
a neighbouring mat, regardless of whether it was the same or a different strain (Fig. 3.3). Cells at the rim away from a neighbouring inoculum continued to grow and were highly filamentous. When two inocula were close enough, filamentous growth was completely inhibited. In the case of a larger distance between inocula, filamentous growth was initiated but stopped when the gap reached approximately $3 \mu \mathrm{~m}$.


Figure 3.3: Paired SLAD mats at a close distance between $\Sigma 1278$ b and AWRI796 (top panel) and $\Sigma 1278$ b and $\Sigma 1278$ b (bottom panel) on SLAD low-density agar ( $0.3 \%$ ). Each whole mat is shown (left and right panels) while the middle panel shows a magnified view of the gap between the paired mats. Images were taken 18 days after inoculation. Each of the whole mat images has a scale of 1 mm and the middle images have a scale of $5 \mu \mathrm{~m}$.

### 3.5.4 Conditioned medium affects cell elongation in liquid culture but not invasive growth

Conditioned medium from a $\Sigma 1278$ b stationary-phase culture has been previously shown to stimulate filamentous and invasive growth when it was used as the assay medium (Chen and Fink, 2006). This study tested if pre-exposure to conditioned medium would enhance the filamentous and invasive growth phenotype on SLAD agar. Stationary-phase cultures of $\Sigma 1278$ b and AWRI796 were collected to prepare CM as described. These were then used to culture (in liquid) the same two strains overnight before analysis in a SLAD mat assay. After growing overnight in either CM, cell elongation ratio of both strains increased compared to an overnight culture in fresh SLAD (Fig. 3.4). The CM derived from AWRI796 resulted in a more enhanced response with longer cells formed by both
strains ( $p$-value $<0.0001$ ). However, pre-culturing in CM from either strain did not result in enhanced filamentous invasive growth on SLAD agar for either strain (data not shown).


Figure 3.4: A boxplot showing cell elongation ratio (y-axis) of $\Sigma 1278$ b and AWRI796 cultured in either SLAD, $\Sigma 1278$ b CM or AWRI796 CM for 16 h . Cell elongation ratio is the ratio of major to minor axis of an ellipse (cell). For $\Sigma 1278$ b cells, the mean cell elongation ratios were not significantly greater in $\Sigma 1278$ b CM but significant in AWRI796 CM compared to in SLAD ( $p$-values $=0.145$ and $0.00984 ; \mathrm{df}=111.49$ and 122.60). Mean cell elongation ratios of AWRI796 cells in $\Sigma 1278$ b CM and AWRI796 CM were significantly greater than in SLAD ( $p$-values $=1.291 \mathrm{e}-7$ and $4.873 \mathrm{e}-10 ; \mathrm{df}=117.33$ and 107.39).

### 3.5.5 Effect of aromatic alcohols, ethanol, hydrogen sulfide and sulfite on yeast growing on SLAD mat assays

Aromatic alcohols (tryptophol and 2-phenylethanol in combination) and sulfur compounds ( $\mathrm{H}_{2} \mathrm{~S}$ and sulfite) were examined for any effects on yeast mats growing on SLAD. Stock solutions of aromatic alcohols needed to be first dissolved in ethanol which has been reported to stimulate hyperfilamentation in diploid $\Sigma 1278$ b (Lorenz et al., 2000). Therefore, the impact of ethanol alone was evaluated, in addition to aromatic alcohols, $\mathrm{H}_{2} \mathrm{~S}$ (supplied as sodium sulfide) and sulfite. Without any additions to the medium, $\Sigma 1278 \mathrm{~b}$ had a larger proportion of cells that initiated agar invasion and filamentation compared to AWRI796 (Fig. 3.5A). $\Sigma 1278 \mathrm{~b}$ is commonly observed to rapidly undergo filamentation and invasive growth, and subsequently results in difficulty in deciphering differences in filamentous/invasive growth between conditions, except for the addition of sodium
metabisulfite (SMS) (Fig. 3.5A-E and F-J). SMS addition (0.01\%) resulted in delays in both agar surface and invasive growth (Fig. 3.5F-J).

For AWRI796, the addition of $0.05 \%$ ethanol in SLAD increased the number of invasive foci and triggered early development of agar invasion (Fig. 3.5A and B). The presence of a total $100 \mu \mathrm{M}$ aromatic alcohols, however, suppressed this effect (Fig. 3.5C compared to B ). The addition of $0.4 \mathrm{mg}^{-1}$ sodium sulfide produced large numbers of invasive foci and reduced biomass on the agar surface (Fig. 3.5D). The effect remained with the combination of both aromatic alcohols and sulfide (Fig. 3.5E). All media containing SMS (Fig. 3.5F-J) resulted in reduced biomass (both surface and invasive). When ethanol, sodium sulfide and SMS were added, the majority of AWRI796 cells grew invasively (Fig. $3.5 \mathrm{I})$. However, inclusion of aromatic alcohols returned cells to almost exclusively surface growth (Fig. 3.5J). Thus, it seems that the suppressive effect on invasive growth of aromatic alcohols is alleviated when sulfide is present and is supported in the presence of SMS, indicating an interplay between sulfide and sulfite.


Figure 3.5: SLAD mat morphologies of $\Sigma 1278$ b and AWRI796 on Day 3 (D3), 6 (D6) and 9 (D9) on SLAD low-density agar ( $0.3 \%$ ) (A) without any additions, with the addition of (B) ethanol (EtOH), (C) combination of ethanol and aromatic alcohols (AA), (D) combination of ethanol and sulfide $\left(\mathrm{H}_{2} \mathrm{~S}\right)$, (E) combination of ethanol, aromatic alcohols and sulfide. Please refer to next page for $(\mathrm{F}-\mathrm{J})$.

|  |  | With SMS |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  |  |  | EtOH | $\begin{gathered} \mathrm{EtOH}+ \\ \mathrm{AA} \end{gathered}$ | $\begin{gathered} \mathrm{EtOH}+ \\ \mathrm{H}_{2} \mathrm{~S} \end{gathered}$ | $\begin{gathered} \mathrm{EtOH}+ \\ \mathrm{AA}+\mathrm{H}_{2} \mathrm{~S} \end{gathered}$ |
|  | m |  |  |  | $\frac{6}{6+5}$ |  |
|  | \| $0$ |  |  |  |  |  |
|  | $\sigma$ |  |  |  |  |  |
|  | $m$ |  |  |  |  |  |
| 10 0 2 2 3 | טٌ |  |  |  |  |  |
|  | $0$ |  |  |  |  |  |

Figure 3.5: $(\mathrm{F}-\mathrm{J})$ the same combinations as in $\mathrm{A}-\mathrm{E}$ with the addition of sulfite (SMS).

### 3.6 Discussion

Yeast grow into a large mat of a thin layer of cells across the surface of low-density YPD agar with some strains forming complex architecture (Reynolds and Fink, 2001; Hope and Dunham, 2014). Karunanithi and colleagues (2012) showed that filamentous mats can also be formed by $\Sigma 1278$ b on YP medium in which glucose is limited. This study reports a different mat morphology formed by $\Sigma 1278$ b and wine yeast strains on SLAD, where nitrogen is limited. Mat size was reduced, no complex architecture was formed and a proportion of cells switched to filamentous and invasive growth. This study further show that addition of some key yeast metabolic compounds affects invasive growth of these mats.

The low nitrogen conditions of SLAD agar limited cell spreading across the agar and instead, a subset of cells underwent pseudohyphal growth and invaded the agar. This response is consistent with the findings reported in other studies investigating nitrogen limitation on medium-density agar (Gimeno et al., 1992; Zupan and Raspor, 2010). Whilst there were no obvious morphology variations in the surface growing cells between strains, the number of invasive foci did vary between strains. The invasive foci of wine yeasts were more rounded in structure compared to those of $\Sigma 1278$ b (Fig. 3.1B). This may simply represent more rapidly growing or less pseudohyphal cells. One reason may be that wine yeast have developed the ability to utilise nitrogen more efficiently, and thus be able to grow rapidly in the presence of limited nutrients compared to laboratory yeast, since they have evolved to survive multiple stresses in the winemaking environment. This is supported by the observations of increased nitrogen content in SLAD, $\Sigma 1278$ b also grew into rounded invasive structures similar to wine yeasts (Fig. 3.2). This indicates that nutrient sufficiency may be reflected by rounded invasive structures. The increase in overall mat size also suggests that nitrogen is important for mat expansion, primarily for cellular growth.

Within each mat, (filamentous) invasive growth continued over time and was most rapid at the mat rim compared to the centre. This may be a result of less competition for nutrients at the rim due to lower cell density, and therefore cell division is supported and more likely to expand. In order to determine if filamentous growth can be induced by another filamentous mat in close proximity, cells of AWRI796 (less filamentous) and $\Sigma 1278$ b (highly filamentous) were inoculated close to each other. In this experiment, filamentous growth was inhibited on the side closest to the neighbouring mat. The same occurred when two inocula of $\Sigma 1278$ b were spotted next to each other, suggesting that the inhibition is neither strain dependent nor unidirectional. This observation is consistent with the repulsion between two neighbouring filamentous colonies of bacteria (Matsushita and Fujikawa, 1990). The inhibition was not evident in yeast surface filamentation colonies in other study in medium-density agar, but it may be due to the shorter incubation time i.e. three days (Liu et al., 1993). Non-filamentous yeast colony growth has been shown to be
affected by the presence of a neighbouring colony. This was due to the release of ammonia via the amino acid permease Shr3p as a signalling molecule from colonies to prevent growth towards a neighbouring colony (Palková et al., 1997). The ammonia signalling may be involved in the filamentous growth inhibition between the two neighbouring mats.

In this study, several compounds were found to affect filamentous and invasive growth of mats on SLAD agar. However, the effect was not obvious for $\Sigma 1278$ b. This strain readily forms filamentous and invasive cells, even in the control condition (SLAD). $\Sigma 1278$ b is well known for its expeditious ability to invasively grow and is chosen for filamentous studies since it seems to be extremely sensitive to ammonia repression of nitrogen assimilation pathways (Rytka, 1975; Wiame et al., 1985; Gimeno et al., 1992).

For AWRI796, the transition to invasive growth in response to low nitrogen was enahnced by the addition of ethanol (Fig. 3.5A and B). FLO11 is required for filamentous and invasive growth during nitrogen starvation (Braus et al., 2003; Lo and Dranginis, 1998; Robertson and Fink, 1998). This gene can be regulated epigenetically by the binding of Sflp which requires histone deacetylase Hda1p (Halme et al., 2004; Octavio et al., 2009). Immunofluorescence analysis has shown that Flo11p was present on the cell surfaces of pseudohyphal or filament-forming cells and was silenced in the yeast form cells derived from the same clone (Guo et al., 2000; Halme et al., 2004). This may explain observations in this study that only a subset of cells transitioned to grow invasively. Ethanol has been previously shown to abolish Sfl1p-mediated silencing (Octavio et al., 2009), which is consistent with the observation that ethanol addition to SLAD increased and induced an early development of agar invasion and filamentous growth. Interestingly, no enhancement of invasive growth by aromatic alcohols was observed, as was reported by Chen and Fink (2006) on $2 \%$ agar, but instead their addition suppressed the enhancement effect of ethanol (Fig. 3.5B and C). This may be due to variation in experimental preparation as Chen and Fink (2006) did not report the method for preparation of the aromatic alcohols.

The effect of addition of $\mathrm{H}_{2} \mathrm{~S}$ was also analysed, since evidence suggests that $\mathrm{H}_{2} \mathrm{~S}$ is a signalling mediator for stress resistance and longevity. $\mathrm{H}_{2} \mathrm{~S}$ offers protection against nutrient and oxygen deprivation in mammals (Blackstone and Roth, 2007; Hine and Mitchell, 2015). Similar $\mathrm{H}_{2} \mathrm{~S}$-mediated biological benefits are also found in yeast. For example, the mutant $\Delta$ met17 has increased $\mathrm{H}_{2} \mathrm{~S}$ production and an extended chronological lifespan (Johnson and Johnson, 2014; Linderholm et al., 2008). The mutant also had increased resistance to heat shock, oxidative and heavy metal stresses, and metal chelate toxicity, suggesting that $\mathrm{H}_{2} \mathrm{~S}$ could lead to an adaptive response to environmental stresses (Singh and Sherman, 1974; Brown et al., 2006; Hwang et al., 2007; Johnson et al., 2014). This study reports a novel response to $\mathrm{H}_{2} \mathrm{~S}$, which is to enhance invasive growth. Historically, invasive growth has been hypothesised to be a survival strategy adopted by yeast during nitrogen starvation that is believed to be a mode of action to forage for nutrients. $\mathrm{H}_{2} \mathrm{~S}$ is well known to be released by yeast upon nitrogen limitation, perhaps this extruded sulfide is sensed by nearby cells as a cue to switch to invasive growth. The mechanism that may
allow cells to respond to this putative $\mathrm{H}_{2} \mathrm{~S}$ cue is not yet known, however evidence supports involvement of the Retrograde-MAPK pathway. RTG3 that activates the mitochondrial retrograde (RTG) signalling was shown to be required by a $\Delta$ met17 mutant to confer longevity and stress tolerance (Johnson and Johnson, 2014). The RTG pathway is usually activated when mitochondrial function is compromised, but the signalling pathway is unclear (Liu and Butow, 2006). Several eukaryotic models have demonstrated a tight inverse relationship between oxygen availability and $\mathrm{H}_{2} \mathrm{~S}$ production in mitochondria, leading to the proposal of sulfide metabolism as an oxygen sensor (Doeller et al., 2005; Furne et al., 2008; Olson and Whitfield, 2010; Olson et al., 2010; Olson, 2012). Fission yeast, Schizosaccharomyces pombe, exposed to $\mathrm{H}_{2} \mathrm{~S}$ results in downregulation of many mitochondrial genes and reduced mitochondrial oxygen consumption, which may result in RTG pathway activation (Jia et al., 2011). Many genes involved in the RTG pathway have been identified as positive regulators of filamentous MAPK cascade, thus supporting the enhancement of filamentous and invasive growth by $\mathrm{H}_{2} \mathrm{~S}$ via the RTG-MAPK pathway (Chavel et al., 2014).

Exposure to sulfite delayed cellular and invasive growth in both $\Sigma 1278$ b and AWRI796 (Fig. 3.5F-J). Less filamentous growth was also observed in $\Sigma 1278$ b in the presence of sulfite. Cells undergoing filamentous growth display prolonged apical growth leading to highly polarised growth at the bud tip, and this is tightly regulated with cell cycle (Pruyne and Bretscher, 2000). A transcriptomics study of S. cerevisiae strain 3090-1d showed that sulfite exposure downregulated cell cycle and polarity-related genes including MYO1, BNR1 and PCL1 (Park and Hwang, 2008). This may reduce the hyperpolarisation event and in turn filamentous growth upon sulfite exposure. Growth, although delayed, did occur upon sulfite exposure suggesting adaption and tolerance to sulfite. Sulfite is produced as part of the sulfate assimilation pathway. The effect of sulfite is of interest to this study because sulfite is usually converted to sulfide and eventually metabolised into methionine, cysteine and glutathione. However, sulfite can be produced and excreted in the form of sulfur dioxide $\left(\mathrm{SO}_{2}\right)$. Excess sulfite has antioxidant and antimicrobial activity and has previously been shown to reduce invasive growth (Zupan and Raspor, 2010). In comparison, this study used a lower concentration of sulfite ( 1.05 vs 9.61 mM ) and hence did not completely block invasive growth.

Pre-exposure of CM was found to have no impact on invasive growth despite having triggered cell elongation in liquid culture (Fig. 3.4). This result suggests that cells decide their phenotypic fate based on an environmental trigger after inoculation onto agar plates. This supports the claim that yeast have developed mechanisms to quickly adapt to environmental changes. Several studies have investigated short and long term responses to the fluctuations in environmental factors. A transient transcriptional change was found immediately after temperature shifts before an adaptation to a new steady state of transcript levels (Gasch et al., 2000). Another transcriptomics study also showed that yeast re-programmed a number of metabolic networks rapidly towards nutritional perturbation (Dikicioglu et al., 2011). The findings from integrated data from both transcriptomics
and metabolomics studies showed that glucose impulse in glucose-starved conditions provoked changes in carbon metabolism, purine and pyrimidine biosynthetic pathways, folate metabolism, superpathway of serine and glycine and the methionine biosynthetic pathways, and aspartate and glutamate biosynthetic pathways (Dikicioglu et al., 2012). Ammonium impulse in nitrogen-starved conditions also affected these metabolic pathways with different profiles. These reports suggest that in the present study, it could be possible that the yeast cells were re-programmed to elongate when cultured in CM, and quickly re-programmed again when transferred to SLAD agar.

The findings of this study build upon the current understanding of the effect of nitrogen limitation on mat formation and the influence of yeast metabolites, ethanol, aromatic alcohols, $\mathrm{H}_{2} \mathrm{~S}$ and sulfite. Further study should involve genetic analysis of the induction or inhibition of invasive growth by these compounds. These observations provide a further opportunity to study the physiological role of each of the metabolites and the pathways leading to the effect upon cellular differentiation.

### 3.7 Funding

This work was supported by Wine Australia [GWR Ph1305] and Australian Research Council [DP 20111529]. ELT was supported by an Adelaide Graduate Research Scholarship. Conflict of interest: None declared.

### 3.8 Acknowledgements

Prototrophic $\Sigma 1278$ b was kindly donated by Dr Charles Boone (University of Toronto). The authors thank Dr Michelle Walker (University of Adelaide) for generating strain I1.

### 3.9 Supplementary Data

### 3.9.1 Methods

## Mat image stitching and stacking

1. Create a folder for stitching process, only import the group of images needing to be stitched one at one time.
2. Download and install Fiji from http://imagej.net/Fiji/Downloads.
3. Open the application.
4. Click Plugins from the menu, select Stitching, and select Grid/Collection stitching.
5. Choose Sequential Images from the drop-down menu for Type, click OK.
6. In the Directory, choose the path to the folder created for stitching containing images to be stitched, click OK.
7. Click OK to confirm image files to be stitched.
8. A stitched image will be generated. Save the image as a TIFF file.
9. For images that cannot be stitched using the method above, use MosaicJ to manually assemble the images.
10. Click Plugins from the menu, select Stitching, and select MosaicJ.
11. A new window will open.
12. Click File, select Open Image Sequence.
13. Select the first image in the stitching folder, click Open.
14. All images in the folder will be loaded.
15. Click an image, the image will be in the working space. Drag images to assemble at the correct position.
16. Click File from the menu, select Create Mosaic.
17. A stitched image will be generated. Save the image as a JPEG file as the TIFF image created using this method is very large.
18. For stacking, open the largest image which all other images will be normalised to.
19. Open other images to be normalised.
20. Click Image from the menu, select Stacks, and select Images to Stack.
21. Click OK. Images are now stacked.
22. Click Image from the menu, select Stacks, and select Stack to Images.
23. Individual images are shown with the normalised size.
24. To fill black area with background colour of the original image, click Colour Picker icon, and then click on the background to pick up colour. Click Blood Fill Tool icon, and click on the black area to fill with background colour.
25. Save the image.

## Cell elongation ratio measurement

1. Open the image that needs to be measured (in this example, images were taken at $400 \times$ magnification).
2. Click Analyze from the menu, select Set Scale. Enter 64 pixels $=10 \mu \mathrm{~m}$ (Note: this needs to be checked for each individual microscope), check Global and click OK. Now the image and the following images opened within this session have been calibrated.
3. Click Process from the menu, select Subtract Background. Input 40 pixels for Rolling ball radius, check Light background, click OK.
4. To convert into a black and white image, click Image from the menu, choose Adjust and select Threshold. Select Default and $\mathbf{B} \& \mathbf{W}$ from the drop-down menu, click Apply and Close.
5. Click Process from the menu, select Binary, and select Fill Holes.
6. Click Process from the menu, select Binary, and select Watershed.
7. To remove non-cell particles, click Colour Picker icon, and then click on the white area in the image. Click Paintbrush Tool icon, double right-click the icon to set brush width, and click OK.
8. Click (and drag) on the non-cell particles to be removed. Save the processed image if necessary.
9. To set measurements that need to be performed (only need to do this once), click Analyze from the menu, select Set Measurements. Check Area, Shape descriptors, Fit ellipse, Feret's diameter and Display label. Choose None for Redirect to and $\mathbf{3}$ for Decimal places. Click OK.
10. To measure, click Analyze, select Analyze particles. Size ( $\mu \mathrm{m}^{\wedge} 2$ ): 5-infinity; Circularity: 0-1; Show: Overlay Outlines; check Display results, Summarize, Exclude on edges, click OK.
11. Save Results table for later use. Save the outline image if necessary.
12. Use AR (aspect ratio) in the Results table as the cell elongation ratio for statistical analysis.

## Chapter 4

## Understanding wine yeast invasive growth through transcriptional analysis

## Contextual statement

Chapter 3 highlighted that nitrogen limitation leads to yeast invasive growth in low-density agar medium. This response was consistent across all strains except for one which had poor overall growth. Several environmental factors could manipulate this invasive growth. Chapter 4 addresses the final aim of the project: to investigate the triggers and regulation of wine yeast biofilms and invasive growth. The manuscript in this chapter presents genes and biological processes associated with invasive growth in low-nitrogen mat conditions.

## Statement of Authorship

| Title of Paper | Transcriptional analysis of invasively growing wine strains of Saccharomyces cerevisiae |
| :--- | :--- |
| Publication Status | Г Published $\quad$ T Accepted for Publication |
|  | Гsubmitted for Publication $\quad$ Unpublished and Unsubmitted work written in |
| manuscript style |  |

Principal Author

| Name of Principal Author (Candidate) | Ee Lin Tek |
| :--- | :--- |
| Contribution to the Paper | Performed all experiments and data analysis, interpreted data, and wrote manuscript. |
| Overall percentage (\%) | $80 \%$ |
| Certification: | This paper reports on original research I conducted during the period of my Higher Degree by <br> Research candidature and is not subject to any obligations or contractual agreements with a <br> third party that would constrain its inclusion in this thesis. I am the primary author of this paper. |
| Signature |  |

## Co-Author Contributions

By signing the Statement of Authorship, each author certifies that:
i. the candidate's stated contribution to the publication is accurate (as detailed above);
ii. permission is granted for the candidate in include the publication in the thesis; and
iii. the sum of all co-author contributions is equal to $100 \%$ less the candidate's stated contribution.

| Name of Co-Author | Andrew R. Hesketh |  |
| :--- | :--- | :--- |
| Contribution to the Paper | Supervised RNA-sequencing data processing and analysis, editing of the manuscript. |  |
|  |  |  |
| Signature |  | Date |


| Name of Co-Author | Joanna F. Sundstrom |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |  |  |  |  |
| Signature |  | Date | 4 | 091 | 2017 |
| Name of Co-Author | Jennie M. Gardner |  |  |  |  |



| Name of Co-Author | Stephen G. Oliver |  |
| :--- | :--- | :--- |
| Contribution to the Paper | Supervised development of work and helped in data interpretation. |  |
|  |  |  |
| Signature |  | Date |


| Name of Co-Author | Vladimir Jiranek |
| :--- | :--- |
| Contribution to the Paper | Supervised development of work, helped in data interpretation and editing of the manuscript. |
|  |  |
| Signature |  |

Please cut and paste additional co-author panels here as required.

# Transcriptional analysis of invasively growing wine strains of Saccharomyces cerevisiae 

Ee Lin Tek ${ }^{1}$, Andrew R. Hesketh ${ }^{2}$, Joanna F. Sundstrom ${ }^{1}$, Jennie M. Gardner ${ }^{1}$, Stephen G. Oliver ${ }^{2}$, Vladimir Jiranek ${ }^{1,3 *}$<br>${ }^{1}$ Department of Wine and Food Science, University of Adelaide, Waite Campus, South Australia 5064, Australia.<br>${ }^{2}$ Department of Biochemistry \& Cambridge System Biology Centre, University of Cambridge, United Kingdom.<br>${ }^{3}$ Australian Research Council Training Centre for Innovative Wine Production.

*Corresponding author: PMB 1, Glen Osmond, South Australia 5064, Australia. Tel: 618-8313-6651; E-mail: vladimir.jiranek@adelaide.edu.au

### 4.1 Keywords

Invasive growth; diploid wine yeast; FPS1; low nitrogen; hexose transporter

### 4.2 Summary

In response to unfavourable conditions such as nutritional and environmental stress, the yeast Saccharomyces cerevisiae can switch to filamentous growth and/or invasive growth by re-programing cellular systems. A number of signal transduction pathways have been identified that regulate these processes, some of which are common to both filamentous and invasive growth. Previous genome-wide studies have identified biological pathways specific to invasive growth, however, the regulation of these is yet to be completely understood. Using differential transcriptome analysis of surface and invasively growing cells of a diploid wine yeast strain, this study found genes and biological processes that have not previously been associated with invasive growth. The analysis identified 272 genes that were upregulated and 84 genes downregulated in invasively growing cells. Enriched Gene Ontology categories of upregulated genes included medium-chain fatty acid biosynthetic process, carbohydrate metabolic process, cellular water homeostasis, fungal-type cell wall organisation, and glucose import. Further analysis of deletion mutants confirmed that FPS1, encoding for the glycerol export protein, is required for invasive growth. This work also identified a hypothetical gene, that has a portion of translated gene sequence homologous to an amidase domain, may have a role in invasive growth.

### 4.3 Introduction

The budding yeast $S$. cerevisiae is able to adapt in response to various nutritional stresses (e.g. glucose and nitrogen limitation) to aid survival. This yeast is dimorphic, in that it can undergo a developmental switch from round, single cells to an elongated (pseudohyphal) multicellular filamentous form (Gimeno et al., 1992; Kron et al., 1994). This results in both haploid and diploid cell types capable of invasion into agar (Gimeno et al., 1992; Cullen and Sprague, 2000). Since yeast cells are non-motile, it is believed that this change in morphology allows them to forage for nutrients. These modes of growth have also been shown to be influenced by strain genetic backgrounds and other physiochemical factors rather than simply nutrient depletion, for example the presence of fusel alcohols, pH , temperature, salt and atmosphere (Zupan and Raspor, 2010; Dickinson, 1996). Yeast can also switch from fluffy and smooth colonies in response to environmental conditions and is accompanied with change in gene expression (Kuthan et al., 2003).

Four signalling pathways shown to regulate pseudohyphal growth have been
well documented and reviewed by Cullen and Sprague (2012). These include the cyclic AMP-dependent protein kinase A (cAMP-PKA) pathway, the Snf1 pathway, the target of rapamycin (TOR) pathway and the mitogen-activated protein kinase (MAPK) pathway. Some proteins in these pathways are also required for invasive growth. For example, components of the MAPK pathway, required for pseudohyphal formation, Ste20p, Ste11p, Ste7p, Kss1p, and Ste12p, are also required for invasive growth (Roberts and Fink, 1994; Cook et al., 1997). Likewise, Tpk2p of the cAMP-PKA pathway is essential for both pseudohyphal and invasive growth (Robertson and Fink, 1998). In relation to the Snf1 pathway, yeast with a deletion of SNF1 were unable to invasively grow or undergo cell elongation (Vyas et al., 2003; Cullen and Sprague, 2000). Rapamycin inhibits invasive growth, which can be restored by overexpression of TAP42, showing that the TOR pathway is involved (Cutler et al., 2001). The cell surface flocculin, Flo11p, is widely regarded as the primary mechanism for cell-cell and cell-surface adhesion, important for pseudohyphal and invasive growth. Regulation of Flo11p is shared by the cAMP-PKA, Snf1 and MAPK pathways, i.e. Tpk2p, Snf1p, and Ste12p are all involved (Lo and Dranginis, 1998; Rupp et al., 1999; Kuchin et al., 2002; Pan and Heitman, 2002).

In diploid cells, pseudohyphal and invasive growth can occur simultaneously or independently, suggesting that apart from the shared core signalling pathways, it is likely there are invasive growth specific pathways. A number of studies have identified genes and biological pathways necessary for invasive growth, and these have involved screening of loss-of-function and overexpression mutants in a range of media (Jin et al., 2008; Ryan et al., 2012; Shively et al., 2013). Jin and colleagues (2008) screened a transposon insertion gene disruption and overexpression library in a haploid version of the filamentous strain of $S$. cerevisiae, $\Sigma 1278$ b, to identify genes necessary for filamentous growth induced by butanol. They found 243 out of 487 genes were also necessary for haploid invasive growth. Ryan and colleagues (2012) screened both haploid and diploid $\Sigma 1278$ bene deletion libraries and identified 577 genes required for haploid invasive growth in rich medium, of these 132 were also required for diploid pseudohyphal growth. However, this group measured relative filamentous outgrowth to determine extent of pseudohyphal growth, which does not take into account agar invasion. In contrast, Shively and colleagues (2013) found 551 genes that when overexpressed exaggerated diploid invasive growth in sufficient nitrogen. The loss-of-function and overexpression studies were comprehensive, yet they are limited by the resources (i.e. number of mutants in the libraries versus number of verified ORFs) and they were studied in different media. Studying gene expression profiles offers an additional layer of information to understand active physiological processes that are associated with the condition of interest and potentially predict novel functions of genes.

In this study, RNA-sequencing technology was used to compare transcriptomes of diploid wine yeast cells collected from the agar surface to cells growing invasively which also included the filamentous phenotype. In the invasively growing population, 272 genes were upregulated and 84 genes were downregulated. Surprisingly, no transcripts from the mentioned four signalling pathways were differentially expressed. Enriched Gene Ontology
(GO) terms of the upregulated gene sets showed that medium-chain fatty acid biosynthetic process, carbohydrate metabolic process, cellular water homeostasis, fungal-type cell wall organisation, and glucose import may be important processes for invasive growth. A number of the upregulated genes identified in this study are common to previous mutant screening studies. The association of cellular water homeostasis to invasive growth is novel, and thus further deletion analysis of genes within this group identified FPS1 as being necessary for invasive growth. Results from this work also uncovered a potential role for a hypothetical gene.

### 4.4 Results and Discussion

### 4.4.1 Global change in gene expression between surface and invasively growing cells

Total RNA was extracted from cells of the diploid wine yeast, AWRI796, collected from the surface and invasively growing into a low percentage ( $0.3 \%$ ), low nitrogen agar medium. Three replicates for each growth type were used with an RNA-sequencing approach to profile global changes in gene expression between surface and invasively growing cells. Sequencing yielded between 35 and 37 million reads from each RNA sample. Differentially expressed genes were defined as those deemed to be statistically significant based on a t-test relative to a 1.3 -fold-change threshold using the limma TREAT method of McCarthy and Smyth (2009). In the invasively growing population, 272 genes were upregulated and 84 genes downregulated, compared to surface growing cells (Table S1). Four of the ten genes having the largest change in expression were hexose transporter genes (HXT3, HXT4, HXT6 and HXT7; Table 4.1). Among these genes, HXT4 has been reported to affect filamentous growth and is required for invasive growth under butanol induction (Jin et al., 2008).

Table 4.1: Top 10 genes with the largest change in gene expression in invasively growing cells.

| Gene Symbol | Name | $\log _{2}$ Fold Change | Adj. $p$-value |
| :--- | :--- | :--- | :--- |
| HXT7 | HeXose Transporter | +3.78 | $1.39 \mathrm{E}-8$ |
| HXT4 | HeXose Transporter | +3.04 | $1.58 \mathrm{E}-8$ |
| AWRI796_5153 | Amidase | +2.69 | $3.30 \mathrm{E}-7$ |
| SSA2 | Stress-Seventy subfamily A | +2.26 | $1.34 \mathrm{E}-7$ |
| HXT6 | HeXose Transporter | +2.25 | $5.40 \mathrm{E}-8$ |
| RGI1 | Respiratory Growth Induced | +1.92 | $5.77 \mathrm{E}-8$ |
| AWRI796_2017 | NA | +1.79 | $3.30 \mathrm{E}-7$ |
| HXT3 | HeXose Transporter | +1.74 | $3.72 \mathrm{E}-7$ |
| CAR1 | Catabolism of ARginine | +1.73 | $3.30 \mathrm{E}-7$ |
| NCE103 | NonClassical Export | -1.72 | $6.93 \mathrm{E}-8$ |

To investigate the biological processes that are associated with invasive growth, GO enrichment analysis was performed. This analysis revealed 37 enriched GO terms for upregulated genes, while none were identified for downregulated genes (Table S2). The enriched GO terms were summarised into five main groups by clustering similar GO terms using REVIGO (Supek et al., 2011), these were medium-chain fatty acid biosynthetic process, carbohydrate metabolic process, cellular water homeostasis, fungal-type cell wall organisation, and glucose import (Fig. 4.1). KEGG pathway analysis of the upregulated and downregulated genes did not identify any overrepresented pathways, including signal transduction pathways required for invasive growth. This may be due to strain differences i.e. wine yeast versus laboratory yeast. Wine yeast may have conserved signalling pathways involving genes that have not yet been characterised, and thus not represented in this transcriptomics analysis.


Figure 4.1: Enriched GO terms (37) of upregulated genes of the invasively growing cells submitted to the REVIGO program. Representative GO categories are shown by circles and visualised by clusters of semantically similar GO terms. Circle colour indicates $\log _{10}$ adjusted $p$-value from the GO enrichment analysis whereas size represents the frequency of the GO term in the underlying GOA database (circles of more general terms are larger).

A number of interesting findings were obtained from differential expression analysis. Approximately $25 \%$ ( 67 genes) of upregulated genes have been reported in other studies as important for invasive growth or associated phenotypes (i.e. diploid pseudohyphal growth, haploid and diploid invasive growth, and differential expression between fluffy and smooth colonies; Table S3). Ten genes were found in more than one other data set, these being ARG8, ERG6, FLO11, IKI3, PMT2, SIN3, SLA1, MGA1, PUT4 and HXT4. However, this is not an exact comparison since: (1) each study used a different conditioned medium (e.g. rich YPD, low nitrogen SLAD, butanol treatment or alternative carbon source GMA); (2) strain ploidy and phenotypes assayed were different.

The present study focuses on the differences between surface and invasive growth, regardless of elongated or ovoid cells, expecting to identify genes and/or biological processes that are important but not easily detected in single gene deletion or overexpression screen studies. Interestingly, a handful of upregulated genes identified in invasively growing cells are common to previously reported upregulated genes of fluffy and downregulated genes of smooth colonies (19 of 165 and 14 of 147, respectively; Kuthan et al., 2003). Yeast colonies with fluffy structure were suggested as a metabolic strategy in unfavourable conditions (Kuthan et al., 2003). This structure changed to smooth when culturing in laboratory conditions and accompanied with a change in gene expression. The presence of common genes expressed in fluffy colonies as well as in invasive growth may indicate a similar strategy used for hostile conditions.

### 4.4.2 Glucose import

Four hexose transporter genes (HXT3, HXT4, HXT6 and HXT7) with increased in gene expression ranging from 3.34- to 13.7 -fold in the invasively growing cells may be related to the availability of nutrients in the medium. Previous studies have shown that these genes are important to recover glucose uptake after ammonium supplementation following a nitrogen-limited sluggish fermentation (Palma et al., 2012). Luyten and colleagues (2002) showed that HXT6 and HXT7 are essential at the end of alcoholic fermentation where the uptake of sugar is often perturbed by the stressful environment of low nutrient and high ethanol. It seems that these genes encoding high-affinity glucose transporters are equally important in the SLADS (containing limited nitrogen supplied solely by ammonium sulfate) conditions of this study. Furthermore, the expression of these four genes was also associated with structured morphologies (Table S3), suggesting a strategy to cope with unfavourable conditions (Kuthan et al., 2003).

### 4.4.3 Carbohydrate metabolism / fungal-type cell wall organisation

Transcriptomics analysis showed genes of carbohydrate metabolic processes were significantly upregulated in invasively growing cells (Fig. 4.1, Table S2). These included glucose phosphorylation (GLK1, HXK1, HXK2), phosphoglucomutase (PGM2), galactokinase (GAL1), and maltose permease (MAL31). Some genes present in both carbohydrate metabolic process and fungal-type cell wall organisation GO categories were also upregulated in invasively growing cells. For example, YEA4, EXG2, GAS1 and GAS5 are involved in chitin and $\beta$-glucan maintenance. Other genes encoding cell wall components, especially fungal-type cell wall components (GO:0009277; $p<2.07 \mathrm{E}-5$ ) were also upregulated in invasively growing cells (Table S2).

Since yeast cells are non-motile, access to nutrients is largely dependent on a cell's access to proximal space. For cells growing on a surface, the expansion of a colony is limited by the agar concentration and nutrients (Chen et al., 2014). If cells were pushed upward, access to nutrients from solid medium becomes limited. Eventually, these cells undergo chronological aging differentiation (Palková et al., 2014). The action of invasion into a medium results in three dimensional access to nutrients, allowing cellular growth and division to continue. Many genes encoding cell wall components were upregulated in the invasively growing cells compared to surface growing cells (Fig. 4.1; Table S2). This suggests cell wall construction is strongly coordinated with cell cycle progress and cell growth activity in the invasively growing population (Klis et al., 2006). Together with the upregulation of genes involved in glucose import and carbohydrate metabolic processes (Fig. 4.1; Table S2), and the time series images of limited surface cell expansion whilst continual invasive population growth occurred (Fig. 4.6B and S2), data in this study supports the hypothesis that invading cells have greater access to nutrients, which aids growth.

AWRI796_5153 is a hypothetical gene with the third largest change in expression (increased expression by 6.45 -fold; Table 4.1). Interestingly, a portion of the gene sequence, when translated, is homologous to an amidase domain. Amidases (KEGG identifier EC 3.5.1.4) function by catalysing the hydrolysis of short-chain amides to organic acids, thereby releasing ammonia. Ammonia is known to be a yeast colony signalling molecule produced during starvation (Palková et al., 1997). To date, amidase is poorly characterised in yeast. However, in bacteria, this protein is normally used to breakdown peptidoglycan for cell wall recycling (Litzinger et al., 2010; Johnson et al., 2013). Other studies have also reported that amidase is involved in the regulation of quorum sensing, biofilms and virulence in bacteria (Ochiai et al., 2014; Clamens et al., 2017).

### 4.4.4 Medium-chain fatty acid biosynthesis pathway

All three genes, EEB1, EHT1 and MGL2, categorised under the medium-chain fatty acid biosynthetic process (GO:0051792; $p<0.015$ ) were upregulated in invasively growing cells. EEB1 is required for invasive growth upon butanol induction whereas EHT1 is required for pseudohyphal growth (Jin et al., 2008; Ryan et al., 2012). Eeb1p and Eht1p are part of medium-chain fatty acid ethyl ester production (Saerens et al., 2006). Ethyl ester is known to contribute to aroma and flavour in alcoholic beverages, but its role in yeast is unclear (Swiegers and Pretorius, 2005; Swiegers et al., 2005). Several reasons have been given for ethyl ester production: (1) to reduce the toxicity of medium-chain fatty acids, (2) to regenerate free co-enzyme A, and (3) to attract Drosophila for dispersal in nature (Thurston et al., 1982; Bardi et al., 1998; Lilly et al., 2006; Saerens et al., 2010; Christiaens et al., 2014).
phosphatidylcholine and phosphatidylethanolamine in the cell, indicating a change in lipid profile (Selvaraju et al., 2016). An increase in phospholipids as a result of increased MGL2 expression may suggest a demand for plasma membrane synthesis, which may be due to an increase in cell size or cellular growth in the invasively growing population.

### 4.4.5 Genetic interaction network analysis predicts genes modulating invasive growth

Genetic interaction network analysis was used (see Experimental Procedures) to determine if any of the differentially expressed genes exhibited extensive connectivity. Network-based approaches are particularly useful in characterising complex biological systems (Barabási and Oltvai, 2004). By establishing a network graph using both differentially expressed genes in this study and interaction data from the Data Repository of Yeast Genetic Interactions, sum of interactions between genes in invasively growing cells can be shown at system-scale and this allowed determination of significant genes from their centrality and connectivity (Zotenko et al., 2008; Koh et al., 2010). In the hub of the largest connected network, three genes were shown to have high connectivity: MSC1, SIN3 and ARO1, with each having at least 30 edges (degree) connected to the node (Fig. S1). Of the three genes, SIN3, which encodes a component of Rpd3 histone deacetylase complexes, has also been identified as being required for pseudohyphal and invasive growth (Carrozza et al., 2005; Ryan et al., 2012). After analysing the network, the connectivity (Betweenness Centrality) value of each gene was examined with the change in expression level. This allowed the discovery of genes that have a larger role in modulating or association with invasive growth. Several genes have been highlighted to have a relatively large value in both Betweenness Centrality and change in expression (Fig. 4.2).


Figure 4.2: Relationship between Betweenness Centrality within the genetic interaction network of differentially expressed genes and changes in gene expression. Each circle represents a gene. Gene names are shown only for those meeting both criteria of absolute $\log _{2}$ fold change greater than 0.7 and Betweenness Centrality greater than 0.015.

Some of these are related to previously identified enriched GO categories: (fungaltype) cell wall organisation and carbohydrate metabolic process such as HXK2, GAS1 and FKS1. Notably, ARO1 and ARO8 both upregulated in invasively growing cells, encode proteins that are involved in phenylalanine and tyrosine biosynthesis, which are precursors of suggested quorum sensing aromatic alcohols in S. cerevisiae (Chen and Fink, 2006). ARO1 is downregulated in smooth colonies compared to fluffy colonies (Kuthan et al., 2003). Genes IME1, MSH4 and EMI2 are involved in meiotic events. IME1 and MSH4 were downregulated in invasively growing cells, while EMI2 was upregulated. EMI2 has a paralog, GLK1, which encodes for glucokinase. In this case, the upregulation of EMI2 may not be due to meiotic function, but could be linked to glucose metabolism. The plot also identified genes related to mitochondria such as CIS1, NUM1 and CSF1, and genes related to cell cycle: DYN1, encodes for protein involved in spindle assembly and orientation and CLB2, encodes for cyclin involved in cell cycle progression. CLB2 overexpression delays $G_{2} / \mathrm{M}$ transition, which means apical growth is prolonged to induce invasive growth (Simpson-Lavy et al., 2009; Shively et al., 2013). Prolonged apical growth that is required for surface filamentation may also be involved in the induction of invasive growth.

RGI1, whose expression increased by 3.78 -fold in the invasively growing cells (Table 4.1), has been reported to be involved in aerobic sugar metabolism (Rep et al., 2000; Domitrovic et al., 2010). Anaerobiosis within a nitrogen atmosphere inhibits invasive growth (Zupan and Raspor, 2010). Previous work in this laboratory has also shown that invasive growth is inhibited in the absence of oxygen as well as in 'petite' strains (Joanna

Sundstrom and Vladimir Jiranek, pers. comm.). Together with the upregulation of several genes related to or found in mitochondria, as identified from the plot in Figure 4.2 and AIM17 (Table S1; Hess et al., 2009), this suggests that respiration may be required for invasive growth.

### 4.4.6 Protein interaction network analysis suggests Ssa 2 p as the major determinant of invasive growth

Protein-protein interactions were visualised (see Experimental Procedures) between the differentially expressed genes in a network graph using the mentha database (Calderone et al., 2013). Similar to the genetic network analysis, this enabled the discovery of high connectivity proteins, thereby reflecting their biological importance in invasive growth. In comparison to genetic interactions that provide information on how genes control cellular processes, protein interactions present functional connections. In the latter, Ssa2p was identified as the key node of the largest connected network, having the most number of edges $($ degree $=14)$ and the largest Betweenness Centrality value (0.77; Fig. 4.3). In addition, SSA2 had the fourth largest change in gene expression with nearly a five-fold increase in invasively growing cells (Table 4.1).


Figure 4.3: Protein-protein interaction network of differentially expressed genes between surface and invasively growing cells. A $25 \%$ fold-change threshold was applied for the differential expression analysis. The largest connected network with an interaction confidence score of at least 0.3 is shown. Red and green node colours represent upregulation and downregulation in invasively growing cells respectively; larger node size represents higher values of Betweenness Centrality, and vice versa.

SSA2 is required for pseudohyphal growth but not haploid invasive growth (Ryan et al., 2012). However, Shively and colleagues (2013) reported that it enhanced invasive growth (agar invasion score 0.96 ) when overexpressed in diploids. This protein is involved in protein folding and transport, suggesting that it may act as a checkpoint protein to ensure functionality of other proteins involving in invasive growth. The importance of this gene, along with NOG2 and HSP26, is also shown in the relationship plot between their protein connectivity and change in expression (Fig. 4.4). Nog2p is a putative GTPase involved in exporting the large ribosomal subunit while Hsp26p is a chaperone which binds and prevents unfolded proteins forming large aggregates (Saveanu et al., 2001; White et al., 2006).


Figure 4.4: Relationship between the Betweenness Centrality of each gene in the protein interaction network and their corresponding change in gene expression. Each circle represents a single gene. Gene names are shown only for those meeting both criteria of absolute $\log _{2}$ fold change greater than 0.8 and Betweenness Centrality greater than 0.125 .

### 4.4.7 Expression levels of transcription factor genes do not correlate with their previously reported involvement in invasive growth

Interestingly, in this study the differentially expressed genes encoding transcription factors did not correlate with previous studies that highlighted their involvement in invasive growth (Jin et al., 2008; Van Mulders et al., 2009; Shively et al., 2013). Fifteen genes encoding known transcription factors increased expression and 12 decreased gene expression in invasively growing cells (Fig. 4.5).


Figure 4.5: Change in gene expression of genes encoding transcription factors in invasively growing cells compared to surface growing cells. Genes with black bars were shown to be involved in invasive growth in other studies (overexpression results in increased invasive growth or deletion results in no invasive growth).

Of these, MGA1, whose encoded protein restores filamentation defects by multicopy expression (Lorenz and Heitman, 1998), had the largest increase in expression. This was followed by MTH1, which encodes for a negative regulator of the glucose-sensing signal transduction pathway for $H X T$ gene expression (Lafuente et al., 2000). The upregulation of many glucose transporter genes in the invasively growing cells suggests that MTH1 had released its repression on these genes. Similarly, NRG2, encoding a negative glucose regulator that interacts with Snf1p (Kuchin et al., 2002), was also upregulated in invasively growing cells. SNF2, encoding for a transcriptional activator of FLO11 under glucose limitation (Barrales et al., 2008), had increased expression. Conversely, ROX1, CIN5 and IME1 had the largest decrease in gene expression (approx. two-fold). When comparing to previously reported genes encoding transcription factor required for or to enhance invasive growth when overexpressed, four were upregulated in this study: MGA1, HMS2, FLO11 and RGT1 (Harashima and Heitman, 2002; Shively et al., 2013). Several genes reported to be involved in invasive or pseudohyphal growth had decreased in expression in invasively growing cells, these being MSN2, RSC30, PHD1, RME1 and CIN5.

### 4.4.8 Cellular water homeostasis: aquaglyceroporin gene FPS1 is required for invasive growth

Cellular water homeostasis (GO:0009992; $p<0.0032$ ) was one of the enriched GO categories identified in the upregulated gene set (Fig. 4.1). All five genes classified within this biological process showed an increase in gene expression (four were significant) in invasively growing cells compared to surface growing cells (AQY1, AQY2, YLL053C, FPS1 and $A Q Y 3$; increased by $1.43-2.25$ fold; Fig. 4.6A). None of these genes have previously been identified as being required for invasive growth, although $A Q Y 1$ was reported to have increased gene expression in fluffy colonies compared to smooth colonies (Kuthan et al., 2003). To confirm if these genes are important for invasive growth, yeast deletants were constructed for each gene of interest and the deletants were screened for reduced invasive growth. Yeast deletants $\Delta f p s 1$ and $\Delta a q y 3$ had a reduced number of invasive growth foci whereas $\Delta a q y 2$ and $\Delta y l l 053 c$ had a similar number of invasive growth foci compared to the wild type AWRI796 on Day 4 (Fig. 4.6B). By Day 10, the invasive foci that had formed developed to a comparable size in all strains. Therefore, the decreased invasive growth observed for $\Delta f p s 1$ and $\Delta a q y 3$ was more related to fewer foci rather than due to reduced or delayed growth. The reduced number of invasive growth foci was still observed on Day 10. These deletants and other progeny from the same spore were further evaluated to ensure the differences were due to the gene deletion and not spore variability. In this assay, the $\Delta f p s 1$ progeny had less invasive growth than the wild type progeny whilst $\Delta a q y 3$ progeny gave mixed results (Fig. S2). $\Delta a q y 1$ was not evaluated in this analysis due to difficulties in generating the strain (Appendix C).


Figure 4.6: Evaluation of genes encoding proteins involved in cellular water homeostasis and their importance for invasive growth. (A) Comparison of aquaporin and aquaglyceroporin gene expression between invasively (white) and surface (black) growing cells SLADS-agar ( $0.3 \%$ ). Please refer to next page for (B).
(B)


Figure 4.6: (B) Invasive growth evaluation of AWRI796 and homozygous deletants of indicated genes on SLADS-agar ( $0.3 \%$ ). Images were photographed from the underside of the agar plates. Surface growing cells were in a large round mat. Multiple small spots on top of that were invasively growing cells. Scale bar, 1 mm .

The deletion analysis confirmed that FPS1 is important for invasive growth. FPS1 encodes a channel protein that regulates glycerol export (Oliveira et al., 2003). Lack of Fps1p results in cell wall stress due to high turgor pressure from accumulation of glycerol (Tamas et al., 1999). Cells then fortify their cell wall by displaying less sensitivity to the cell wall degrading enzyme, zymolyase (Beese et al., 2009). As the transcriptomics profile indicates that cell wall remodelling and organisation is actively performed in invasive growth, this fortified cell wall may have prevented the wall from being flexibly modified for growing invasively. This suggests that high turgor pressure or fortified cell wall may not be beneficial when growing invasively. Alternatively, invasive growth may also require the export of glycerol.

### 4.5 Conclusions

In summary, this study has identified that genes of glucose import and carbohydrate metabolic process are upregulated in invasively growing cells compared to those growing on the agar surface, indicating improved access to nutrients. Fungal-type cell wall organisation is involved in invasive growth, potentially to enhance cell wall stability and adhesion. The protein of a hypothetical gene that has an amidase domain may have a role in invasive growth through the involvement of cell wall recycling process or cell-cell signalling. Ssa2p, which is involved in protein folding and transport, was identified as being significant in association with invasive growth from the protein interaction network analysis. Cellular water homeostasis is also important, especially the glycerol export channel protein Fps1p. Genes involved in medium-chain fatty acid biosynthetic process and ethyl ester production were upregulated in invasive growth but their roles in invasive growth remain elusive.

### 4.6 Experimental Procedures

### 4.6.1 Yeast strains

Yeast strains used in this study are listed in Table 4.2. To generate deletants of genes of interest (GOI) in AWRI796, the corresponding gene deletant in a BY4741 background was used. The GOI KanMX gene replacement cassettes were generated by PCR using GOI specific primer pairs (GOI_A and GOI_D, Table S4) and genomic DNA of the corresponding BY4741 deletant (Wach et al., 1994; Winzeler et al., 1999). Deletion in AWRI796 was generated by transformation of the GOI KanMX gene replacement cassette, followed by selection on YPD agar ( $1 \%$ yeast extract, $2 \%$ bacto peptone, $2 \%$ glucose, $2 \%$ bacteriological agar) $+200 \mathrm{mg} \mathrm{L}^{-1}$ G418-sulfate (Gietz and Schiestl, 2007). Homozygous deletants were isolated by sporulation, dissection and re-diploidisation, followed by verification with PCR amplification and sequencing using GOI specific primer pairs GOI_A2 and GOI_D2 (Table S4) located outside the original gene replacement cassette. AQY1 deletion in AWRI796 was omitted in this study due to difficulties in generating the correct strain (Appendix C).

Table 4.2: Yeast strains used in this study.

| Yeast strain | Genotype | Reference |
| :---: | :---: | :---: |
| AWRI796 | Commercial wine yeast strain; diploid | Mauri Yeast Australia |
| AWRI796 $\Delta$ aqy 2 | aqy2 $\Delta:: K a n \mathrm{MX} / a q y 2 \Delta:: K a n \mathrm{MX}$ | This study |
| AWRI796 $\Delta$ aqy 3 | aqy3 $::$ Kan MX/aqy $3 \Delta:: K a n \mathrm{MX}$ | This study |
| AWRI796 $\Delta$ fps1 | fps1 $\triangle::$ Kan MX/fps1 $\Delta:: K a n M X$ | This study |
| AWRI796 $\Delta$ yll053c | yll053c $\Delta:: K a n \mathrm{MX} / \mathrm{yll0} 53 c \Delta:: K a n \mathrm{MX}$ | This study |
| BY4741 aqu $^{\text {2 }}$ | MATa his3D1 leurД0 met15 0 ura3 $\Delta 0$ aqy2 $\Delta:: K a n M X$ | Thermo Fisher Scientific Australia |
| BY4741 $\Delta$ aqy 3 | MATa his3 1 leu2 $\Delta 0$ met15 0 ura3 00 aqy3 $\Delta:: K a n \mathrm{MX}$ | Thermo Fisher Scientific Australia |
| BY4741 $\Delta f p s 1$ | MATa his3 1 leu2 $\Delta 0$ met15 0 ura3 $\Delta 0$ fps1 $\Delta:: K a n M X$ | Thermo Fisher Scientific Australia |
| BY4741 $\Delta$ yll053c | MATa his3 1 leu2 $\Delta 0$ met15 0 ura3 $\Delta 0$ yll053c $\Delta:: K a n M X$ | Thermo Fisher Scientific Australia |

### 4.6.2 Genomic DNA preparation and PCR conditions

Genomic DNA was extracted according to Lõoke et al. (2011). TE buffer ( 10 mM Tris- HCl $\mathrm{pH} 8.0,1 \mathrm{mM}$ EDTA) was used to solubilise DNA, and $2 \mu \mathrm{~L}$ was used as the template in a $50 \mu \mathrm{~L}$ PCR reaction. PCR reactions were performed with Bioline Velocity DNA Polymerase (Cat No. BIO-21098), according to the manufacturer's instructions. PCR products were separated on a $0.8-1 \%$ TAE-agarose gel containing GelRed nucleic acid stain (Biotin; Cat No. 41003). DNA fragments of GOI KanMX gene replacement cassettes
were purified using the Wizard SV Gel and PCR Clean-Up System (Promega, Madison, WI; Cat No. A9282).

### 4.6.3 Low nitrogen invasive growth assays

AWRI796 was grown in 10 mL SLAD ( $0.17 \%$ Yeast Nitrogen Base without amino acids and ammonium sulfate, $2 \%$ glucose, $50 \mu \mathrm{M}$ ammonium sulfate, prepared according to Binder et al., 2015) for 48 h at $30^{\circ} \mathrm{C}$ before re-inoculation into 25 mL SLAD at $1 \times 10^{4}$ cells $\mathrm{mL}^{-1}$ in an Erlenmeyer flask and grown for a further 24 h . Prior to plating, the exponential-phase culture was diluted in Phosphate Buffered Saline (PBS; 137 mM NaCl , $2.7 \mathrm{mM} \mathrm{KCl}, 10 \mathrm{mM} \mathrm{Na} 2 \mathrm{HPO}_{4}, 1.8 \mathrm{mM} \mathrm{KH}_{2} \mathrm{PO}_{4}$, pH 7.4) to $2 \times 10^{5}$ cells $\mathrm{mL}^{-1}$. An aliquot of $5 \mu \mathrm{~L}$ was spotted at the centre of SLADS-agar ( 10 mL SLAD, $0.4 \mathrm{mg} \mathrm{L}^{-1}$ sodium sulfide $\left(\mathrm{Na}_{2} \mathrm{~S} .9 \mathrm{H}_{2} \mathrm{O}\right), 0.3 \%$ agar) in a 60 mm Petri dish (Techno Plas; Cat No. S6014S10). For RNA-sequencing, cells were harvested after 8 days of incubation at $25^{\circ} \mathrm{C}$. Three independent assays were conducted; the number of agar plates from which cells were harvested for each independent assay were 188, 190 and 192 respectively. For invasive growth screening of AWRI796 GOI deletants, invasive growth mats were imaged from the underside of the plate on Day 4 and 10 at $0.5 \times 0.63$ magnification using a Nikon SMZ1270 stereomicroscope and an attached DS-Fi3 camera with NIS-Elements F4.60 software.

### 4.6.4 Sample harvest and RNA extraction

Cells growing on the agar surface were harvested with a disposable plastic inoculation loop and resuspended in 1 mL Trizol (Life Technologies; Cat No. 15596-018). Any remaining surface cells were rinsed off with ultrapure water. A scalpel blade was used to slice out the piece of agar containing invasively growing cells and transferred to a separate 1 mL Trizol. The cells from all agar plates making up each replicate were pooled for each of the three assays for both surface and invasively growing cells (i.e. six samples in total). Harvested cells in Trizol were heated at $60^{\circ} \mathrm{C}$ for 3 min and then centrifuged at $3,824 \times g$ for 30 s . Supernatant was removed and 1 mL fresh Trizol was added before being snap frozen in liquid nitrogen.

RNA extraction was performed using a combination of Trizol reagent and a Qiagen RNeasy Mini kit (Cat No. 74104). Samples were thawed on ice. Glass beads were added up to the halfway mark of the meniscus. Six cycles of 45 s of vortexing and 45 s of rest on ice were used to disrupt cells. Tubes were incubated at $65^{\circ} \mathrm{C}$ for 3 min and $200 \mu \mathrm{~L}$ of chloroform was added, followed by vortexing for 15 s before leaving at room temperature for 5 min . Tubes were centrifuged at $20,817 \times g$ for 10 min at $4{ }^{\circ} \mathrm{C}$. Supernatant was recovered to a fresh tube and an equal volume of $70 \% \mathrm{v} / \mathrm{v}$ ethanol was added, mixed by pipetting, before continuing according to the Qiagen RNeasy Mini kit manufacturer's instructions. RNA quality and quantity were checked using a Nanodrop

ND-1000 UV-visible light spectrophotometer (Thermo Fisher Scientific), separation on 1\% TAE-agarose gel and an Experion Automated Electrophoresis System (Bio-Rad).

### 4.6.5 RNA sequencing and analysis

RNA-sequencing was performed with an Illumina Hiseq instrument in one lane (Australian Genome Research Facility, Melbourne, Australia). Reads were mapped to the $S$. cerevisiae AWRI796 genome sequence located at the NCBI (GenBank assembly accession: GCA_000190195.1) with TopHat (Trapnell et al., 2009). Reads were counted for each gene using featureCounts in the Rsubread software package (Liao et al., 2013). The translation sequence of genes annotated as "hypothetical protein" was used to search for any domain hits in the Pfam database (Finn et al., 2016). Gene Ontology IDs for the matched protein domains were extracted from InterPro database (Mitchell et al., 2015). These GO IDs were added to the latest gene association file downloaded from the Saccharomyces Genome Database (Date: 04/02/2016). This was used for downstream GO analysis. Counts and gene lengths were merged for genes that had sequences located next to each other in the genome and have matched part of the same domain. Genes with counts less than 50 were not considered in the downstream analysis. Differential expression analysis was performed using the limma package (Ritchie et al., 2015) in R with voom (Law et al., 2014) and TREAT (McCarthy and Smyth, 2009) functions, incorporating a $30 \%$ fold-change threshold in the hypothesis test. GOseq was used to perform GO enrichment and KEGG analysis (Young et al., 2010). The significantly enriched GO list was summarised and visualised using REVIGO (Supek et al., 2011).

### 4.6.6 Network analysis

The interactions between significant differentially expressed genes were visualised using a network graph in Cytoscape (Shannon et al., 2003). The protein-protein interaction database of $S$. cerevisiae was downloaded from mentha (Calderone et al., 2013, Date: 24/04/2016) while genetic interaction data was obtained from the DRYGIN database (Costanzo et al., 2010; Koh et al., 2010). For protein-protein network graphs, interactions with a confidence score of at least 0.3 were used with the resulting differentially expressed genes from the hypothesis test with a $25 \%$ fold-change threshold. Basic network analysis was performed in Cytoscape. Some parameters were visualised in graphs: node color was mapped to up- or down-regulation whereas node size was mapped to Betweenness Centrality value which represents connectivity of each node in the graph. The Betweenness Centrality of each node was plotted with the change in gene expression value. The betweenness of a node $v$ is obtained by counting the number of all shortest paths, connecting any pair of nodes within the network, which are going through that particular node $v$. The value is divided by the number of all shortest paths connecting two nodes.

The $S$. cerevisiae transcription factor database was downloaded from YEASTRACT and was used to determine the differentially expressed transcription factor genes (Teixeira et al., 2014). A graph was plotted to show change in gene expression levels of differentially expressed transcription factor genes.

### 4.7 Acknowledgements

This work was supported by Wine Australia [GWR Ph1305] and the Australian Research Council [DP 20111529]. ELT was supported by an Adelaide Graduate Research Scholarship, a DR Stranks Postgraduate Travelling Fellowship and a Research Abroad Scholarship provided by the University of Adelaide. The authors thank Dr Valarie Wood for providing suggestions on annotations for hypothetical proteins.

The authors have no conflict of interest to declare.

### 4.8 Supporting Information

### 4.8.1 Tables

Table S1: Due to the size of the table, this can be found in Appendix D.

Table S2: List of enriched Gene Ontology terms from the upregulated gene set in invasively growing cells.

| Category | Number of DE Genes in Category | Number of GO Term Genes in Category | $\begin{aligned} & \hline \text { Ont } \\ & \text { olog } \\ & \mathrm{y} \end{aligned}$ | $\text { Adj. } p-$ value |  |
| :---: | :---: | :---: | :---: | :---: | :---: |
| GO:0005886 | 60 | 398 plasma membrane | CC | $5.67 \mathrm{E}$ | AQR1, AQY1, AQY2, ATO2, ATO3, BEM2, BNII, BULI, CCH1, CIS3, CWH43, CYRI, DIP5, DNFI, DNF2, DUR3, ENAI, EXG2, FET3, FKSI, FLOI1, FUII, GAPI, GASI, GLK1, HKR1, HSP30, HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, INAl, KRE6, MCH5, MEPI, MMPI, PDRIO, PDR11, PDR15, PDR5, PHM7, PHO90, PUNI, PUT4, RGII, SLAI, SRO77, SSA2, SSUI, STT4, TCB3, TDHI, THI7, TORI, TOR2, TPOI, TPO4, YLR194C |
| GO:0009277 | 17 | 75 fungal-type cell wall | CC | $2.06 \mathrm{E}$ | CIS3, CWP1, DSE2, EXG2, FIT1, FIT3, FLO5, GAS1, GAS5, PIR1, PRY3, SIM1, SSA2, SUN4, TDH1, ZPSI, YLR194C |
| GO:0005618 | 14 | 54 cell wall | CC | $2.06 \mathrm{E}-0$ | CIS3, CWPI, DSE2, FITI, FIT3, FLOII, FLO5, GASI, GAS5, PIRI, PRY3, SIMI, SSA2, SUN4 |
| GO:0005887 | 22 | 95 integral component of plasma membrane | CC | $3.91 \mathrm{E}-0$ | AGP2, AQY1, AQY2, CWH43, DIP5, ENAI, FUSI, GAP1, HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31, MEPI, MMPI, PMCl, PUT4, YPK9, YFL054C, YLL053C |
| GO:0046323 | 10 | 22 glucose import | BP | $6.14 \mathrm{E}-0$ | 5 GLK1, HXK1, HXK2, HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL3I |
| GO:0005353 | 6 | 7 fructose transmembrane transporter activity | MF | $9.28 \mathrm{E}-0$ | HXT1, HXT2, HXT3, HXT4, HXT6, HXT7 |
| GO:0015578 | 6 | 7 mannose transmembrane transporter activity | MF | $9.28 \mathrm{E}-0$ | HXT1, HXT2, HXT3, HXT4, HXT6, HXT7 |
| GO:0005215 | 16 | 69 transporter activity | MF | $9.28 \mathrm{E}-0$ | AQR1, AQYY, AQY2, DUR3, FUII, HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31, THI7, TPO4, YFL054C, YLL053C |
| GO:0055085 | 34 | 205 transmembrane transport | BP | $9.65 \mathrm{E}-0$ | AGP2, AQR1, AQY1, AQY2, ATO3, AVT6, CCH1, DIP5, DUR3, ECM3, ENA1, FUII, GAPI, HXT1, HXT2, HXT3, HXT4, HXT6, |
| GO:0005576 | 15 | 81 extracellular region | CC | $0.0006$ | 4 CIS3, CWPI, DSE2, FITI, FIT3, FLOI1, FLO5, GASI, GAS5, PIR1, PRY3, SIMI, SSA2, SUN4, ZPSI |
| GO:0008643 | 8 | 19 carbohydrate transport | BP | 0.00078 | 9 HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31, YEA4 |
| GO:0005975 | 17 | 91 carbohydrate metabolic process | BP | 0.00116 | 1 EMI2, EXG2, GALI, GAS1, GAS5, GDB1, GLC3, GLK1, GPH1, |
| GO:0031225 | 11 | 49 anchored component of membrane | CC | $0.0013$ | CWP1, DSE2, EXG2, FIT1, FIT3, FLOI1, FLO5, GAS1, GAS5, PRY3, YLR194C |
| GO:0015146 | 4 | 4 pentose transmembrane transporter activity | MF | 0.00321 | 2 HXT1, HXT2, HXT4, HXT7 |
| GO:0009992 | 4 | 5 cellular water homeostasis | BP | 0.00321 | AQYI, AQY2, YFL054C, YLL053C |
| GO:0015250 | 4 | 5 water channel activity | MF | 0.00321 | 2 AQYI, AQY2, YFL054C, YLL053C |
| GO:0015254 | 4 | 5 glycerol channel activity | MF | 0.00321 | 2 AQYI, AQY2, YFL054C, YLL053C |
| GO:0005355 | 7 | 18 glucose transmembrane transporter activity | MF | 0.00645 | 9 HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31 |
| GO:0001678 | 4 | 5 cellular glucose homeostasis | BP | 0.006772 | 2 EMI2, GLK1, HXK1, HXK2 |
| GO:0004340 | 4 | 5 glucokinase activity | MF | 0.006772 | 2 EMI2, GLK1, HXK1, HXK2 |
| GO:0004396 | 4 | 5 hexokinase activity | MF | 0.00677 | EMI2, GLK1, HXK1, HXK2 |
| GO:0008865 | 4 | 5 fructokinase activity | MF | 0.00677 | 2 EMI2, GLK1, HXK1, HXK2 |
| GO:0019158 | 4 | 5 mannokinase activity | MF | 0.006772 | 2 EMI2, GLK1, HXK1, HXK2 |
| GO:0008645 | 4 | 5 hexose transport | BP | 0.00682 | 6 HXT3, HXT4, HXT6, HXT7 |
| GO:0005351 | 7 | 19 sugar:proton symporter activity | MF | 0.00709 | 5 HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31 |
| GO:0035428 | 7 | 19 hexose transmembrane transport | BP | 0.00709 | 5 HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31 |
| GO:0031505 | 17 | 95 fungal-type cell wall organization | BP | 0.00974 | CIS3, CWH43, CWPI, EXG2, GASI, HKRI, KRE6, MHP1, MYO3, |
| GO:0006833 | 3 | 3 water transport | BP | 0.00974 | 6 AQY1, AQY2, YFL054C |
| GO:0051792 | 3 | 3 medium-chain fatty acid biosynthetic process | BP | 0.01176 | 4 EEBI, EHT1, MGL2 |
| GO:0071555 | 15 | 79 cell wall organization | BP | $0.01434$ | CIS3, DSE1, DSE2, ECM3, EXG2, FKS1, GAS1, GAS5, GSC2, KRE6, PIRI, SIM1, SUN4, YPK2, YLR194C |
| GO:0006006 | 7 | 21 glucose metabolic process | BP | 0.0179 | 1 DOG2, GLK1, HXK1, HXK2, PGM2, RGT1, TDH1 |
| GO:0034220 | 6 | 13 ion transmembrane transport | BP | 0.018779 | 9 AQY1, AQY2, CCHI, MCH5, YFL054C, YLL053C |
| GO:0022891 | 7 | 23 substrate-specific transmembrane transporter activity | MF | 0.02216 | HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31 |
| GO:0005536 | 4 | 7 glucose binding | MF | 0.04825 | 7 EMI2, GLKI, HXK1, HXK2 |
| GO:0005199 | 4 | 13 structural constituent of cell wall | MF | 0.04825 | 7 CIS3, CWPI, PIRI, YLR194C |
| GO:0022857 | 7 | 26 transmembrane transporter activity | MF | 0.04825 | 7 HXT1, HXT2, HXT3, HXT4, HXT6, HXT7, MAL31 |
| GO:0046835 | 5 | 14 carbohydrate phosphorylation | BP | 0.04825 | EMI2, GALI, GLK1, HXK1, HXK2 |

Table S3: Genes upregulated in invasively growing cells in this study and common to other related studies. Genes in bold are those that are reported in more than one of these studies.

| Study | Phenotype | Medium | Common genes |
| :--- | :--- | :--- | :--- |
| Ryan | Haploid null mutant | YPD agar | ARG8, ERG6, FLO11, IKI3, <br> et al. |
| with reduced invasive |  | MEF2, PMT2, PUT4, SIN3, <br> $(2012)$ | growth |

Table S4: Primers used in this study for amplification of gene of interest KanMX gene replacement cassettes and sequencing.

| Primer | Sequence $\left(5^{\prime}\right.$ to $\left.\mathbf{3}^{\prime}\right)$ |
| :--- | :--- |
| AQY2_A $^{1}$ | AATAATGACTTTACCTCCTCCAATCC |
| AQY2_D $^{1}$ | TTTCGGCATTAACGTATGTAGTGTA |
| AQY3_A |  |
| AQY3_D $^{1}$ | CTCCCTATTTGGTACTACGATACGA |
| FPS1_A $^{1}$ | GCACAATTAGTTTATTTGGCAACTT |
| FPS1_D $^{1}$ | ATGTATAGTAGGTATGATACCGTCCCTT |
| YLL053C_A $^{1}$ | ATGTCTAACGAATCTAACGACCTTG |
| YLL053C_D $^{1}$ | TACTTCACATCATCTTTGTTTCCAA |
| AQY2_A2 | GCACCGTAACTACTACAGT |
| AQY2_D2 | TACGATGGGAGCGTTATG |
| AQY3_A2 | TTATCCAACTATGGTGACG |
| AQY3_D2 | TGGTCAATCATACAGAACG |
| FPS1_A2 | GGACGGAGAGAGTTACGGC |
| FPS1_D2 | CGAATCGCTGCTTGATGTT |
| YLL053C_A2 | TATCGTGAATCATATCTGCC |
| YLL053C_D2 | GTCCTGGTTCCACTTCGTAG |

${ }^{1}$ GOI_A and GOI_D primers are from Yeast Deletion Project
(www-sequence.stanford.edu/group/yeast_deletion_project/deletions3.html).

### 4.8.2 Figures

Figure S1: Genetic interaction network between differentially expressed genes (only the largest connected network is shown). Red and green node colours represent upregulated and downregulated genes in invasively growing cells; larger node size represents high value of Betweenness Centrality, and vice versa.


Figure S2: Invasive growth evaluation of strains from a tetrad set produced by sporulation and spontaneous re-diploidisation of a heterozygous deletion AWRI796 on SLADS-agar. Scale bar, 1 mm .


## Chapter 5

## Conclusions

### 5.1 Summary of findings

The studies reported in this dissertation led to the following main conclusions:

1. Commercial wine yeast strains are able to form biofilms as determined by mat formation on a rich medium with low density ( $0.3 \%$ ) agar. These mats consisted of replicative and non-replicative cells and featured invasive growth, bud elongation, sporulation, and in one case, a sector that was morphologically distinct. The use of a medium containing grape pulp resulted in enhanced invasive growth of yeast mats, while the ability to adhere to plastic was variable between strains.
2. Nitrogen limitation resulted in reduced mat sizes (maximum size was approximately 5 mm in diameter in comparison to up to a full 90 mm plate on rich medium) and induced filamentous and invasive growth. The mat regions where invasive growth occurred were in distinct foci, which did not increase in number markedly over the course of the experiment, indicating that invasively growing cells were triggered soon after inoculation. The number of invasive foci in each mat was strain dependent. Many factors were shown to influence the formation of filamentous invasive foci, these being nitrogen content, the presence of a neighbouring mat and the presence of exogenous yeast metabolites. For instance, ethanol and hydrogen sulfide enhanced filamentous invasive growth, while aromatic alcohols and sulfite inhibited their formation.
3. Differential expression analysis by RNA-sequencing of surface and invasively growing cells on low nitrogen, low density agar medium revealed genes associated with glucose import, carbohydrate metabolic processes, fungal-type cell wall organisation, mediumchain fatty acid biosynthesis and cellular water homeostasis were upregulated in invasively growing cells. Evaluation of deletants of genes involved in cellular water homeostasis confirmed that the aquaglyceroporin gene, FPS1, is important for

### 5.2 Contribution to knowledge

The characterisation of mat architecture and visualisation of cell morphologies formed by commercial wine yeast strains broaden the current knowledge beyond the typical and simple 'hub and spokes' description of mat structures. The complexity of cell morphologies within a mat suggests that cells may differentiate for different roles. This may be advantageous for the mat community since they are likely to adapt quicker to changing conditions as opposed to an individual cell morphology. This interesting feature challenges the current knowledge and calls for investigation of how each differentiated cell interacts with others and contributes to mat survival. The simple macro features (petal-like formation) of these mat structures have recently been described mathematically with a collaborating group determining algorithms that result in strikingly similar computer-generated patterns (Alexander Tam, pers. comm. 2017). It is important to understand the formation of these structures as this will aid knowledge of how non-laboratory yeast biofilms occur in nature. The findings of grape-pulp mat assays and winery hose plastic adhesion contribute to the knowledge of biofilm formation in relation to a winery/vineyard environment. The capability of commercial wine yeasts to form invasive biofilms on grape pulp agar supports this as a method for residency and persistence in and on damaged wine grapes, which might lead to a change in the profiles of indigenous microflora in vineyards and wineries in the long-term. The surprising ability of wine yeasts to adhere to commonly used winery hose suggests that in the absence of rigorous sanitation, yeast could remain in these hoses, and potentially be transferred between fermentations and wines. Other plastics or rubbers also commonly found in wineries have not been examined here. Plastic tanks, valve caps or internal components of pumps, presses and crushers warrant attention as these surfaces may also serve as areas for yeast residence.

This work is the first to report mat morphologies under low nitrogen conditions. Nitrogen limitation was chosen since this is a common environment that yeast in the vineyard and winery are exposed to. Previous studies as well as in this laboratory on non-mat ( $2 \%$ agar) conditions reported morphological changes when cells were limited for nitrogen, which lead to a hypothesis for this study that these conditions may also trigger similar responses to yeast mats (low density agar) enabling survival. Consistent with previous reports on $2 \%$ agar, yeast cells switched to filamentous and invasive growth in a low nitrogen environment on $0.3 \%$ agar. This morphological switch is believed to extend access to nutrients since limited proliferation prevents non-motile cells moving towards fresh nutrients. In order to develop filamentous and invasive growth, yeast cells undergo polarised growth, resulting in extension of the growth periphery and existence at a less crowded position, and thus having reduced competition for nutrients. In the vineyard, wine yeast that colonise damaged grapes may consume available nitrogen rapidly. As
nitrogen is depleted, these cells may differentiate into filamentous growth, accompanied with their ability to invade grape pulp, to access fresh nutrients, enhance residency and survival. In the winery, nitrogen is usually exhausted within the first 48 hours of must fermentation. Filamentous growth that will increase surface area to mass ratios of a cell may aid nutrient exposure and facilitate uptake during fermentation.

The invasive growth response can also be influenced by the presence of several yeast metabolites, such as ethanol (previously shown to induce elongation), aromatic alcohols (previously reported to enhance filamentous and invasive growth), hydrogen sulfide (novel), and sulfite (previously shown to inhibit growth). These were chosen since they are common metabolites produced by wine yeast in fermentation and have an effect on filamentous and/or invasive growth on $2 \%$ agar. The involvement of metabolites of the yeast sulfur metabolic pathway infers their involvement in the nutrient stress response. Particularly, hydrogen sulfide enhanced the morphological switch that occurs in response to nutrient starvation; the release of this compound is also linked to nutrient starvation, suggesting that this metabolite may be an intermediate signalling molecule enabling the response. This is important since hydrogen sulfide has so far been only linked to resistance to other stresses such as heat shock, heavy metal and oxidative stresses in yeast. The connection between nutrient starvation response and sulfur metabolism could help to understand hydrogen sulfide-related fermentation problems or biofilm formation occurring in a sulfur-rich environment.

The transcriptomics analysis revealed that many genes are upregulated in invasively growing cells and the processes involved were glucose import and carbohydrate metabolism, reflecting better access to fresh nutrients and potentially breakdown and utilisation of agar to allow invasive growth. Upregulation of genes involved in fungal-type cell wall organisation suggests biogenesis, assembly, re-arrangement and disassembly of cell wall components are associated with invasive growth, which infers certain composition or arrangement of the cell wall may be required for growing invasively. Upregulation of FLO11 also suggests the encoded protein is not just required for initial attachment to agar where invasive growth began, but is also required during growth inside the agar. The attachment facilitated by Flo11p may hold invaded cells in place to push daughter cells further into the agar instead of being replaced by the buds and moving away from the agar. A hypothetical gene (AWRI796_5153) having part of its translation sequence homologous to an amidase, was one of the few genes with a large increase in transcript abundance ( 6.45 -fold) in invasively growing cells, suggesting an important role in invasive growth. Amidases have not been linked to invasive growth or biofilm formation but have been shown to be involved in cell wall recycling processes in bacteria. The identification of several biological processes, previously not associated with invasive growth significantly expands the current knowledge of this field. In particular, gene deletant analysis revealed that FPS1, encoding the glycerol exporter, is important for invasive growth in low nitrogen agar. These are novel findings in nitrogen-limited conditions as opposed to glucose limitation in other genome-wide studies. As part of the transcriptomics studies, an RNA extraction
method has also been developed for yeast cells growing into agar.

### 5.3 Limitations and future directions

The study of mat formation is challenging due to a variety of factors, including genetic variation between strains, occurrence of multiple events such as cell differentiation, cellcell communication, adhesion and invasive growth. Future work could involve a deeper understanding of how a mat is formed, which factors influence their structure, and how cells choose their fate. Incorporation of mathematical modelling will help identify parameters resulting in the structures or formation of interest and make hypotheses for subsequent experimental design. The experimental approach could also include onsite experiments in a winery setting, followed by confirmation with laboratory experiments. The ultimate output would aid decision making in winemaking management regarding microbial impact.

For the first time, hydrogen sulfide is reported to enhance invasive growth in this study. Nitrogen limitation induces invasive growth and the liberation of hydrogen sulfide by yeast often occurs when nitrogen is insufficient. It has been suggested that hydrogen sulfide, alike to ammonia, may be involved in cell-cell signalling. Future work should investigate how hydrogen sulfide is detected by cells and the mechanism to stimulate invasive growth. The work could also be extended to confirm if hydrogen sulfide is a yeast cell-cell signalling molecule.

While assessing the impact of gene deletions involved in cellular water homeostasis on invasive growth, one deletant, $\Delta a q y 1$, could not be generated, and hence was not evaluated. It appears that the gene replacement cassette was mis-targeted, and thus although transformants were obtained, unexpected amplified allele sizes were observed from spore progeny (Appendix C). Further work needs to be done to investigate why deletion of $A Q Y 1$ was unsuccessful, for instance, study the AWRI796 genome sequence and investigate PCR conditions to optimise cassette generation and transformation.

Although the transcriptomics analysis has provided new information on invasive growth, there were limitations. For instance, transcriptomics analysis only examined gene expression, while post-translational modifications and protein activity were not examined. Assumptions have been made that an increase in gene expression results in an increase in protein levels. However, the regulation of many genes and their products can occur at many stages post transcription. Furthermore, gene expression may not directly support the phenotype observed. For example, ARO1 and ARO8, encoding for enzymes that are responsible for aromatic amino acid production, were upregulated in invasively growing cells. These amino acids are precursors to aromatic alcohols which were shown to inhibit invasive growth in this work. This result is contradictory to the findings that aromatic alcohols enhanced invasive growth as reported by Chen and Fink (2006), which could be due to different medium preparation such as $2 \%$ versus $0.3 \%$ agar or ethanol concentration
in preparation of aromatic alcohols. Metabolite analysis could be undertaken to identify if the amino acids were in fact produced. Future work could include both proteomics and metabolomics studies to gain a holistic view on the process.

Differential transcriptome analysis requires a well-annotated genome of a strain to be analysed. AWRI796 was chosen for this analysis since this strain has its genome annotated close to completion. The genome sequence is also very similar to the reference sequence of S288C. All currently annotated genes in AWRI796 are also present in the S288C genome. In addition, the AWRI796 genome has several hypothetical genes predicted. The translation sequence of these genes was blasted for homology to protein families. Most translated sequences were matched to a protein family, suggesting they are protein coding genes. GO information was obtained and used in the analysis. A number of the hypothetical genes, previously predicted to be individual genes, were merged based on the evidence of their location in the genome and the matching protein domain region. Further annotation of this reference sequence has contributed to an understanding of these hypothetical genes. Future work could evaluate the functions of these, including whether they appear in the commonly used S288C reference genome. This will continue to improve the annotation for the AWRI796 genome.

Deletion of FPS1, encoding the glycerol exporter led to reduced invasive growth. Previous work reports accumulation of glycerol inside the cell of FPS1 deletants which could therefore alter turgor pressure and cause cell wall fortification that may disable invasive growth. Further analysis of deletants that similarly result in glycerol accumulation ( $\Delta a d k 1, \Delta s c h 9$ ) would contribute to this understanding. Cells could also be stained with Calcofluor White to determine the intensity of chitin and $\beta$-glucan, and consequently examine if an increased glycerol accumulation results in fortification of the cell wall. Enzyme digestibility of cell walls could also be tested and compared between both wild type and mutant. Alternatively, the presence of glycerol in extracellular fluid may be important for invasive growth. Filamentous invasive growth was induced when glycerol was used to replace glucose in a medium (Palecek et al., 2002). Addition of glucose was shown to repress invasive growth in a dose-dependent manner. Future experiments could use glycerol in SLAD in the presence and absence of glucose to test if this would rescue invasive growth in the $\Delta f p s 1$ deletant. This would also confirm the role of extracellular glycerol in invasive growth.

This study is significant since $S$. cerevisiae is a well-studied model organism, but processes such as mat formation are still not fully understood, especially for nonlaboratory strains. Mat formation forms the basic understanding of biofilm formation, which has implications such as persistence and survival of clinical yeasts in medical devices, invasiveness into human and plant tissues, interactions between microorganisms and the use of metabolites in wastewater, and in this study, survival of commercial wine yeasts in the wine environment. Many tantalising questions and possibilities have been revealed by this work.

## Appendix A

# Method development for mat formation and plastic adhesion assays 

## A. 1 Mat formation assays

## A.1.1 Reproduction of results by Reynolds and Fink (2001) and test mat formation ability of commercial wine yeast strains

## Background and methods

Mat formation methods described by Reynolds and Fink (2001) were reviewed in order to test if common commercial wine yeast strains also have the ability to form mats. Unfortunately, some steps were not detailed in this short form publication. For example, how the medium was prepared and whether the plates were incubated yeast inoculum side up or down since the agar concentration was very low. In this first preliminary study, the method reported was repeated with some modifications and additional details. Laboratory yeast strain prototrophic diploid $\Sigma 1278$ b and two wine yeast strains, L2056 and AWRI796, were used. Yeast Peptone Dextrose (YPD; $1 \%$ yeast extract, $2 \%$ bacto peptone, $2 \%$ glucose) with $0.3 \%$ agar was made by dissolving all components in RO water and autoclaved to sterilise. Instead of inoculation with a toothpick as reported, to standardise initial cell number, this experiment used inoculation of $5 \mu \mathrm{~L}$ of a diluted overnight YPD culture $\left(1 \times 10^{4}\right.$ cells $\left.\mathrm{mL}^{-1}\right)$. Plates were incubated yeast inoculum side down. Plate images were photographed after 16 days of incubation using a Samsung Galaxy S3 camera. Mats were washed with a stream of ultrapure water from a laboratory squeeze bottle for approximately 30 s to check for adhesive cells.

## Results

Mats were small ( $<40 \mathrm{~mm}$; Fig. A.1) and $\Sigma 1278$ b had a different mat structure (no spokes) compared to those reported by Reynolds and Fink (2001) where mats were described to have a 'hub and spokes' structure. Post-wash observations showed cells adhered to the agar near the mat rim.


Figure A.1: Mat formation pre- and post-wash by $\Sigma 1278$ b, L2056 and AWRI796 on YPD with $0.3 \%$ agar on 90 mm Petri dishes on Day 16 .

Liquid YPD discharged from agar during incubation, and the medium agar concentration may have increased, which may explain the differences in mat size and structure compared to those described by Reynolds and Fink (2001).

## A.1.2 Evaluation of medium preparation methods for mat assays

## Background and methods

In this experiment, three approaches were tested to find the best solution to prepare dry low-density agar YPD:

1. YPD with $0.5 \%$ Bacto agar, autoclaved (increased agar concentration)
2. YPD with $0.5 \%$ agarose, autoclaved (alternative gelling agent)
3. Filtered $2 \times$ YPD and autoclaved $2 \times$ Bacto agar ( $0.6 \%$ ) (washed twice with 800 mL ultrapure water in a 1 L Schott bottle, swirled to mix and rested for 15 min before decanting), then mixed equal volumes before pouring into Petri dishes
4. Filtered $2 \times$ YPD and autoclaved $2 \times$ Bacto agar ( $0.6 \%$ ), then mixed equal volumes before pouring into Petri dishes

## Results

Agar medium made using all approaches was dry even after two-week incubation. However, the $\Sigma 1278$ b mat was smaller on YPD with $0.5 \%$ agar than $0.3 \%$ agar whereas the mat structure on YPD with $0.3 \%$ agar resembled those commonly reported (Fig. A.2).


Figure A.2: Mat formation by $\Sigma 1278$ b on medium prepared using four different approaches: (A) autoclaved YPD with $0.5 \%$ Bacto agar; (B) autoclaved YPD with $0.5 \%$ agarose; (C) filtered YPD with $0.3 \%$ washed and autoclaved Bacto agar; (D) filtered YPD with $0.3 \%$ autoclaved Bacto agar. 90 mm Petri dishes were used.

## Conclusions

The mat shape and size between washed and non-washed agar were similar. Therefore, approach ' 4 ' was used for the preparation of medium.

## A.1.3 Evaluation of mat inoculation with cells at exponential growth phase

## Background and methods

Biological variability of mat size and structure had been observed across replications. In order to decrease this, mats were inoculated with cells standardised for initial cellular metabolic state. Following the initial overnight YPD culture, a fresh YPD culture was inoculated and incubated for a set amount of time to achieve exponential-phase cultures (instead of stationary phase). The following experiment was set up to identify the incubation time required after the re-inoculation. Overnight YPD cultures of prototrophic $\Sigma 1278$ b, auxotrophic $\Sigma 1278$ b and auxotrophic $\Sigma 1278$ b $\Delta$ flo $11 / \Delta$ flo11 were re-inoculated into 25 mL fresh YPD at $1.25 \times 10^{6}$ cells $\mathrm{mL}^{-1}$. Cells were counted using a haemocytometer at several time points to determine the time required for cells to produce approximately three generations.

## Results

All strains achieved three generations ( $\sim 1 \times 10^{7}$ cells $\mathrm{mL}^{-1}$ ) within 4.5 h and approximately four generations within 7 h , indicating rapid growth (Fig. A.3).


Figure A.3: Growth curve after re-inoculation of an overnight YPD culture into fresh YPD. Inoculation rate was $1.25 \times 10^{6}$ cells $\mathrm{mL}^{-1}$. (•) Prototrophic $\Sigma 1278$ b, (■) auxotrophic $\Sigma 1278$ b, (o) auxotrophic $\Sigma 1278$ b $\Delta$ flo $11 / \Delta$ flo11.

## Conclusions

The mat assay method was modified to include a re-inoculation step using an overnight culture, inoculated into fresh YPD at a rate of $1.25 \times 10^{6}$ cells $\mathrm{mL}^{-1}$ and incubated for 6
h prior to inoculation of YPD agar (0.3\%).

## A. 2 Plastic adhesion assays

## A.2.1 Refinement of staining and washing methods

## Background and methods

This experiment followed plastic adhesion methods described by Reynolds and Fink (2001) with modifications and additional details described below. Three strains used were kindly donated by J. Gardner (Uni. of Adelaide): (a) ISO C9 C (L2056 MATa $\Delta h o$ ); (b) ISO C9 D (L2056 MATa $\Delta h o$ ); and (c) ISO C9 C/D (L2056 $\Delta h o / \Delta h o)$. In brief, these strains are derivatives of the commercial wine yeast strain L2056, considered to be very close to isogenic. They were created by three rounds of meiosis and re-diploidisation of the haploid wine yeast C9 (originally derived from L2056, as described in Walker et al., 2003). Homothallism was enabled by introduction of a functional HO gene carried on a plasmid also enabling G418-sulfate resistance. Loss of resistance and inability to sporulate were used to confirm plasmid loss. Mitochondrial RFLP analysis was used to check genetic similarity.

Media used were Synthetic Complete (SC; $0.17 \%$ Yeast Nitrogen Base without amino acids and ammonium sulfate, $0.079 \%$ Complete Supplement Mixture, $0.5 \%$ ammonium sulfate, $0.1 \%$ glucose) and Synthetic Low Ammonium Dextrose (SLAD; 0.17\% Yeast Nitrogen Base without amino acids and ammonium sulfate, $50 \mu \mathrm{M}$ ammonium sulfate, $0.1 \%$ glucose). Following a one-hour incubation, cells were stained with $1 \%$ Crystal Violet solution for 15 min as described by Reynolds and Fink (2001). To remove unbound Crystal Violet, cells were washed with ultrapure water using a pipette to load water and a tipping and tapping motion to remove water. Cells adhered to the plastic were observed not to have been stained by the Crystal Violet. Therefore, cells were stained again for 20 min. For subsequent experiments, cells were stained twice for 20 min each time.

## Results

The number of adhered cells was reflected by differences in absorbance values at 570 nm (Fig. A.4).


Figure A.4: Plastic adhesion of yeast strains, as measured by absorbance of Crystal Violet-stained residual cells post-washing at 570 nm . (•) ISO C9 C, (०) ISO C9 D, ISO C9 C/D, and ( $\square$ ) no cell control in SC and SLAD.

## Conclusions

The plastic adhesion assay was modified with cells stained twice after incubation. Washing steps would include adding ultrapure water by pipetting, followed by inverting the microplate to tap the water out.

## A.2.2 Determination of the maximum absorption of Crystal Violet

## Background and methods

Several publications have used either 570 or 590 nm to quantify absorbance of Crystal Violet (Reynolds and Fink, 2001; Zara et al., 2009; Gori et al., 2011; Granek et al., 2013). This experiment determined the best wavelength to use by performing an absorbance scan on three samples after one-hour incubation in specified medium: (a) no cell control in SLAD; (b) AWRI796 in SLAD; (c) L2056 in SC. The scan was performed using a Tecan Infinite M200 PRO microplate reader from 230 nm to 1000 nm in 10 nm increments.

## Results

Maximum absorption of Crystal Violet was observed at 590 nm (Fig. A.5).


Figure A.5: Wavelength scan for Crystal Violet-stained cultures adhered to plastic. (o) AWRI796 incubated in SLAD, ( $\square$ )L2056 incubated in SC, (•) no cell control.

## Conclusions

For all future assays, absorbance at 590 nm was chosen to quantify cell adhesion on plastic.

## Appendix B

# Method development for mat formation assays in a low nitrogen medium (SLAD) 

## B.0.1 Determination of inoculation rate

## Background and methods

Mat formation was performed as described by Reynolds and Fink (2001) with the substitution of SLAD for YPD and several defined inoculation rates instead of the undefined toothpick inoculation. $\Sigma 1278$ b and two commercial wine strains, L2056 and AWRI796, were tested in this experiment. Inoculation rates were $5 \mu \mathrm{~L}$ of $2 \times 10^{2}, 2 \times 10^{3}, 2 \times 10^{4}$ and $2 \times 10^{5}$ cells $\mathrm{mL}^{-1}$ of an overnight Synthetic Low Ammonium Dextrose (SLAD; $0.17 \%$ Yeast Nitrogen Base without amino acids and ammonium sulfate, $2 \%$ glucose, $50 \mu \mathrm{M}$ ammonium sulfate) culture, equating to approximately $1,10,100$ and 1000 cells. Four to six images were photographed for each mat to capture all sectors on Day 3, 5, 7 and 9 using a Nikon Eclipse 50i microscope at $40 \times$ magnification and an attached Digital Sight DS-2MBWc camera with NIS-Elements F3.0 imaging software. The image of a whole mat was generated by stitching the sector images using Fiji software (Thévenaz and Unser, 2007; Preibisch et al., 2009; Schindelin et al., 2012).

## Results

In general, a higher inoculation rate led to a greater number of invasive growth foci initiated at an early stage (Fig. B.1). Replications from higher inoculation rates produced more consistent results than lower inoculation rates (data not shown). Independent of the initial inoculum used, all mats reached a very similar maximum mat size, suggesting that growth is limited by a factor independent of initial cell numbers. This may be nitrogen
availability. Maximum mat size was approximately $4-5 \mathrm{~mm}$ in diameter, and this was often observed at the first time point analysed (Day 3), except when only 1 cell was used as the inoculum. In comparison, the maximum size of a colony grown from the same strains on SLAD with $2 \%$ agar reaches approximately 1 mm (Joanna Sundstrom, pers. comm.). As the maximum mat size is at least 4-fold wider than colonies formed on SLAD with $2 \%$ agar, and cell growth occurs as a thin layer across the surface, these were defined as mats rather than colonies. Mat expansion also extends beyond the boundary of the inoculum drop. This can also be visualised in Figure B.1A, where growth of the mat inoculated with a single cell doubles in size between 3 and 9 days.

## Conclusions

An inoculation rate of $5 \mu \mathrm{~L}$ of $2 \times 10^{5}$ cells $\mathrm{mL}^{-1}$ ( 1000 cells) was selected for all future SLAD mat assays. Use of rapidly growing cells (exponential phase) as the inoculum was also introduced as in the YPD mat assays to standardise the growth phase of cells. When capturing microscopic images, phase contrast was changed from dark field to the phase corresponding to the objective lens to obtain a white background image.


Figure B.1: Mat formation in a low nitrogen medium (SLAD with $0.3 \%$ agar) for a range of initial inoculum over time. (A) Prototrophic $\Sigma 1278$ b inoculated with either 1, 10, 100 or 1000 cells. Scale bar, 1 mm . Please refer to next two pages for (B) and (C).


Figure B.1: (B) L2056 inoculated with either 1, 10, 100 or 1000 cells. Scale bar, 1 mm . Please refer to next page for (C).


Figure B.1: (C) AWRI796 inoculated with either 1, 10, 100 or 1000 cells. Scale bar, 1 mm .

## B.0.2 Preliminary study on the effect of sulfide on mat formation in SLAD

## Background and methods

Sulfide is of interest to this project since it is a yeast metabolite that preliminary evidence from this laboratory suggests a possible role in cell signalling and it has a significant impact on wine quality. This experiment compared mats from a low nitrogen medium (SLAD) formed by prototrophic $\Sigma 1278$ b, L2056, AWRI796, EC1118, PDM and Distinction with and without the influence of sulfide. Yeast cultures were grown in either SLAD or SLADS (SLAD with $0.4 \mathrm{mg} \mathrm{L}^{-1}$ sodium sulfide) for two overnights before being re-inoculated into a fresh SLAD or SLADS at $1 \times 10^{4}$ cells $\mathrm{mL}^{-1}$ and incubated for 16 h . The cell concentration of cultures was adjusted to $2 \times 10^{5}$ cells $\mathrm{mL}^{-1}$ with PBS. A $5 \mu \mathrm{~L}$ aliquot was spotted to Petri dishes containing SLAD or SLADS with $0.3 \%$ agar (i.e. 1000 cells were inoculated). EC1118, PDM and Distinction were evaluated in a separate experiment, and therefore there was a slight variation in the days where images were captured. Imaging and stitching methods were as described in Study B.0.1.

## Results

All strains consistently showed an enhancement of invasive growth in the presence of exogenous sulfide (Fig. B.2A and B). $\Sigma 1278$ b, EC1118, PDM and Distinction also had reduced surface growth.

## Conclusions

Cell counts of liquid cultures confirmed that the re-inoculation rate and incubation period described achieved more than three generations and cultures had not reached saturation. Sulfide enhanced invasive growth and the addition would be tested in combinations with other compounds.

Figure B.2: Mat formation of yeast strains in a low nitrogen medium over time. (A) $\Sigma 1278$ b, L2056, AWRI796, (B) EC1118, PDM and Distinction on SLAD and SLADS (containing $0.4 \mathrm{mg} \mathrm{L}^{-1}$ sodium sulfide).



## Appendix C

## Attempt to construct $\Delta a q y 1$ in AWRI796

## C.0.1 Transformation with homologous recombination

## Methods

A KanMX gene replacement cassette was generated by PCR from the genomic DNA of BY4741 $\Delta$ aqy1 using the primers AQY1_A (5'-TAGAAGTGGTAAATTGCAGGATAGC$\left.3^{\prime}\right)$ and AQY1_D (5'-TCAACCATATGACTACTTGGGATTT-3') (Winzeler et al., 1999; Wach et al., 1994). AQY1 deletion in AWRI796 was attempted by transformation of the cassette, followed by selection on YPD $+200 \mathrm{mg} \mathrm{L}^{-1}$ G418-sulfate (Gietz and Schiestl, 2007). Homozygous deletants were isolated by sporulation, dissection and re-diploidisation, followed by verification with PCR amplification.

## Results

The resulting progeny showed $2: 2$ segregation of the alleles with two corresponding to the wild type allele size and the other two corresponding to both wild type and deletion allele sizes (Fig. D.1A). When the alleles were amplified with the primer pairs located outside the gene replacement cassette, AQY1_A2 (5'-TTCCAAGTGAATATCTGC-3') and AQY1_D2 (5'-GATTCCTAGATCCTAACAT-3'), all four progenies showed wild type allele sizes (Fig. D.1B).

## Conclusion

The results suggest that the KanMX cassette has a preferential recombination locus other than $A Q Y 1$ in AWRI796.


Figure D.1: AQY1 PCR products from genomic DNA of four spore progenies (1-4), BY4741 Daqy1 and AWRI796 using primers (A) AQY1_A and AQY1_D, (B) AQY1_A2 and AQY1_D2.

## C.0.2 Construction of KanMX gene replacement cassette from a plasmid

## Methods

To increase specificity to AWRI796, a KanMX gene replacement construct was PCR amplified from a plasmid (pBS418; kindly donated by M. Walker, Uni. of Adelaide) using a long primer pair with 40 bp specific to the AWRI796 sequence and 20 bp homologous to either the TEF promoter or terminator on the plasmid. These primers were AQY1_TEFp_fwd ( 5 '-CCTTACACAGTAGGATTAGTCTAGAAGTGGTAAATTGAAGC CTTGACAGTCTTGACGTGC-3') and AQY1_TEFt_rev (5'-CGCACTTAACTTCGC ATCTGGACTACTTGGGATTTCAAGGACAAGATATACATCAACGAT-3’).

## Results

The PCR product quantity was low. When the product was used as a template in a new PCR reaction, no products were obtained.

## Appendix D

## Supporting information for Chapter

 4Table S1: Results of differential gene expression analysis comparing transcriptomes of cells growing invasively and on the surface of SLADS-agar ( $0.3 \%$ ). Genes with low read counts $(<50)$ were excluded. Differentially expressed genes were selected on the basis of satisfying testing significance ( $\mathrm{FDR}<0.05$ ) relative to a 1.3 -fold-change threshold. Adjusted $p$-value is shown zero for less than $1 \times 10^{-6}$. Significantly upregulated, no change and downregulated genes in invasively growing cells are indicated by 1,0 and -1 in the column Score.

| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $\boldsymbol{p}$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $\boldsymbol{p}$-value | Sco |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1051 | HXT7 | 3.781 | 0 | 1 | AWRI796_2590 | TDH1 | 0.731 | 0.002984 |  |
| AWRI796_2159 | HXT4 | 3.039 | 0 | 1 | AWRI796_0070 | PaU5 | 0.729 | 0.007187 |  |
| AWRI796_5153 | AWRI796_5153 | 2.686 | 1.00E-06 | 1 | AWRI796_1561 | IRC7 | 0.729 | 0.003954 |  |
| AWRI796_3083 | SSA2 | 2.26 | 0 | 1 | AWRI796_4656 | YPK9 | 0.726 | 0.001067 |  |
| AWRI796_5256 | HXT6 | 2.251 | 0 | 1 | AWRI796_0144 | YBL029W | 0.724 | $4.40 \mathrm{E}-05$ |  |
| AWRI796_1349 | RGII | 1.919 | 0 | 1 | AWRI796_0617 | DLD1 | 0.72 | 0.000194 |  |
| AWRI796_2017 | AWRI796_2017 | 1.789 | 1.00E-06 | 1 | AWRI796_3327 | HAP1 | 0.72 | $4.10 \mathrm{E}-05$ |  |
| AWRI796_5255 | нхт3 | 1.742 | 1.00E-06 | 1 | AWRI796_1703 | SRM1 | 0.719 | 0.001178 |  |
| AWRI796_4889 | CAR1 | 1.727 | 1.00E-06 | 1 | AWRI796_3329 | GSY2 | 0.718 | 0.000191 |  |
| AWRI796_1052 | HXT3 | 1.524 | 0 | 1 | AWRI796_4406 | CSI2 | 0.718 | 0.149065 |  |
| AWRI796_1560 | HXK1 | 1.434 | 0 | 1 | AWRI796_0449 | MGR1 | 0.716 | 0.003327 |  |
| AWRI796_0081 | SRO77 | 1.417 | 1.00E-06 | 1 | AWRI796_4902 | EEB1 | 0.713 | 0.022128 |  |
| AWRI796-4257_58 | AWRI796_4257_58 | 1.35 | $2.00 \mathrm{E}-06$ | 1 | AWRI796_1619 | GCN1 | 0.712 | $7.00 \mathrm{E}-05$ |  |
| AWRI796_2502 | CIS3 | 1.336 | 0.003327 | 1 | AWRI796_4905 | SSU1 | 0.712 | 0.002694 |  |
| AWRI796_2813 | PIR1 | 1.297 | 0.000181 | 1 | AWRI796_4187 | ATO2 | 0.71 | 0.000402 |  |
| AWRI796_1614 | ARO8 | 1.275 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_1273 | GLC3 | 0.708 | 0.000167 |  |
| AWRI796_0236 | HSP26 | 1.245 | $2.90 \mathrm{E}-05$ | 1 | AWRI796_4077 | KRE33 | 0.707 | 0.000697 |  |
| AWRI796_2240 | GND1 | 1.21 | 1.00E-06 | 1 | AWRI796_2284 | RRD1 | 0.705 | 0.000133 |  |
| AWRI796_3653 | FET3 | 1.184 | $1.80 \mathrm{E}-05$ | 1 | AWRI796_3222 | DIP2 | 0.705 | 0.000825 |  |
| AWRI796_2160 | HXT1 | 1.183 | 0 | 1 | AWRI796_3647 | ERB1 | 0.703 | $3.20 \mathrm{E}-05$ |  |
| AWRI796_3611 | HXT2 | 1.183 | 1.00E-06 | 1 | AWRI796_4752 | DIP5 | 0.703 | 0.000359 |  |
| AWRI796_3060 | YLL053C | 1.168 | 0.00017 | 1 | AWRI796_1809 | GSC2 | 0.701 | 0.000204 |  |
| AWRI796_5047 | TKL1 | 1.162 | 0 | 1 | AWRI796_1530 | FAB1 | 0.699 | 0.002214 |  |
| AWRI796_0102 | YBL081W | 1.139 | 0.000225 | 1 | AWRI796_3079 | TPO1 | 0.699 | 0.000908 |  |
| AWRI796_2568 | PRY3 | 1.125 | 0.000608 | 1 | AWRI796_4700 | RPA190 | 0.699 | 0.000289 |  |
| AWRI796_1119B | HKR1 | 1.094 | $3.20 \mathrm{E}-05$ | 1 | AWRI796_3468 | CAR2 | 0.696 | 0.001067 |  |
| AWRI796_2201 | SPS 100 | 1.076 | $2.70 \mathrm{E}-05$ | 1 | AWRI796_0875 | DOP1 | 0.695 | 0.00034 |  |
| AWRI796_1107 | PDR15 | 1.068 | $1.30 \mathrm{E}-05$ | 1 | AWRI796_4135 | GCD10 | 0.687 | 0.000268 |  |
| AWRI796_1988 | MGA1 | 1.059 | 0.000144 | 1 | AWRI796_0280 | TPS1 | 0.684 | 0.000194 |  |
| AWRI796_3020 | YKR075C | 1.044 | 0 | 1 | AWRI796_2600 | MHP1 | 0.684 | 0.000484 |  |
| AWRI796_3274 | YLR194C | 1.044 | $4.10 \mathrm{E}-05$ | 1 | AWRI796_1964 | CCH1 | 0.681 | 0.000408 |  |
| AWRI796_4782 | FAS2 | 1.038 | 0 | 1 | AWRI796_3438 | DUS3 | 0.678 | 0.000351 |  |
| AWRI796_0883B | NUM1 | 1.031 | 1.00E-06 | 1 | AWRI796_1446 | BRR2 | 0.674 | 0.000728 |  |
| AWRI796_3414 | ELO3 | 1.009 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_4995 | RPA135 | 0.674 | 0.001538 |  |
| AWRI796_4912 | SEC16 | 0.996 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_4837 | OYE3 | 0.673 | 0.08583 |  |
| AWRI796_3204 | MDN1 | 0.987 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_5151 | ERR2 | 0.672 | 0.000955 |  |
| AWRI796_1873 | CLB1 | 0.96 | 0.000841 | 1 | AWRI796_1402 | DSE1 | 0.67 | 0.001535 |  |
| AWRI796_3553 | IMD4 | 0.954 | 0.000268 | 1 | AWRI796_1771 | ERG4 | 0.67 | 0.000631 |  |
| AWRI796_3677 | YMR085W | 0.951 | $8.00 \mathrm{E}-06$ | 1 | AWRI796_2893 | NUP100 | 0.668 | 0.00031 |  |
| AWRI796_2041 | GUT1 | 0.944 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_0378 | YBR238C | 0.667 | 0.005337 |  |
| AWRI796_5135 | GDB1 | 0.944 | $5.00 \mathrm{E}-06$ | 1 | AWRI796_3695 | YPK2 | 0.666 | 0.003246 |  |
| AWRI796_1463 | YJL225C | 0.94 | $4.00 \mathrm{E}-06$ | 1 | AWRI796_0983 | EXG2 | 0.664 | 0.027963 |  |
| AWRI796_2282 | GUT2 | 0.94 | $2.00 \mathrm{E}-06$ | 1 | AWRI796_4003 | POP1 | 0.66 | 0.000217 |  |
| AWRI796_3447 | INA1 | 0.927 | 0.001756 | 1 | AWRI796_3309 | THI7 | 0.657 | 0.001704 |  |
| AWRI796_3186 | CSF1 | 0.926 | $2.30 \mathrm{E}-05$ | 1 | AWRI796_0041 | PMT2 | 0.656 | 0.000508 |  |
| AWRI796_4670 | MCH5 | 0.924 | 0.000387 | 1 | AWRI796_2782 | PTK1 | 0.656 | 0.000337 |  |
| AWRI796_1730 | PUS2 | 0.92 | 0.00037 | 1 | AWRI796_1505 | BLM10 | 0.655 | 0.001481 |  |
| AWRI796_0995 | MTH1 | 0.919 |  | 1 | AWRI796_4614 | SSP2 | 0.655 | 0.143366 |  |
| AWRI796_4272 | ZPS1 | 0.919 | 0.000214 | 1 | AWRI796_1323 | SAH1 | 0.654 | 0.00406 |  |
| AWRI796_5083 | CLB2 | 0.915 | 0.01243 | 1 | AWRI796_4455 | RSB1 | 0.651 | 0.084879 |  |
| AWRI796_3696 | PGM2 | 0.912 | $2.00 \mathrm{E}-06$ | 1 | AWRI796_0527 | YCR061W | 0.647 | 0.001089 |  |
| AWRI796_4069 | AAH1 | 0.909 | $7.00 \mathrm{E}-05$ | 1 | AWRI796_4705 | PUT4 | 0.647 | 0.001156 |  |
| AWRI796_1525 | GSY1 | 0.907 | $3.60 \mathrm{E}-05$ | 1 | AWRI796_3978 | NRD1 | 0.646 | 0.006427 |  |
| AWRI796_3391 | FKS1 | 0.904 | $1.10 \mathrm{E}-05$ | 1 | AWRI796_3679 | YMR087W | 0.641 | 0.001037 |  |
| AWRI796_4676 | SPS4 | 0.901 | 0.018242 | 1 | AWRI796_5114 | GPH1 | 0.641 | 0.001116 |  |
| AWRI796_0432 | MAL31 | 0.899 | 0.000421 | 1 | AWRI796_0534 | RSA4 | 0.638 | 0.003246 |  |
| AWRI796_3061 | AQY2 | 0.897 | 0.001162 | 1 | AWRI796_5243 | FLO5 | 0.638 | 0.005408 |  |
| AWRI796_3070 | VPS13 | 0.896 | $4.00 \mathrm{E}-06$ | 1 | AWRI796_2311 | SIM1 | 0.637 | 0.00837 |  |
| AWRI796_0293 | IRA1 | 0.892 | $1.00 \mathrm{E}-06$ | 1 | AWRI796_4495 | NUP1 | 0.636 | 0.000773 |  |
| AWRI796_4731 | GDH1 | 0.888 | 1.70E-05 | 1 | AWRI796_4503 | LeU9 | 0.636 | 0.0013 |  |
| AWRI796_2472 | PHO90 | 0.871 | $1.00 \mathrm{E}-05$ | 1 | AWRI796_0524 | PWP2 | 0.635 | 0.006427 |  |
| AWRI796_3443 | UTP21 | 0.87 | 0.000157 | 1 | AWRI796_1883 | MEP1 | 0.635 | 0.00084 |  |
| AWRI796_4491 | ECM3 | 0.858 | $3.60 \mathrm{E}-05$ | 1 | AWRI796_3801 | GUA1 | 0.635 | 0.000101 |  |
| AWRI796_0464 | FUS1 | 0.856 | 0.005336 | 1 | AWRI796_1482 | RIM15 | 0.634 | 0.000156 |  |
| AWRI796_2204 | DSE2 | 0.85 | 0.00219 | 1 | AWRI796_4641 | TPO4 | 0.633 | 0.004081 |  |
| AWRI796_3893 | GAS1 | 0.848 | 1.30E-05 | 1 | AWRI796_0592 | HEM3 | 0.632 | 0.006036 |  |
| AWRI796_3482 | FMP27 | 0.845 | $8.00 \mathrm{E}-06$ | 1 | AWRI796_3048 | YKR104W | 0.632 | 0.010288 |  |
| AWRI796_0835 | DNF2 | 0.839 | $5.00 \mathrm{E}-05$ | 1 | AWRI796_0197 | RPL4A | 0.63 | 0.000523 |  |
| AWRI796_0286 | AGP2 | 0.837 | 0.000168 | 1 | AWRI796_0187 | GAL1 | 0.629 | 0.016585 |  |
| AWRI796_2458 | ZNF1 | 0.832 | 0.00017 | 1 | AWRI796_1527 | IGD1 | 0.629 | 0.225841 |  |
| AWRI796_4285 | ARG8 | 0.827 | 0.000126 | 1 | AWRI796_1141 | ADA2 | 0.626 | 0.017211 |  |
| AWRI796_1087 | ATO3 | 0.826 | 0.000901 | 1 | AWRI796_1461 | YRFl-7 | 0.625 | 0.036767 |  |
| AWRI796_2780 | TOR2 | 0.824 | 0.000131 | 1 | AWRI796_0878 | MKC7 | 0.624 | 0.140556 |  |
| AWRI796_0496 | HSP30 | 0.823 | 0.013751 | 1 | AWRI796_2501 | HSP150 | 0.623 | 0.574468 |  |
| AWRI796_2626 | CYR1 | 0.819 | 1.70E-05 | 1 | AWRI796_4383 | GAS5 | 0.622 | 0.002543 |  |
| AWRI796_3001 | DYN1 | 0.817 | 0.000283 | 1 | AWRI796_3461 | SEN1 | 0.62 | 0.000211 |  |
| AWRI796_3961 | BNI1 | 0.817 | 0.00014 | 1 | AWRI796_3845 | AWRI796_3845 | 0.62 | 0.090731 |  |
| AWRI796_2111 | SRB2 | 0.813 | 0.034664 | 1 | AWRI796_4356 | MAM3 | 0.619 | 0.000937 |  |
| AWRI796_4737 | FIT3 | 0.813 | 0.001375 | 1 | AWRI796_0130 | FUII | 0.618 | 0.000327 |  |
| AWRI796-4234 | NOG2 | 0.808 | $2.60 \mathrm{E}-05$ | 1 | AWRI796-4132 | SUN4 | 0.618 | 0.007419 |  |
| AWRI796_1211 | FIT1 | 0.807 | 0.002506 | 1 | AWRI796_2119 | FSH1 | 0.616 | 0.03499 |  |
| AWRI796_0698 | MRK1 | 0.804 | $2.90 \mathrm{E}-05$ | 1 | AWRI796_4334 | PHM7 | 0.616 | 0.001008 |  |
| AWRI796_2868 | CWP1 | 0.802 | 0.000162 | 1 | AWRI796_2682 | TOR1 | 0.614 | 0.000803 |  |
| AWRI796_5142 | AQY1 | 0.802 | $7.00 \mathrm{E}-05$ | 1 | AWRI796_3365 | STT4 | 0.614 | 0.002408 |  |
| AWRI796_3149 | YLR046C | 0.799 | 0.000265 | 1 | AWRI796_4688 | PDR10 | 0.614 | 0.00301 |  |
| AWRI796_2026 | MAL31 | 0.798 | 0.037474 | 1 | AWRI796_0552 | CDC39 | 0.612 | 0.001107 |  |
| AWRI796_0451 | GLK1 | 0.797 | $3.10 \mathrm{E}-05$ | 1 | AWRI796_2008 | SLH1 | 0.61 | 0.006695 |  |
| AWRI796_2750 | HMS2 | 0.797 | 0.003833 | 1 | AWRI796_4255_56 | AWRI796_4255_56 | 0.608 | 0.006771 |  |
| AWRI796_2407 | FAA3 | 0.793 | $4.10 \mathrm{E}-05$ | 1 | AWRI796_0024 | CLN3 | 0.606 | 0.300806 |  |
| AWRI796_0166 | UTP20 | 0.789 | 0.000156 | 1 | AWRI796_2988 | GAP1 | 0.603 | 0.003409 |  |
| AWRI796_0133 | URA7 | 0.783 | $2.70 \mathrm{E}-05$ | 1 | AWRI796_0493 | CWH43 | 0.601 | 0.003833 |  |
| AWRI796_0789 | ENA1 | 0.779 | 0.003133 | 1 | AWRI796_0685 | PMT1 | 0.599 | 0.005214 |  |
| AWRI796-4998 | YPR015C | 0.774 | 0.001538 | 1 | AWRI796_1368 | AWRI796_1368 | 0.596 | 0.037497 |  |
| AWRI796_4067 | YNL144C | 0.771 | 0.000204 | 1 | AWRI796_0546 | YCR087C-A | 0.595 | 0.013038 |  |
| AWRI796_1197 | EMI2 | 0.769 | 6.10E-05 | 1 | AWRI796_1761 | STT3 | 0.594 | 0.00837 |  |
| AWRI796_0864 | ARO1 | 0.768 | 0.000131 | 1 | AWRI796_3718 | ECM16 | 0.594 | 0.002275 |  |
| AWRI796_0007 | BDH1 | 0.767 | $5.40 \mathrm{E}-05$ | 1 | AWRI796_4729 | ALD4 | 0.594 | 0.006771 |  |
| AWRI796_2431 | FLO11 | 0.767 | 0.006992 | 1 | AWRI796_3448 | PUN1 | 0.593 | 0.011501 |  |
| AWRI796_5193 | YRF1-6 | 0.763 | 0.00011 | 1 | AWRI796_4511 | RPO31 | 0.591 | 0.005763 |  |
| AWRI796_1278 | YEA4 | 0.759 | 0.020327 | 1 | AWRI796_2238 | OYE2 | 0.59 | 0.003327 |  |
| AWRI796_4745 | SAM4 | 0.759 | 0.006878 | 1 | AWRI796_1351 | ARG5,6 | 0.587 | 0.007087 |  |
| AWRI796_3904 | ADH6 | 0.75 | 0.000582 | 1 | AWRI796_2798 | FAS1 | 0.583 | 0.003833 |  |
| AWRI796_3986 | ATG2 | 0.748 | 0.000268 | 1 | AWRI796-4287 | RTC1 | ${ }^{0.583}$ | 0.005287 |  |
| AWRI796_2279 | AIM20 | 0.747 | 0.017069 | 1 | AWRI796_1935 | UBR1 | 0.578 | 0.002163 |  |
| AWRI796_2456 | YFL054C | 0.741 | 0.000139 | 1 | AWRI799_3098 | DRS1 ${ }^{\text {PMR25C }}$ | ${ }_{0}^{0.578}$ | 0.016281 |  |
| $\begin{aligned} & \text { AWRI796_0362 } \\ & \text { AWRI796_1571 } \end{aligned}$ | PYC2 HXK2 | 0.734 0.734 | $9.20 \mathrm{E}-05$ $3.80 \mathrm{E}-05$ | 1 1 | AWRI796_3855 AWRI796_3812 | YMR265C RRP5 | 0.578 0.577 | 0.018991 0.021872 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{l o g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1325 | ACA1 | 0.576 | 0.002414 | 1 | AWRI796_4592 | SPR2 | 0.494 | 1 | 0 |
| AWRI796_0645 | RPO21 | 0.575 | 0.027963 | 1 | AWRI796_0694 | NDE2 | 0.493 | 0.081069 | 0 |
| AWRI796_0229 | NRG2 | 0.574 | 0.010703 | 1 | AWRI796_2222 | MPC2 | 0.492 | 0.049849 | 1 |
| AWRI796_0300 | YSW1 | 0.574 | 0.032219 | 1 | AWRI796_0068 | KIN3 | 0.49 | 0.499814 | 0 |
| AWRI796_4574 | ULS1 | 0.574 | 0.010703 | 1 | AWRI796_1373 | TSC11 | 0.489 | 0.077414 | 0 |
| AWRI796_4746 | PBII | 0.574 | 0.055349 | 0 | AWRI796_0822 | SED1 | 0.488 | 1 | 0 |
| AWRI796_0934 | EBS1 | 0.573 | 0.003126 | 1 | AWRI796_1929 | ATF2 | 0.488 | 0.998045 | 0 |
| AWRI796_2225 | PRP8 | 0.573 | 0.025081 | 1 | AWRI796_3557 | SUR7 | 0.488 | 0.419134 | 0 |
| AWRI796_3891 | SCW10 | 0.573 | 0.331383 | 0 | AWRI796_4465 | RPL3 | 0.488 | 0.085525 | 0 |
| AWRI796_4655 | SNF2 | 0.572 | 0.00618 | 1 | AWRI796_1949 | ELP2 | 0.487 | 0.161312 | 0 |
| AWRI796_0788 | KRS1 | 0.57 | 0.001442 | 1 | AWRI796_2016 | PXR1 | 0.487 | 0.339458 | 0 |
| AWRI796_3594 | ERG6 | 0.57 | 0.001099 | 1 | AWRI796_3047 | NFT1 | 0.487 | 1 |  |
| AWRI796-4543 | PDR5 | 0.57 | 0.011218 | 1 | AWRI796_4636 | HRK1 | 0.487 | 0.312734 | 0 |
| AWRI796_3864 | BUL1 | 0.565 | 0.007286 | 1 | AWRI796_0375 | VHC1 | 0.484 | 0.124417 | 0 |
| AWRI796_0519 | ARE1 | 0.564 | 0.01127 | 1 | AWRI796_2306 | TAO3 | 0.483 | 0.171666 | 0 |
| AWRI796_1657 | RPL9A | 0.564 | 0.006771 | 1 | AWRI796_0167 | HTA2 | 0.482 | 0.384813 | 0 |
| AWRI796_2546 | MEF2 | 0.564 | 0.03499 | 1 | AWRI796_5224 | ENA1 | 0.482 | 0.081818 | 0 |
| AWRI796_4111 | NST1 | 0.564 | 0.000841 | 1 | AWRI796_1885 | PPT1 | 0.479 | 0.360763 | 0 |
| AWRI796_5051 | TEF1 | 0.564 | 0.058011 | 0 | AWRI796_2440 | DAL2 | 0.479 | 0.198057 | 0 |
| AWRI796_0327 | EHT1 | 0.563 | 0.005577 | 1 | AWRI796_2540 | UTP10 | 0.479 | 0.136223 | 0 |
| AWRI796_5141 | QCR2 | 0.563 | 0.014402 | 1 | AWRI796-4826 | RTT10 | 0.477 | 0.707279 | 0 |
| AWRI796_0513 | TAF2 | 0.562 | 0.026974 | 1 | AWRI796_5029 | SMK1 | 0.477 | 0.728989 | 0 |
| AWRI796_1685 | YGL117W | 0.561 | 0.080163 | 0 | AWRI796_1355 | ALD5 | 0.476 | 0.18698 | 0 |
| AWRI796_2716 | LIH1 | 0.561 | 0.019518 | 1 | AWRI796_3046 | FLO10 | 0.476 | 0.485835 | 0 |
| AWRI796_2404 | PDR11 | 0.56 | 0.006771 | 1 | AWRI796_3436 | SKI2 | 0.476 | 0.152831 | 0 |
| AWRI796_1440 | DNF1 | 0.559 | 0.002568 | 1 | AWRI796_4203 | ARE2 | 0.476 | 0.135731 | 0 |
| AWRI796_1776 | PMC1 | 0.557 | 0.020233 | 1 | AWRI796_5078 | YPR114W | 0.476 | 0.690813 | 0 |
| AWRI796_3388 | VRP1 | 0.555 | 0.071279 | 0 | AWRI796_2088 | ARG4 | 0.475 | 0.464202 | 0 |
| AWRI796_0154 | PEP1 | 0.553 | 0.011871 | 1 | AWRI796_4792 | FLC1 | 0.475 | 0.337584 | 0 |
| AWRI796_4200 | ACC1 | 0.553 | 0.005028 | 1 | AWRI796_5011 | CSR2 | 0.475 | 0.17496 | 0 |
| AWRI796_2925 | MAE1 | 0.551 | 0.112574 | 0 | AWRI796_4602 | HER1 | 0.471 | 0.214497 | 0 |
| AWRI796_3528 | YML082W | 0.551 | 0.023854 | 1 | AWRI796_2166 | KIC1 | 0.47 | 0.238884 | 0 |
| AWRI796_0215 | REG2 | 0.55 | 0.097384 | 0 | AWRI796_0424 | SNF5 | 0.469 | 0.700881 | 0 |
| AWRI796_2919 | RGT1 | 0.549 | 0.005596 | 1 | AWRI796_0428 | SUL1 | 0.468 | 1 | 0 |
| AWRI796_1299 | SPC25 | 0.548 | 0.039632 | 1 | AWRI796_0745 | OSH2 | 0.468 | 0.38368 | 0 |
| AWRI796_2113 | DOG2 | 0.548 | 0.041796 | 1 | AWRI796_2264 | SET5 | 0.468 | 0.652644 | 0 |
| AWRI796_4133 | AQR1 | 0.547 | 0.035965 | 1 | AWRI796_3454 | DCK1 | 0.468 | 0.219935 | 0 |
| AWRI796_5201 | YRF1-7 | 0.547 | 0.378139 | 0 | AWRI796_5096 | RRP9 | 0.468 | 0.487406 | 0 |
| AWRI796_1758 | TRP5 | 0.545 | 0.025594 | 1 | AWRI796_5181 | CRH1 | 0.468 | 1 | 0 |
| AWRI796_1953 | TDA10 | 0.544 | 0.011501 | 1 | AWRI796_2993 | YKR045C | 0.467 | 1 | 0 |
| AWRI796_2425 | SQT1 | 0.543 | 0.014463 | 1 | AWRI796_3360 | ECM38 | 0.465 | 0.112574 | 0 |
| AWRI796_1565 | YPS5 | 0.542 | 0.437484 | 0 | AWRI796_3463 | IMD3 | 0.465 | 0.16451 | 0 |
| AWRI796_2105 | NEL1 | 0.54 | 0.136688 | 0 | AWRI796_0619 | GLT1 | 0.464 | 0.366947 | 0 |
| AWRI796_5158 | AWRI796_5158 | 0.539 | 0.23021 | 0 | AWRI796_1577 | GUS1 | 0.464 | 0.159048 | 0 |
| AWRI796_1831 | SPR3 | 0.538 | 0.627803 | 0 | AWRI796_2018 | YOR1 | 0.463 | 0.560707 | 0 |
| AWRI796_2298 | TMA108 | 0.538 | 0.026549 | 1 | AWRI796_0916 | ATC1 | 0.462 | 0.965612 |  |
| AWRI796_2507 | INO1 | 0.538 | 0.013751 | 1 | AWRI796_3064 | YBT1 | 0.46 | 0.174723 | 0 |
| AWRI796_3180 | GAL2 | 0.538 | 1 | 0 | AWRI796_1137 | APT2 | 0.459 | 1 | 0 |
| AWRI796_3162 | FRS1 | 0.537 | 0.003954 | 1 | AWRI796_0247 | MIS1 | 0.458 | 0.455464 | 0 |
| AWRI796_5113 | KRE6 | 0.537 | 0.034567 | 1 | AWRI796_1192 | GNP1 | 0.458 | 1 | 0 |
| AWRI796_0465 | HBN1 | 0.536 | 0.252784 | 0 | AWRI796_0263 | VID24 | 0.457 | 0.464202 | 0 |
| AWRI796_1824 | FMP48 | 0.536 | 0.014843 | 1 | AWRI796_0355 | DUR1,2 | 0.457 | 0.438589 |  |
| AWRI796_3053 | MMP1 | 0.536 | 0.015807 | 1 | AWRI796_0082 | PKC1 | 0.456 | 0.373255 | 0 |
| AWRI796_3299 | IFH1 | 0.536 | 0.009361 | 1 | AWRI796_3869 | CAT8 | 0.456 | 0.540032 | 0 |
| AWRI796_4409 | SIN3 | 0.536 | 0.017069 | 1 | AWRI796_4701 | YOR342C | 0.455 | 0.442478 | 0 |
| AWRI796_2567 | PRY1 | 0.535 | 0.813497 | 0 | AWRI796_4915 | MOT1 | 0.455 | 0.281108 | 0 |
| AWRI796_0203 | CHS2 | 0.532 | 0.08767 | 0 | AWRI796_2525 | URA2 | 0.454 | 0.437481 | 0 |
| AWRI796_2054 | AIM17 | 0.531 | 0.010209 | 1 | AWRI796_3291 | CRR1 | 0.454 | 0.668226 | 0 |
| AWRI796_3424 | IKI3 | 0.531 | 0.022776 | 1 | AWRI796_1231 | PRB1 | 0.453 | 0.690813 | 0 |
| AWRI796_0548B | FIG2 | 0.53 | 0.194484 | 0 | AWRI796_2616 | BBC1 | 0.453 | 0.566396 | 0 |
| AWRI796_3094 | PUF3 | 0.53 | 0.038635 | 1 | AWRI796_3721 | RRB1 | 0.453 | 0.205346 | 0 |
| AWRI796_4733 | AMF1 | 0.53 | 0.158011 | 0 | AWRI796_1259 | SNU13 | 0.451 |  | 0 |
| AWRI796_0078 | FLO1 | 0.528 | 0.526974 | 0 | AWRI796_0841 | ARX1 | 0.45 | 0.473642 | 0 |
| AWRI796_5097 | MEP3 | 0.528 | 0.424087 | 0 | AWRI796_2447 | IRC24 | 0.448 | 0.280158 | 0 |
| AWRI796_0104 | NUP170 | 0.526 | 0.040223 | 1 | AWRI796_2291 | PAN6 | 0.447 | 1 | 0 |
| AWRI796_1635 | XRN1 | 0.526 | 0.021872 | 1 | AWRI796_0732 | PUS9 | 0.446 | 0.751808 | 0 |
| AWRI796_4888 | PEX25 | 0.525 | 0.037714 | 1 | AWRI796_2920 | UGP1 | 0.446 | 0.278208 | 0 |
| AWRI796_3257 | CBF5 | 0.523 | 0.021297 | 1 | AWRI796_0076 | SWH1 | 0.445 | 0.538055 | 0 |
| AWRI796_3878 | HAS1 | 0.522 | 0.032219 | 1 | AWRI796_0748 | NOP1 | 0.444 | 1 | 0 |
| AWRI796_2428 | YIR016W | 0.52 | 0.021872 | 1 | AWRI796_0172 | GPI18 | 0.443 | 1 | 0 |
| AWRI796_3067 | FPS1 | 0.52 | 0.050173 | 0 | AWRI796_0028 | RBG1 | 0.441 | 0.52669 | 0 |
| AWRI796_5191 | YML133C | 0.52 | 0.148872 | 0 | AWRI796_3783 | CLN1 | 0.44 | 1 | 0 |
| AWRI796_0272 | LYS2 | 0.519 | 0.035114 | 1 | AWRI796_1112 | DFM1 | 0.439 | 0.373255 | 0 |
| AWRI796_0455 | GFD2 | 0.519 | 0.461205 | 0 | AWRI796_1586 | мто1 | 0.439 | 0.814725 | 0 |
| AWRI796_2059 | DUR3 | 0.519 | 0.032219 | 1 | AWRI796_5251 | PAU3 | 0.438 | 1 | 0 |
| AWRI796_2117 | AAP1 | 0.519 | 0.15397 | 0 | AWRI796_0182 | MNN2 | 0.437 | 0.52669 | 0 |
| AWRI796_1342 | FCY22 | 0.518 | 0.781044 | 0 | AWRI796_1466 | ALR2 | 0.437 | 1 | 0 |
| AWRI796_0035 | MYO4 | 0.517 | 0.03341 | 1 | AWRI796_3645 | NUP116 | 0.437 | 1 | 0 |
| AWRI796_1430 | BEM2 | 0.517 | 0.011502 | 1 | AWRI796_0600 | SEC31 | 0.436 | 0.584003 | 0 |
| AWRI796_2840 | MYO3 | 0.517 | 0.022802 | 1 | AWRI796_1650 | AMS1 | 0.436 | 1 | 0 |
| AWRI796_4028 | CHS1 | 0.517 | 0.419134 | 0 | AWRI796_1915 | NSR1 | 0.436 | 0.701509 | 0 |
| AWRI796_0188 | FUR4 | 0.516 | 0.678758 | 0 | AWRI796_1419 | UBP5 | 0.435 | 1 | 0 |
| AWRI796_1839 | ART5 | 0.515 | 0.135431 | 0 | AWRI796_3606 | PLB2 | 0.434 | 0.690813 | 0 |
| AWRI796_1528 | YFR018C | 0.514 | 0.045177 | 1 | AWRI796_4832 | TRE1 | 0.434 | 0.686491 | 0 |
| AWRI796_2642 | ILV3 | 0.514 | 0.050633 | 0 | AWRI796_4919 | GCR1 | 0.434 | 0.788578 | 0 |
| AWRI796_3095 | YEH1 | 0.514 | 0.08767 | 0 | AWRI796_2029 | ARN2 | 0.433 | 1 | 0 |
| AWRI796_3608 | PLB1 | 0.514 | 0.091116 | 0 | AWRI796_3034 | TGL4 | 0.433 | 0.642353 | 0 |
| AWRI796_1427 | YER152C | 0.513 | 0.020552 | 1 | AWRI796_3255 | YLR173W | 0.432 | 0.743273 | 0 |
| AWRI796_3535 | HMG1 | 0.51 | 0.038446 | 1 | AWRI796_4236 | HOL1 | 0.432 | 1 | 0 |
| AWRI796_3537 | TCB3 | 0.51 | 0.034998 | 1 | AWRI796_2101 | ERC1 | 0.431 | 0.891607 | 0 |
| AWRI796_3780 | YMR196W | 0.51 | 0.161658 | 0 | AWRI796-4192 | LRO1 | 0.431 | 1 | 0 |
| AWRI796_3981 | RPA49 | 0.51 | 0.022479 | 1 | AWRI796_3950 | WSC2 | 0.43 | 1 | 0 |
| AWRI796_1397 | AVT6 | 0.509 | 0.017018 | 1 | AWRI796_5230 | YOR389W | 0.43 | 0.95918 | 0 |
| AWRI796_1643 | RAD54 | 0.508 | 0.122635 | 0 | AWRI796_0570 | SSB1 | 0.429 | 0.988704 | 0 |
| AWRI796_4640 | YTM1 | 0.508 | 0.027963 | 1 | AWRI796_2190 | FUR1 | 0.429 | 1 | 0 |
| AWRI796_1683 | PRP43 | 0.507 | 0.046019 | 1 | AWRI796_3952 | HCH1 | 0.429 | 1 | 0 |
| AWRI796_4735 | FRE3 | 0.507 | 0.770615 | 0 | AWRI796_1243 | GLY1 | 0.428 | 1 | 0 |
| AWRI796_0163 | SLA1 | 0.505 | 0.049586 | 1 | AWRI796_3988 | NAR1 | 0.427 | 1 | 0 |
| AWRI796_3516 | TSL1 | 0.505 | 0.474875 | 0 | AWRI796_1450 | ECM32 | 0.426 | , | 0 |
| AWRI796_1708 | NUP145 | 0.504 | 0.050633 | 0 | AWRI796_1827 | MUP1 | 0.425 | 1 | 0 |
| AWRI796_1369 | DOT6 | 0.502 | 0.327954 | 0 | AWRI796_4652 | RRP36 | 0.425 | 1 | 0 |
| AWRI796_3791 | HFA1 | 0.5 | 0.106623 | 0 | AWRI796-0711 | SYO1 | 0.424 | 1 | 0 |
| AWRI796_3794 | MGL2 | 0.5 | 0.045177 | 1 | AWRI796_3564 | RRN11 | 0.424 | 1 | 0 |
| AWRI796_0273 | TKL2 | 0.499 | 0.300067 | 0 | AWRI796_2944 | UFD4 | 0.423 | 1 | 0 |
| AWRI796-4195 | PRP2 | 0.499 | 0.083998 | 0 | AWRI796_3569 | AMD1 | 0.421 | , | 0 |
| AWRI796_0518 AWRI796_148 | BUD23 TOM1 | 0.498 0.494 | 0.223283 0.022507 | 0 1 | AWRI796_0766 AWRI796_1352 | GAL3 RNR1 | 0.419 0.419 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 0 g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_0242 | RPG1 | 0.418 | 1 | 0 | AWRI796_1098 | SXM1 | 0.368 | 1 | 0 |
| AWRI796_2153 | RTC3 | 0.418 | 1 | 0 | AWRI796_3521 | UTP14 | 0.368 | 1 | 0 |
| AWRI796_4787 | NEW1 | 0.418 | 1 | 0 | AWRI796_4747 | MDL2 | 0.368 | 1 | 0 |
| AWRI796_2138 | ERG7 | 0.417 | 1 | 0 | AWRI796_0359 | SDS24 | 0.367 | 1 | 0 |
| AWRI796_4673 | NOP58 | 0.415 | 1 | 0 | AWRI796_2265 | BAT1 | 0.367 | 1 | 0 |
| AWRI796_1438 | CHD1 | 0.414 | 1 | 0 | AWRI796_3823 | YHM2 | 0.367 | 1 | 0 |
| AWRI796_0216 | RFS1 | 0.413 | 1 | 0 | AWRI796_4075 | YNL134C | 0.367 | 1 | 0 |
| AWRI796_1492 | FRS2 | 0.413 | 1 | 0 | AWRI796_4796 | BMS1 | 0.367 | 1 | 0 |
| AWRI796_1036 | UTP4 | 0.412 | 1 | 0 | AWRI796_3503 | DAT1 | 0.366 | 1 | 0 |
| AWRI796_1295 | HEM14 | 0.412 | 1 | 0 | AWRI796_1806 | ERV1 | 0.365 | 1 | 0 |
| AWRI796_0468 | AGP1 | 0.411 | 1 | 0 | AWRI796_2031 | YHL044W | 0.365 | 1 | 0 |
| AWRI796_1384 | NUP157 | 0.411 | 1 |  | AWRI796_4186 | CIT1 | 0.365 | 1 | 0 |
| AWRI796_0266 | AIM3 | 0.409 | 1 | 0 | AWRI796_2278 | BNR1 | 0.364 | 1 | 0 |
| AWRI796_1375 | RAD51 | 0.409 | 1 | 0 | AWRI796_2346 | KTR7 | 0.364 | 1 | 0 |
| AWRI796_2091 | YHR022C | 0.408 | 1 | 0 | AWRI796_3122 | MEU1 | 0.364 | 1 | 0 |
| AWRI796_1994 | COQ6 | 0.407 | 1 | 0 | AWRI796_3223 | ZRT2 | 0.364 | 1 | 0 |
| AWRI796_4342 | YoL075C | 0.406 | 1 | 0 | AWRI796_4201 | TIM23 | 0.364 | 1 | 0 |
| AWRI796_2442 | DAL7 | 0.405 | 1 | 0 | AWRI796_2368 | YIL055C | 0.363 | 1 | 0 |
| AWRI796_2768 | OXP1 | 0.405 | 1 | 0 | AWRI796_3676 | ADH3 | 0.363 | 1 | 0 |
| AWRI796_0483 | CIT2 | 0.404 | 1 | 0 | AWRI796_4052 | RIA1 | 0.363 | 1 | 0 |
| AWRI796_0942 | ADR1 | 0.404 | 1 | 0 | AWRI796_4223 | COQ2 | 0.363 | 1 | 0 |
| AWRI796_1363 | UTP7 | 0.404 | 1 | 0 | AWRI796_3052 | MHT1 | 0.362 | 1 | 0 |
| AWRI796_1495 | PaU5 | 0.404 | 1 | 0 | AWRI796_4768 | YPL247C | 0.362 | 1 | 0 |
| AWRI796_0381 | YBR241C | 0.403 | 1 | 0 | AWRI796_2015 | SCW4 | 0.361 | 1 | 0 |
| AWRI796_0901 | SEC7 | 0.403 | 1 | 0 | AWRI796_0561 | ADY3 | 0.36 | 1 | 0 |
| AWRI796_2881 | TEF4 | 0.403 | 1 | 0 | AWRI796_2799 | PRS1 | 0.36 | 1 | 0 |
| AWRI796_4858 | PPT2 | 0.403 | 1 | 0 | AWRI796_2736 | NMD5 | 0.359 | 1 | 0 |
| AWRI796_2829 | LTV1 | 0.402 | 1 | 0 | AWRI796_2981 | SPO14 | 0.359 | 1 | 0 |
| AWRI796_3719 | POM152 | 0.402 | 1 | 0 | AWRI796_3968 | POL2 | 0.359 | 1 | 0 |
| AWRI796_4337 | IRA2 | 0.402 | 1 | 0 | AWRI796_5102 | ASN1 | 0.358 | 1 | 0 |
| AWRI796_1808 | IMO32 | 0.4 | 1 | 0 | AWRI796_2253 | UTP9 | 0.357 | 1 | 0 |
| AWRI796_1833 | ADE6 | 0.399 | 1 | 0 | AWRI796_2405 | TIR3 | 0.357 | 1 | 0 |
| AWRI796_4237 | BIO5 | 0.399 | 1 | 0 | AWRI796_2862 | APE1 | 0.357 | 1 | 0 |
| AWRI796_4357 | GPD2 | 0.399 | 1 | 0 | AWRI796_2258 | PPX1 | 0.356 | 1 | 0 |
| AWRI796_2471 | ACO2 | 0.398 | 1 | 0 | AWRI796_4642 | MOD5 | 0.356 | 1 | 0 |
| AWRI796_3929 | KRI1 | 0.397 | 1 | 0 | AWRI796_4844 | SVS1 | 0.356 | 1 | 0 |
| AWRI796_1000 | GCN2 | 0.396 | 1 | 0 | AWRI796_0069 | CDC15 | 0.354 | 1 | 0 |
| AWRI796_1502 | WWM1 | 0.396 | 1 | 0 | AWRI796_1503 | CDC4 | 0.354 | 1 | 0 |
| AWRI796_0031 | FUN19 | 0.395 | 1 | 0 | AWRI796_3106 | YLR001C | 0.354 | 1 | 0 |
| AWRI796_1664 | YGL140C | 0.395 | 1 | 0 | AWRI796_3232 | SLS1 | 0.354 | 1 | 0 |
| AWRI796_3707 | ASC1 | 0.395 | 1 | 0 | AWRI796_4996 | YPR011C | 0.354 | 1 | 0 |
| AWRI796_4821 | GUP2 | 0.395 | 1 | 0 | AWRI796_0730 | PRM7 | 0.353 | 1 | 0 |
| AWRI796_2289 | SLN1 | 0.394 | 1 | 0 | AWRI796_1119A | HKR1 | 0.353 | 1 | 0 |
| AWRI796_1930 | PBP1 | 0.393 | 1 | 0 | AWRI796_1691 | NSA1 | 0.353 | 1 | 0 |
| AWRI796_2090 | YHR020W | 0.393 | 1 | 0 | AWRI796_2789 | DPH2 | 0.353 | 1 | 0 |
| AWRI796_3233 | RRN5 | 0.393 | 1 | 0 | AWRI796_3195 | KIN2 | 0.353 | 1 | 0 |
| AWRI796_3254 | DPH5 | 0.393 | 1 | 0 | AWRI796_3369 | CDC25 | 0.353 | 1 | 0 |
| AWRI796_0743 | GPM2 | 0.392 | 1 | 0 | AWRI796_4384 | YOL029C | 0.353 | 1 | 0 |
| AWRI796_0958 | LYS4 | 0.392 | 1 | 0 | AWRI796_0668 | TRM3 | 0.352 | 1 | 0 |
| AWRI796_1344 | GPP2 | 0.392 | 1 | 0 | AWRI796_3514 | CAC2 | 0.352 | 1 | 0 |
| AWRI796_3525 | ALO1 | 0.392 | 1 | 0 | AWRI796_2137 | TRM5 | 0.351 | 1 | 0 |
| AWRI796_4653 | MPD1 | 0.392 | 1 | 0 | AWRI796_4753 | YPL264C | 0.35 | 1 | 0 |
| AWRI796_4754 | KEL3 | 0.392 | 1 | 0 | AWRI796_1246 | GDA1 | 0.348 | 1 | 0 |
| AWRI796_4806 | TYW1 | 0.392 | 1 | 0 | AWRI796_1886 | ASN2 | 0.348 | 1 | 0 |
| AWRI796_3158 | ERG3 | 0.391 | 1 | 0 | AWRI796_3349 | CTS1 | 0.348 | 1 | 0 |
| AWRI796_4527 | BAG7 | 0.391 | 1 | 0 | AWRI796_1198 | GRH1 | 0.347 | 1 | 0 |
| AWRI796_1403 | RSP5 | 0.39 | 1 | 0 | AWRI796_3258 | RFX1 | 0.347 | 1 | 0 |
| AWRI796_1900 | BTN2 | 0.39 | 1 | 0 | AWRI796_3345 | YLR278C | 0.347 | 1 | 0 |
| AWRI796_3800 | SKY1 | 0.39 | 1 | 0 | AWRI796_3888 | YME2 | 0.346 | 1 | 0 |
| AWRI796_0583 | PRR2 | 0.389 | 1 | 0 | AWRI796_1602 | KIP3 | 0.345 | 1 | 0 |
| AWRI796_1420 | FTR1 | 0.389 | 1 | 0 | AWRI796_1904 | ECL1 | 0.345 | 1 | 0 |
| AWRI796_2140 | QNS1 | 0.389 | 1 | 0 | AWRI796_2945 | MRT4 | 0.345 | 1 | 0 |
| AWRI796_5076 | MRD1 | 0.389 | 1 | 0 | AWRI796_0970 | VHS1 | 0.343 | 1 | 0 |
| AWRI796_0536 | SOL2 | 0.388 | 1 | 0 | AWRI796_3774 | GCV2 | 0.343 | 1 | 0 |
| AWRI796_0121 | YBL055C | 0.387 | 1 | 0 | AWRI796_0421 | APE3 | 0.342 | 1 | 0 |
| AWRI796_0941 | AHA1 | 0.387 | 1 | 0 | AWRI796_4484 | LPX1 | 0.342 | 1 | 0 |
| AWRI796_1491 | BUD27 | 0.386 | 1 | , | AWRI796_4526 | EFT2 | 0.342 | 1 | 0 |
| AWRI796_3123 | POM34 | 0.385 | 1 | 0 | AWRI796_4980 | NCR1 | 0.342 | 1 | 0 |
| AWRI796_4504 | INP53 | 0.385 | 1 | 0 | AWRI796_4033 | SWT21 | 0.341 | 1 | 0 |
| AWRI796_3652 | AAC1 | 0.384 | 1 |  | AWRI796_4353 | CRT10 | 0.341 | 1 | 0 |
| AWRI796_4293 | ALR1 | 0.384 | 1 | 0 | AWRI796_0025 | CYC3 | 0.34 | 1 | 0 |
| AWRI796_1484 | AGX1 | 0.383 | 1 | 0 | AWRI796_2398 | HIS6 | 0.34 | 1 | 0 |
| AWRI796_3330 | HSP60 | 0.383 | 1 | 0 | AWRI796_3141 | PAU23 | 0.34 | 1 | 0 |
| AWRI796_3519 | YML096W | 0.383 | 1 | 0 | AWRI796_5154_55 | AWRI796_5154_55 | 0.34 | 1 | 0 |
| AWRI796_4442 | AKR2 | 0.383 | 1 | 0 | AWRI796_2148 | KSP1 | 0.339 | 1 | 0 |
| AWRI796_0756 | MCD1 | 0.382 | , | 0 | AWRI796_4063 | RPC31 | 0.339 | 1 | 0 |
| AWRI796_1569 | ZRT1 | 0.382 | 1 | 0 | AWRI796_4333 | ADH1 | 0.339 | 1 | 0 |
| AWRI796_2254 | RIX1 | 0.382 | 1 | 0 | AWRI796_0865 | MTC5 | 0.338 | 1 | 0 |
| AWRI796_3285 | HRD3 | 0.382 | 1 | 0 | AWRI796_2746 | PMT4 | 0.338 | 1 | 0 |
| AWRI796_5008 | ATH1 | 0.382 | 1 | 0 | AWRI796_2177 | BZZ1 | 0.337 | 1 | 0 |
| AWRI796_0871 | YCF1 | 0.38 | 1 | 0 | AWRI796_3761 | ECM5 | 0.337 | 1 | 0 |
| AWRI796_1655 | INO80 | 0.379 | 1 | 0 | AWRI796_1341 | FCY21 | 0.336 | 1 | 0 |
| AWRI796_2043 | ECM29 | 0.379 | 1 | 0 | AWRI796_3000 | YSR3 | 0.336 | 1 | 0 |
| AWRI796_3879 | TDA1 | 0.379 | 1 | 0 | AWRI796_0006 | BDH2 | 0.335 | 1 | 0 |
| AWRI796_1677 | SCS3 | 0.377 | 1 | 0 | AWRI796_0159 | SCT1 | 0.335 | 1 | 0 |
| AWRI796_3018 | SIS2 | 0.377 | 1 | 0 | AWRI796_2124 | CPR2 | 0.335 | 1 | 0 |
| AWRI796_3218 | YLR125W | 0.377 | 1 | 0 | AWRI796_4321 | WRS1 | 0.335 | 1 | 0 |
| AWRI796_0733 | GPR1 | 0.376 | 1 | 0 | AWRI796_3963 | LYP1 | 0.334 | 1 | 0 |
| AWRI796_3790 | YMR206W | 0.376 | 1 | 0 | AWRI796_1155 | RMT2 | 0.333 | 1 | 0 |
| AWRI796_4070 | THO2 | 0.376 | , | 0 | AWRI796_1287 | NUG1 | 0.333 | 1 | 0 |
| AWRI796_2003 | YGR266W | 0.374 | 1 | 0 | AWRI796_2161 | HXT5 | 0.333 | 1 | 0 |
| AWRI796_2102 | YHR033W | 0.374 | 1 | 0 | AWRI796_4567 | LAS17 | 0.333 | 1 | 0 |
| AWRI796_2396 | TIM44 | 0.374 | 1 | 0 | AWRI796_4364 | SPE2 | 0.332 | 1 | 0 |
| AWRI796_2628 | AVT1 | 0.374 | 1 | 0 | AWRI796_5209 | YML133C | 0.332 | 1 | 0 |
| AWRI796_0461 | HIS4 | 0.373 | 1 | 0 | AWRI796_1210 | HSP31 | 0.331 | 1 | 0 |
| AWRI796_0488 | ADP1 | 0.373 | 1 | 0 | AWRI796_3851 | TPS3 | 0.331 | 1 | 0 |
| AWRI796_0640 | COP1 | 0.373 | 1 | 0 | AWRI796_0223 | AKL1 | 0.33 | 1 | 0 |
| AWRI796_2331 | DPH1 | 0.373 | 1 | 0 | AWRI796_1370 | PTC2 | 0.33 | 1 | 0 |
| AWRI796_1233 | SDD1 | 0.372 | 1 | 0 | AWRI796_2321 | SDP1 | 0.33 | 1 | 0 |
| AWRI796_2995 | NAP1 | 0.371 | 1 | 0 | AWRI796_2341 | UTP25 | 0.329 | 1 | 0 |
| AWRI796_1846 | PAC10 | 0.37 | , | 0 | AWRI796_4713 | CIR2 | 0.329 | 1 | 0 |
| AWRI796_3496 | NDII | 0.37 | , | 0 | AWRI796-0168 | HTB2 | 0.328 | 1 | 0 |
| AWRI796_4358 | ARG1 | 0.37 | 1 | 0 | AWRI796_2112 | NCP1 | 0.328 | 1 | 0 |
| AWRI796_4963 | MET12 | 0.37 | 1 | 0 | AWRI796_2688 | OPI3 | 0.328 | 1 | 0 |
| AWRI796_3945 | PCL1 | 0.369 | 1 | 0 | AWRI796_2884 | DHR2 | 0.328 | 1 | 0 |
| AWRI796_4839 AWRI796_0474 | $\underset{\text { MEX27 }}{\text { GBP }}$ | 0.369 0.368 | 1 1 | 0 | AWRI796_3413 AWRI796_4210 | ${ }_{\text {ROM2 }}{ }_{\text {BUD17 }}$ | 0.328 0.328 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_0608 | VMA1 | 0.327 | 1 | 0 | AWRI796_4778 | RVB2 | 0.296 | 1 | 0 |
| AWRI796_0723 | STP4 | 0.327 | 1 | 0 | AWRI796_2974 | DBP7 | 0.295 | 1 | 0 |
| AWRI796_1862 | vas1 | 0.327 | 1 | 0 | AWRI796_5101 | NOC4 | 0.295 | 1 | 0 |
| AWRI796_0346 | TAF5 | 0.326 | 1 | 0 | AWRI796_0022 | ERV46 | 0.294 | 1 | 0 |
| AWRI796_0577 | CDC13 | 0.326 | 1 | 0 | AWRI796_3908 | SAM3 | 0.294 | 1 | 0 |
| AWRI796_2326 | YIL108W | 0.326 | 1 | 0 | AWRI796_4402 | PLB3 | 0.294 | 1 | 0 |
| AWRI796_0231 | TIP1 | 0.325 | 1 | 0 | AWRI796_1984 | SDA1 | 0.293 | 1 | 0 |
| AWRI796_1889 | YGR127W | 0.325 | 1 | 0 | AWRI796_4598 | ODC2 | 0.293 | 1 | 0 |
| AWRI796_2597 | YJL045W | 0.325 | 1 | 0 | AWRI796_4849 | TGS1 | 0.293 | 1 | 0 |
| AWRI796_3259 | YLR177W | 0.325 | 1 | 0 | AWRI796_2116 | INM1 | 0.292 | 1 | 0 |
| AWRI796_4486 | TCB1 | 0.325 | 1 | 0 | AWRI796_2575 | UTP18 | 0.292 | 1 | 0 |
| AWRI796_1195 | YDR514C | 0.324 | 1 | 0 | AWRI796_2735 | MNS1 | 0.292 | 1 | 0 |
| AWRI796_3499 | NAB6 | 0.324 | 1 | 0 | AWRI796_4084 | ESBP6 | 0.292 | 1 | 0 |
| AWRI796_0116 | SKT5 | 0.323 | 1 | 0 | AWRI796_0452 | GID7 | 0.291 | 1 | 0 |
| AWRI796_1143 | YHP1 | 0.323 | 1 |  | AWRI796_1428 | PET122 | 0.291 | 1 | 0 |
| AWRI796_4586 | RET1 | 0.323 | 1 | 0 | AWRI796_1950 | YGR201C | 0.291 | 1 | 0 |
| AWRI796_3133 | ADE16 | 0.322 | 1 | 0 | AWRI796_2796 | SPE1 | 0.291 | 1 | 0 |
| AWRI796_3767 | RGM1 | 0.322 | 1 | 0 | AWRI796_3444 | VIP1 | 0.291 | 1 | 0 |
| AWRI796_4743 | FDH1 | 0.322 | 1 | 0 | AWRI796_3513 | NUP188 | 0.291 | 1 | 0 |
| AWRI796_4847 | CDC60 | 0.322 | 1 | 0 | AWRI796_0580 | TIM22 | 0.29 | 1 | 0 |
| AWRI796_1254 | MCM3 | 0.321 | 1 | 0 | AWRI796_1958 | YGR210C | 0.29 | 1 | 0 |
| AWRI796_2604 | IRC18 | 0.321 | 1 | 0 | AWRI796_3078 | FRA1 | 0.29 | 1 | 0 |
| AWRI796_2652 | RaV1 | 0.321 | 1 | 0 | AWRI796_3803 | ESC1 | 0.29 | 1 | 0 |
| AWRI796_4407 | TOP1 | 0.321 | 1 | 0 | AWRI796_1479 | RPO41 | 0.289 | 1 | 0 |
| AWRI796_0601 | SNF3 | 0.32 | 1 | 0 | AWRI796_3583 | YML020W | 0.289 | 1 | 0 |
| AWRI796_0796 | HEM12 | 0.32 | 1 | 0 | AWRI796_4583 | DED1 | 0.289 | 1 | 0 |
| AWRI796_4425 | AWRI796_4425 | 0.32 | 1 | 0 | AWRI796_4726 | GPB1 | 0.289 | 1 | 0 |
| AWRI796_5156 | AWRI796_5156 | 0.32 | 1 | 0 | AWRI796_4945 | NOP4 | 0.289 | 1 | 0 |
| AWRI796_0257 | VPS 15 | 0.319 | 1 | 0 | AWRI796_3138 | SMF3 | 0.288 | 1 | 0 |
| AWRI796_1014 | BFR2 | 0.319 | 1 | 0 | AWRI796_3276 | PWP1 | 0.288 | 1 | 0 |
| AWRI796_3467 | DIF1 | 0.319 | 1 | 0 | AWRI796_4214 | SSK2 | 0.288 | 1 | 0 |
| AWRI796_3470 | SEC39 | 0.319 | 1 | 0 | AWRI796_5089 | YPR127W | 0.288 | 1 | 0 |
| AWRI796_3992 | SIN4 | 0.318 | 1 | 0 | AWRI796_1759 | PGD1 | 0.287 | 1 | 0 |
| AWRI796_1410 | PMD1 | 0.317 | 1 | 0 | AWRI796_2395 | YKE4 | 0.287 | 1 | 0 |
| AWRI796_2058 | YHL017W | 0.317 | 1 | 0 | AWRI796_3793 | YMR209C | 0.287 | 1 | 0 |
| AWRI796_4302 | MCH4 | 0.317 | 1 | 0 | AWRI796_4441 | EXO1 | 0.287 | 1 | 0 |
| AWRI796_2233 | ENO2 | 0.316 | 1 | 0 | AWRI796_0096 | TEL1 | 0.286 | 1 | 0 |
| AWRI796_4575 | THI72 | 0.316 | 1 | 0 | AWRI796_2443 | DAL3 | 0.286 | 1 | 0 |
| AWRI796_0306 | RPB5 | 0.315 | 1 | 0 | AWRI796_3422 | NAM2 | 0.286 | 1 | 0 |
| AWRI796_0504 | SNT1 | 0.315 | 1 | 0 | AWRI796_3565 | CAT2 | 0.286 | 1 | 0 |
| AWRI796_2451 | AWRI796_2451 | 0.315 | 1 | 0 | AWRI796_3806 | FSH2 | 0.286 | 1 | 0 |
| AWRI796_4094 | DBP2 | 0.315 | 1 | 0 | AWRI796_4696 | TEA1 | 0.286 | 1 | 0 |
| AWRI796_4699 | RPA43 | 0.315 | 1 | 0 | AWRI796_0812 | RTR2 | 0.285 | 1 | 0 |
| AWRI796_0712 | TSR1 | 0.314 | 1 | 0 | AWRI796_2449 | YPS6 | 0.285 | 1 | 0 |
| AWRI796_1238 | AFG1 | 0.314 | 1 | 0 | AWRI796_2526 | TRK1 | 0.285 | 1 | 0 |
| AWRI796_2808 | NNK1 | 0.314 | 1 | 0 | AWRI796_0540 | PTC6 | 0.284 | 1 | 0 |
| AWRI796_1940 | HIP1 | 0.313 | 1 | 0 | AWRI796_1887 | YGR125W | 0.284 | 1 | 0 |
| AWRI796_3987 | ZWF1 | 0.312 | 1 | 0 | AWRI796_2277 | POT1 | 0.284 | 1 | 0 |
| AWRI796_0274 | TEF1 | 0.311 | 1 | 0 | AWRI796_3025 | MTD1 | 0.284 | 1 | 0 |
| AWRI796_2283 | IMP2' | 0.311 | 1 | 0 | AWRI796_3633 | HOF1 | 0.284 | 1 | 0 |
| AWRI796_2766 | JEN1 | 0.311 | 1 | 0 | AWRI796_4415 | YSP3 | 0.284 | 1 | 0 |
| AWRI796_3830 | GAD1 | 0.311 | 1 | 0 | AWRI796_4893 | SSE1 | 0.284 | 1 | 0 |
| AWRI796_3831 | GTO3 | 0.311 | 1 | 0 | AWRI796_4997 | CMR3 | 0.284 | 1 | 0 |
| AWRI796_0045 | FUN30 | 0.31 | 1 | 0 | AWRI796_0043 | CCR4 | 0.283 | 1 | 0 |
| AWRI796_2445 | LYS1 | 0.31 | 1 | 0 | AWRI796_3555 | CYB2 | 0.283 | 1 | 0 |
| AWRI796_2559 | ARG3 | 0.31 | 1 | 0 | AWRI796_2438 | DAL1 | 0.282 | 1 | 0 |
| AWRI796_4350 | RIB2 | 0.31 | 1 | 0 | AWRI796_2664 | ANB1 | 0.282 | 1 | 0 |
| AWRI796_0351 | COS111 | 0.309 | 1 | 0 | AWRI796_3074 | RIX7 | 0.282 | 1 | 0 |
| AWRI796_1678 | MET13 | 0.309 | 1 | 0 | AWRI796_0634 | SAS10 | 0.281 | 1 | 0 |
| AWRI796_2564 | IML2 | 0.309 | 1 | 0 | AWRI796_3092 | BPT1 | 0.281 | 1 | 0 |
| AWRI796_2592 | MTR4 | 0.309 | 1 | 0 | AWRI796_0219 | PRP6 | 0.28 | 1 | 0 |
| AWRI796_0140 | RIB1 | 0.308 | 1 | 0 | AWRI796_1926 | RBG2 | 0.28 | 1 | 0 |
| AWRI796_2608 | HCA4 | 0.308 | 1 | 0 | AWRI796_3894 | PSE1 | 0.28 | 1 | 0 |
| AWRI796_2732 | RSF2 | 0.308 | 1 | 0 | AWRI796_0195 | CDS1 | 0.279 | 1 | 0 |
| AWRI796_3657 | ARG7 | 0.308 | 1 | 0 | AWRI796_1162 | JIP4 | 0.279 | 1 | 0 |
| AWRI796_4403 | RCL1 | 0.308 | 1 | 0 | AWRI796_1312 | YPT31 | 0.279 | 1 | 0 |
| AWRI796_2490 | CPS1 | 0.307 | 1 | 0 | AWRI796_1371 | TRP2 | 0.279 | 1 | 0 |
| AWRI796_3183 | RAX2 | 0.307 | 1 | 0 | AWRI796_2164 | TRA1 | 0.279 | 1 | 0 |
| AWRI796_3433 | CST9 | 0.307 | 1 | 0 | AWRI796_2904 | TMA19 | 0.279 | 1 | 0 |
| AWRI796_0598 | GGC1 | 0.306 | 1 | 0 | AWRI796_1282 | MNN1 | 0.278 | 1 | 0 |
| AWRI796_3007 | KTR2 | 0.306 | 1 | 0 | AWRI796_4021 | YNL200C | 0.278 | 1 | 0 |
| AWRI796_3308 | TOP3 | 0.306 | 1 | 0 | AWRI796_1110 | SIZ1 | 0.277 | 1 | 0 |
| AWRI796_4281 | NOP8 | 0.306 | 1 | 0 | AWRI796_2940 | URB1 | 0.277 | 1 | 0 |
| AWRI796_0184 | KAP104 | 0.305 | 1 | 0 | AWRI796_4974 | RRP12 | 0.277 | 1 | 0 |
| AWRI796_2350 | THS1 | 0.305 | 1 | 0 | AWRI796_5022 | THP3 | 0.277 | 1 | 0 |
| AWRI796_4718 | PRT1 | 0.305 | , | 0 | AWRI796_2224 | DNA2 | 0.276 | 1 | 0 |
| AWRI796_2109 | MSC7 | 0.304 | 1 | 0 | AWRI796_1309 | MIG3 | 0.275 | 1 | 0 |
| AWRI796_3732 | YMR144W | 0.304 | 1 | 0 | AWRI796_2548 | LSB6 | 0.275 | 1 | 0 |
| AWRI796_4564 | GAC1 | 0.304 | 1 | 0 | AWRI796_4343 | DSC2 | 0.274 | 1 | 0 |
| AWRI796_0616 | AIR2 | 0.303 | 1 | 0 | AWRI796_5203 | COS3 | 0.274 | 1 | 0 |
| AWRI796_1023 | SUM1 | 0.303 | 1 | 0 | AWRI796_4246 | YNR065C | 0.273 | 1 | 0 |
| AWRI796_2342 | ICE2 | 0.303 | 1 | 0 | AWRI796_2095 | PPA1 | 0.273 | 1 | 0 |
| AWRI796_4224 | MVD1 | 0.303 | 1 | 0 | AWRI796_0781 | REG1 | 0.272 | 1 | 0 |
| AWRI796_4791 | FMP40 | 0.303 | 1 | 0 | AWRI796_1377 | UBP9 | 0.272 | 1 | 0 |
| AWRI796_0697 | THI3 | 0.302 | 1 | 0 | AWRI796_1982 | YAP1802 | 0.272 | 1 | 0 |
| AWRI796_3529 | TDA9 | 0.302 | 1 | 0 | AWRI796_2155 | GAR1 | 0.272 | 1 | 0 |
| AWRI796_4541 | RPB2 | 0.302 | 1 | 0 | AWRI796_2793 | FAT3 | 0.272 | 1 | 0 |
| AWRI796_4820 | NAB3 | 0.302 | 1 | 0 | AWRI796_3862 | ZDS1 | 0.272 | 1 | 0 |
| AWRI796_1769 | PUF4 | 0.301 | 1 | 0 | AWRI796_3230 | RKM5 | 0.271 | 1 | 0 |
| AWRI796_4016 | RIO2 | 0.301 | , | 0 | AWRI796_3261 | YLR179C | 0.271 | 1 | 0 |
| AWRI796_4582 | HIS3 | 0.301 | 1 | 0 | AWRI796_2729 | YJR124C | 0.27 | 1 | 0 |
| AWRI796_4235 | ESF2 | 0.299 | 1 | 0 | AWRI796_3802 | TRS130 | 0.27 | 1 | 0 |
| AWRI796_4986 | CIT3 | 0.299 | , | 0 | AWRI796_4150 | LAP2 | 0.27 | 1 | 0 |
| AWRI796_0567 | MFG1 | 0.298 | 1 | 0 | AWRI796_4852 | PEP4 | 0.27 | 1 | 0 |
| AWRI796_3172 | LAM6 | 0.298 | 1 | 0 | AWRI796_5058 | SRP54 | 0.27 | 1 | 0 |
| AWRI796_4060 | YCK2 | 0.298 | 1 | 0 | AWRI796_0052 | CYS3 | 0.269 | 1 | 0 |
| AWRI796_4166 | EFM6 | 0.298 | 1 | 0 | AWRI796_0434 | HMLALPHA2 | 0.269 | 1 | 0 |
| AWRI796_1606 | NCS6 | 0.297 | 1 | 0 | AWRI796_1903 | ENP2 | 0.269 | 1 | 0 |
| AWRI796_5133 | SEC23 | 0.297 | 1 | 0 | AWRI796_2086 | YSC84 | 0.269 | 1 | 0 |
| AWRI796_0200 | PDX3 | 0.296 | 1 | 0 | AWRI796_2961 | TOF2 | 0.269 | 1 | 0 |
| AWRI796_0389 | ARO4 | 0.296 | , | 0 | AWRI796_3895 | NIP1 | 0.269 | 1 | 0 |
| AWRI796_1613 | KEX1 | 0.296 | 1 | - | AWRI796_1270 | EDC3 | 0.268 | 1 | 0 |
| AWRI796_3043 | BAS1 | 0.296 | 1 | 0 | AWRI796_1699 | YGL101W | 0.268 | 1 | 0 |
| AWRI796_3128 | IZH3 | 0.296 | 1 | 0 | AWRI796_1890 | UTP8 | 0.268 | 1 | 0 |
| AWRI796_3380 | PEX30 | 0.296 | 1 |  | AWRI796_4355 | PRS5 | 0.268 | 1 | 0 |
| AWRI796_4320 AWRI796_455 | SDD3 | 0.296 0.296 | - $\begin{array}{r}1 \\ 1\end{array}$ | 0 | AWRI796_1429 AWRI796_1598 | OXA1 EDC1 | 0.267 0.267 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 0 g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1720 | HNM1 | 0.267 | 1 | 0 | AWRI796_3269 | ATG26 | 0.241 | 1 | 0 |
| AWRI796_1881 | NUP57 | 0.267 | 1 | 0 | AWRI796_3941 | MSB3 | 0.241 | 1 | 0 |
| AWRI796_4043 | NOP13 | 0.267 | 1 | 0 | AWRI796_4147 | ALG11 | 0.241 | 1 | 0 |
| AWRI796_1183 | ITR1 | 0.266 | 1 | 0 | AWRI796_5050 | MRL1 | 0.241 | 1 | 0 |
| AWRI796_1603 | CLG1 | 0.266 | 1 | 0 | AWRI796_0287 | HSL7 | 0.24 | 1 | 0 |
| AWRI796_2139 | OSH3 | 0.266 | 1 | 0 | AWRI796_0759 | NTH1 | 0.24 | 1 | 0 |
| AWRI796_2656 | YJR039W | 0.266 | 1 | 0 | AWRI796_1611 | CHC1 | 0.24 | 1 | 0 |
| AWRI796_3884 | PRC1 | 0.266 | 1 | 0 | AWRI796_3460 | CRN1 | 0.24 | 1 | 0 |
| AWRI796_4228 | FPK1 | 0.266 | 1 | 0 | AWRI796_4269 | HPF1 | 0.24 | 1 | 0 |
| AWRI796_2841 | PMU1 | 0.265 | 1 | 0 | AWRI796_4732 | ATF1 | 0.24 | 1 | 0 |
| AWRI796_2873 | YKL091C | 0.265 | 1 | 0 | AWRI796_0169 | NTH2 | 0.239 | 1 | 0 |
| AWRI796_5210 | YHL049C | 0.265 | 1 | 0 | AWRI796_0988 | HEL2 | 0.239 | 1 | 0 |
| AWRI796_0550 | KIN82 | 0.264 | 1 | 0 | AWRI796_1116 | SYF1 | 0.239 | 1 | 0 |
| AWRI796_1275 | MIT1 | 0.264 | 1 | 0 | AWRI796_2743 | HIR3 | 0.239 | 1 | 0 |
| AWRI796_3362 | HRII | 0.264 | 1 | 0 | AWRI796_3938 | MON2 | 0.239 | 1 | 0 |
| AWRI796_2714 | ADO1 | 0.263 | 1 | 0 | AWRI796_0190 | CHS3 | 0.238 | 1 | 0 |
| AWRI796_0370 | ROT2 | 0.262 | 1 | 0 | AWRI796_0734 | SLM3 | 0.238 | 1 | 0 |
| AWRI796_2020 | YGR283C | 0.262 | 1 | 0 | AWRI796_1177 | PKH1 | 0.238 | 1 | 0 |
| AWRI796_2167 | SBE22 | 0.262 | 1 | 0 | AWRI796_2228 | MTG2 | 0.238 | 1 | 0 |
| AWRI796_2822 | YKL151C | 0.262 | 1 | 0 | AWRI796_3024 | TRZ1 | 0.238 | 1 | 0 |
| AWRI796_3990 | KEX2 | 0.262 | 1 | 0 | AWRI796_0262 | YMC2 | 0.237 | 1 | 0 |
| AWRI796_4456 | ETT1 | 0.262 | 1 | 0 | AWRI796_0767 | SNQ2 | 0.237 | 1 | 0 |
| AWRI796_0217 | YBR053C | 0.261 | 1 | 0 | AWRI796_2202 | YHR140W | 0.237 | 1 | 0 |
| AWRI796_0503 | BPH1 | 0.261 | 1 | 0 | AWRI796_2275 | SUC2 | 0.237 | 1 | 0 |
| AWRI796_2922 | YKL033W-A | 0.261 | 1 | 0 | AWRI796_3900 | PRE5 | 0.237 | 1 | 0 |
| AWRI796_5111 | TDA6 | 0.261 | 1 | 0 | AWRI796_4101 | POL1 | 0.237 | 1 | 0 |
| AWRI796_0058 | SSA1 | 0.26 | 1 | 0 | AWRI796_4848 | AIM44 | 0.237 | 1 | 0 |
| AWRI796_0418 | SSH1 | 0.26 | 1 | 0 | AWRI796_0515 | PER1 | 0.236 | 1 | 0 |
| AWRI796_0623 | NRP1 | 0.26 | 1 | 0 | AWRI796_2073 | TCD1 | 0.236 | 1 | 0 |
| AWRI796_2889 | STB6 | 0.26 | 1 | 0 | AWRI796_2797 | LOT5 | 0.236 | 1 | 0 |
| AWRI796_4131 | RPL9B | 0.26 | 1 | 0 | AWRI796_3027 | NUP133 | 0.236 | 1 | 0 |
| AWRI796_1391 | TMN3 | 0.259 | 1 | 0 | AWRI796_4378 | YOL036W | 0.236 | 1 | 0 |
| AWRI796_0059 | VPS8 | 0.258 | 1 | 0 | AWRI796_0039 | MAK16 | 0.235 | 1 | 0 |
| AWRI796_1050 | YDR341C | 0.258 | 1 | 0 | AWRI796_2495 | HAL5 | 0.235 | 1 | 0 |
| AWRI796_2602 | NUP192 | 0.258 | 1 | 0 | AWRI796_2583 | YHC3 | 0.235 | 1 | 0 |
| AWRI796_4298 | TRM11 | 0.258 | 1 | 0 | AWRI796_2680 | CCT5 | 0.235 | 1 | 0 |
| AWRI796_4605 | WTM1 | 0.258 | 1 | 0 | AWRI796_4872 | RPL5 | 0.234 | 1 | 0 |
| AWRI796_1096 | SHE9 | 0.257 | 1 | 0 | AWRI796_0817 | IPT1 | 0.233 | 1 | 0 |
| AWRI796_4559 | DCS2 | 0.257 | 1 | 0 | AWRI796_2120 | SMF2 | 0.233 | 1 | 0 |
| AWRI796_0400 | SHM1 | 0.256 | 1 | 0 | AWRI796_0768 | RPL4B | 0.232 | 1 | 0 |
| AWRI796_0477 | STP22 | 0.256 | 1 | 0 | AWRI796_1936 | TYS 1 | 0.232 | 1 | 0 |
| AWRI796_1587 | ADE5,7 | 0.256 | 1 | 0 | AWRI796_2045 | WSC4 | 0.232 | 1 | 0 |
| AWRI796_1719 | DBP3 | 0.256 | 1 | 0 | AWRI796_2437 | YVH1 | 0.232 | 1 | 0 |
| AWRI796_1858 | UTP22 | 0.256 | 1 | 0 | AWRI796_4624 | SEC63 | 0.232 | 1 | 0 |
| AWRI796_2128 | GIC1 | 0.256 | 1 | 0 | AWRI796_0005 | GDH3 | 0.231 | 1 | 0 |
| AWRI796_4089 | DCP2 | 0.256 | 1 | 0 | AWRI796_1680 | RPS2 | 0.231 | 1 | 0 |
| AWRI796_4110 | YNL092W | 0.256 | 1 | 0 | AWRI796_2007 | YTA7 | 0.231 | 1 | 0 |
| AWRI796_4770 | YPL245W | 0.256 | 1 | 0 | AWRI796_3628 | YMR027W | 0.231 | 1 | 0 |
| AWRI796_0238 | PFF1 | 0.255 | 1 | 0 | AWRI796_3914 | EGT2 | 0.231 | 1 | 0 |
| AWRI796_1228 | CAN1 | 0.255 | 1 | 0 | AWRI796_4209 | SEC12 | 0.231 | 1 | 0 |
| AWRI796_2049 | SNF6 | 0.255 | 1 | 0 | AWRI796_0441 | SPB1 | 0.23 | 1 | 0 |
| AWRI796_2741 | IML1 | 0.255 | 1 | 0 | AWRI796_1300 | ISC1 | 0.23 | 1 | 0 |
| AWRI796_2965 | YKR015C | 0.255 | 1 | 0 | AWRI796_2686 | LIA1 | 0.23 | 1 | 0 |
| AWRI796-4802 | NIP7 | 0.255 | 1 | 0 | AWRI796-4020 | PSY2 | 0.23 | 1 | 0 |
| AWRI796_0539 | PAT1 | 0.254 | 1 | 0 | AWRI796_1636 | NUP49 | 0.229 | 1 | 0 |
| AWRI796_2243 | KOG1 | 0.254 | 1 | 0 | AWRI796_3586 | PSP2 | 0.229 | 1 | 0 |
| AWRI796_2712 | URA8 | 0.254 | 1 | 0 | AWRI796_4825 | MRN1 | 0.229 | 1 | 0 |
| AWRI796_0774 | GCV1 | 0.253 | 1 | 0 | AWRI796_0647 | RGT2 | 0.228 | 1 | 0 |
| AWRI796_2349 | AIR1 | 0.253 | 1 | 0 | AWRI796_0896 | TRM82 | 0.228 | 1 | 0 |
| AWRI796_3260 | TFS 1 | 0.253 | 1 | 0 | AWRI796_1121 | SIP1 | 0.228 | 1 | 0 |
| AWRI796_4046 | PSD1 | 0.253 | 1 | 0 | AWRI796_1800 | MTL1 | 0.228 | 1 | 0 |
| AWRI796_1265 | PXP1 | 0.252 | 1 | 0 | AWRI796_4174 | HEF3 | 0.228 | 1 | 0 |
| AWRI796_1531 | ATG18 | 0.252 | 1 | 0 | AWRI796_0548A | FIG2 | 0.227 | 1 | 0 |
| AWRI796_2721 | RSM7 | 0.252 | 1 | 0 | AWRI796_2806 | SNU114 | 0.227 | 1 | 0 |
| AWRI796_2860 | SEG2 | 0.252 | 1 | 0 | AWRI796_4876 | NAN1 | 0.227 | 1 | 0 |
| AWRI796_3469 | MRPL4 | 0.252 | 1 | 0 | AWRI796_0020 | GCV3 | 0.226 | 1 | 0 |
| AWRI796_4170 | KTR5 | 0.252 | 1 | 0 | AWRI796_1688 | YGL114W | 0.226 | 1 | 0 |
| AWRI796_4950 | MET31 | 0.252 | 1 | 0 | AWRI796_1792 | SNU71 | 0.226 | 1 | 0 |
| AWRI796_1128 | CYM1 | 0.251 | 1 | 0 | AWRI796_3209 | HOG1 | 0.226 | 1 | 0 |
| AWRI796_2034 | ARN1 | 0.251 | 1 | 0 | AWRI796_2488 | KRE9 | 0.225 | 1 | 0 |
| AWRI796-4695 | KRE5 | 0.251 | 1 | 0 | AWRI796-4173 | PUB1 | 0.225 | , | 0 |
| AWRI796_1496 | LPD1 | 0.25 | 1 | 0 | AWRI796_5036 | FCY1 | 0.225 | 1 | 0 |
| AWRI796_3951 | POP3 | 0.25 | 1 | 0 | AWRI796_0729 | NAT1 | 0.224 | 1 | 0 |
| AWRI796-4887 | YPL113C | 0.25 | 1 | 0 | AWRI796_2752 | YJR149W | 0.224 | , | 0 |
| AWRI796_1667 | SEC27 | 0.249 | 1 | 0 | AWRI796_4766 | GYP5 | 0.224 | 1 | 0 |
| AWRI796-2002 | MES1 | 0.249 | 1 | 0 | AWRI796_5134 | DPM1 | 0.224 | 1 | 0 |
| AWRI796_2330 | SHQ1 | 0.249 | 1 | 0 | AWRI796_1656 | ARO2 | 0.223 | 1 | 0 |
| AWRI796_2896 | MNR2 | 0.249 | 1 | 0 | AWRI796_2223 | SOL3 | 0.223 | 1 | 0 |
| AWRI796_3021 | ECM4 | 0.249 | 1 | 0 | AWRI796_3697 | YKU80 | 0.223 | , | 0 |
| AWRI796_3866 | FCP1 | 0.249 | 1 | 0 | AWRI796_4579 | MCA1 | 0.223 | 1 | 0 |
| AWRI796_0482 | YCP4 | 0.248 | 1 | 0 | AWRI796_1557 | RET2 | 0.222 | 1 | 0 |
| AWRI796_4697 | YOR338W | 0.248 | 1 | 0 | AWRI796_4520 | RGA1 | 0.222 | 1 | 0 |
| AWRI796_4704 | PYK2 | 0.248 | 1 | 0 | AWRI796_4744 | SAM3 | 0.222 | 1 | 0 |
| AWRI796_0662 | HEM25 | 0.247 | 1 | 0 | AWRI796_0009 | CNE1 | 0.221 | 1 | 0 |
| AWRI796_4001 | ATG4 | 0.247 | 1 | 0 | AWRI796_1416 | COX15 | 0.221 | , | 0 |
| AWRI796_0720 | SLC1 | 0.246 | 1 | 0 | AWRI796_1946 | SNG1 | 0.221 | 1 | 0 |
| AWRI796_0833 | YDR089W | 0.246 | 1 | 0 | AWRI796_0244 | SPT7 | 0.22 | , | 0 |
| AWRI796_0903 | HSP42 | 0.246 | 1 | 0 | AWRI796_0793 | HEM13 | 0.22 | 1 | 0 |
| AWRI796_0956 | HEM1 | 0.246 | 1 | 0 | AWRI796_1115 | YDR415C | 0.22 | 1 | 0 |
| AWRI796_3173 | RFU1 | 0.246 | 1 | 0 | AWRI796_1658 | RRT6 | 0.22 | , | 0 |
| AWRI796_3306 | BNA5 | 0.246 | 1 | 0 | AWRI796_3277 | NOP56 | 0.22 | , | 0 |
| AWRI796_3714 | EPO1 | 0.246 | 1 | 0 | AWRI796_3560 | RSE1 | 0.22 | 1 | 0 |
| AWRI796_4025 | YNL195C | 0.246 | 1 | 0 | AWRI796_3786 | ERG2 | 0.22 | 1 | 0 |
| AWRI796_2064 | PRS3 | 0.245 | 1 | 0 | AWRI796_4022 | GCR2 | 0.22 | , | 0 |
| AWRI796_3179 | EMP46 | 0.245 | 1 | 0 | AWRI796_4529 | SIA1 | 0.22 | 1 | 0 |
| AWRI796_5166 | AAD4 | 0.245 | 1 | 0 | AWRI796_0106 | ILS1 | 0.219 | 1 | 0 |
| AWRI796_1100 | UTP5 | 0.244 | 1 | 0 | AWRI796_0156 | ACH1 | 0.218 | 1 | 0 |
| AWRI796_1617 | MDS3 | 0.244 | 1 | 0 | AWRI796_0157 | RRN6 | 0.218 | 1 | 0 |
| AWRI796_1917 | TIF4631 | 0.244 | 1 | 0 | AWRI796_2763 | FRE2 | 0.218 | , | 0 |
| AWRI796_3089_90 | AWRI796_3089_90 | 0.244 | 1 | 0 | AWRI796_3835 | ROY1 | 0.218 | 1 | 0 |
| AWRI796_2663 | TAH11 | 0.243 | 1 | 0 | AWRI796_4155 | BDP1 | 0.218 | 1 | 0 |
| AWRI796_3320 | RCK2 | 0.243 | 1 | 0 | AWRI796-4450 | WHI2 | 0.218 | , | 0 |
| AWRI796_3550 | NTE1 | 0.243 | 1 | 0 | AWRI796_1139 | YDR444W | 0.217 | 1 | 0 |
| AWRI796_3953 | ERG24 | 0.243 | 1 | 0 | AWRI796_2083 | ARD1 | 0.217 | 1 | 0 |
| AWRI796_0126 | EDE1 | 0.241 | , | 0 | AWRI796_2309 | KGD1 | 0.217 | 1 | 0 |
| AWRI796_1741 AWRI796_1912 | ${ }_{\text {TIFII }}{ }_{\text {PT32 }}$ | 0.241 0.241 | 1 1 | 0 0 | AWRI796_4202 AWRI796_4638 | RCF2 VPH1 | 0.217 0.217 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_0502 | SYP1 | 0.216 | 1 | 0 | AWRI796_3188 | ALT1 | 0.191 | 1 |  |
| AWRI796_1748 | HEM2 | 0.216 | 1 | 0 | AWRI796_3663 | NAT4 | 0.191 | 1 |  |
| AWRI796_2367 | VHR1 | 0.216 | 1 | 0 | AWRI796_0295 | MAK5 | 0.189 | 1 |  |
| AWRI796_2907 | ASK1 | 0.216 | 1 | 0 | AWRI796_0411 | RIF1 | 0.189 | 1 |  |
| AWRI796_3171 | RGR1 | 0.216 | 1 | 0 | AWRI796_2908 | YKL050C | 0.189 | 1 |  |
| AWRI796_3939 | MRX6 | 0.216 | - | 0 | AWRI796_1168 | PHO8 | 0.188 | 1 |  |
| AWRI796_0388 | HIS7 | 0.215 | 1 | 0 | AWRI796_2480 | MNN5 | 0.188 | 1 |  |
| AWRI796_1324 | ERG28 | 0.215 | 1 | 0 | AWRI796_2569 | NET1 | 0.188 | 1 |  |
| AWRI796_2773 | UBA1 | 0.215 | 1 | 0 | AWRI796_2861 | GFA1 | 0.188 | 1 |  |
| AWRI796_3081 | HSP104 | 0.215 | 1 | 0 | AWRI796_4517 | UBP2 | 0.188 | 1 |  |
| AWRI796_3685 | UTP15 | 0.215 | 1 | 0 | AWRI796_4615 | PUS7 | 0.188 | 1 |  |
| AWRI796_4325 | TRM10 | 0.215 | 1 | 0 | AWRI796_1364 | AWRI796_1364 | 0.187 | 1 |  |
| AWRI796_1458 | PUG1 | 0.214 | 1 | 0 | AWRI796_1952 | ADE3 | 0.187 | 1 |  |
| AWRI796_2107 | PUT2 | 0.214 | 1 | 0 | AWRI796_2118 | YHK8 | 0.187 | 1 |  |
| AWRI796_2193 | ECM14 | 0.214 | 1 | 0 | AWRI796_3267 | SKG3 | 0.187 | 1 |  |
| AWRI796_3042 | UBP11 | 0.214 | 1 | 0 | AWRI796_3700 | MYO5 | 0.187 | 1 |  |
| AWRI796_3573 | NDC1 | 0.214 | 1 | 0 | AWRI796_0499 | NPP1 | 0.186 | 1 |  |
| AWRI796_1701 | LSG1 | 0.213 | 1 | 0 | AWRI796_3175 | RPL10 | 0.186 | 1 |  |
| AWRI796_0170 | RER2 | 0.212 | 1 | 0 | AWRI796_0921 | RVB1 | 0.185 | 1 |  |
| AWRI796_2103 | YHR033W | 0.212 | 1 | 0 | AWRI796_1863 | TPC1 | 0.185 | 1 |  |
| AWRI796_2990 | UTH1 | 0.212 | 1 | 0 | AWRI796_2094 | THR1 | 0.185 | 1 |  |
| AWRI796_3883 | LCB1 | 0.212 | 1 | 0 | AWRI796_3602 | CDC5 | 0.185 | 1 |  |
| AWRI796_1870 | NOP7 | 0.211 | 1 | 0 | AWRI796_3912 | PEX6 | 0.185 | 1 |  |
| AWRI796_2025 | MAL33 | 0.211 | 1 | 0 | AWRI796_1404 | NSA2 | 0.184 | 1 |  |
| AWRI796_2466 | LAA1 | 0.211 | 1 | 0 | AWRI796_1407 | SAK1 | 0.184 | 1 |  |
| AWRI796_3312 | VPS34 | 0.211 | 1 | 0 | AWRI796_1854 | PIL1 | 0.184 | 1 |  |
| AWRI796_3919 | VNX1 | 0.211 | 1 | 0 | AWRI796_2286 | ESL1 | 0.184 | 1 |  |
| AWRI796_3958 | GOR1 | 0.21 | 1 | 0 | AWRI796_2374 | SYG1 | 0.184 | 1 |  |
| AWRI796_4877 | KAP120 | 0.21 | 1 | 0 | AWRI796_4107 | YNL095C | 0.184 | 1 |  |
| AWRI796_2978 | SAP190 | 0.209 | 1 | 0 | AWRI796_5015 | ARP7 | 0.184 | 1 |  |
| AWRI796_3212 | MSL5 | 0.209 | 1 | 0 | AWRI796_4689 | SCD5 | 0.183 | 1 |  |
| AWRI796_4085 | NAF1 | 0.209 | 1 | 0 | AWRI796_4725 | MRS6 | 0.183 | 1 |  |
| AWRI796_5160 | AWRI796_5160 | 0.209 | 1 | 0 | AWRI796_2097 | DAP2 | 0.182 | 1 |  |
| AWRI796_0819 | TPS2 | 0.208 | 1 | 0 | AWRI796_4890 | GDE1 | 0.182 | 1 |  |
| AWRI796_4193 | NRM1 | 0.208 | 1 | 0 | AWRI796_5013 | SRO7 | 0.182 | 1 |  |
| AWRI796_4934 | PDR12 | 0.208 | 1 | 0 | AWRI796_4521 | ADE2 | 0.181 | 1 |  |
| AWRI796_1046 | MSN5 | 0.207 | 1 | 0 | AWRI796_0639 | LDB17 | 0.18 | 1 |  |
| AWRI796_1692 | CUE3 | 0.207 | 1 | 0 | AWRI796_1164 | SNF1 | 0.18 | 1 |  |
| AWRI796_2370 | MMF1 | 0.207 | 1 | 0 | AWRI796_1891 | SYF2 | 0.18 | 1 |  |
| AWRI796_3013 | GPT2 | 0.207 | 1 | 0 | AWRI796_3396 | DIC1 | 0.18 | 1 |  |
| AWRI796_3231 | NHA1 | 0.207 | 1 | 0 | AWRI796_3925 | EMW1 | 0.18 | 1 |  |
| AWRI796_4618 | ENV9 | 0.207 | 1 | 0 | AWRI796_4948 | ISM1 | 0.18 | 1 |  |
| AWRI796_2182 | SET1 | 0.206 | 1 | 0 | AWRI796_3982 | YNL247W | 0.179 | 1 |  |
| AWRI796_2934 | SPT23 | 0.206 | 1 | 0 | AWRI796_4612 | ABP140 | 0.179 | 1 |  |
| AWRI796_3738 | IMP1 | 0.206 | 1 | 0 | AWRI796_0626 | CDC9 | 0.178 | 1 |  |
| AWRI796_0568 | BRE4 | 0.205 | 1 | 0 | AWRI796_0955 | COX20 | 0.178 | 1 |  |
| AWRI796_0276 | GRS1 | 0.204 | 1 | 0 | AWRI796_1679 | MON1 | 0.178 | 1 |  |
| AWRI796_0395 | RIB5 | 0.204 | 1 | 0 | AWRI796_1997 | RAD2 | 0.178 | 1 |  |
| AWRI796_2299 | OM45 | 0.204 | 1 | 0 | AWRI796_2666 | UTR1 | 0.178 |  |  |
| AWRI796_2637 | MET3 | 0.204 | 1 | 0 | AWRI796_3674 | NAM7 | 0.178 | 1 |  |
| AWRI796_4595 | STE13 | 0.204 | 1 | 0 | AWRI796_5062 | SYT1 | 0.178 | 1 |  |
| AWRI796_1009 | DPL1 | 0.203 | 1 | 0 | AWRI796_0597 | YDL199C | 0.177 | 1 |  |
| AWRI796_1967 | PET54 | 0.203 | 1 | 0 | AWRI796_2162 | YHR097C | 0.177 | 1 |  |
| AWRI796_2504 | SSY5 | 0.203 | 1 | 0 | AWRI796_3119 | PPR1 | 0.177 | 1 |  |
| AWRI796_0128 | COR1 | 0.202 | 1 | 0 | AWRI796_1083 | ARO10 | 0.176 | 1 |  |
| AWRI796_0940 | UPC2 | 0.202 | 1 | 0 | AWRI796_1134 | TH174 | 0.176 | 1 |  |
| AWRI796_1337 | FCY2 | 0.202 | 1 | 0 | AWRI796_1271 | VAC8 | 0.176 | 1 |  |
| AWRI796_3012 | CCP1 | 0.202 | 1 | 0 | AWRI796_1766 | ATE1 | 0.176 | 1 |  |
| AWRI796_0387 | ENP1 | 0.201 | 1 | 0 | AWRI796_0491 | CTO1 | 0.175 | 1 |  |
| AWRI796_2256 | AIM46 | 0.201 | 1 | 0 | AWRI796_0918 | YDR186C | 0.175 | 1 |  |
| AWRI796_2675 | PTK2 | 0.201 | 1 | 0 | AWRI796_2325 | SEC24 | 0.175 | 1 |  |
| AWRI796_2933 | MAK11 | 0.201 | 1 | 0 | AWRI796_3763 | YMR178W | 0.175 | 1 |  |
| AWRI796_3354 | GCD7 | 0.201 | 1 | 0 | AWRI796_4061 | GIM3 | 0.175 | 1 |  |
| AWRI796_3593 | SPT5 | 0.201 | 1 | 0 | AWRI796_4983 | ULA1 | 0.175 | 1 |  |
| AWRI796_4536 | PNO1 | 0.201 | 1 | 0 | AWRI796_0406 | BIT2 | 0.174 | 1 |  |
| AWRI796_1612 | POX1 | 0.2 | 1 | 0 | AWRI796_3022 | MSA2 | 0.174 | 1 |  |
| AWRI796_2281 | UBP7 | 0.2 | 1 | 0 | AWRI796_3096 | SOF1 | 0.174 | 1 |  |
| AWRI796_3107 | NOC3 | 0.2 | 1 | 0 | AWRI796_3517 | ARG81 | 0.174 | 1 |  |
| AWRI796_4086 | NMA111 | 0.2 | 1 | 0 | AWRI796_1437 | GCG1 | 0.173 | 1 |  |
| AWRI796_4418 | TSR3 | 0.2 | 1 | 0 | AWRI796_2322 | HOS4 | 0.173 | 1 |  |
| AWRI796_3174 | BUD20 | 0.199 | 1 | 0 | AWRI796_2476 | YJL193W | 0.173 | 1 |  |
| AWRI796_4339 | AVO1 | 0.199 | 1 | 0 | AWRI796_2758 | AAD10 | 0.173 | 1 |  |
| AWRI796_4446 | HIR2 | 0.199 | 1 | 0 | AWRI796_2093 | MAS2 | 0.172 | 1 |  |
| AWRI796_4952 | PMA2 | 0.199 | 1 | 0 | AWRI796_2491 | TOH1 | 0.172 | 1 |  |
| AWRI796_2332 | XBP1 | 0.198 | 1 | 0 | AWRI796_2963 | PRY2 | 0.172 | 1 |  |
| AWRI796_3829 | RKR1 | 0.198 | 1 | 0 | AWRI796_3157 | SPT8 | 0.172 | 1 |  |
| AWRI796_4739 | YOR385W | 0.198 | 1 | 0 | AWRI796_3374 | TAD3 | 0.172 | 1 |  |
| AWRI796_1251 | RAD23 | 0.197 | 1 | 0 | AWRI796_4188 | RPC34 | 0.172 | 1 |  |
| AWRI796_1362 | SER3 | 0.197 | 1 | 0 | AWRI796_5080 | RRG8 | 0.172 | 1 |  |
| AWRI796_2411 | CFD1 | 0.197 | 1 | 0 | AWRI796_5110 | TPO3 | 0.172 | 1 |  |
| AWRI796_3272 | HCR1 | 0.197 | 1 | 0 | AWRI796_0516 | RRT12 | 0.171 | 1 |  |
| AWRI796_1899 | VPS62 | 0.196 | 1 | 0 | AWRI796_4769 | RBD2 | 0.171 | 1 |  |
| AWRI796_2110 | BCD1 | 0.196 | 1 | 0 | AWRI796_4931 | ALD6 | 0.171 | 1 |  |
| AWRI796_2262 | SCH9 | 0.196 | 1 | 0 | AWRI796_5140 | RPC82 | 0.171 | 1 |  |
| AWRI796_3680 | VBA1 | 0.196 | 1 | 0 | AWRI796_0783 | PST2 | 0.17 | 1 |  |
| AWRI796_0980 | HSP78 | 0.195 | 1 | 0 | AWRI796_2146 | LAM4 | 0.17 | 1 |  |
| AWRI796_2040 | RPL8A | 0.195 | 1 | 0 | AWRI796_2320 | POR2 | 0.17 | 1 |  |
| AWRI796_2250 | EGD2 | 0.195 | 1 | 0 | AWRI796-4959 | ERG10 | 0.17 | 1 |  |
| AWRI796_2419 | PAN1 | 0.195 | 1 | 0 | AWRI796_4181 | LST8 | 0.169 | 1 |  |
| AWRI796_3395 | KAP95 | 0.195 | 1 | 0 | AWRI796_4900 | MSY1 | 0.169 | 1 |  |
| AWRI796_4464 | YOR062C | 0.195 | 1 | 0 | AWRI796_4969 | IRC15 | 0.169 | 1 |  |
| AWRI796_0363 | YBR220C | 0.194 | 1 | 0 | AWRI796_0914 | CDC1 | 0.168 | 1 |  |
| AWRI796_0696 | RPP1A | 0.194 | 1 | 0 | AWRI796_1743 | ALG13 | 0.168 | 1 |  |
| AWRI796_4573 | SPR1 | 0.194 | 1 | 0 | AWRI796_3753 | MME1 | 0.168 | 1 |  |
| AWRI796_0029 | FUN12 | 0.193 | 1 | 0 | AWRI796_1621 | IME4 | 0.167 | 1 |  |
| AWRI796_0202 | SCO1 | 0.193 | 1 | 0 | AWRI796_3985 | SLA2 | 0.167 | 1 |  |
| AWRI796_2388 | BCY1 | 0.193 | 1 | 0 | AWRI796_3176 | FMP25 | 0.166 | 1 |  |
| AWRI796_2541 | PRM10 | 0.193 | 1 | 0 | AWRI796_3600 | YML002W | 0.166 | 1 |  |
| AWRI796_3321 | YEF3 | 0.193 | 1 | 0 | AWRI796_4551 | YRR1 | 0.166 | 1 |  |
| AWRI796_4331 | DUF1 | 0.193 | 1 | 0 | AWRI796_5016 | GLN1 | 0.166 | 1 |  |
| AWRI796_0594 | ACK1 | 0.192 | 1 | 0 | AWRI796_5042 | SPE3 | 0.166 | 1 |  |
| AWRI796_4921 | UBP16 | 0.192 | 1 | 0 | AWRI796_1928 | ERG1 | 0.165 | 1 |  |
| AWRI796_5117 | TIF3 | 0.192 | 1 | 0 | AWRI796_2465 | NUC1 | 0.165 | 1 |  |
| AWRI796_0919 | CCT6 | 0.191 | 1 | 0 | AWRI796_2771 | SAC1 | 0.165 | 1 |  |
| AWRI796_2640 | GPI14 | 0.191 | 1 | 0 | AWRI796_2776 | EMC3 | 0.165 | 1 |  |
| AWRI796_2954 AWRI796_3148 | PAP1 STU2 | 0.191 0.191 | 1 1 | 0 | AWRI796_3177 AWRI796_3887 | BOS1 ATM1 | 0.165 0.165 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{l o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_4599 | DSC3 | 0.165 | 1 | 0 | AWRI796_1943 | XKS1 | 0.146 | 1 | 0 |
| AWRI796_1868 | PCP1 | 0.164 | 1 | 0 | AWRI796_2397 | RPB3 | 0.146 | 1 | 0 |
| AWRI796_3477 | FPR4 | 0.164 | 1 | 0 | AWRI796_2687 | NPA3 | 0.146 | 1 | 0 |
| AWRI796_1481 | MIL1 | 0.163 | 1 | 0 | AWRI796_2774 | STE6 | 0.146 | 1 | 0 |
| AWRI796_1760 | PIB2 | 0.163 | 1 | 0 | AWRI796_4231 | LYS9 | 0.146 | 1 | 0 |
| AWRI796_1892 | YGR130C | 0.163 | 1 | 0 | AWRI796_0147 | NCL1 | 0.145 | 1 | 0 |
| AWRI796_2089 | DED81 | 0.163 | 1 | 0 | AWRI796_0595 | TRM8 | 0.145 | 1 | 0 |
| AWRI796_2163 | SFB3 | 0.163 | 1 | 0 | AWRI796_1823 | SCM4 | 0.145 | 1 | 0 |
| AWRI796_3297 | CCC1 | 0.163 | 1 | 0 | AWRI796_3169 | MEF1 | 0.145 | 1 | 0 |
| AWRI796_3632 | EIS1 | 0.163 | 1 | 0 | AWRI796_5005 | EAF3 | 0.145 | 1 | 0 |
| AWRI796_4671 | SLY41 | 0.163 | 1 | 0 | AWRI796_0340 | RIM2 | 0.144 | 1 | 0 |
| AWRI796_0358 | MET8 | 0.162 | 1 | 0 | AWRI796_0484 | YCR007C | 0.144 | 1 | 0 |
| AWRI796_0641 | YDL144C | 0.162 | 1 | 0 | AWRI796_0620 | UGA3 | 0.144 | 1 | 0 |
| AWRI796_1568 | ADH4 | 0.162 | 1 | 0 | AWRI796_1297 | BIM1 | 0.144 | 1 | 0 |
| AWRI796_2946 | LAC1 | 0.162 | , | 0 | AWRI796_1993 | ENO1 | 0.144 | 1 | 0 |
| AWRI796_5115 | SGV1 | 0.162 | 1 | 0 | AWRI796_2154 | RPF1 | 0.144 | 1 | 0 |
| AWRI796_0353 | KTR3 | 0.161 | 1 | 0 | AWRI796_2251 | MDM31 | 0.144 | 1 | 0 |
| AWRI796_0659 | UBP1 | 0.161 | 1 | 0 | AWRI796_3852 | YMR262W | 0.144 | 1 | 0 |
| AWRI796_2794 | MTR2 | 0.161 | 1 | 0 | AWRI796_4280 | NOP8 | 0.144 | 1 | 0 |
| AWRI796_3449 | VPS36 | 0.161 | 1 | 0 | AWRI796_0633 | MSH5 | 0.143 | 1 | 0 |
| AWRI796_4232 | BRE5 | 0.161 | 1 | 0 | AWRI796_1422 | SCC4 | 0.143 | 1 | 0 |
| AWRI796_0399 | TAE1 | 0.16 | 1 | 0 | AWRI796_1998 | TNA1 | 0.143 | 1 | 0 |
| AWRI796_0917 | UPS3 | 0.16 | 1 | 0 | AWRI796_2135 | DYS1 | 0.143 | 1 | 0 |
| AWRI796_1563 | COS12 | 0.16 | 1 | 0 | AWRI796_2826 | AVT3 | 0.143 | 1 | 0 |
| AWRI796_2023 | BIO2 | 0.16 | 1 | 0 | AWRI796_3150 | FRE8 | 0.143 | 1 | 0 |
| AWRI796_2577 | MPM1 | 0.16 | 1 | 0 | AWRI796_3545 | TEM1 | 0.143 | 1 | 0 |
| AWRI796_2650 | GEA1 | 0.16 | 1 | 0 | AWRI796_1625 | TPN1 | 0.142 | 1 | 0 |
| AWRI796_4665 | BUD7 | 0.16 | 1 | 0 | AWRI796_2454 | AAD4 | 0.142 | 1 | 0 |
| AWRI796_1469 | RGD2 | 0.159 | 1 | 0 | AWRI796_2956 | YKR005C | 0.141 | 1 | 0 |
| AWRI796_2060 | RPS20 | 0.159 | 1 | 0 | AWRI796_3886 | ADE4 | 0.141 | 1 | 0 |
| AWRI796_3493 | TUB3 | 0.159 | 1 | 0 | AWRI796_4071 | SRV2 | 0.141 | 1 | 0 |
| AWRI796_3918 | KRE1 | 0.159 | 1 | 0 | AWRI796_4490 | TMA46 | 0.141 | 1 | 0 |
| AWRI796_4180 | SIS1 | 0.159 | 1 | 0 | AWRI796_0192 | OLA1 | 0.14 | 1 | 0 |
| AWRI796_2188 | ANS1 | 0.158 | 1 | 0 | AWRI796_1462 | YPR204W | 0.14 | 1 | 0 |
| AWRI796_2375 | MET30 | 0.158 | 1 | 0 | AWRI796_2115 | YHR045W | 0.14 | 1 | 0 |
| AWRI796_4911 | ELP3 | 0.158 | 1 | 0 | AWRI796_3747 | YMR160W | 0.14 | 1 | 0 |
| AWRI796_1781 | ERG26 | 0.157 | 1 | 0 | AWRI796_1011 | MHR1 | 0.139 | 1 | 0 |
| AWRI796_2136 | RRP4 | 0.157 | 1 | 0 | AWRI796_3948 | CUS2 | 0.139 | 1 | 0 |
| AWRI796_2323 | COX5B | 0.157 | 1 | 0 | AWRI796_4230 | MSO1 | 0.139 | 1 | 0 |
| AWRI796_3097 | PSR1 | 0.157 | 1 | 0 | AWRI796_4461 | LPL1 | 0.139 | 1 | 0 |
| AWRI796_3650 | STV1 | 0.157 | 1 | 0 | AWRI796_5030 | SEC8 | 0.139 | 1 | 0 |
| AWRI796_3775 | SGS1 | 0.157 | 1 | 0 | AWRI796_0661 | YFH1 | 0.138 | 1 | 0 |
| AWRI796_0805 | TGL2 | 0.156 | 1 | 0 | AWRI796_0780 | VPS54 | 0.138 | 1 | 0 |
| AWRI796_0866 | SAC6 | 0.156 | 1 | 0 | AWRI796_1054 | MRP1 | 0.138 | 1 | 0 |
| AWRI796_2333 | SGA1 | 0.156 | 1 | 0 | AWRI796_1059 | YPQ2 | 0.138 | 1 | 0 |
| AWRI796_2553 | KHA1 | 0.156 | 1 | 0 | AWRI796_1298 | AFG3 | 0.138 | 1 | 0 |
| AWRI796_3031 | PRP16 | 0.156 | 1 | 0 | AWRI796_2748 | RPS4B | 0.138 | 1 | 0 |
| AWRI796_4341 | MDM20 | 0.156 | 1 | 0 | AWRI796_2779 | EAP1 | 0.138 | 1 | 0 |
| AWRI796_4374 | NOP12 | 0.156 | 1 | 0 | AWRI796_2982 | DAL80 | 0.138 | 1 | 0 |
| AWRI796_4650 | RDL1 | 0.156 | 1 | 0 | AWRI796_3159 | MNL2 | 0.138 | 1 | 0 |
| AWRI796_0764 | SOK1 | 0.155 | 1 | 0 | AWRI796_3227 | PDC5 | 0.138 | 1 | 0 |
| AWRI796_3752 | PAH1 | 0.155 | 1 | 0 | AWRI796_3973 | FOL1 | 0.138 | 1 | 0 |
| AWRI796_4124 | IMP4 | 0.155 | 1 | 0 | AWRI796_0825 | VPS41 | 0.137 | 1 | 0 |
| AWRI796_4142 | MSG5 | 0.155 | 1 | 0 | AWRI796_0857 | TRM1 | 0.137 | 1 | 0 |
| AWRI796_4859 | PXA1 | 0.155 | 1 | 0 | AWRI796_1542 | QCR6 | 0.137 | 1 | 0 |
| AWRI796_0053 | SWC3 | 0.154 | 1 | 0 | AWRI796_3937 | CLA4 | 0.137 | 1 | 0 |
| AWRI796_1948 | PMT6 | 0.154 | 1 | 0 | AWRI796_4197 | PHO91 | 0.137 | 1 | 0 |
| AWRI796_2180 | TOM71 | 0.154 | 1 | 0 | AWRI796_0083 | SEA4 | 0.136 | 1 | 0 |
| AWRI796_3005 | TIF1 | 0.154 | 1 | 0 | AWRI796_0321 | NPL4 | 0.136 | 1 | 0 |
| AWRI796_4068 | MEP2 | 0.154 | 1 | 0 | AWRI796_0635 | RPC53 | 0.136 | 1 | 0 |
| AWRI796_4556 | GLN4 | 0.154 | 1 | 0 | AWRI796_1378 | PRS2 | 0.136 | 1 | 0 |
| AWRI796_4896 | FMP30 | 0.154 | 1 | 0 | AWRI796_2157 | MSR1 | 0.136 | 1 | 0 |
| AWRI796_0047 | PSK1 | 0.153 | 1 | 0 | AWRI796_2580 | LAS21 | 0.136 | 1 | 0 |
| AWRI796_0066 | BUD14 | 0.153 | 1 | 0 | AWRI796_2622 | NOP9 | 0.136 | 1 | 0 |
| AWRI796_1049 | YDR338C | 0.153 | 1 | 0 | AWRI796_2701 | JSN1 | 0.136 | 1 | 0 |
| AWRI796_2679 | RPA12 | 0.153 | 1 | 0 | AWRI796_2004 | FOL2 | 0.135 | 1 | 0 |
| AWRI796_4413 | RRP6 | 0.153 | 1 | 0 | AWRI796_4053 | CBK1 | 0.135 | 1 | 0 |
| AWRI796_1202 | SPS1 | 0.152 | 1 | 0 | AWRI796_4808 | HRR25 | 0.135 | 1 | 0 |
| AWRI796_1222 | DLD3 | 0.152 | 1 | 0 | AWRI796_4856 | YPL150W | 0.135 | 1 | 0 |
| AWRI796_1489 | BST1 | 0.152 | 1 | 0 | AWRI796_4904 | NOG1 | 0.135 | 1 | 0 |
| AWRI796_1740 | TYW3 | 0.152 | 1 | 0 | AWRI796_4949 | YPL039W | 0.135 | 1 | 0 |
| AWRI796_3399 | YLR352W | 0.152 | 1 | 0 | AWRI796_0779 | NSII | 0.134 | 1 | 0 |
| AWRI796_3506 | COQ5 | 0.152 | 1 | 0 | AWRI796_2523 | YJL132W | 0.134 | 1 | 0 |
| AWRI796_3684 | AIP1 | 0.152 | 1 | 0 | AWRI796_4136 | NOP2 | 0.134 | 1 | 0 |
| AWRI796_4106 | PHO23 | 0.152 | 1 | 0 | AWRI796_0323 | SMY2 | 0.133 | , | 0 |
| AWRI796_0786 | ARO3 | 0.151 | 1 | 0 | AWRI796_1142 | UTP6 | 0.133 | 1 | 0 |
| AWRI796_1249 | CYC7 | 0.151 | 1 | 0 | AWRI796_1405 | LCP5 | 0.133 | 1 | 0 |
| AWRI796_2068 | STE20 | 0.151 | 1 | 0 | AWRI796_1510 | DEG1 | 0.133 | 1 | 0 |
| AWRI796_2338 | LYS12 | 0.151 | 1 | 0 | AWRI796_3298 | UTP13 | 0.133 | 1 | 0 |
| AWRI796_2576 | YJL068C | 0.151 | 1 | 0 | AWRI796_3615 | SEC59 | 0.133 | 1 | 0 |
| AWRI796_2692 | MIR1 | 0.151 | 1 | 0 | AWRI796_3890 | UBP15 | 0.133 | , | 0 |
| AWRI796_3071 | ENT4 | 0.151 | 1 | 0 | AWRI796_3993 | YNL234W | 0.133 | 1 | 0 |
| AWRI796_3410 | MDM30 | 0.151 | 1 | 0 | AWRI796_4717 | PDE2 | 0.133 | 1 | 0 |
| AWRI796_4363 | AIM39 | 0.151 | 1 | 0 | AWRI796_0201 | CSG2 | 0.132 | , | 0 |
| AWRI796_2077 | ERG11 | 0.15 | 1 | 0 | AWRI796_0403 | REI1 | 0.132 | 1 | 0 |
| AWRI796_2230 | NMD3 | 0.15 | 1 | 0 | AWRI796_0776 | FAL1 | 0.132 | 1 | 0 |
| AWRI796_2409 | YIA6 | 0.15 | 1 | 0 | AWRI796_1005 | RTT103 | 0.132 | , | 0 |
| AWRI796_2552 | BCK1 | 0.15 | 1 | 0 | AWRI796_2226 | CDC23 | 0.132 | 1 | 0 |
| AWRI796_2912 | DCW1 | 0.15 | 1 | 0 | AWRI796_2390 | SSM4 | 0.132 | 1 | 0 |
| AWRI796_2987 | KAE1 | 0.15 | 1 | 0 | AWRI796_1182 | PUF6 | 0.131 | , | 0 |
| AWRI796_1269 | NPP2 | 0.149 | 1 | 0 | AWRI796_1909 | RSR1 | 0.131 | , | 0 |
| AWRI796_1474 | FET5 | 0.149 | 1 | 0 | AWRI796_1951 | PCT1 | 0.131 | 1 | 0 |
| AWRI796_3526 | TUB1 | 0.149 | 1 | 0 | AWRI796_2517 | RPB4 | 0.131 | , | 0 |
| AWRI796_0521 | RSC6 | 0.148 | 1 | 0 | AWRI796_2927 | TCD2 | 0.131 | , | 0 |
| AWRI796_0535 | SSK22 | 0.148 | 1 | 0 | AWRI796_4112 | RHO2 | 0.131 | 1 | 0 |
| AWRI796_1545 | RSC8 | 0.148 | 1 | 0 | AWRI796_4216 | ABZ1 | 0.131 | 1 | 0 |
| AWRI796_3026 | RPF2 | 0.148 | 1 | 0 | AWRI796_1016 | CFT1 | 0.13 | 1 | 0 |
| AWRI796_3217 | YPS3 | 0.148 | 1 | 0 | AWRI796_1244 | IES6 | 0.13 | 1 | 0 |
| AWRI796_4771 | HUT1 | 0.148 | 1 | 0 | AWRI796_2837 | YKL133C | 0.13 | , | 0 |
| AWRI796_2114 | DOG1 | 0.147 | 1 | 0 | AWRI796_4525 | VPS17 | 0.13 | 1 | 0 |
| AWRI796_2424 | STS1 | 0.147 | , | 0 | AWRI796_0107 | SSA3 | 0.129 | 1 | 0 |
| AWRI796_2479 | SWE1 | 0.147 | 1 | 0 | AWRI796_1281 | IRC22 | 0.129 | 1 | 0 |
| AWRI796_4581 | MRM1 | 0.147 | 1 | 0 | AWRI796_1406 | vFA1 | 0.129 | 1 | 0 |
| AWRI796_4917 | ATP4 | 0.147 | 1 | 0 | AWRI796_1684 | COQ8 | 0.129 | 1 | 0 |
| AWRI796_5128 | DPB2 | 0.147 | 1 | 0 | AWRI796_1925 | YIP1 | 0.129 | 1 | 0 |
| AWRI796_0533 AWRI796_0870 | CPR4 CCW12 | 0.146 0.146 | 1 1 | 0 0 | AWRI796_3614 AWRI796_4468 | CLU1 MSA1 | 0.129 0.129 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_0227 | YBR063C | 0.128 | , | 0 | AWRI796_4463 | CKA2 | 0.111 |  |
| AWRI796_0354 | FTH1 | 0.128 | 1 | 0 | AWRI796_4482 | TGL5 | 0.111 |  |
| AWRI796_0993 | DON1 | 0.128 | 1 | 0 | AWRI796_0415 | SAF1 | 0.11 |  |
| AWRI796_1744 | RIM8 | 0.128 | 1 | 0 | AWRI796_1512 | NIC96 | 0.11 |  |
| AWRI796_2203 | CHS7 | 0.128 | 1 | 0 | AWRI796_1529 | AWRI796_1529 | 0.11 |  |
| AWRI796_2221 | YAP1801 | 0.128 | 1 | 0 | AWRI796_2046 | RIM101 | 0.11 |  |
| AWRI796_2496 | TPK1 | 0.128 | 1 | 0 | AWRI796_2433 | SEC11 | 0.11 |  |
| AWRI796_2668 | OSM1 | 0.128 | 1 | 0 | AWRI796_1538 | PTR3 | 0.109 |  |
| AWRI796_4964 | RAD1 | 0.128 | 1 | 0 | AWRI796_1840 | ROM1 | 0.109 |  |
| AWRI796_1524 | CMK1 | 0.127 | 1 | 0 | AWRI796_2376 | PIG2 | 0.109 |  |
| AWRI796_2001 | SAY1 | 0.127 | 1 | 0 | AWRI796_2870 | YJU3 | 0.109 |  |
| AWRI796_3832 | YMR252C | 0.127 | 1 | 0 | AWRI796_4649 | YOR283W | 0.109 |  |
| AWRI796_0314 | TOS1 | 0.126 | 1 | 0 | AWRI796_5108 | PIN3 | 0.109 |  |
| AWRI796_1132 | PPZ2 | 0.126 | 1 | 0 | AWRI796_0728 | SIR2 | 0.108 |  |
| AWRI796_1315 | EDC2 | 0.126 | 1 | 0 | AWRI796_0848 | YDR109C | 0.108 |  |
| AWRI796_2080 | TDA3 | 0.126 | 1 | 0 | AWRI796_1707 | SPC105 | 0.108 |  |
| AWRI796_2192 | YHR131C | 0.126 | 1 | 0 | AWRI796_1867 | MDR1 | 0.108 |  |
| AWRI796_2362 | EFM4 | 0.126 | 1 | 0 | AWRI796_2245 | GP116 | 0.108 |  |
| AWRI796_5139 | SKI3 | 0.126 | 1 | 0 | AWRI796_3009 | LAS1 | 0.108 |  |
| AWRI796_1637 | ROK1 | 0.125 | 1 | 0 | AWRI796_3125 | YEH2 | 0.108 |  |
| AWRI796_3431 | ART10 | 0.125 | 1 | 0 | AWRI796_0072 | UIP3 | 0.107 |  |
| AWRI796_4562 | HEM15 | 0.125 | 1 | 0 | AWRI796_0566 | GYP7 | 0.107 |  |
| AWRI796_1018 | CPR5 | 0.124 | 1 | 0 | AWRI796_2562 | ALY2 | 0.107 |  |
| AWRI796_1245 | YEL043W | 0.124 | 1 | 0 | AWRI796_3216 | YPS1 | 0.107 |  |
| AWRI796_1628 | GTS1 | 0.124 | 1 | 0 | AWRI796_3322 | SSP120 | 0.107 |  |
| AWRI796_3870 | GPI12 | 0.124 | 1 | 0 | AWRI796_3458 | TDA5 | 0.107 |  |
| AWRI796_4037 | IPI3 | 0.124 | 1 | 0 | AWRI796_3785 | RAD14 | 0.107 |  |
| AWRI796_4684 | PRO2 | 0.124 | 1 | 0 | AWRI796_4251 | PDR18 | 0.107 |  |
| AWRI796_5048 | OPY2 | 0.124 | 1 | 0 | AWRI796_4629 | RPT4 | 0.107 |  |
| AWRI796_1144 | PPN1 | 0.123 | 1 | 0 | AWRI796_0946 | GTB1 | 0.106 |  |
| AWRI796_2772 | TRP3 | 0.123 | 1 | 0 | AWRI796_5214 | YCR102C | 0.106 |  |
| AWRI796_2792 | PXA2 | 0.123 | 1 | 0 | AWRI796_0419 | YBR284W | 0.105 |  |
| AWRI796_3316 | MAP1 | 0.123 | 1 | 0 | AWRI796_0652 | CDC53 | 0.105 |  |
| AWRI796_3356 | GSP1 | 0.123 | 1 | 0 | AWRI796_0753 | PTC1 | 0.105 |  |
| AWRI796_3073 | GRC3 | 0.122 | 1 | 0 | AWRI796_1069 | ESF1 | 0.105 |  |
| AWRI796_3742 | YMR155W | 0.122 | 1 | 0 | AWRI796_2654 | RAD26 | 0.105 |  |
| AWRI796_3799 | GAS3 | 0.122 | 1 | 0 | AWRI796_3713 | PKR1 | 0.105 |  |
| AWRI796_4781 | SSO1 | 0.122 | 1 | 0 | AWRI796_3796 | EFR3 | 0.105 |  |
| AWRI796_0101 | ALG3 | 0.121 | 1 | 0 | AWRI796_1537 | CDC14 | 0.104 |  |
| AWRI796_0379 | ERT1 | 0.121 | 1 | 0 | AWRI796_2021 | ERV29 | 0.104 |  |
| AWRI796_2386 | CKA1 | 0.121 | 1 | 0 | AWRI796_2293 | SSL2 | 0.104 |  |
| AWRI796_0309 | ICS2 | 0.12 | 1 | 0 | AWRI796_2473 | UBP12 | 0.104 |  |
| AWRI796_1240 | RML2 | 0.12 | 1 | 0 | AWRI796_2985 | CAF4 | 0.104 |  |
| AWRI796-4908 | RLM1 | 0.12 | 1 | 0 | AWRI796_3465 | TSR2 | 0.104 |  |
| AWRI796_5129 | BET2 | 0.12 | 1 | 0 | AWRI796_4208 | MPP6 | 0.104 |  |
| AWRI796_0390 | SPO23 | 0.119 | 1 | 0 | AWRI796_4215 | PPG1 | 0.104 |  |
| AWRI796_1539 | MET10 | 0.119 | 1 | 0 | AWRI796_4977 | RQC2 | 0.104 |  |
| AWRI796_2657 | GEF1 | 0.119 | 1 | 0 | AWRI796_0122 | TOD6 | 0.103 |  |
| AWRI796_4149 | YNL046W | 0.119 | 1 | 0 | AWRI796_0311 | IFA38 | 0.103 |  |
| AWRI796_4666 | RaX1 | 0.119 | 1 | 0 | AWRI796_0699 | MDH3 | 0.103 |  |
| AWRI796_5017 | VMA13 | 0.119 | - 1 | 0 | AWRI796_1007 | SRP101 | 0.103 |  |
| AWRI796_1426 | UBP3 | 0.118 | 1 | 0 | AWRI796_1445 | RAD3 | 0.103 |  |
| AWRI796_1543 | PHO4 | 0.118 | 1 | 0 | AWRI796_1626 | YGL185C | 0.103 |  |
| AWRI796_1751 | PNC1 | 0.118 | 1 | 0 | AWRI796_2308 | STH1 | 0.103 |  |
| AWRI796_1762 | ALK1 | 0.118 | 1 | 0 | AWRI796_2997 | TRK2 | 0.103 |  |
| AWRI796_1813 | CAX4 | 0.118 | 1 | 0 | AWRI796_3264 | SWI6 | 0.103 |  |
| AWRI796_2132 | RRP3 | 0.118 | 1 | 0 | AWRI796_4218 | ARC35 | 0.103 |  |
| AWRI796_2844 | RRN3 | 0.118 | 1 | 0 | AWRI796_4550 | PNS1 | 0.103 |  |
| AWRI796_3972 | SIP3 | 0.118 | 1 | 0 | AWRI796_4639 | FSF1 | 0.103 |  |
| AWRI796_4606 | MKK1 | 0.118 | 1 | 0 | AWRI796_0038 | DRS2 | 0.102 |  |
| AWRI796_5014 | HTS1 | 0.118 | 1 | 0 | AWRI796_1646 | AIM14 | 0.102 |  |
| AWRI796_5237 | AIF1 | 0.118 | 1 | 0 | AWRI796_1681 | NAB2 | 0.102 |  |
| AWRI796_0149 | PIM1 | 0.117 | 1 | 0 | AWRI796_2801 | COY1 | 0.102 |  |
| AWRI796_0489 | PGK1 | 0.117 | 1 | 0 | AWRI796_2810 | KKQ8 | 0.102 |  |
| AWRI796_1225 | HPA3 | 0.117 | 1 | 0 | AWRI796_3039 | MLP1 | 0.102 1 |  |
| AWRI796_1663 | HUL5 | 0.117 | 1 | 0 | AWRI796_4424 | YOR012W | 0.102 |  |
| AWRI796_3113 | PAM18 | 0.117 | 1 | 0 | AWRI796_4968 | CTF19 | 0.102 |  |
| AWRI796_3497 | YML119W | 0.117 | 1 | 0 | AWRI796_5118 | MMS1 | 0.102 1 |  |
| AWRI796_4716 | VTS1 | 0.117 | 1 | 0 | AWRI796_0520 | YCR051W | 0.101 |  |
| AWRI796_4840 | MRX4 | 0.117 | 1 | 0 | AWRI796_0663 | CYK3 | 0.101 1 |  |
| AWRI796_0171 | COQ1 | 0.116 | - 1 | 0 | AWRI796_1020 | PMT7 | $0.101 \quad 1$ |  |
| AWRI796_2767 | URA1 | 0.116 | 1 | 0 | AWRI796_1038 | YSP2 | 0.101 |  |
| AWRI796_4054 | YGP1 | 0.116 | 1 | 0 | AWRI796_2276 | YIL161W | 0.101 1 |  |
| AWRI796_4266 | IMA4 | 0.116 | 1 | 0 | AWRI796_2700 | GRR1 | 0.101 1 |  |
| AWRI796_4894 | SYH1 | 0.116 | 1 | 0 | AWRI796_4519 | IAH1 | 0.101 1 |  |
| AWRI796_1483 | HAC1 | 0.115 | 1 | 0 | AWRI796_0118 | SHP1 | 0.1 1 |  |
| AWRI796_1788 | ECT1 | 0.115 | 1 | 0 | AWRI796_0342 | AIM4 | 0.1 |  |
| AWRI796_2050 | SNF6 | 0.115 | 1 | 0 | AWRI796_1507 | VTC2 | 0.1 |  |
| AWRI796_2751 | BAT2 | 0.115 | 1 | 0 | AWRI796_1551 | DUG1 | 0.1 |  |
| AWRI796_4376 | RPP2A | 0.115 | 1 | 0 | AWRI796_1779 | CDH1 | 0.1 |  |
| AWRI796_4686 | MYO2 | 0.115 | 1 | 0 | AWRI796_2145 | IRE1 | 0.1 |  |
| AWRI796_4779 | VMA11 | 0.115 | 1 | 0 | AWRI796_2932 | CDC16 | 0.1 1 |  |
| AWRI796_3673 | SEC14 | 0.114 | 1 | 0 | AWRI796_3035 | PXL1 | 0.1 |  |
| AWRI796_3795 | DML1 | 0.114 | 1 | 0 | AWRI796_4314 | WSC3 | 0.1 |  |
| AWRI796_4007 | YNL217W | 0.114 | 1 | 0 | AWRI796_4799 | THI6 | 0.1 1 |  |
| AWRI796_4411 | IZH2 | 0.114 | 1 | 0 | AWRI796_0086 | ECM21 | 0.099 |  |
| AWRI796_4657 | YOR292C | 0.114 | 1 | 0 | AWRI796_0410 | CHK1 | 0.099 |  |
| AWRI796_0407 | EFM2 | 0.113 | - 1 | 0 | AWRI796_0742 | GPD1 | 0.099 1 |  |
| AWRI796_0508 | PH087 | 0.113 | 1 | 0 | AWRI796_1789 | SEC9 | 0.099 |  |
| AWRI796_0889 | ном2 | 0.113 | 1 | 0 | AWRI796_2497 | YJL163C | 0.099 |  |
| AWRI796_0960 | FMN1 | 0.113 | 1 | 0 | AWRI796_3457 | TUS1 | 0.099 |  |
| AWRI796_1166 | PEX29 | 0.113 | 1 | 0 | AWRI796_3750 | INP2 | 0.099 |  |
| AWRI796_4381 | OPI10 | 0.113 | 1 | 0 | AWRI796_3892 | FKS3 | 0.099 |  |
| AWRI796_5079 | RGC1 | 0.113 | 1 | 0 | AWRI796_0838 | GRX3 | 0.098 |  |
| AWRI796_0367 | YBR225W | 0.112 | 1 | 0 | AWRI796_0974 | BTT1 | 0.098 |  |
| AWRI796_0686 | PMT5 | 0.112 | 1 | 0 | AWRI796_1336 | HIS1 | 0.098 |  |
| AWRI796_1235 | POL5 | 0.112 | 1 | 0 | AWRI796_2069 | MRP4 | 0.098 |  |
| AWRI796_1944 | SKI6 | 0.112 | 1 | 0 | AWRI796_2129 | RPP1 | 0.098 |  |
| AWRI796_3054 | GTT2 | 0.112 | 1 | 0 | AWRI796_2655 | HUL4 | 0.098 |  |
| AWRI796_3198 | ICT1 | 0.112 | 1 | 0 | AWRI796_3662 | AVO2 | 0.098 |  |
| AWRI796_3237 | RMP1 | 0.112 | 1 | 0 | AWRI796_4761 | BBP1 | 0.098 |  |
| AWRI796_3617 | ERG5 | 0.112 | 1 | 0 | AWRI796_4774 | HSP82 | 0.098 |  |
| AWRI796_4594 | RFC1 | 0.112 | 1 | 0 | AWRI796_1756 | SCW11 | 0.097 |  |
| AWRI796_1154 | SPP41 | 0.111 | 1 | 0 | AWRI796_3710 | ASII | 0.097 |  |
| AWRI796_3273 | UPS1 | 0.111 | 1 | 0 | AWRI796_4552 | DDP1 | 0.097 1 |  |
| AWRI796_3281 AWRI796_3983 | MSS51 VPS55 | 0.111 0.111 | 1 1 | 0 | AWRI796_4600 AWRI796_4719 | RPB8 PRE10 | 0.097 0.097 |  |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_5202 | YRF1-7 | 0.097 | , | 0 | AWRI796_4163 | HDA1 | 0.08 | 1 |  |
| AWRI796_1595 | VRG4 | 0.096 | 1 | 0 | AWRI796_5061 | ASR1 | 0.08 | 1 |  |
| AWRI796_3435 | AFG2 | 0.096 | 1 | 0 | AWRI796_5268 | FLP1 | 0.08 | 1 |  |
| AWRI796_4755 | FUM1 | 0.096 | 1 | 0 | AWRI796_1610 | SPT16 | 0.079 | 1 |  |
| AWRI796_0271 | RAD16 | 0.095 | 1 | 0 | AWRI796_1945 | FYV8 | 0.079 | 1 |  |
| AWRI796_1791 | YGR012W | 0.095 | 1 | 0 | AWRI796_4099 | LEU4 | 0.079 | 1 |  |
| AWRI796_1901 | SKN1 | 0.095 | 1 | 0 | AWRI796_4184 | PET8 | 0.079 | 1 |  |
| AWRI796_2312 | POG1 | 0.095 | 1 | 0 | AWRI796_4453 | Rati | 0.079 | 1 |  |
| AWRI796_3124 | PSR2 | 0.095 | 1 | 0 | AWRI796_0628 | DHH1 | 0.078 | 1 |  |
| AWRI796_3420 | CSR1 | 0.095 | 1 | 0 | AWRI796_1923 | PSD2 | 0.078 | 1 |  |
| AWRI796_4212 | YNR029C | 0.095 | 1 | 0 | AWRI796_3478 | HMG2 | 0.078 | 1 |  |
| AWRI796_4219 | MRPS 12 | 0.095 | 1 | 0 | AWRI796_0746 | CDC7 | 0.077 | 1 |  |
| AWRI796_4834 | NIP100 | 0.095 | 1 | 0 | AWRI796_1242 | AWRI796_1242 | 0.077 | 1 |  |
| AWRI796_4943 | CAM1 | 0.095 | 1 | 0 | AWRI796_1382 | SSA4 | 0.077 | 1 |  |
| AWRI796_1333 | HOM3 | 0.094 | 1 | 0 | AWRI796_2764 | COS9 | 0.077 | 1 |  |
| AWRI796_2790 | CNB1 | 0.094 | 1 | 0 | AWRI796_3416 | STP3 | 0.077 | 1 |  |
| AWRI796_3575 | USA1 | 0.094 | 1 | 0 | AWRI796_1252 | ANP1 | 0.076 | 1 |  |
| AWRI796_4306 | PTH4 | 0.094 | 1 | 0 | AWRI796_1434 | BuR6 | 0.076 | 1 |  |
| AWRI796_4617 | DGA1 | 0.094 | 1 | 0 | AWRI796_2594 | UBX6 | 0.076 | 1 |  |
| AWRI796_4683 | LDB19 | 0.094 | 1 | 0 | AWRI796_2734 | STR2 | 0.076 | 1 |  |
| AWRI796_0143 | PET9 | 0.093 | 1 | 0 | AWRI796_3087 | KNS1 | 0.076 | 1 |  |
| AWRI796_0332 | YPC1 | 0.093 | 1 | 0 | AWRI796_3377 | MMS22 | 0.076 | 1 |  |
| AWRI796_0637 | NOP14 | 0.093 | 1 | 0 | AWRI796_4664 | MBF1 | 0.076 | 1 |  |
| AWRI796_1045 | SWR1 | 0.093 | 1 | 0 | AWRI796_0859 | KIN1 | 0.075 | 1 |  |
| AWRI796_1330 | TPA1 | 0.093 | 1 | 0 | AWRI796_1851 | GCD2 | 0.075 | 1 |  |
| AWRI796_2055 | OPI1 | 0.093 | 1 | 0 | AWRI796_3387 | SGD1 | 0.075 | 1 |  |
| AWRI796_2237 | AWRI796_2237 | 0.093 | 1 | 0 | AWRI796_3964 | PIK1 | 0.075 | 1 |  |
| AWRI796_2619 | CCT3 | 0.093 | 1 | 0 | AWRI796_2261 | MNL1 | 0.074 | 1 |  |
| AWRI796_2966 | MIC60 | 0.093 | 1 | 0 | AWRI796_3324 | MCP2 | 0.074 | 1 |  |
| AWRI796_4204 | ATP23 | 0.093 | 1 | 0 | AWRI796_3741 | RIM13 | 0.074 | 1 |  |
| AWRI796_0042 | FUN26 | 0.092 | 1 | 0 | AWRI796_4213 | ALG12 | 0.074 | 1 |  |
| AWRI796_0110 | AST1 | 0.092 | 1 | 0 | AWRI796_4604 | WTM2 | 0.074 | 1 |  |
| AWRI796_0840 | TVP15 | 0.092 | 1 | 0 | AWRI796_0505 | FEN1 | 0.074 | 1 |  |
| AWRI796_1698 | RPL28 | 0.092 | 1 | 0 | AWRI796_0135 | APL3 | 0.073 | 1 |  |
| AWRI796_2414 | SGN1 | 0.092 | 1 | 0 | AWRI796_0718 | MCH1 | 0.073 | 1 |  |
| AWRI796_5146 | SGE1 | 0.092 | 1 | 0 | AWRI796_2104 | PIH1 | 0.073 | 1 |  |
| AWRI796_0806 | MAK21 | 0.091 | 1 | 0 | AWRI796_2144 | YHR078W | 0.073 | 1 |  |
| AWRI796_1519 | GCN20 | 0.091 | 1 | 0 | AWRI796_2259 | YHR202W | 0.073 | 1 |  |
| AWRI796_2172 | GGA2 | 0.091 | 1 | 0 | AWRI796_2378 | CBR1 | 0.073 | 1 |  |
| AWRI796_2770 | DOA1 | 0.091 | 1 | 0 | AWRI796_3182 | EMP70 | 0.073 | 1 |  |
| AWRI796_2818 | APE2 | 0.091 | 1 | 0 | AWRI796_4238 | BIO4 | 0.073 | 1 |  |
| AWRI796_4370 | PSK2 | 0.091 | 1 | 0 | AWRI796_4783 | USV1 | 0.073 | 1 |  |
| AWRI796_1897 | TPO2 | 0.09 | 1 | 0 | AWRI796_4797 | YPL216W | 0.073 | 1 |  |
| AWRI796_2949 | AUR1 | 0.09 | 1 | 0 | AWRI796_1250 | UTR4 | 0.072 | 1 |  |
| AWRI796_3235 | DPH6 | 0.09 | 1 | 0 | AWRI796_1589 | TAN1 | 0.072 | 1 |  |
| AWRI796_4815 | APL5 | 0.09 | 1 | 0 | AWRI796_1757 | CWH41 | 0.072 | 1 |  |
| AWRI796_0556 | YCR099C | 0.089 | 1 | 0 | AWRI796_2019 | BGL2 | 0.072 | 1 |  |
| AWRI796_2096 | RPN1 | 0.089 | 1 | 0 | AWRI796_2199 | ARO9 | 0.072 | 1 |  |
| AWRI796_2420 | EGH1 | 0.089 | 1 | 0 | AWRI796_3991 | YTP1 | 0.072 |  |  |
| AWRI796_2717 | CPA2 | 0.089 | 1 | 0 | AWRI796_0693 | YDL086W | 0.071 | 1 |  |
| AWRI796_3105 | DNM1 | 0.089 | 1 | 0 | AWRI796_0892 | ACL4 | 0.071 | 1 |  |
| AWRI796_4108 | APP1 | 0.089 | 1 | 0 | AWRI796_3532 | CPR3 | 0.071 | 1 |  |
| AWRI796_0529 | HCM1 | 0.088 | 1 | 0 | AWRI796_4869 | ODC1 | 0.071 | 1 |  |
| AWRI796_0578 | DTD1 | 0.088 | 1 | 0 | AWRI796_0392 | DUT1 | 0.07 | 1 |  |
| AWRI796_2234 | FMO1 | 0.088 | 1 | 0 | AWRI796_0849 | FOB1 | 0.07 | 1 |  |
| AWRI796_3134 | RPL15A | 0.088 | 1 | 0 | AWRI796_0904 | SUP35 | 0.07 | 1 |  |
| AWRI796_3542 | ERV41 | 0.088 | 1 | 0 | AWRI796_0574 | WHI4 | 0.069 | 1 |  |
| AWRI796_4198 | YNR014W | 0.088 | 1 | 0 | AWRI796_1301 | GPA2 | 0.069 | 1 |  |
| AWRI796_1937 | TFG1 | 0.087 | 1 | 0 | AWRI796_1554 | BNA6 | 0.069 | 1 |  |
| AWRI796_3817 | RNA1 | 0.087 | 1 | 0 | AWRI796_2339 | RSM25 | 0.069 | 1 |  |
| AWRI796_3833 | YMR253C | 0.087 | 1 | 0 | AWRI796_2636 | TDH2 | 0.069 | 1 |  |
| AWRI796_4359 | YOL057W | 0.087 | 1 | 0 | AWRI796_3598 | GLO1 | 0.069 | 1 |  |
| AWRI796_5026 | ATG11 | 0.087 | 1 | 0 | AWRI796_3989 | LAP3 | 0.069 | 1 |  |
| AWRI796_5152 | AWRI796_5152 | 0.087 | 1 | 0 | AWRI796_4459 | NOB1 | 0.069 | 1 |  |
| AWRI796_2474 | ELO1 | 0.086 | 1 | 0 | AWRI796_4473 | SGO1 | 0.069 | 1 |  |
| AWRI796_3419 | SEC61 | 0.086 | 1 | 0 | AWRI796_4530 | RUP1 | 0.069 | 1 |  |
| AWRI796_3544 | ORC1 | 0.086 | 1 | 0 | AWRI796_0279 | PTC4 | 0.068 | 1 |  |
| AWRI796_4682 | PMT3 | 0.086 | 1 | 0 | AWRI796_0671 | YDL109C | 0.068 | 1 |  |
| AWRI796_5004 | SDD4 | 0.086 | 1 | 0 | AWRI796_0968 | MNN10 | 0.068 | 1 |  |
| AWRI796_0357 | NGR1 | 0.085 | 1 | 0 | AWRI796_1120 | ARO80 | 0.068 | 1 |  |
| AWRI796_0791 | YDR042C | 0.085 | - 1 | 0 | AWRI796_1826 | YGR054W | 0.068 | 1 |  |
| AWRI796_0828 | RRP8 | 0.085 | 1 | 0 | AWRI796_2379 | PKP1 | 0.068 | 1 |  |
| AWRI796_1478 | TUB2 | 0.085 | 1 | 0 | AWRI796_2710 | RSM26 | 0.068 | 1 |  |
| AWRI796_3402 | ILV5 | 0.085 | 1 | 0 | AWRI796_3861 | SCS7 | 0.068 | 1 |  |
| AWRI796_3789 | PFK2 | 0.085 | 1 | 0 | AWRI796_4049 | BNI5 | 0.068 | 1 |  |
| AWRI796_4724 | RPS 12 | 0.085 | 1 | 0 | AWRI796_4288 | BSC6 | 0.068 | 1 |  |
| AWRI796_5019 | TIP41 | 0.085 | 1 | 0 | AWRI796_0183 | YBR016W | 0.067 | 1 |  |
| AWRI796_1088 | EFT2 | 0.084 | 1 | 0 | AWRI796_1869 | GTF1 | 0.067 | 1 |  |
| AWRI796_2078 | YHR007C-A | 0.084 | 1 | 0 | AWRI796_1983 | LSC2 | 0.067 | 1 |  |
| AWRI796_2133 | SSF1 | 0.084 | 1 | 0 | AWRI796_2461 | YJL213W | 0.067 | 1 |  |
| AWRI796_2823 | MCR1 | 0.084 | 1 | 0 | AWRI796_3348 | NNT1 | 0.067 | 1 |  |
| AWRI796_3063 | LDB18 | 0.084 | 1 | 0 | AWRI796_4310 | SHR5 | 0.067 | 1 |  |
| AWRI796_0296 | SUP45 | 0.083 | 1 | 0 | AWRI796_0093 | MAP2 | 0.066 | 1 |  |
| AWRI796_2403 | MNT3 | 0.083 | 1 | 0 | AWRI796_0653 | LYS21 | 0.066 | 1 |  |
| AWRI796_2457 | DAK2 | 0.083 | 1 | 0 | AWRI796_0740 | RTK1 | 0.066 | 1 |  |
| AWRI796_4901 | PNG1 | 0.083 | 1 | 0 | AWRI796_1056 | YPS7 | 0.066 | 1 |  |
| AWRI796_0288 | CKS1 | 0.082 | 1 | 0 | AWRI796_2024 | IMA1 | 0.066 | 1 |  |
| AWRI796_0445 | YCL049C | 0.082 | 1 | 0 | AWRI796_2065 | ETP1 | 0.066 | 1 |  |
| AWRI796_0855 | APC4 | 0.082 | 1 | 0 | AWRI796_2566 | SCP160 | 0.066 | 1 |  |
| AWRI796_1599 | NIF3 | 0.082 | 1 | 0 | AWRI796_3226 | CKI1 | 0.066 | 1 |  |
| AWRI796_3376 | BUD6 | 0.082 | 1 | 0 | AWRI796_3265 | TOS4 | 0.066 | 1 |  |
| AWRI796_4780 | NSL1 | 0.082 | 1 | 0 | AWRI796_3825 | ZRC1 | 0.066 | 1 |  |
| AWRI796_4838 | DAP1 | 0.082 | 1 | 0 | AWRI796_4129 | RPL16B | 0.066 | 1 |  |
| AWRI796_0060 | TFC3 | 0.081 | 1 | 0 | AWRI796_4152 | BOP3 | 0.066 | 1 |  |
| AWRI796_0345 | YBR197C | 0.081 | 1 | 0 | AWRI796_2518 | YUR1 | 0.065 | 1 |  |
| AWRI796_1629 | ATG1 | 0.081 | 1 | 0 | AWRI796_2880 | RRP14 | 0.065 | 1 |  |
| AWRI796_2042 | GOS1 | 0.081 | 1 | 0 | AWRI796_2976 | GCN3 | 0.065 | 1 |  |
| AWRI796_2883 | SMY1 | 0.081 | 1 | 0 | AWRI796_3579 | YML6 | 0.065 | 1 |  |
| AWRI796_4002 | SSU72 | 0.081 | 1 | 0 | AWRI796_4156 | GPI15 | 0.065 | 1 |  |
| AWRI796_0051 | DEP1 | 0.08 | 1 | 0 | AWRI796_4814 | OXR1 | 0.065 | 1 |  |
| AWRI796_0808 | LCB2 | 0.08 | 1 | 0 | AWRI796_4898 | ATG21 | 0.065 | 1 |  |
| AWRI796_0885 | GIR2 | 0.08 | 1 | 0 | AWRI796_5060 | NVJ2 | 0.065 | 1 |  |
| AWRI796_2317 | PRM5 | 0.08 | 1 | 0 | AWRI796_0336 | GDT1 | 0.064 | 1 |  |
| AWRI796_2510 | RPA34 | 0.08 | 1 | 0 | AWRI796_2673 | YJR056C | 0.064 | 1 |  |
| AWRI796_2960 | FOX2 | 0.08 | 1 | 0 | AWRI796_3501 | VAN1 | 0.064 | 1 |  |
| AWRI796_3114 AWRI796_3540 | RLP24 POB3 | 0.08 0.08 | 1 1 | 0 | AWRI796_3589 AWRI796_3638 | TRM9 CCS1 | 0.064 0.064 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 0 g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_3692 | MUB1 | 0.064 | 1 | 0 | AWRI796_1591 | SAP4 | 0.05 | 1 | 0 |
| AWRI796_3749 | DNF3 | 0.064 | 1 | 0 | AWRI796_1700 | SEH1 | 0.05 | 1 | 0 |
| AWRI796_3804 | ERG8 | 0.064 | 1 | 0 | AWRI796_2659 | NUP85 | 0.05 | 1 | 0 |
| AWRI796_4765 | ATG41 | 0.064 | 1 | 0 | AWRI796_3045 | SIR1 | 0.05 | 1 | 0 |
| AWRI796_4882 | DBP1 | 0.064 | 1 | 0 | AWRI796_3527 | YML083C | 0.05 | 1 | 0 |
| AWRI796_0193 | ETR1 | 0.063 | 1 | 0 | AWRI796_4091 | DMA2 | 0.05 | 1 | 0 |
| AWRI796_2081 | DIA4 | 0.063 | 1 | 0 | AWRI796_4909 | YPL088W | 0.05 | 1 | 0 |
| AWRI796_2134 | HTD2 | 0.063 | 1 | 0 | AWRI796_0088 | BNA4 | 0.049 | 1 | 0 |
| AWRI796_2629 | MPP10 | 0.063 | 1 | 0 | AWRI796_0412 | PPS1 | 0.049 | 1 | 0 |
| AWRI796_3120 | BRE2 | 0.063 | 1 | 0 | AWRI796_0765 | TRP1 | 0.049 | 1 | 0 |
| AWRI796_3160 | SHM2 | 0.063 | 1 | 0 | AWRI796_4328 | MSH2 | 0.049 | 1 | 0 |
| AWRI796_4913 | BRO1 | 0.063 | 1 |  | AWRI796_4626 | TRE2 | 0.049 | 1 | 0 |
| AWRI796_0307 | CNS1 | 0.062 | 1 | 0 | AWRI796_0270 | CYC8 | 0.048 | 1 | 0 |
| AWRI796_0547 | ABP1 | 0.062 | 1 | 0 | AWRI796_0475 | SGF29 | 0.048 | 1 | 0 |
| AWRI796_0584 | NOP6 | 0.062 | 1 | 0 | AWRI796_1286 | YND1 | 0.048 | 1 | 0 |
| AWRI796_1358 | MRX1 | 0.062 | 1 | 0 | AWRI796_1622 | CDC55 | 0.048 | 1 | 0 |
| AWRI796_2340 | YIL092W | 0.062 | 1 | 0 | AWRI796_3452 | URA4 | 0.048 | 1 | 0 |
| AWRI796_2499 | FMP33 | 0.062 | 1 | 0 | AWRI796_4674 | DGK1 | 0.048 | 1 | 0 |
| AWRI796_2916 | vPS24 | 0.062 | 1 | 0 | AWRI796_4807 | PGC1 | 0.048 | 1 | 0 |
| AWRI796_4183 | HRB1 | 0.062 | 1 | 0 | AWRI796_0008 | ECM1 | 0.047 | 1 | 0 |
| AWRI796_4284 | PPM2 | 0.062 | 1 | 0 | AWRI796_0478 | LDB16 | 0.047 | 1 | 0 |
| AWRI796_4322 | COQ3 | 0.062 | 1 | 0 | AWRI796_0544 | TUP1 | 0.047 | 1 | 0 |
| AWRI796_4585 | NOC2 | 0.062 | 1 | 0 | AWRI796_0658 | YDL124W | 0.047 | 1 | 0 |
| AWRI796_4694 | alal | 0.062 | 1 | 0 | AWRI796_1775 | PMA1 | 0.047 | 1 | 0 |
| AWRI796_0040 | LTE1 | 0.061 | 1 | 0 | AWRI796_1793 | MSB2 | 0.047 | 1 | 0 |
| AWRI796_0473 | BUD3 | 0.061 | 1 | 0 | AWRI796_2412 | INP51 | 0.047 | 1 | 0 |
| AWRI796_0532 | ATG15 | 0.061 | 1 | 0 | AWRI796_2785 | MIA40 | 0.047 | 1 | 0 |
| AWRI796_0925 | REF2 | 0.061 | 1 | 0 | AWRI796_2895 | YET1 | 0.047 | 1 | 0 |
| AWRI796_1084 | YRA1 | 0.061 | 1 | 0 | AWRI796_4828 | TCO89 | 0.047 | 1 | 0 |
| AWRI796_1163 | YDR476C | 0.061 | 1 | 0 | AWRI796_5126 | VPS4 | 0.047 | 1 | 0 |
| AWRI796_2579 | MRPL8 | 0.061 | 1 | 0 | AWRI796_0409 | UBX7 | 0.046 | 1 | 0 |
| AWRI796_3147 | PDC1 | 0.061 | 1 | 0 | AWRI796_0497 | YCR023C | 0.046 | 1 | 0 |
| AWRI796_4009 | IES2 | 0.061 | 1 | 0 | AWRI796_0588 | CWC2 | 0.046 | 1 | 0 |
| AWRI796_4270_71 | AWRI796_4270_71 | 0.061 | 1 | 0 | AWRI796_1004 | NSE3 | 0.046 | 1 | 0 |
| AWRI796_4736 | FIT2 | 0.061 | 1 | 0 | AWRI796_1085 | RPP2B | 0.046 | 1 | 0 |
| AWRI796_4897 | ELP4 | 0.061 | 1 | 0 | AWRI796_1431 | YER156C | 0.046 | 1 | 0 |
| AWRI796_0394 | MTC4 | 0.06 | 1 | 0 | AWRI796_1965 | CRM1 | 0.046 | 1 | 0 |
| AWRI796_0611 | YDL180W | 0.06 | 1 | 0 | AWRI796_2176 | APE4 | 0.046 | 1 | 0 |
| AWRI796_1425 | SPI1 | 0.06 | 1 |  | AWRI796_2178 | DMA1 | 0.046 | 1 | 0 |
| AWRI796_1672 | SNT2 | 0.06 | 1 | 0 | AWRI796_2648 | BNA1 | 0.046 | 1 | 0 |
| AWRI796_2092 | MYO1 | 0.06 | 1 | 0 | AWRI796_3373 | CDC3 | 0.046 | 1 | 0 |
| AWRI796_2131 | SSZ1 | 0.06 | 1 | 0 | AWRI796_4220 | DBP6 | 0.046 | 1 | 0 |
| AWRI796_2165 | GEP4 | 0.06 | 1 | 0 | AWRI796_4571 | MSB1 | 0.046 | 1 | 0 |
| AWRI796_3389 | RPP0 | 0.06 | 1 | 0 | AWRI796_4864 | MKK2 | 0.046 | 1 | 0 |
| AWRI796_3488 | ERO1 | 0.06 | 1 | 0 | AWRI796_1392 | BOI2 | 0.045 | 1 | 0 |
| AWRI796_4282 | RIB4 | 0.06 | 1 | 0 | AWRI796_1454 | ISC10 | 0.045 | 1 | 0 |
| AWRI796_4994 | SUT2 | 0.06 | 1 | 0 | AWRI796_1847 | YGR079W | 0.045 | 1 | 0 |
| AWRI796_0090 | MRX3 | 0.059 | 1 | 0 | AWRI796_2415 | MPH1 | 0.045 | 1 | 0 |
| AWRI796_0938 | GCD6 | 0.059 | 1 | 0 | AWRI796_2611 | vPS53 | 0.045 | 1 | 0 |
| AWRI796_1975 | PH081 | 0.059 | 1 | 0 | AWRI796_3510 | URA5 | 0.045 | 1 | 0 |
| AWRI796_3404 | RSC2 | 0.059 | 1 | 0 | AWRI796_4205 | YNR021W | 0.045 | 1 | 0 |
| AWRI796_4547 | PUP1 | 0.059 | 1 | 0 | AWRI796_0877 | SAN1 | 0.044 | 1 | 0 |
| AWRI796_0383 | ALG7 | 0.058 | 1 | 0 | AWRI796_1493 | GAT1 | 0.044 | 1 | 0 |
| AWRI796_1572 | RTG2 | 0.058 | 1 | 0 | AWRI796_2038 | VMR1 | 0.044 | 1 | 0 |
| AWRI796_2151 | IPI1 | 0.058 | 1 | 0 | AWRI796_2207 | MRPL6 | 0.044 | 1 | 0 |
| AWRI796_3344 | YSH1 | 0.058 | 1 | 0 | AWRI796_2843 | YPK1 | 0.044 | 1 | 0 |
| AWRI796_3944 | RFC3 | 0.058 | 1 | 0 | AWRI796_3136 | RAD5 | 0.044 | 1 | 0 |
| AWRI796_3956 | MET2 | 0.058 | 1 | 0 | AWRI796_3797 | CEF1 | 0.044 | 1 | 0 |
| AWRI796_4749 | PLC1 | 0.058 | 1 | 0 | AWRI796_4121 | NIS1 | 0.044 | 1 | 0 |
| AWRI796_0260 | EXO84 | 0.057 | 1 | 0 | AWRI796_4734 | RDR1 | 0.044 | 1 | 0 |
| AWRI796_0382 | YBR242W | 0.057 | 1 | 0 | AWRI796_4855 | PRP46 | 0.044 | 1 | 0 |
| AWRI796_2171 | CDC12 | 0.057 | 1 | 0 | AWRI796_0373 | PBP2 | 0.043 | 1 | 0 |
| AWRI796_2702 | BUD4 | 0.057 | 1 | 0 | AWRI796_0665 | IWR1 | 0.043 | 1 | 0 |
| AWRI796_2754 | DAN4 | 0.057 | 1 | 0 | AWRI796_1075 | VPS74 | 0.043 | 1 | 0 |
| AWRI796_1066 | TFC6 | 0.056 | 1 | 0 | AWRI796_3818 | TAF9 | 0.043 | 1 | 0 |
| AWRI796_1620 | HOS2 | 0.056 | 1 | 0 | AWRI796_4305 | PAP2 | 0.043 | 1 | 0 |
| AWRI796_2811 | TPK3 | 0.056 | 1 | 0 | AWRI796_1175 | PAC11 | 0.042 | 1 | 0 |
| AWRI796_3091 | DPS1 | 0.056 | 1 | 0 | AWRI796_1875 | CLD1 | 0.042 | 1 | 0 |
| AWRI796_3121 | PML1 | 0.056 | 1 | 0 | AWRI796_2319 | NUP159 | 0.042 | 1 | 0 |
| AWRI796_3199 | ERG27 | 0.056 | 1 | 0 | AWRI796_2537 | MDV1 | 0.042 | 1 | 0 |
| AWRI796_3798 | SCJ1 | 0.056 | 1 | 0 | AWRI796_3077 | GPI13 | 0.042 | 1 | 0 |
| AWRI796_5168 | AWRI796_5168 | 0.056 | 1 | 0 | AWRI796_3214 | YLR118C | 0.042 | 1 | 0 |
| AWRI796_0292 | YBR139W | 0.055 | 1 | 0 | AWRI796_3283 | HMX1 | 0.042 | 1 | 0 |
| AWRI796_0936 | MSS4 | 0.055 | , | 0 | AWRI796_3319 | IRC20 | 0.042 | 1 | 0 |
| AWRI796_1319 | HVG1 | 0.055 | 1 | 0 | AWRI796_3678 | SEG1 | 0.042 | 1 | 0 |
| AWRI796_3822 | CUS1 | 0.055 | , | 0 | AWRI796_3911 | RPD3 | 0.042 | 1 | 0 |
| AWRI796_3865 | DSK2 | 0.055 | 1 | 0 | AWRI796_4140 | POR1 | 0.042 | 1 | 0 |
| AWRI796_4865 | UME1 | 0.055 | 1 | 0 | AWRI796_5024 | MSF1 | 0.042 | 1 | 0 |
| AWRI796_0162 | HIR1 | 0.054 | 1 | 0 | AWRI796_0343 | MSII | 0.041 | 1 | 0 |
| AWRI796_0881 | EKII | 0.054 | 1 | 0 | AWRI796_2022 | ZUO1 | 0.041 | 1 | 0 |
| AWRI796_0991 | CCC2 | 0.054 | 1 | 0 | AWRI796_4397 | CMK2 | 0.041 | 1 | 0 |
| AWRI796_1305 | YAT2 | 0.054 | 1 | 0 | AWRI796_0036 | FRT2 | 0.04 | 1 | 0 |
| AWRI796_1745 | RNA15 | 0.054 | 1 | 0 | AWRI796_0326 | ECM31 | 0.04 | 1 | 0 |
| AWRI796_4545 | ISN1 | 0.054 | 1 | 0 | AWRI796_0372 | SWC5 | 0.04 | 1 | 0 |
| AWRI796_0457 | LSB5 | 0.053 | 1 | 0 | AWRI796_0613 | DLD2 | 0.04 | 1 | 0 |
| AWRI796_1008 | SSD1 | 0.053 | 1 | 0 | AWRI796_1459 | AWRI796_1459 | 0.04 | 1 | 0 |
| AWRI796_1105 | RPB7 | 0.053 | 1 | 0 | AWRI796_1799 | YGR021W | 0.04 | 1 | 0 |
| AWRI796_2897 | YKL063C | 0.053 | , | 0 | AWRI796_2257 | RPN10 | 0.04 | 1 | 0 |
| AWRI796_4264 | ENB1 | 0.053 | 1 | 0 | AWRI796_2290 | ATG32 | 0.04 | 1 | 0 |
| AWRI796_0161 | ALK2 | 0.052 | 1 | 0 | AWRI796_3867 | PRM15 | 0.04 | 1 | 0 |
| AWRI796_0209 | TCM62 | 0.052 | , | 0 | AWRI796_4244 | YNR063W | 0.04 | 1 | 0 |
| AWRI796_0954 | IVY1 | 0.052 | 1 | 0 | AWRI796_5020 | TIF5 | 0.04 | 1 | 0 |
| AWRI796_1616 | EMP24 | 0.052 | 1 | 0 | AWRI796_5161 | AWRI796_5161 | 0.04 | 1 | 0 |
| AWRI796_1919 | MRPS 35 | 0.052 | 1 | 0 | AWRI796_1092 | SAC7 | 0.039 | 1 | 0 |
| AWRI796_3004 | GLG1 | 0.052 | 1 | 0 | AWRI796_2633 | POL31 | 0.039 | 1 | 0 |
| AWRI796_3971 | DSL1 | 0.052 | 1 | 0 | AWRI796_0657 | CDC48 | 0.038 | 1 | 0 |
| AWRI796_0113 | SEF1 | 0.051 | 1 | 0 | AWRI796_0891 | SSY1 | 0.038 | 1 | 0 |
| AWRI796_0957 | RTN1 | 0.051 | 1 | 0 | AWRI796_1314 | ZRG8 | 0.038 | 1 | 0 |
| AWRI796_1255 | SPF1 | 0.051 | 1 | 0 | AWRI796_2082 | VPS29 | 0.038 | 1 | 0 |
| AWRI796_1866 | TEL2 | 0.051 | 1 | 0 | AWRI796_2361 | RNR3 | 0.038 | 1 | 0 |
| AWRI796_2316 | RHO3 | 0.051 | 1 | 0 | AWRI796_3040 | ESL2 | 0.038 | 1 | 0 |
| AWRI796_2516 | YAK1 | 0.051 | , | 0 | AWRI796_5056 | ASA1 | 0.038 | 1 | 0 |
| AWRI796_2825 | SDH1 | 0.051 | 1 | 0 | AWRI796_1905 | NAT2 | 0.037 | 1 | 0 |
| AWRI796_3006 | UTP30 | 0.051 | 1 | 0 | AWRI796_2141 | PPE1 | 0.037 | 1 | 0 |
| AWRI796-4034 | UBP10 | 0.051 | - 1 | 0 | AWRI796-3959 | TOF1 | 0.037 | 1 | 0 |
| AWRI796_0982 AWRI796_1366 | $\underset{\text { LLV1 }}{\text { SWM1 }}$ | 0.05 0.05 | 1 1 | 0 | AWRI796_4412 AWRI796_4764 | PHO80 YAH1 | 0.037 0.037 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_2098 | YHI9 | 0.036 | 1 | 0 | AWRI796_3479 | LEU3 | 0.022 | 1 |  |
| AWRI796_2288 | MLP2 | 0.036 | 1 | 0 | AWRI796_3626 | MRPL3 | 0.022 | 1 |  |
| AWRI796_2740 | MET5 | 0.036 | 1 | 0 | AWRI796_5066 | RPL11A | 0.022 | 1 |  |
| AWRI796_2833 | CTK1 | 0.036 | 1 | 0 | AWRI796_1449 | TMT1 | 0.021 | 1 |  |
| AWRI796_3591 | ERV25 | 0.036 | 1 | 0 | AWRI796_3129 | UBR2 | 0.021 | 1 |  |
| AWRI796_3616 | BUD22 | 0.036 | 1 | 0 | AWRI796_3500 | ATR1 | 0.021 | 1 |  |
| AWRI796_3927 | ZIM17 | 0.036 | 1 | 0 | AWRI796_4207 | SNF12 | 0.021 | 1 |  |
| AWRI796_4570 | TUF1 | 0.036 | 1 | 0 | AWRI796_4498 | RAS1 | 0.021 | 1 |  |
| AWRI796_2048 | YHL026C | 0.035 | 1 | 0 | AWRI796_4827 | CTI6 | 0.021 | 1 |  |
| AWRI796_4227 | TRM112 | 0.035 | 1 | 0 | AWRI796_4854 | RRD2 | 0.021 | 1 |  |
| AWRI796_0132 | ERD2 | 0.034 | 1 | 0 | AWRI796_2324 | HPM1 | 0.02 | 1 |  |
| AWRI796_0269 | YSA1 | 0.034 | 1 | 0 | AWRI796_2713 | SOD1 | 0.02 | 1 |  |
| AWRI796_2149 | SAM35 | 0.034 | 1 | 0 | AWRI796_3051 | AYT1 | 0.02 | 1 |  |
| AWRI796_2174 | ERP5 | 0.034 | 1 | 0 | AWRI796_3115 | TEN1 | 0.02 | 1 |  |
| AWRI796_2427 | YIR014W | 0.034 | 1 | 0 | AWRI796_3511 | SEC65 | 0.02 | 1 |  |
| AWRI796_2532 | ALB1 | 0.034 | 1 | 0 | AWRI796_3551 | SML1 | 0.02 | 1 |  |
| AWRI796_3017 | DRE2 | 0.034 | 1 | 0 | AWRI796_3934 | RPS 19B | 0.02 | 1 |  |
| AWRI796_3029 | HBS1 | 0.034 | 1 | 0 | AWRI796_4047 | FMP41 | 0.02 | 1 |  |
| AWRI796_3353 | COQ11 | 0.034 | 1 | 0 | AWRI796_4058 | NSG2 | 0.02 | 1 |  |
| AWRI796_4918 | GPI2 | 0.034 | 1 | 0 | AWRI796_4507 | CEX1 | 0.02 | 1 |  |
| AWRI796_0444 | APA1 | 0.033 | 1 | 0 | AWRI796_4936 | LGE1 | 0.02 | 1 |  |
| AWRI796_0651 | SRF1 | 0.033 | 1 | 0 | AWRI796_1079 | ARH1 | 0.019 | 1 |  |
| AWRI796_1709 | NBP35 | 0.033 | 1 | 0 | AWRI796_3241 | YLR149C | 0.019 | 1 |  |
| AWRI796_2328 | MOB1 | 0.033 | 1 | 0 | AWRI796_3561 | GSF2 | 0.019 | 1 |  |
| AWRI796_3062 | FRE6 | 0.033 | 1 | 0 | AWRI796_4372 | NTG2 | 0.019 | 1 |  |
| AWRI796_3286 | SEC13 | 0.033 | 1 | 0 | AWRI796_4907 | RPS6B | 0.019 | 1 |  |
| AWRI796_3333 | RED1 | 0.033 | 1 | 0 | AWRI796_5081 | YPR117W | 0.019 | 1 |  |
| AWRI796_3787 | TOM40 | 0.033 | 1 | 0 | AWRI796_0798 | TPI1 | 0.018 | 1 |  |
| AWRI796_0971 | YDR248C | 0.032 | 1 | 0 | AWRI796_0856 | VBA4 | 0.018 | 1 |  |
| AWRI796_1199 | EUG1 | 0.032 | 1 | 0 | AWRI796_1473 | LAM5 | 0.018 | 1 |  |
| AWRI796_1262 | YEL023C | 0.032 | 1 | 0 | AWRI796_2478 | RPS22A | 0.018 | 1 |  |
| AWRI796_1828 | RSC1 | 0.032 | 1 | 0 | AWRI796_2696 | YJR084W | 0.018 | 1 |  |
| AWRI796_3189 | XDJ1 | 0.032 | 1 | 0 | AWRI796_0463 | RNQ1 | 0.017 | 1 |  |
| AWRI796_3200 | APC9 | 0.032 | 1 | 0 | AWRI796_2970 | VPS51 | 0.017 | 1 |  |
| AWRI796_3530 | DUS1 | 0.032 | 1 | 0 | AWRI796_3104 | RTT109 | 0.017 | 1 |  |
| AWRI796_3889 | ADH2 | 0.032 | 1 | 0 | AWRI796_3897 | GLC8 | 0.017 | 1 |  |
| AWRI796_4092 | YNL115C | 0.032 | 1 | 0 | AWRI796_4920 | YTA6 | 0.017 | 1 |  |
| AWRI796_4435 | HST3 | 0.032 | 1 | 0 | AWRI796_0402 | TSC10 | 0.016 | 1 |  |
| AWRI796_4005 | ALG9 | 0.031 | 1 | 0 | AWRI796_0569 | PTP1 | 0.016 | 1 |  |
| AWRI796_4751 | DIM1 | 0.031 | 1 | 0 | AWRI796_0852 | MRX14 | 0.016 | 1 |  |
| AWRI796_4885 | HOS3 | 0.031 | 1 | 0 | AWRI796_1439 | PAB1 | 0.016 | 1 |  |
| AWRI796_0255 | PBY1 | 0.03 | 1 | 0 | AWRI796_1645 | YIP5 | 0.016 | 1 |  |
| AWRI796_0294 | BMT2 | 0.03 | 1 | 0 | AWRI796_2150 | STE12 | 0.016 | 1 |  |
| AWRI796_0377 | PRP5 | 0.03 | 1 | 0 | AWRI796_3665 | TVP18 | 0.016 | 1 |  |
| AWRI796_0844 | TMS1 | 0.03 | 1 | 0 | AWRI796_5170 | AWRI796_5170 | 0.016 | 1 |  |
| AWRI796_2494 | ERG20 | 0.03 | 1 | 0 | AWRI796_0545 | CSM1 | 0.015 | 1 |  |
| AWRI796_2554 | TOK1 | 0.03 | 1 | 0 | AWRI796_1257 | BUD16 | 0.015 | 1 |  |
| AWRI796_4514 | RIO1 | 0.03 | 1 | 0 | AWRI796_1264 | URA3 | 0.015 | 1 |  |
| AWRI796_4870 | RDS2 | 0.03 | 1 | 0 | AWRI796_2130 | PaN5 | 0.015 | 1 |  |
| AWRI796_0127 | PSY4 | 0.029 | 1 | 0 | AWRI796_2581 | NUP82 | 0.015 | 1 |  |
| AWRI796_0935 | UME6 | 0.029 | - 1 | 0 | AWRI796_2726 | ATP2 | 0.015 | 1 |  |
| AWRI796_2882 | VMA5 | 0.029 | 1 | 0 | AWRI796_3318 | ERF2 | 0.015 |  |  |
| AWRI796_2930 | URA6 | 0.029 | 1 | 0 | AWRI796_0716 | MBP1 | 0.014 | 1 |  |
| AWRI796_4151 | YIP3 | 0.029 | 1 | 0 | AWRI796_1436 | RAD4 | 0.014 | 1 |  |
| AWRI796_4260 | YIR042C | 0.029 | 1 | 0 | AWRI796_1888 | YGR126W | 0.014 | 1 |  |
| AWRI796_4668 | ISW2 | 0.029 | 1 | 0 | AWRI796_2239 | YHR182W | 0.014 | 1 |  |
| AWRI796_4925 | YPL068C | 0.029 | 1 | 0 | AWRI796_2247 | ERG9 | 0.014 | 1 |  |
| AWRI796_1395 | RPL23B | 0.028 | 1 | 0 | AWRI796_2838 | RMA1 | 0.014 | 1 |  |
| AWRI796_1669 | RPL1B | 0.028 | 1 | 0 | AWRI796_3810 | TAF7 | 0.014 | 1 |  |
| AWRI796_1864 | ASK10 | 0.028 | 1 | 0 | AWRI796_4122 | APJ1 | 0.014 | 1 |  |
| AWRI796_2212 | SPO12 | 0.028 | 1 | 0 | AWRI796_4182 | MRP7 | 0.014 | 1 |  |
| AWRI796_2344 | AVT7 | 0.028 | 1 | 0 | AWRI796_5103 | YPR147C | 0.014 | 1 |  |
| AWRI796_3487 | YML131W | 0.028 | 1 | 0 | AWRI796_0953 | PCF11 | 0.013 | 1 |  |
| AWRI796_0615 | YDL176W | 0.027 | 1 | 0 | AWRI796_1588 | SEC15 | 0.013 | 1 |  |
| AWRI796_1812 | YGR035C | 0.027 | 1 | 0 | AWRI796_1961 | RTA1 | 0.013 | 1 |  |
| AWRI796_2627 | OST1 | 0.027 | 1 | 0 | AWRI796_2301 | FLX1 | 0.013 | 1 |  |
| AWRI796_4330 | MPD2 | 0.027 | 1 | 0 | AWRI796_3827 | COA6 | 0.013 | 1 |  |
| AWRI796_4408 | RPB11 | 0.027 | 1 | 0 | AWRI796_4414 | ALG6 | 0.013 | 1 |  |
| AWRI796_4549 | MTR10 | 0.027 | 1 | 0 | AWRI796_0581 | RRI1 | 0.012 | 1 |  |
| AWRI796_0089 | BRN1 | 0.026 | 1 | 0 | AWRI796_1006 | HRQ1 | 0.012 | 1 |  |
| AWRI796_0453 | ${ }_{\text {ATG22 }}$ | 0.026 | - 1 | 0 | AWRI796-1237 | MAK10 | 0.012 | 1 |  |
| AWRI796_1091 | RVS167 | 0.026 | 1 | 0 | AWRI796_2047 | AWRI796_2047 | 0.012 | 1 |  |
| AWRI796_1596 | SDT1 | 0.026 | 1 | 0 | AWRI796_2707 | YJR098C | 0.012 | 1 |  |
| AWRI796_2318 | His5 | 0.026 | 1 | 0 | AWRI796_3127 | SDO1 | 0.012 | 1 |  |
| AWRI796_2514 | YJL144W | 0.026 | 1 | 0 | AWRI796_3654 | SEN15 | 0.012 | 1 |  |
| AWRI796_3398 | NIT3 | 0.026 | 1 | 0 | AWRI796_3931 | MRPS18 | 0.012 | 1 |  |
| AWRI796_3849 | TRM732 | 0.026 | 1 | 0 | AWRI796_5099 | TAZ1 | 0.012 | 1 |  |
| AWRI796_3949 | MRPL10 | 0.026 | 1 | 0 | AWRI796_0301 | ARA1 | 0.011 | 1 |  |
| AWRI796_4241 | FRE4 | 0.026 | 1 | 0 | AWRI796_0320 | SSE2 | 0.011 | 1 |  |
| AWRI796_5046 | LTP1 | 0.026 | 1 | 0 | AWRI796_0401 | YPT10 | 0.011 | 1 |  |
| AWRI796_5123 | JIP5 | 0.026 | 1 | 0 | AWRI796_0738 | MPS1 | 0.011 | 1 |  |
| AWRI796_0097 | RPL23A | 0.025 | 1 | 0 | AWRI796_0760 | YRB1 | 0.011 | 1 |  |
| AWRI796_1532 | ROG3 | 0.025 | 1 | 0 | AWRI796_1326 | SPO73 | 0.011 | 1 |  |
| AWRI796_1583 | CSE1 | 0.025 | 1 | 0 | AWRI796_2399 | FAF1 | 0.011 | 1 |  |
| AWRI796_2585 | IKS1 | 0.025 | 1 | 0 | AWRI796_2508 | SNA3 | 0.011 | 1 |  |
| AWRI796_3225 | USB1 | 0.025 | 1 | 0 | AWRI796_3335 | PDR8 | 0.011 | 1 |  |
| AWRI796_4669 | RRG7 | 0.025 | 1 | 0 | AWRI796_3658 | AEP1 | 0.011 | 1 |  |
| AWRI796_1102 | URH1 | 0.024 | 1 | 0 | AWRI796_3955 | CAF120 | 0.011 | 1 |  |
| AWRI796_1348 | RRT13 | 0.024 | 1 | 0 | AWRI796_4421 | TIR4 | 0.011 | 1 |  |
| AWRI796_1548 | SAP155 | 0.024 | 1 | 0 | AWRI796_4458 | vHS3 | 0.011 | 1 |  |
| AWRI796_1796 | YGR017W | 0.024 | 1 | 0 | AWRI796_4497 | CRC1 | 0.011 | 1 |  |
| AWRI796_1999 | APL6 | 0.024 | 1 | 0 | AWRI796_4589 | MGM1 | 0.011 | 1 |  |
| AWRI796_3271 | PEX13 | 0.024 | 1 | 0 | AWRI796_0164 | LDB7 | 0.01 | 1 |  |
| AWRI796_4470 | VPS5 | 0.024 | 1 | 0 | AWRI796_0758 | RMD1 | 0.01 | 1 |  |
| AWRI796_4630 | GCD1 | 0.024 | 1 | 0 | AWRI796_0834 | RLI1 | 0.01 | 1 |  |
| AWRI796_0735 | DBP10 | 0.023 | 1 | 0 | AWRI796_1876 | YGR111W | 0.01 | 1 |  |
| AWRI796_1268 | GTT3 | 0.023 | 1 | 0 | AWRI796_2731 | VPS70 | 0.01 | 1 |  |
| AWRI796_1963 | GPI1 | 0.023 | 1 | 0 | AWRI796_2943 | CCE1 | 0.01 | 1 |  |
| AWRI796_2076 | STP2 | 0.023 | 1 | 0 | AWRI796_3032 | OMA1 | 0.01 | 1 |  |
| AWRI796-4993 | HAA1 | 0.023 | 1 | 0 | AWRI796_4247 | YNR066C | 0.01 | 1 |  |
| AWRI796_5034 | ARO7 | 0.023 | 1 | 0 | AWRI796_4654 | YOR289W | 0.01 | 1 |  |
| AWRI796_0117 | YEL1 | 0.022 | 1 | 0 | AWRI796_5006 | YME1 | 0.01 | 1 |  |
| AWRI796_0175 | DSF2 | 0.022 | 1 | 0 | AWRI796_0888 | RPA14 | 0.009 | 1 |  |
| AWRI796_1146 | GUK1 | 0.022 | 1 | 0 | AWRI796_3249 | PUS5 | 0.009 | 1 |  |
| AWRI796_1726 | NPY1 | 0.022 | 1 | 0 | AWRI796_3635 | IMP2 | 0.009 | 1 |  |
| AWRI796_2778 AWRI796_2991 | $\stackrel{\text { LOS1 }}{\text { SHB17 }}$ | 0.022 0.022 | 1 1 | 0 | AWRI796_4221 AWRI796_4299 | ${ }_{\text {LRP1 }}^{\text {ZRG17 }}$ | 0.009 0.009 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_4492 | CMR2 | 0.009 | , | 0 | AWRI796_5150 | HSP33 | -0.005 | 1 |  |
| AWRI796_4714 | SNX3 | 0.009 | 1 | 0 | AWRI796_1082 | RGA2 | -0.006 | 1 |  |
| AWRI796_0317 | TYR1 | 0.008 | 1 | 0 | AWRI796_1535 | HIS2 | -0.006 | 1 |  |
| AWRI796_1037 | YCG1 | 0.008 | 1 | 0 | AWRI796_1593 | VID30 | -0.006 | 1 |  |
| AWRI796_1367 | AIM10 | 0.008 | 1 | 0 | AWRI796_1753 | MIG1 | -0.006 | 1 |  |
| AWRI796_1697 | vPS73 | 0.008 | 1 | 0 | AWRI796_1924 | MSM1 | -0.006 | 1 |  |
| AWRI796_1723 | HSF1 | 0.008 | 1 | 0 | AWRI796_2142 | PTC7 | -0.006 | 1 |  |
| AWRI796_1818 | NQM1 | 0.008 | 1 | 0 | AWRI796_2169 | YPT35 | -0.006 | 1 |  |
| AWRI796_2678 | NTA1 | 0.008 | 1 | 0 | AWRI796_2236 | STB5 | -0.006 | 1 |  |
| AWRI796_2783 | PEX1 | 0.008 | 1 | 0 | AWRI796_3853 | SAP30 | -0.006 | 1 |  |
| AWRI796_2928 | GPX1 | 0.008 | 1 | 0 | AWRI796_4623 | NAT5 | -0.006 | 1 |  |
| AWRI796_3907 | AWRI796_3907 | 0.008 | 1 | 0 | AWRI796_0253 | PHO3 | -0.007 | 1 |  |
| AWRI796_4304 | MSN1 | 0.008 | 1 | 0 | AWRI796_0277 | MRPL36 | -0.007 | 1 |  |
| AWRI796_0589 | NHP2 | 0.007 | 1 | 0 | AWRI796_0325 | SWD3 | -0.007 | 1 |  |
| AWRI796_2183 | MSH1 | 0.007 | 1 | 0 | AWRI796_0446 | SPS22 | -0.007 | 1 |  |
| AWRI796_3278 | PBA1 | 0.007 | 1 | 0 | AWRI796_1452 | PDA1 | -0.007 | 1 |  |
| AWRI796_3724 | ERG29 | 0.007 | 1 | 0 | AWRI796_3346 | YLR283W | -0.007 | 1 |  |
| AWRI796_3828 | FAA4 | 0.007 | 1 | 0 | AWRI796_0224 | ORC2 | -0.008 | 1 |  |
| AWRI796_4621 | TUM1 | 0.007 | 1 | 0 | AWRI796_0416 | DUG2 | -0.008 | 1 |  |
| AWRI796_4710 | SOG2 | 0.007 | 1 | 0 | AWRI796_0858 | DPB4 | -0.008 | 1 |  |
| AWRI796_1307 | CHO1 | 0.006 | 1 | 0 | AWRI796_0932 | COQ4 | -0.008 | 1 |  |
| AWRI796_2762 | MCH2 | 0.006 | 1 | 0 | AWRI796_2216 | Lin1 | -0.008 | 1 |  |
| AWRI796_3581 | APT1 | 0.006 | 1 | 0 | AWRI796_2671 | KCH1 | -0.008 | 1 |  |
| AWRI796_4233 | POP2 | 0.006 | 1 | 0 | AWRI796_2852 | APN1 | -0.008 | 1 |  |
| AWRI796_5025 | TAH18 | 0.006 | 1 | 0 | AWRI796_3675 | ISF1 | -0.008 | 1 |  |
| AWRI796_0826 | PDC2 | 0.005 | 1 | 0 | AWRI796_4661 | YOR296W | -0.008 | 1 |  |
| AWRI796_0966 | PRP28 | 0.005 | 1 | 0 | AWRI796_5071 | YTH1 | -0.008 | 1 |  |
| AWRI796_1061 | TRP4 | 0.005 | 1 | 0 | AWRI796_0603 | ARF1 | -0.009 | 1 |  |
| AWRI796_2807 | EBP2 | 0.005 | 1 | 0 | AWRI796_0792 | NRG1 | -0.009 | 1 |  |
| AWRI796_3208 | CCW12 | 0.005 | 1 | 0 | AWRI796_2351 | YIL077C | -0.009 | 1 |  |
| AWRI796_3220 | APC2 | 0.005 | 1 | 0 | AWRI796_2777 | ADD66 | -0.009 | 1 |  |
| AWRI796_4387 | MIM1 | 0.005 | 1 | 0 | AWRI796_3253 | APS1 | -0.009 | 1 |  |
| AWRI796_0687 | SRP14 | 0.004 | 1 | 0 | AWRI796_4891 | YPL109C | -0.009 | 1 |  |
| AWRI796_1033 | ASP1 | 0.004 | 1 | 0 | AWRI796_0259 | FES1 | -0.01 | 1 |  |
| AWRI796_1208 | CAB1 | 0.004 | 1 | 0 | AWRI796_0948 | CRF1 | -0.01 | 1 |  |
| AWRI796_1386 | GLE2 | 0.004 | 1 | 0 | AWRI796_2057 | YHL018W | -0.01 | 1 |  |
| AWRI796_1418 | DDI1 | 0.004 | 1 | 0 | AWRI799 - 3210 | AVL9 | -0.01 | 1 |  |
| AWRI796_1632 | YGL176C | 0.004 | 1 | 0 | AWRI796_4015 | YNL208W | -0.01 | 1 |  |
| AWRI796_2718 | YMR1 | 0.004 | 1 | 0 | AWRI796_4102 | AVT4 | -0.01 | 1 |  |
| AWRI796_2996 | FMP46 | 0.004 | 1 | 0 | AWRI796_0376 | ABD1 | -0.011 | 1 |  |
| AWRI796_3236 | ACF2 | 0.004 | 1 | 0 | AWRI796_0528 | BUD31 | -0.011 | 1 |  |
| AWRI796_3917 | LEM3 | 0.004 | 1 | 0 | AWRI796_0642 | CCT4 | -0.011 | 1 |  |
| AWRI796_4467 | CYT1 | 0.004 | 1 | 0 | AWRI796_0727 | PRP11 | -0.011 | 1 |  |
| AWRI796_5172 | PAU6 | 0.004 | 1 | 0 | AWRI796_1316 | ARB1 | -0.011 | 1 |  |
| AWRI796_1737 | SDS23 | 0.003 | 1 | 0 | AWRI796_1486 | CAF16 | -0.011 | 1 |  |
| AWRI796_1767 | KAP122 | 0.003 | 1 | 0 | AWRI796_2125 | MED6 | -0.011 | 1 |  |
| AWRI796_2725 | JHD2 | 0.003 | 1 | 0 | AWRI796_3427 | REH1 | -0.011 | 1 |  |
| AWRI796_4348 | HST1 | 0.003 | 1 | 0 | AWRI796_4817 | RSA1 | -0.011 | 1 |  |
| AWRI796_0364 | PDB1 | 0.002 | 1 | 0 | AWRI796_5068 | FHL1 | -0.011 | 1 |  |
| AWRI796_1263 | GEA2 | 0.002 | 1 | 0 | AWRI796_0606 | PPH22 | -0.012 | 1 |  |
| AWRI796_1959 | ZPR1 | 0.002 | - 1 | 0 | AWRI796_1226 | SIT1 | -0.012 | 1 |  |
| AWRI796_4366 | GSH2 | 0.002 | 1 | 0 | AWRI796_3428 | STE23 | -0.012 | 1 |  |
| AWRI796_1280 | WBP1 | 0.001 | 1 | 0 | AWRI796_3505 | BUL2 | -0.012 | 1 |  |
| AWRI796_3294 | CPR6 | 0.001 | 1 | 0 | AWRI796_3668 | SDD2 | -0.012 | 1 |  |
| AWRI796_3507 | ZDS2 | 0.001 | 1 | 0 | AWRI796_5216 | COS3 | -0.012 | 1 |  |
| AWRI796_4647 | FSH3 | 0.001 | 1 | 0 | AWRI796_1060 | TRR1 | -0.013 | 1 |  |
| AWRI796_4978 | CHL1 | 0.001 | 1 | 0 | AWRI796_1152 | MRPL28 | -0.013 | 1 |  |
| AWRI796_0810 | RPS13 | 0 | 1 | 0 | AWRI796_1853 | RPL11B | -0.013 | 1 |  |
| AWRI796_1534 | LSB3 | 0 | 1 | 0 | AWRI796_1962 | RSM27 | -0.013 | 1 |  |
| AWRI796_3304 | ECM22 | 0 | 1 | 0 | AWRI796_3168 | FYV7 | -0.013 | 1 |  |
| AWRI796_4762 | HFI1 | 0 | 1 | 0 | AWRI796_3407 | STE11 | -0.013 | 1 |  |
| AWRI796_0196 | RKM3 | -0.001 | 1 | 0 | AWRI796_4390 | TSR4 | -0.013 | 1 |  |
| AWRI796_0312 | CDC28 | -0.001 | 1 | 0 | AWRI796_4394 | YOL019W | -0.013 | 1 |  |
| AWRI796_0541 | SRB8 | -0.001 | 1 | 0 | AWRI796_1615 | MCM6 | -0.014 | 1 |  |
| AWRI796_0710 | UBC9 | -0.001 | 1 | 0 | AWRI796_2513 | SFH5 | -0.014 | 1 |  |
| AWRI796_1343 | CEM1 | -0.001 | 1 | 0 | AWRI796_2719 | YJR111C | -0.014 | 1 |  |
| AWRI796_2506 | VPS35 | -0.001 | 1 | 0 | AWRI796_4146 | SFB2 | -0.014 | 1 |  |
| AWRI796_2529 | GCD14 | -0.001 | 1 | 0 | AWRI796_4466 | YNG1 | -0.014 | 1 |  |
| AWRI796_2720 | NNF1 | -0.001 | 1 | 0 | AWRI796_0208 | QDR3 | -0.015 | 1 |  |
| AWRI796_2876 | CAB3 | -0.001 | 1 | 0 | AWRI796_0422 | YBR287W | -0.015 | 1 |  |
| AWRI796-4789 | MMT2 | -0.001 | - 1 | 0 | AWRI796_0724 | SIT4 | -0.015 | 1 |  |
| AWRI796_0751 | APC11 | -0.002 | 1 | 0 | AWRI796_1387 | FLO8 | -0.015 | 1 |  |
| AWRI796_2722 | TDA4 | -0.002 | 1 | 0 | AWRI796_1941 | TDH3 | -0.015 | 1 |  |
| AWRI796_3044 | SKG1 | -0.002 | 1 | 0 | AWRI796_0012 | ACS1 | -0.016 | 1 |  |
| AWRI796_3381 | YLR326W | -0.002 | 1 | 0 | AWRI796_0669 | RRP42 | -0.016 | 1 |  |
| AWRI796_4316 | ITR2 | -0.002 | 1 | 0 | AWRI796_1396 | SHO1 | -0.016 | 1 |  |
| AWRI796_4385 | YAP7 | -0.002 | 1 | 0 | AWRI796_1477 | YPT1 | -0.016 | 1 |  |
| AWRI796_4906 | GLR1 | -0.002 | 1 | 0 | AWRI796_2000 | BUD32 | -0.016 | 1 |  |
| AWRI796_4941 | MNN9 | -0.002 | 1 | 0 | AWRI796_2067 | YHL008C | -0.016 | 1 |  |
| AWRI796_0160 | YbL010C | -0.003 | 1 | 0 | AWRI796_2877 | CYT2 | -0.016 | 1 |  |
| AWRI796_0256 | YBR096W | -0.003 | 1 | 0 | AWRI796_3782 | CIK1 | -0.016 | 1 |  |
| AWRI796_0605 | RBS1 | -0.003 | 1 | 0 | AWRI796_3811 | MTF1 | -0.016 | 1 |  |
| AWRI796_1973 | PHB2 | -0.003 | 1 | 0 | AWRI796_4109 | YPT53 | -0.016 | 1 |  |
| AWRI796_1995 | GND2 | -0.003 | 1 | 0 | AWRI796_4115 | MKT1 | -0.016 | 1 |  |
| AWRI796_2432 | MRS1 | -0.003 | 1 | 0 | AWRI796_5021 | PUF2 | -0.016 | 1 |  |
| AWRI796_2643 | ESS1 | -0.003 | 1 | 0 | AWRI796_0305 | RIB7 | -0.017 | 1 |  |
| AWRI796_3008 | TFA2 | -0.003 | 1 | 0 | AWRI796_0562 | GUD1 | -0.017 | 1 |  |
| AWRI796_3664 | MOT3 | -0.003 | 1 | 0 | AWRI796_1081 | LSM6 | -0.017 | 1 |  |
| AWRI796_4199 | SMM1 | -0.003 | 1 | 0 | AWRI796_1451 | BMH1 | -0.017 | 1 |  |
| AWRI796_5189 | IMD2 | -0.003 | 1 | 0 | AWRI796_1835 | SPT4 | -0.017 | 1 |  |
| AWRI796_0782 | RAD28 | -0.004 | 1 | 0 | AWRI796_2463 | PEX2 | -0.017 | 1 |  |
| AWRI796_2229 | DBP8 | -0.004 | 1 | 0 | AWRI796_3342 | MCM5 | -0.017 | 1 |  |
| AWRI796_3549 | OGG1 | -0.004 | 1 | 0 | AWRI796_3587 | PPZ1 | -0.017 | 1 |  |
| AWRI796_4294 | VPS68 | -0.004 | 1 | 0 | AWRI796_4958 | suv3 | -0.017 | 1 |  |
| AWRI796_1131 | PPM1 | -0.005 | 1 | 0 | AWRI796_4967 | VTC3 | -0.017 | 1 |  |
| AWRI796_2108 | RRF1 | -0.005 | 1 | 0 | AWRI796_0013 | FLC2 | -0.018 | 1 |  |
| AWRI796_2360 | YIL067C | -0.005 | 1 | 0 | AWRI796_0559 | AAD4 | -0.018 | 1 |  |
| AWRI796_2848 | OAC1 | -0.005 | 1 | 0 | AWRI796_1353 | TDA2 | -0.018 | 1 |  |
| AWRI796_2911 | ANR2 | -0.005 | 1 | 0 | AWRI796_1608 | MIG2 | -0.018 | 1 |  |
| AWRI796_3495 | GTR1 | -0.005 | 1 | 0 | AWRI796_1750 | OCH1 | -0.018 | 1 |  |
| AWRI796_3699 | ILV2 | -0.005 | 1 | 0 | AWRI796_1786 | TFG2 | -0.018 | 1 |  |
| AWRI796_3896 | YMR310C | -0.005 | 1 | 0 | AWRI796_1787 | PRP18 | -0.018 | 1 |  |
| AWRI796_4045 | APC1 | -0.005 | 1 | 0 | AWRI796_2697 | YJR085C | -0.018 | 1 |  |
| AWRI796_4082 | FAR11 | -0.005 | 1 | 0 | AWRI796_2866 | MTC2 | -0.018 | 1 |  |
| AWRI796_4344 | THP1 | -0.005 | 1 | 0 | AWRI796_0226 | YBR062C | -0.019 | 1 |  |
| AWRI796_4388 AWRI796_4956 | $\stackrel{\text { LAG2 }}{\text { PHO85 }}$ | -0.005 -0.005 | 1 1 | 0 | AWRI796_0831 AWRI796_0900 | RRP1 STB3 | -0.019 -0.019 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1109 | ADE8 | -0.019 | 1 | 0 | AWRI796_4168 | SAM50 | -0.031 | 1 |  |
| AWRI796_1174 | RIB3 | -0.019 | 1 | 0 | AWRI796_0992 | GLO2 | -0.032 | 1 |  |
| AWRI796_2745 | YJR142W | -0.019 | 1 | 0 | AWRI796_1213 | PAD1 | -0.032 | 1 |  |
| AWRI796_3016 | YKR070W | -0.019 | 1 | 0 | AWRI796_1376 | SHC1 | -0.032 | 1 |  |
| AWRI796_3642 | ARG80 | -0.019 | 1 | 0 | AWRI796_1540 | SMC2 | -0.032 | 1 |  |
| AWRI796_0391 | MRPS5 | -0.02 | 1 | 0 | AWRI796_2220 | PEX18 | -0.032 | 1 |  |
| AWRI796_0845 | ARP10 | -0.02 | 1 | 0 | AWRI796_2387 | CAP2 | -0.032 | 1 |  |
| AWRI796_2011 | RTT102 | -0.02 | 1 | 0 | AWRI796_3244 | YLR152C | -0.032 | 1 |  |
| AWRI796_2730 | ENT3 | -0.02 | 1 | 0 | AWRI796_3622 | FMS1 | -0.032 | 1 |  |
| AWRI796_4999 | TIF6 | -0.02 | 1 | 0 | AWRI796_3755 | CEP3 | -0.032 | 1 |  |
| AWRI796_5098 | LOA1 | -0.02 | 1 | 0 | AWRI796_4279 | CTR9 | -0.032 | 1 |  |
| AWRI796_0439 | PRD1 | -0.021 | 1 | 0 | AWRI796_4727 | NDD1 | -0.032 | 1 |  |
| AWRI796_0557 | YCR 100C | -0.021 | 1 | 0 | AWRI796_4942 | DIG1 | -0.032 | 1 |  |
| AWRI796_1399 | YER121W | -0.021 | 1 | 0 | AWRI796_4946 | SSN3 | -0.032 | 1 |  |
| AWRI796_1871 | SRB5 | -0.021 | 1 | 0 | AWRI796_0264 | PH088 | -0.033 | 1 |  |
| AWRI796_4851 | KIP2 | -0.021 | 1 | 0 | AWRI796_0324 | UMP1 | -0.033 | 1 |  |
| AWRI796_0472 | DCC1 | -0.022 | 1 | 0 | AWRI796_0501 | FEN2 | -0.033 | 1 |  |
| AWRI796_0667 | ATG20 | -0.022 | 1 | 0 | AWRI796_0908 | NGG1 | -0.033 | 1 |  |
| AWRI796_1068 | CDC40 | -0.022 | 1 | 0 | AWRI796_1229 | NPR2 | -0.033 | 1 |  |
| AWRI796_1968 | HSV2 | -0.022 | 1 | 0 | AWRI796_1687 | SNF4 | -0.033 | 1 |  |
| AWRI796_2185 | CIA2 | -0.022 | 1 | 0 | AWRI796_2755 | DAL5 | -0.033 | 1 |  |
| AWRI796_3015 | MET1 | -0.022 | 1 | 0 | AWRI796_3509 | PML39 | -0.033 | 1 |  |
| AWRI796_3351 | MEC3 | -0.022 | 1 | 0 | AWRI796_0181 | GRX7 | -0.034 | 1 |  |
| AWRI796_3727 | PSO2 | -0.022 | 1 | 0 | AWRI796_1855 | PDC6 | -0.034 | 1 |  |
| AWRI796_3765 | CTL1 | -0.022 | 1 | 0 | AWRI796_3019 | AIM29 | -0.034 | 1 |  |
| AWRI796_4866 | SPP1 | -0.022 | 1 | 0 | AWRI796_1032 | SWA2 | -0.035 | 1 |  |
| AWRI796_4884 | IDI1 | -0.022 | 1 | 0 | AWRI796_1423 | SPT15 | -0.035 | 1 |  |
| AWRI796_0176 | FLR1 | -0.023 | 1 | 0 | AWRI796_2521 | LCB3 | -0.035 | 1 |  |
| AWRI796_1127 | TIF35 | -0.023 | 1 | 0 | AWRI796_3242 | STM1 | -0.035 | 1 |  |
| AWRI796_1308 | GAL83 | -0.023 | 1 | 0 | AWRI796_3268 | MDL1 | -0.035 | 1 |  |
| AWRI796_1843 | PRP38 | -0.023 | 1 | 0 | AWRI796_3270 | MMR1 | -0.035 | 1 |  |
| AWRI796_2197 | YCK1 | -0.023 | 1 | 0 | AWRI796_3434 | VPS33 | -0.035 | 1 |  |
| AWRI796_2373 | NEO1 | -0.023 | 1 | 0 | AWRI796_4006 | MGS1 | -0.035 | 1 |  |
| AWRI796_3967 | YIF1 | -0.023 | 1 | 0 | AWRI796_0173 | RCR1 | -0.036 | 1 |  |
| AWRI796_4103 | MIC27 | -0.023 | 1 | 0 | AWRI796_0225 | TRM7 | -0.036 | 1 |  |
| AWRI796_4947 | MRX11 | -0.023 | 1 | 0 | AWRI796_0289 | MEC1 | -0.036 | 1 |  |
| AWRI796_0023 | CDC24 | -0.024 | 1 | 0 | AWRI796_0344 | PGII | -0.036 | 1 |  |
| AWRI796_1335 | GIP2 | -0.024 | 1 | 0 | AWRI796_0722 | KNH1 | -0.036 | 1 |  |
| AWRI796_1546 | IRC5 | -0.024 | 1 | 0 | AWRI796_1640 | PMR1 | -0.036 | 1 |  |
| AWRI796_1734 | PKP2 | -0.024 | 1 | 0 | AWRI796_2052 | NPR3 | -0.036 | 1 |  |
| AWRI796_2122 | CIC1 | -0.024 | 1 | 0 | AWRI796_2100 | RRM3 | -0.036 | 1 |  |
| AWRI796_3856 | RSN1 | -0.024 | 1 | 0 | AWRI796_2232 | SPC97 | -0.036 | 1 |  |
| AWRI796_4000 | SQS1 | -0.024 | 1 | 0 | AWRI796_2235 | YHR177W | -0.036 | 1 |  |
| AWRI796_0245 | UBC4 | -0.025 | 1 | 0 | AWRI796_2436 | MND2 | -0.036 | 1 |  |
| AWRI796_1090 | YDR387C | -0.025 | 1 | 0 | AWRI796_2854 | ABF1 | -0.036 | 1 |  |
| AWRI796_1218 | YDR541C | -0.025 | 1 | 0 | AWRI796_4300 | SMF1 | -0.036 | 1 |  |
| AWRI796_1306 | GCD11 | -0.025 | 1 | 0 | AWRI796_0056 | FUN14 | -0.037 | 1 |  |
| AWRI796_1798 | VMA7 | -0.025 | 1 | 0 | AWRI796_0366 | TDP1 | -0.037 | 1 |  |
| AWRI796_2531 | MTC1 | -0.025 | 1 | 0 | AWRI796_1266 | MMS21 | -0.037 | 1 |  |
| AWRI796_2644 | TES1 | -0.025 | 1 | 0 | AWRI796_1350 | MOT2 | -0.037 | 1 |  |
| AWRI796_3816 | RNH1 | -0.025 | 1 | 0 | AWRI796_2014 | CWC22 | -0.037 | 1 |  |
| AWRI796_3850 | TIF11 | -0.025 | 1 | 0 | AWRI796_2079 | SOD2 | -0.037 | 1 |  |
| AWRI796_0240 | SLM4 | -0.026 | 1 | 0 | AWRI796_2416 | AIM21 | -0.037 | 1 |  |
| AWRI796_0715 | YDL057W | -0.026 | 1 | 0 | AWRI796_2665 | CYC1 | -0.037 | 1 |  |
| AWRI796_1113 | RRP17 | -0.026 | 1 | 0 | AWRI796_2874 | CUE2 | -0.037 | 1 |  |
| AWRI796_1411 | GLC7 | -0.026 | 1 | 0 | AWRI796_3439 | SFP1 | -0.037 | 1 |  |
| AWRI796_1714 | GUP1 | -0.026 | 1 | 0 | AWRI796_4004 | ADE12 | -0.037 | 1 |  |
| AWRI796_1893 | PHB1 | -0.026 | 1 | 0 | AWRI796_4057 | IGO1 | -0.037 | 1 |  |
| AWRI796_3466 | ECM30 | $-0.026$ | 1 | 0 | AWRI796_4093 | RPC19 | -0.037 | 1 |  |
| AWRI796_3539 | DAK1 | -0.026 | 1 | 0 | AWRI796_5057 | SUA7 | -0.037 | 1 |  |
| AWRI796_4659 | RRS1 | -0.026 | 1 | 0 | AWRI796_0103 | PET112 | -0.038 | 1 |  |
| AWRI796_1374 | PUP3 | -0.027 | 1 | 0 | AWRI796_0151 | RFT1 | -0.038 | 1 |  |
| AWRI796_1412 | YER134C | -0.027 | 1 | 0 | AWRI796_1236 | RPL12A | -0.038 | 1 |  |
| AWRI796_1820 | TAM41 | -0.027 | 1 | 0 | AWRI796_1774 | LEU1 | -0.038 | 1 |  |
| AWRI796_2485 | ATG27 | -0.027 | 1 | 0 | AWRI796_2547 | GSH1 | -0.038 | 1 |  |
| AWRI796_3010 | OAF3 | -0.027 | 1 | 0 | AWRI796_3139 | MLH2 | -0.038 | 1 |  |
| AWRI796_4405 | COQ10 | $-0.027$ | 1 | 0 | AWRI796_3582 | UNG1 | -0.038 | 1 |  |
| AWRI796_0714 | USO1 | -0.028 | 1 | 0 | AWRI796_3860 | RRN9 | -0.038 | 1 |  |
| AWRI796_0752 | RPT2 | -0.028 | 1 | 0 | AWRI796_4518 | CAT5 | -0.038 | 1 |  |
| AWRI796_0967 | PEX5 | -0.028 | 1 | 0 | AWRI796_4620 | CLP1 | -0.038 | , |  |
| AWRI796-1706 | PAN2 | -0.028 | 1 | 0 | AWRI796_0261 | SIF2 | -0.039 | 1 |  |
| AWRI796_2389 | ULP2 | -0.028 | 1 | 0 | AWRI796_0498 | SLM5 | -0.039 | 1 |  |
| AWRI796_2747 | MGM101 | -0.028 | 1 | 0 | AWRI796_0811 | RRG1 | -0.039 | 1 |  |
| AWRI796_2817 | RCN1 | -0.028 | 1 |  | AWRI796_0905 | ${ }_{\text {ARG82 }}$ | -0.039 | 1 |  |
| AWRI796_2887 | MUD2 | -0.028 | 1 | 0 | AWRI796_3201 | CDC45 | -0.039 | 1 |  |
| AWRI796_3430 | CCW14 | -0.028 | 1 | 0 | AWRI796_3567 | YMD8 | -0.039 | 1 |  |
| AWRI796_3740 | NUP53 | -0.028 | 1 | 0 | AWRI796_3998 | JJJ1 | -0.039 | 1 |  |
| AWRI796_3807 | UBP8 | -0.028 | 1 | 0 | AWRI796_4957 | TRM44 | -0.039 | 1 |  |
| AWRI796_5246 | YNL284C-A | -0.028 | 1 | 0 | AWRI796_0322 | SEC66 | -0.04 | 1 |  |
| AWRI796_1044 | RQC1 | -0.029 | 1 | 0 | AWRI796_0664 | NUP84 | -0.04 | 1 |  |
| AWRI796_1095 | SPT3 | -0.029 | 1 | 0 | AWRI796_0986 | AKR1 | -0.04 | 1 |  |
| AWRI796_1715 | SCY1 | -0.029 | 1 | 0 | AWRI796_1918 | GTR2 | -0.04 | 1 |  |
| AWRI796_2986 | SPC34 | -0.029 | 1 | 0 | AWRI796_2170 | TRR2 | -0.04 | 1 |  |
| AWRI796_3792 | ERG12 | -0.029 | 1 | 0 | AWRI796_2828 | RPC25 | -0.04 | 1 |  |
| AWRI796_3932 | BXII | -0.029 | 1 | 0 | AWRI796_3142 | RIC1 | -0.04 | , |  |
| AWRI796_4938 | KTR6 | -0.029 | 1 | 0 | AWRI796_3411 | SSQ1 | -0.04 | 1 |  |
| AWRI796_0014 | OAF1 | -0.03 | 1 | 0 | AWRI796_3734 | TIF34 | -0.04 | 1 |  |
| AWRI796_0890 | SAC3 | -0.03 | 1 | 0 | AWRI796_4910 | YDC1 | -0.04 | 1 |  |
| AWRI796_1003 | INM2 | -0.03 | 1 | 0 | AWRI796_5109 | NCA2 | -0.04 | 1 |  |
| AWRI796_1093 | UBA2 | -0.03 | 1 | 0 | AWRI796_0075 | YAT1 | -0.041 | 1 |  |
| AWRI796_1704 | Tos8 | -0.03 | 1 | 0 | AWRI796_1393 | SPR6 | -0.041 | 1 |  |
| AWRI796_2788 | ACP1 | -0.03 | 1 | 0 | AWRI796_2106 | BRL1 | -0.041 | 1 |  |
| AWRI796_3311 | LIP2 | -0.03 | 1 | 0 | AWRI796_2314 | QDR1 | -0.041 | 1 |  |
| AWRI796_3464 | CNA1 | -0.03 | 1 | 0 | AWRI796_3712 | RPL15B | -0.041 | 1 |  |
| AWRI796_3706 | MGR3 | -0.03 | 1 | 0 | AWRI796_4805 | RKM1 | -0.041 | 1 |  |
| AWRI796_4472 | NRT1 | -0.03 | 1 | 0 | AWRI796_1605 | VAM7 | -0.042 | 1 |  |
| AWRI796_5067 | PRE2 | -0.03 | 1 | 0 | AWRI796_2307 | MET18 | -0.042 | 1 |  |
| AWRI796_0134 | MRPL16 | -0.031 | 1 | 0 | AWRI796_3130 | SNF7 | -0.042 | 1 |  |
| AWRI796_0867 | FIN1 | -0.031 | 1 | 0 | AWRI796_3313 | CSC1 | -0.042 | 1 |  |
| AWRI796_1310 | SMB1 | -0.031 | 1 | 0 | AWRI796_4616 | ESA1 | -0.042 | 1 |  |
| AWRI796_1860 | DBF2 | -0.031 | 1 | 0 | AWRI796_4880 | TFB2 | -0.042 | 1 |  |
| AWRI796_2621 | VTC4 | -0.031 | 1 | 0 | AWRI796_4953 | YPL034W | -0.042 | 1 |  |
| AWRI796_2709 | AIM25 | -0.031 | 1 | 0 | AWRI796_5073 | YPR109W | -0.042 | 1 |  |
| AWRI796_2998 | YKR051W | -0.031 | 1 | 0 | AWRI796_0092 | RPL32 | -0.043 | 1 |  |
| AWRI796_3072 | PRP19 | -0.031 | 1 | 0 | AWRI796_0962 | SEC26 | -0.043 | 1 |  |
| AWRI796_3558 AWRI796_3942 | GAL80 PUS4 | -0.031 -0.031 | 1 1 | 0 0 | AWRI796_1327 AWRI796_1441 | SAP1 BCK2 | -0.043 -0.043 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1981 | PFK1 | -0.043 | , | 0 | AWRI796_3112 | NSE1 | -0.059 | 1 |  |
| AWRI796_2527 | PBS2 | -0.043 | 1 | 0 | AWRI796_3940 | RIM21 | -0.059 | 1 |  |
| AWRI796_2556 | GWT1 | -0.043 | 1 | 0 | AWRI796_4841 | REV3 | -0.059 | 1 |  |
| AWRI796_4930 | TIM50 | -0.043 | 1 | 0 | AWRI796_1200 | URC2 | -0.06 | 1 |  |
| AWRI796_1013 | ATP5 | -0.044 | 1 | 0 | AWRI796_1304 | PRO3 | -0.06 | 1 |  |
| AWRI796_1470 | FMP32 | -0.044 | 1 | 0 | AWRI796_1770 | PDR1 | -0.06 | 1 |  |
| AWRI796_2936 | SWD2 | -0.044 | 1 | 0 | AWRI796_2417 | DJP1 | -0.06 | 1 |  |
| AWRI796_4391 | DIS3 | -0.044 | 1 | 0 | AWRI796_2631 | SAG1 | -0.06 | 1 |  |
| AWRI796_4578 | LIP5 | -0.044 | 1 | 0 | AWRI796_3400 | BuD8 | -0.06 | 1 |  |
| AWRI796_4627 | CDC31 | -0.044 | 1 | 0 | AWRI796_4165 | FAP1 | -0.06 | 1 |  |
| AWRI796_2595 | RTT101 | -0.045 | 1 | 0 | AWRI796_5065 | SNT309 | -0.06 | 1 |  |
| AWRI796_2903 | NUP120 | -0.045 | 1 | 0 | AWRI796_1034 | MRPL35 | -0.061 | 1 |  |
| AWRI796_3066 | RPL8B | -0.045 | 1 | 0 | AWRI796_1852 | MRP13 | -0.061 | 1 |  |
| AWRI796_3228 | SLX4 | -0.045 | 1 | 0 | AWRI796_2294 | CCT2 | -0.061 | 1 |  |
| AWRI796_3315 | GPN3 | -0.045 | 1 | 0 | AWRI796_2300 | VHS2 | -0.061 | 1 |  |
| AWRI796_3522 | PRE8 | -0.045 | 1 | 0 | AWRI796_2803 | LST4 | -0.061 | 1 |  |
| AWRI796_4141 | VAC7 | -0.045 | 1 | 0 | AWRI796_3901 | YMR315W | -0.061 | 1 |  |
| AWRI796_4431 | HSP10 | -0.045 | 1 | 0 | AWRI796_4172 | SIW14 | -0.061 | 1 |  |
| AWRI796_4489 | PTC5 | -0.045 | 1 | 0 | AWRI796_4375 | RPS 15 | -0.061 | 1 |  |
| AWRI796_5116 | ORC4 | -0.045 | 1 | 0 | AWRI796_4816 | DDC1 | -0.061 | 1 |  |
| AWRI796_0141 | HEK2 | -0.046 | 1 | 0 | AWRI796_5002 | MCM4 | -0.061 | 1 |  |
| AWRI796_1624 | COX4 | -0.046 | 1 | 0 | AWRI796_0807 | YDR061W | -0.062 | 1 |  |
| AWRI796_3203 | SEN2 | -0.046 | 1 | 0 | AWRI796_0883A | NUM1 | -0.062 | 1 |  |
| AWRI796_3874 | NGL2 | -0.046 | 1 | 0 | AWRI796_1485 | CAK1 | -0.062 | 1 |  |
| AWRI796_3902 | DIA1 | -0.046 | 1 | 0 | AWRI796_2528 | SPT10 | -0.062 | 1 |  |
| AWRI796_4095 | CYB5 | -0.046 | 1 | 0 | AWRI796_4097 | YAF9 | -0.062 | 1 |  |
| AWRI796_4249 | YNR068C | -0.046 | 1 | 0 | AWRI796_4508 | AZF1 | -0.062 | 1 |  |
| AWRI796_1580 | YGL242C | -0.047 | 1 | 0 | AWRI796_5138 | MLC2 | -0.062 | 1 |  |
| AWRI796_2464 | CBP1 | -0.047 | 1 | 0 | AWRI796_0374 | ARC40 | -0.063 | 1 |  |
| AWRI796_2865 | UTP11 | -0.047 | 1 | 0 | AWRI796_1790 | NMA2 | -0.063 | 1 |  |
| AWRI796_3397 | ORM2 | -0.047 | 1 | 0 | AWRI796_3213 | CLF1 | -0.063 | 1 |  |
| AWRI796_3498 | NGL3 | -0.047 | 1 | 0 | AWRI796_3371 | MRPL15 | -0.063 | 1 |  |
| AWRI796_3634 | RCH1 | -0.047 | 1 | 0 | AWRI796_3588 | TAF11 | -0.063 | 1 |  |
| AWRI796_3690 | ATP25 | -0.047 | 1 | 0 | AWRI796_4117 | SAL1 | -0.063 | 1 |  |
| AWRI796_0310 | AMN1 | -0.048 | 1 | 0 | AWRI796_4134 | YDJ1 | -0.063 | 1 |  |
| AWRI796_1832 | ERG25 | -0.048 | 1 | 0 | AWRI796_5106 | SUE1 | -0.063 | 1 |  |
| AWRI796_2992 | UIP5 | -0.048 | - 1 | 0 | AWRI799_2244 | IKI1 | -0.064 | 1 |  |
| AWRI796_3733 | NDE1 | -0.048 | 1 | 0 | AWRI796_3140 | YLR036C | -0.064 | 1 |  |
| AWRI796_4400 | HRD1 | -0.048 | 1 | 0 | AWRI796_3280 | COQ9 | -0.064 | 1 |  |
| AWRI796_5063 | YPR097W | -0.048 | 1 | 0 | AWRI796_4603 | MCP1 | -0.064 | 1 |  |
| AWRI796_1609 | SIP2 | -0.049 | 1 | 0 | AWRI796_1584 | HAP2 | -0.065 | 1 |  |
| AWRI796_4048 | SKO1 | -0.049 | 1 | 0 | AWRI796_3037 | SRP40 | -0.065 | 1 |  |
| AWRI796_4452 | STD1 | -0.049 | 1 | 0 | AWRI796_3757 | ALD2 | -0.065 | 1 |  |
| AWRI796_4809 | TPK2 | -0.049 | 1 | 0 | AWRI796_3922 | PFS2 | -0.065 | 1 |  |
| AWRI796_0778 | SES1 | -0.05 | 1 | 0 | AWRI796_3974 | GIS2 | -0.065 | 1 |  |
| AWRI796_1055 | PAL1 | -0.05 | 1 | 0 | AWRI796_4123 | MKS1 | -0.065 | 1 |  |
| AWRI796_1365 | GET2 | -0.05 | 1 | 0 | AWRI796_4352 | MET22 | -0.065 | 1 |  |
| AWRI796_1381 | RPS8B | -0.05 | 1 | 0 | AWRI796_4546 | NFI1 | -0.065 | 1 |  |
| AWRI796_1764 | CKB1 | -0.05 | 1 | 0 | AWRI796_4835 | MRPL40 | -0.065 | 1 |  |
| AWRI796_2391 | YNL284C-B | -0.05 | 1 | 0 | AWRI796_0299 | RTC2 | -0.066 | 1 |  |
| AWRI796_2563 | TAX4 | -0.05 | 1 | 0 | AWRI796_0526 | TAH1 | -0.066 | 1 |  |
| AWRI796_3111 | SSK1 | -0.05 | 1 | 0 | AWRI796_0963 | YDR239C | -0.066 | 1 |  |
| AWRI796_4935 | SUR1 | -0.05 | 1 | 0 | AWRI796_1302 | RPN3 | -0.066 | 1 |  |
| AWRI796_5137 | PZF1 | -0.05 | 1 | 0 | AWRI796_2515 | TIM17 | -0.066 | 1 |  |
| AWRI796_1724 | AFT1 | -0.051 | 1 | 0 | AWRI796_4644 | CAF20 | -0.066 | 1 |  |
| AWRI796_1727 | SGF73 | -0.051 | 1 | 0 | AWRI796_4883 | MRP51 | -0.066 | 1 |  |
| AWRI796_1977 | MIC26 | -0.051 | 1 | 0 | AWRI796_5035 | JID1 | -0.066 | 1 |  |
| AWRI796_2252 | NVJ1 | -0.051 | 1 | 0 | AWRI796_5159 | AWRI796_5159 | -0.066 | 1 |  |
| AWRI796_2327 | PFK26 | -0.051 | 1 | 0 | AWRI796_1752 | YGL036W | -0.067 | 1 |  |
| AWRI796_3943 | MID1 | -0.051 | 1 | 0 | AWRI796_1986 | CPD1 | -0.067 | 1 |  |
| AWRI796_4488 | VPS21 | -0.051 | 1 | 0 | AWRI796_2352 | SEC28 | -0.067 | 1 |  |
| AWRI796_0119 | PTH2 | -0.052 | 1 | 0 | AWRI796_4196 | URK1 | -0.067 | 1 |  |
| AWRI796_0303 | APD1 | -0.052 | 1 | 0 | AWRI796_5059 | YPR089W | -0.067 | 1 |  |
| AWRI796_1523 | IOC3 | -0.052 | 1 | 0 | AWRI796_0996 | RNH202 | -0.068 | 1 |  |
| AWRI796_1695 | MLC1 | -0.052 | 1 | 0 | AWRI796_1895 | CAF130 | -0.068 | 1 |  |
| AWRI796_1942 | PDX1 | -0.052 | 1 | 0 | AWRI796_2382 | TED1 | -0.068 | 1 |  |
| AWRI796_2533 | RPE1 | -0.052 | 1 | 0 | AWRI796_3266 | EMG1 | -0.068 | 1 |  |
| AWRI796_0507 | RBK1 | -0.053 | 1 | 0 | AWRI796_3423 | SMC6 | -0.068 | 1 |  |
| AWRI796_0538 | FUB1 | -0.053 | 1 | 0 | AWRI796_3694 | YMR102C | -0.068 | 1 |  |
| AWRI796_2967 | HEL1 | -0.053 | 1 | 0 | AWRI796_4018 | SPS18 | -0.068 | 1 |  |
| AWRI796_3310 | FAR10 | -0.053 | - 1 | 0 | AWRI796-4040 | RPS3 | -0.068 | 1 |  |
| AWRI796_4044 | MDG1 | -0.053 | 1 | 0 | AWRI796_4538 | SPP2 | -0.068 | 1 |  |
| AWRI796_4283 | RRP40 | -0.053 | 1 | 0 | AWRI796_5074 | RPC40 | -0.068 | 1 |  |
| AWRI796_4989 | AIM45 | -0.053 | 1 | 0 | AWRI796_0672 | KIN28 | -0.069 | 1 |  |
| AWRI796_1896 | LSB1 | -0.054 | 1 | 0 | AWRI796_0943 | RAD9 | -0.069 | 1 |  |
| AWRI796_1913 | CHO2 | -0.054 | 1 | 0 | AWRI796_1015 | PRO1 | -0.069 | 1 |  |
| AWRI796_3534 | WAR1 | -0.054 | 1 | 0 | AWRI796_1674 | RSM23 | -0.069 | 1 |  |
| AWRI796_4823 | MF(ALPHA) 1 | -0.054 | 1 | 0 | AWRI796_4608 | KIN4 | -0.069 | 1 |  |
| AWRI796_0341 | MED8 | -0.055 | 1 | 0 | AWRI796_0494 | MAK32 | -0.07 | 1 |  |
| AWRI796_0737 | ARP2 | -0.055 | 1 | 0 | AWRI796_0747 | TSC13 | -0.07 | 1 |  |
| AWRI796_3165 | ENV10 | -0.055 | 1 | 0 | AWRI796_1471 | SEC53 | -0.07 | 1 |  |
| AWRI796_4041 | MRPL22 | -0.055 | 1 | 0 | AWRI796_1972 | SMI1 | -0.07 | 1 |  |
| AWRI796_4478 | BUD21 | -0.055 | 1 | 0 | AWRI796_3737 | SWP1 | -0.07 | 1 |  |
| AWRI796_0237 | RDH54 | -0.056 | 1 | 0 | AWRI796_0085 | SFT2 | -0.071 | 1 |  |
| AWRI796_0843 | SPO71 | -0.056 | 1 | 0 | AWRI796_0485 | SAT4 | -0.071 | 1 |  |
| AWRI796_1241 | FRD1 | -0.056 | 1 | 0 | AWRI796_0627 | ENT1 | -0.071 | 1 |  |
| AWRI796_1987 | SOL4 | -0.056 | 1 | 0 | AWRI796_0907 | RSM24 | -0.071 | 1 |  |
| AWRI796_2348 | ${ }^{\text {CAB2 }}$ | -0.056 | - 1 | 0 | AWRI796_2587 | YJL055W | -0.071 | 1 |  |
| AWRI796_4301 | RPS19A | -0.056 | 1 | 0 | AWRI796_3979 | RAD50 | -0.071 |  |  |
| AWRI796_0018 | AIM1 | -0.057 | 1 | 0 | AWRI796_0146 | RRN10 | -0.072 | 1 |  |
| AWRI796_0676 | QRI7 | -0.057 | 1 | 0 | AWRI796_0139 | STU1 | -0.073 | 1 |  |
| AWRI796_1400 | GLO3 | -0.057 | 1 | 0 | AWRI796_0573 | SHS1 | -0.073 | 1 |  |
| AWRI796_3826 | YMR244W | -0.057 | 1 | 0 | AWRI796_0691 | ASM4 | -0.073 | 1 |  |
| AWRI796_4361 | THI20 | -0.057 | 1 | 0 | AWRI796_1448 | GRX4 | -0.073 | 1 |  |
| AWRI796_4533 | LSC1 | -0.057 | 1 | 0 | AWRI796_2851 | PRR1 | -0.073 | 1 |  |
| AWRI796_4775 | YAR1 | -0.057 | 1 | 0 | AWRI796_2935 | RAM2 | -0.073 | 1 |  |
| AWRI796-4777 | ENV7 | -0.057 | 1 | 0 | AWRI796_3859 | TMA23 | -0.073 | 1 |  |
| AWRI796_1180 | RSM28 | -0.058 | 1 | 0 | AWRI796_0365 | PCS60 | -0.074 | 1 |  |
| AWRI796_1597 | COG1 | -0.058 | 1 | 0 | AWRI796_0522 | THR4 | -0.074 | 1 |  |
| AWRI796_3858 | PRP24 | -0.058 | 1 | 0 | AWRI796_1686 | CDC20 | -0.074 | 1 |  |
| AWRI796_1039 | SKP1 | -0.059 | 1 | 0 | AWRI796_3378 | SFH1 | -0.074 | 1 |  |
| AWRI796_1380 | AST2 | -0.059 | 1 | 0 | AWRI796_3819 | BCH1 | -0.074 | 1 |  |
| AWRI796_1555 | RMD8 | -0.059 | 1 | 0 | AWRI796_3821 | RNT1 | -0.074 | 1 |  |
| AWRI796_2208 | IMP3 | -0.059 | 1 | 0 | AWRI796_4031 | SRP1 | -0.074 | 1 |  |
| AWRI796_2487 | SWI3 | -0.059 | 1 | 0 | AWRI796_4609 | DFR1 | -0.074 | 1 |  |
| AWRI796_2544 AWRI796_2977 | PAM16 BCH2 | -0.059 -0.059 | 1 1 | 0 | AWRI796_0067 AWRI796_0622 | ADE1 SFA1 | -0.075 -0.075 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1256 | ECM10 | -0.075 | , | 0 | AWRI796_0700 | VAM6 | -0.091 | 1 |  |
| AWRI796_1332 | JHD1 | -0.075 | 1 | 0 | AWRI796_1204 | RBA50 | -0.091 | 1 |  |
| AWRI796_2477 | SOP4 | -0.075 | 1 | 0 | AWRI796_1274 | GCN4 | -0.091 | 1 |  |
| AWRI796_2669 | RAD7 | -0.075 | 1 | 0 | AWRI796_1938 | HGH1 | -0.091 | 1 |  |
| AWRI796_2690 | H0С1 | -0.075 | 1 | 0 | AWRI796_2964 | YPT52 | -0.091 | 1 |  |
| AWRI796_4903 | SEC62 | -0.075 | 1 | 0 | AWRI796_3994 | BNI4 | -0.091 | 1 |  |
| AWRI796_0087 | ATP1 | -0.076 | 1 | 0 | AWRI796_4010 | PEX17 | -0.091 | 1 |  |
| AWRI796_0802 | PST1 | -0.076 | 1 | 0 | AWRI796_4064 | PGA2 | -0.091 | 1 |  |
| AWRI796_2051 | RIM4 | -0.076 | 1 | 0 | AWRI796_4130 | FKH2 | -0.091 | 1 |  |
| AWRI796_2353 | RPN2 | -0.076 | 1 | 0 | AWRI796_4275 | DCP1 | -0.091 | 1 |  |
| AWRI796_4338 | REX4 | -0.076 | 1 | 0 | AWRI796_4485 | OST3 | -0.091 | 1 |  |
| AWRI796_0688 | UBX3 | -0.077 | 1 | 0 | AWRI796_4537 | MDM32 | -0.091 | 1 |  |
| AWRI796_0989 | CIA1 | -0.077 | 1 | 0 | AWRI796_0010 | GPB2 | -0.092 | 1 |  |
| AWRI796_1035 | PEP7 | -0.077 | 1 | 0 | AWRI796_0629 | STE7 | -0.092 | 1 |  |
| AWRI796_1497 | MDJ1 | -0.077 | 1 | 0 | AWRI796_1205 | HLR1 | -0.092 | 1 |  |
| AWRI796_2598 | GYP6 | -0.077 | 1 | 0 | AWRI796_1673 | CEG1 | -0.092 | 1 |  |
| AWRI796_2618 | YJL016W | -0.077 | 1 | 0 | AWRI796_1842 | UPF3 | -0.092 | 1 |  |
| AWRI796_2968 | YKR018C | -0.077 | 1 | 0 | AWRI796_2470 | ECM25 | -0.092 | 1 |  |
| AWRI796_0987 | PEX10 | -0.078 | 1 | 0 | AWRI796_2821 | GPM1 | -0.092 | 1 |  |
| AWRI796_2195 | NSG1 | -0.078 | 1 | 0 | AWRI796_4137 | ARP5 | -0.092 | 1 |  |
| AWRI796_2434 | DAL81 | -0.078 | 1 | 0 | AWRI796_4483 | WHI5 | -0.092 | 1 |  |
| AWRI796_3187 | GAA1 | -0.078 | 1 | 0 | AWRI796-4793 | RPL1A | -0.092 | 1 |  |
| AWRI796_3282 | QRI5 | -0.078 | 1 | 0 | AWRI796_5130 | PRP4 | -0.092 | 1 |  |
| AWRI796_3552 | CMP2 | -0.078 | 1 | 0 | AWRI796_0772 | KCS1 | -0.093 | 1 |  |
| AWRI796_3644 | IOC4 | -0.078 | 1 | 0 | AWRI796_0830 | AFR1 | -0.093 | 1 |  |
| AWRI796_5107 | URN1 | -0.078 | 1 | 0 | AWRI796_1097 | RPT3 | -0.093 | 1 |  |
| AWRI796_0032 | POP5 | -0.079 | 1 | 0 | AWRI796_1145 | TSA2 | -0.093 | 1 |  |
| AWRI796_0131 | PRE7 | -0.079 | 1 | 0 | AWRI796_1738 | OLE1 | -0.093 | 1 |  |
| AWRI796_1641 | CUP2 | -0.079 | 1 | 0 | AWRI796_2044 | OCA5 | -0.093 | 1 |  |
| AWRI796_1725 | MNP1 | -0.079 | 1 | 0 | AWRI796_2482 | MNN11 | -0.093 | 1 |  |
| AWRI796_3386 | NUP2 | -0.079 | 1 | 0 | AWRI796_3240 | PEP3 | -0.093 | 1 |  |
| AWRI796_3405 | ADE13 | -0.079 | 1 | 0 | AWRI796_3293 | CDC123 | -0.093 | 1 |  |
| AWRI796_0824 | PET100 | -0.08 | 1 | 0 | AWRI796_3476 | VMA6 | -0.093 | 1 |  |
| AWRI796_0836 | GIS1 | -0.08 | 1 | 0 | AWRI796_4038 | YNL181W | -0.093 | 1 |  |
| AWRI796_0863 | SWF1 | -0.08 | 1 | 0 | AWRI796_4051 | IBD2 | -0.093 | 1 |  |
| AWRI796_2623 | CCT8 | -0.08 | 1 | 0 | AWRI796_4074 | FPR1 | -0.093 | 1 |  |
| AWRI796_2749 | RPS4A | -0.08 | 1 | 0 | AWRI796_4382 | SIL1 | -0.093 | 1 |  |
| AWRI796_2901 | MPE1 | -0.08 | 1 | 0 | AWRI796_5077 | PIS1 | -0.093 | 1 |  |
| AWRI796_2973 | YKR023W | -0.08 | 1 | 0 | AWRI796_0797 | VMS1 | -0.094 | 1 |  |
| AWRI796_3030 | MRPL20 | -0.08 | 1 | 0 | AWRI796_0978 | CTA1 | -0.094 | 1 |  |
| AWRI796_1070 | KEI1 | -0.081 | 1 | 0 | AWRI796_1138 | SSN2 | -0.094 | 1 |  |
| AWRI796_3085 | HIF1 | -0.081 | 1 | 0 | AWRI796_1294 | PRP22 | -0.094 | 1 |  |
| AWRI796_3649 | STB2 | -0.081 | 1 | 0 | AWRI796_1487 | GYP8 | -0.094 | 1 |  |
| AWRI796_4239 | BIO3 | -0.081 | 1 | 0 | AWRI796_3099 | LMO1 | -0.094 | 1 |  |
| AWRI796_4494 | RKII | -0.081 | 1 | 0 | AWRI796_3669 | RCO1 | -0.094 | 1 |  |
| AWRI796_5028 | NHP6A | -0.081 | 1 | 0 | AWRI796_4079 | CPT1 | -0.094 | 1 |  |
| AWRI796_5070 | ISR1 | -0.081 | 1 | 0 | AWRI796_4554 | SEY1 | -0.094 | 1 |  |
| AWRI796_1801 | MTL1 | -0.082 | 1 | 0 | AWRI796_4804 | IPL1 | -0.094 | 1 |  |
| AWRI796_2181 | ORC6 | -0.082 | 1 | 0 | AWRI796_5223 | ENA2 | -0.094 |  |  |
| AWRI796_2918 | PTM1 | -0.082 | 1 | 0 | AWRI796_0285 | CCZ1 | -0.095 | 1 |  |
| AWRI796_3336 | BOP2 | -0.082 | 1 | 0 | AWRI796_0708 | IDP1 | -0.095 | 1 |  |
| AWRI796_0525 | YIH1 | -0.083 | 1 | 0 | AWRI796_1151 | TFB3 | -0.095 | 1 |  |
| AWRI796_1581 | KAP114 | -0.083 | 1 | 0 | AWRI796_2184 | LSM12 | -0.095 | 1 |  |
| AWRI796_1794 | YGR015C | -0.083 | 1 | 0 | AWRI796_2715 | ECM27 | -0.095 | 1 |  |
| AWRI796_2072 | OSH7 | -0.083 | 1 | 0 | AWRI796_3442 | YLR407W | -0.095 | 1 |  |
| AWRI796_2538 | CCT7 | -0.083 | 1 | 0 | AWRI796_3762 | MMT1 | -0.095 | 1 |  |
| AWRI796_2819 | RSM22 | -0.083 | 1 | 0 | AWRI796_3970 | LTO1 | -0.095 | 1 |  |
| AWRI796_3243 | PCD1 | -0.083 | 1 | 0 | AWRI796_0868 | YDR131C | -0.096 | 1 |  |
| AWRI796_3728 | CIN4 | -0.083 | 1 | 0 | AWRI796_1457 | TOG1 | -0.096 | 1 |  |
| AWRI796_4178 | IDP3 | -0.083 | 1 | 0 | AWRI796_1668 | MRM2 | -0.096 | 1 |  |
| AWRI796_4380 | MSE1 | -0.083 | 1 | 0 | AWRI796_2606 | TAD2 | -0.096 | 1 |  |
| AWRI796_4871 | COX11 | -0.083 | 1 | 0 | AWRI796_2607 | KAR2 | -0.096 | 1 |  |
| AWRI796_0450 | PDII | -0.084 | 1 | 0 | AWRI796_2738 | MCM22 | -0.096 | 1 |  |
| AWRI796_0512 | MATALPHA1 | -0.084 | 1 | 0 | AWRI796_2999 | MRS4 | -0.096 | 1 |  |
| AWRI796_1074 | CTS2 | -0.084 | 1 | 0 | AWRI796_3153 | FCF2 | -0.096 | 1 |  |
| AWRI796_1260 | YEL025C | -0.084 | 1 | 0 | AWRI796_4290 | MED7 | -0.096 | 1 |  |
| AWRI796_3211 | CFT2 | -0.084 | 1 | 0 | AWRI796_4648 | PLP2 | -0.096 | 1 |  |
| AWRI796_4584 | GEP3 | -0.084 | 1 | 0 | AWRI796_0431 | MAL33 | -0.097 | 1 |  |
| AWRI796_0275 | MUD1 | -0.085 | 1 | 0 | AWRI796_0625 | CDC36 | -0.097 | 1 |  |
| AWRI796_0969 | TRS23 | -0.085 | 1 | 0 | AWRI796_0861 | YDR124W | -0.097 | 1 |  |
| AWRI796-1660 | ROG1 | -0.085 | - 1 | 0 | AWRI796_1631 | MPT5 | -0.097 | 1 |  |
| AWRI796_3303 | ADY4 | -0.085 | 1 | 0 | AWRI796_1728 | ALG2 | -0.097 | 1 |  |
| AWRI796_3406 | DCR2 | -0.085 | 1 | 0 | AWRI796_2952 | MET14 | -0.097 | 1 |  |
| AWRI796_0034 | GIP4 | -0.086 | 1 | 0 | AWRI796_4434 | AHC1 | -0.097 | 1 |  |
| AWRI796_0650 | PPH21 | -0.086 | 1 | 0 | AWRI796_4487 | YVC1 | -0.097 | 1 |  |
| AWRI796_1927 | CBP4 | -0.086 | 1 | 0 | AWRI796_4637 | PAC1 | -0.097 | 1 |  |
| AWRI796_4565 | SYC1 | -0.086 | 1 | 0 | AWRI796_4886 | BEM3 | -0.097 | 1 |  |
| AWRI796_1047 | MRX8 | -0.087 | 1 | 0 | AWRI796_5027 | MAK3 | -0.097 | 1 |  |
| AWRI796_1172 | VPS72 | -0.087 | 1 | 0 | AWRI796_0148 | MCM2 | -0.098 | 1 |  |
| AWRI796_1652 | LYS5 | -0.087 | 1 | 0 | AWRI796_0330 | RPS6B | -0.098 | 1 |  |
| AWRI796_2493 | SET2 | -0.087 | 1 | 0 | AWRI796_0624 | FAP7 | -0.098 | 1 |  |
| AWRI796_4645 | HEM4 | -0.087 | 1 | 0 | AWRI796_1354 | VTC1 | -0.098 | 1 |  |
| AWRI796_4829 | PPQ1 | -0.087 | 1 | 0 | AWRI796_1550 | IRC6 | -0.098 | 1 |  |
| AWRI796_1736 | GEP7 | -0.088 | 1 | 0 | AWRI796_2304 | FKH1 | -0.098 | 1 |  |
| AWRI796_1780 | ERP6 | -0.088 | 1 | 0 | AWRI796_3758 | EAR1 | -0.098 | 1 |  |
| AWRI796_1989 | YGR250C | -0.088 | 1 | 0 | AWRI796_3871 | AEP2 | -0.098 | 1 |  |
| AWRI796_2693 | BNA2 | -0.088 | 1 | 0 | AWRI796_4416 | UTP23 | -0.098 | 1 |  |
| AWRI796_2859 | AAT1 | -0.088 | 1 | 0 | AWRI796_5044 | YPR071w | -0.098 | 1 |  |
| AWRI796_4531 | SFL1 | -0.088 | 1 | 0 | AWRI796_1467 | SWP82 | -0.099 | 1 |  |
| AWRI796_5232 | HSP33 | -0.088 | 1 | 0 | AWRI796_2781 | MNN4 | -0.099 | 1 |  |
| AWRI796_0033 | PRP45 | -0.089 | 1 | 0 | AWRI796_3116 | LOT6 | -0.099 | 1 |  |
| AWRI796_0158 | FMT1 | -0.089 | 1 | 0 | AWRI796_3759 | HOT1 | -0.099 | 1 |  |
| AWRI796_1902 | THI4 | -0.089 | 1 | 0 | AWRI796_4553 | GET4 | -0.099 | 1 |  |
| AWRI796_2765 | SRY1 | -0.089 | 1 | 0 | AWRI796_5124 | BSP1 | -0.099 | 1 |  |
| AWRI796_3338 | DCS1 | -0.089 | 1 | 0 | AWRI796_0114 | PRX1 | -0.1 | 1 |  |
| AWRI796_3702 | YMR111C | -0.089 | 1 | 0 | AWRI796_0872 | RGP1 | -0.1 | 1 |  |
| AWRI796_3899 | TGL3 | -0.089 | 1 | 0 | AWRI796_1206 | QCR7 | -0.1 | 1 |  |
| AWRI796_4513 | RTC5 | -0.089 | 1 | 0 | AWRI796_1894 | PEX4 | -0.1 | 1 |  |
| AWRI796_4622 | TMA16 | -0.089 | 1 | 0 | AWRI796_2364 | ARC15 | -0.1 | 1 |  |
| AWRI796_0939 | TCP1 | -0.09 | 1 | 0 | AWRI796_2551 | MRPL49 | -0.1 | 1 |  |
| AWRI796_1111 | STE14 | -0.09 | 1 | 0 | AWRI796_3279 | YKE2 | -0.1 | 1 |  |
| AWRI796_2189 | YHR127W | -0.09 | 1 | 0 | AWRI796_0438 | KRR1 | -0.101 | 1 |  |
| AWRI796_2369 | GPP1 | -0.09 | 1 | 0 | AWRI796_0572 | GCS1 | -0.101 | 1 |  |
| AWRI796_2879 | MDH1 | -0.09 | 1 | 0 | AWRI796_1073 | DXO1 | -0.101 | 1 |  |
| AWRI796_4451 | DBP5 | -0.09 | 1 | 0 | AWRI796_1104 | DIT1 | -0.101 | 1 |  |
| AWRI796_4471 AWRI796_0199 | GYP1 HMT1 | -0.09 -0.091 | 1 1 | 0 | AWRI796_1169 AWRI796_1978 | $\xrightarrow[\text { YGR237C }]{\text { CWC21 }}$ | -0.101 -0.101 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_2483 | YJL181W | -0.101 | 1 | 0 | AWRI796_1717 | MPC1 | -0.115 | 1 | 0 |
| AWRI796_0071 | YAR023C | -0.102 | 1 | 0 | AWRI796_2099 | SLT2 | -0.115 | 1 | 0 |
| AWRI796_0514 | YCR043C | -0.102 | 1 | 0 | AWRI796_3815 | TRI1 | -0.115 | 1 | 0 |
| AWRI796_0599 | ASF2 | -0.102 | 1 | 0 | AWRI796_0207 | CST26 | -0.116 | 1 | 0 |
| AWRI796_0886 | ENT5 | -0.102 | 1 | 0 | AWRI796_0250 | IST2 | -0.116 | 1 | 0 |
| AWRI796_1130 | GPI17 | -0.102 | 1 | 0 | AWRI796_1053 | SVF1 | -0.116 | 1 | 0 |
| AWRI796_1283 | NOP16 | -0.102 | 1 | 0 | AWRI796_1057 | ATP22 | -0.116 | 1 | 0 |
| AWRI796_1340 | PCL6 | -0.102 | 1 | 0 | AWRI796_1388 | KAP123 | -0.116 | 1 | 0 |
| AWRI796_2674 | CDC8 | -0.102 | 1 | 0 | AWRI796_2400 | VID28 | -0.116 | 1 | 0 |
| AWRI796_3068 | ATG10 | -0.102 | 1 | 0 | AWRI796_2733 | EFM3 | -0.116 | 1 | 0 |
| AWRI796_3219 | YLR126C | -0.102 | 1 | 0 | AWRI796_3290 | TUB4 | -0.116 | 1 | 0 |
| AWRI796_3284 | ENT2 | -0.102 | 1 | 0 | AWRI796_3300 | UCC1 | -0.116 | 1 | 0 |
| AWRI796_3997 | URE2 | -0.102 | 1 | 0 | AWRI796_0654 | YDL129W | -0.117 | 1 | 0 |
| AWRI796_4289 | PFK27 | -0.102 | 1 | 0 | AWRI796_2392 | EMC5 | -0.117 | 1 | 0 |
| AWRI796_4379 | SMC5 | -0.102 | 1 | 0 | AWRI796_2894 | YNK1 | -0.117 | 1 | 0 |
| AWRI796_1861 | DRN1 | -0.103 | 1 | 0 | AWRI796_3084 | POM33 | -0.117 | 1 | 0 |
| AWRI796_2209 | SKG6 | -0.103 | 1 | 0 | AWRI796_3403 | ATG33 | -0.117 | 1 | 0 |
| AWRI796_2804 | ZRT3 | -0.103 | 1 | 0 | AWRI796_3820 | DFG5 | -0.117 | 1 | 0 |
| AWRI796_2971 | ALY1 | -0.103 | 1 | 0 | AWRI796_3885 | DYN3 | -0.117 | 1 | 0 |
| AWRI796_3502 | TAF8 | -0.103 | 1 | 0 | AWRI796_4500 | PIN2 | -0.117 | 1 | 0 |
| AWRI796_3689 | MTG1 | -0.103 | 1 | 0 | AWRI796_0150 | HAP3 | -0.118 | 1 | 0 |
| AWRI796_1058 | SBE2 | -0.104 | 1 | 0 | AWRI796_1705 | VPS45 | -0.118 | 1 | 0 |
| AWRI796_2573 | ARG2 | -0.104 | 1 | 0 | AWRI796_3473 | ECM7 | -0.118 | 1 | 0 |
| AWRI796_2847 | DGR2 | -0.104 | 1 | 0 | AWRI796_0801 | CDC34 | -0.119 | 1 | 0 |
| AWRI796_3103 | SFII | -0.104 | 1 | 0 | AWRI796_0821 | RAD55 | -0.119 | 1 | 0 |
| AWRI796_4327 | SPO21 | -0.104 | 1 | 0 | AWRI796_1849 | SLX9 | -0.119 | 1 | 0 |
| AWRI796_1178 | IZH1 | -0.105 | 1 | 0 | AWRI796_2839 | SHE2 | -0.119 | 1 | 0 |
| AWRI796_1713 | LCL3 | -0.105 | 1 | 0 | AWRI796_3784 | ROT1 | -0.119 | 1 | 0 |
| AWRI796_1811 | RPL26B | -0.105 | 1 | 0 | AWRI796_4143 | COX5A | -0.119 | 1 | 0 |
| AWRI796_1974 | NAS6 | -0.105 | 1 | 0 | AWRI796_4420 | SLG1 | -0.119 | 1 | 0 |
| AWRI796_3580 | NSE5 | -0.105 | 1 | 0 | AWRI796_4988 | YPR003C | -0.119 | 1 | 0 |
| AWRI796_4023 | WHI3 | -0.105 | 1 | 0 | AWRI796_0750 | GRX6 | -0.12 | 1 | 0 |
| AWRI796_4169 | CRZ1 | -0.105 | 1 | 0 | AWRI796_0775 | DAS2 | -0.12 | 1 | 0 |
| AWRI796_4308 | MSB4 | -0.105 | 1 | 0 | AWRI796_0979 | RKM4 | -0.12 | 1 | 0 |
| AWRI796_4914 | SEN54 | -0.105 | 1 | 0 | AWRI796_4065 | ALF1 | -0.12 | , | 0 |
| AWRI796_4951 | EGD1 | -0.105 | 1 | 0 | AWRI796_4426 | RTS1 | -0.12 | 1 | 0 |
| AWRI796_0243 | SEC18 | -0.106 | 1 | 0 | AWRI796_0371 | OM14 | -0.121 | 1 | 0 |
| AWRI796_0832 | SLU7 | -0.106 | 1 | 0 | AWRI796_0393 | TRS20 | -0.121 | 1 | 0 |
| AWRI796_0899 | CDC37 | -0.106 | 1 | 0 | AWRI796_0604 | UFD2 | -0.121 | 1 | 0 |
| AWRI796_3221 | DCN1 | -0.106 | 1 | 0 | AWRI796_0837 | MSH6 | -0.121 | 1 | 0 |
| AWRI796_3508 | YML108W | -0.106 | 1 | 0 | AWRI796_0893 | NBP2 | -0.121 | 1 | 0 |
| AWRI796_3915 | PFA3 | -0.106 | 1 | 0 | AWRI796_1782 | EFM5 | -0.121 | 1 | 0 |
| AWRI796_3954 | PRM1 | -0.106 | 1 | 0 | AWRI796_2305 | ASG1 | -0.121 | 1 | 0 |
| AWRI796_4457 | TMC1 | -0.106 | 1 | 0 | AWRI796_3194 | IOC2 | -0.121 | 1 | 0 |
| AWRI796_1239 | VmA8 | -0.107 | 1 | 0 | AWRI796_3875 | DSS1 | -0.121 | 1 | 0 |
| AWRI796_1288 | PAC2 | -0.107 | 1 | 0 | AWRI796_5064 | MRPL51 | -0.121 | 1 | 0 |
| AWRI796_3936 | TRF5 | -0.107 | 1 | 0 | AWRI796_5082 | MRI1 | -0.121 | 1 | 0 |
| AWRI796_4206 | MRPL50 | -0.107 | 1 | 0 | AWRI796_0862 | ECM18 | -0.122 | 1 | 0 |
| AWRI796_0063 | SWD1 | -0.108 | 1 | 0 | AWRI796_2211 | MTC6 | -0.122 | 1 | 0 |
| AWRI796_0368 | MCX1 | -0.108 | 1 | 0 | AWRI796_2227 | THP2 | -0.122 | 1 | 0 |
| AWRI796_0369 | SLX1 | -0.108 | 1 | 0 | AWRI796_2260 | RPS4B | -0.122 | 1 | 0 |
| AWRI796_0470 | LEU2 | -0.108 | 1 | 0 | AWRI796_4702 | TYE7 | -0.122 | 1 | 0 |
| AWRI796_0923 | NUP42 | -0.108 | 1 | 0 | AWRI796_4818 | PRM3 | -0.122 | 1 | 0 |
| AWRI796_1284 | PMI40 | -0.108 | 1 | 0 | AWRI796_0347 | KTR4 | -0.123 | 1 | 0 |
| AWRI796_1514 | RPN11 | -0.108 | 1 | 0 | AWRI796_1476 | ACT1 | -0.123 | 1 | 0 |
| AWRI796_2218 | KEL1 | -0.108 | 1 | 0 | AWRI796_2950 | MRP17 | -0.123 | 1 | 0 |
| AWRI796_2975 | RPC37 | -0.108 | 1 | 0 | AWRI796_3166 | SPC3 | -0.123 | 1 | 0 |
| AWRI796_3185 | SMC4 | -0.108 | 1 | 0 | AWRI796_3250 | SEC10 | -0.123 | 1 | 0 |
| AWRI796_4050 | YNL165W | -0.108 | 1 | 0 | AWRI796_5033 | YMC1 | -0.123 | 1 | 0 |
| AWRI796_4128 | Lat1 | -0.108 | 1 | 0 | AWRI796_0425 | BSD2 | -0.124 | 1 | 0 |
| AWRI796_0136 | YbL036C | -0.109 | 1 | 0 | AWRI796_0565 | YPD1 | -0.124 | 1 | 0 |
| AWRI796_0804 | Yos9 | -0.109 | 1 | 0 | AWRI796_1556 | PRE4 | -0.124 | 1 | 0 |
| AWRI796_0869 | YDR132C | -0.109 | 1 | 0 | AWRI796_2613 | RNR2 | -0.124 | 1 | 0 |
| AWRI796_2036 | CBP2 | -0.109 | 1 | 0 | AWRI796_2921 | TUL1 | -0.124 | 1 | 0 |
| AWRI796_2219 | TDA11 | -0.109 | 1 | 0 | AWRI796_2948 | BYE1 | -0.124 | 1 | 0 |
| AWRI796_2359 | SEC6 | -0.109 | 1 | 0 | AWRI796_3772 | YMR187C | -0.124 | 1 | 0 |
| AWRI796_2363 | YRB2 | -0.109 | 1 | 0 | AWRI796_3854 | CUE1 | -0.124 | 1 | 0 |
| AWRI796_4340 | BRX1 | -0.109 | 1 | 0 | AWRI796_4430 | YOR019W | -0.124 | 1 | 0 |
| AWRI796_0895 | SEC1 | -0.11 | 1 | 0 | AWRI796_4895 | MSD1 | -0.124 | 1 | 0 |
| AWRI796_1176 | SLD5 | -0.11 | 1 | 0 | AWRI796_5164 | AWRI796_5164 | -0.124 | 1 | 0 |
| AWRI796_1289 | SEC3 | -0.11 | 1 | 0 | AWRI796_0278 | TFC1 | -0.125 | 1 | 0 |
| AWRI796_1696 | ARC1 | -0.11 | 1 | 0 | AWRI796_1160 | TRS31 | -0.125 | 1 | 0 |
| AWRI796_2039 | SBP1 | -0.11 | 1 | 0 | AWRI796_3033 | TVP38 | -0.125 | 1 | 0 |
| AWRI796_3475 | YLR446W | -0.11 | 1 | 0 | AWRI796_3620 | YMR018W | -0.125 | 1 | 0 |
| AWRI796_3554 | SPC2 | -0.11 | 1 | 0 | AWRI796_4756 | YPL260W | -0.125 | 1 | 0 |
| AWRI796_4113 | TOP2 | -0.11 | 1 | 0 | AWRI796_0111 | PRS4 | -0.126 | 1 | 0 |
| AWRI796_0030 | MTW1 | -0.111 | 1 | 0 | AWRI796_0339 | RPL21A | -0.126 | 1 | 0 |
| AWRI796_0610 | LYS20 | -0.111 | 1 | 0 | AWRI796_2355 | SPO22 | -0.126 | 1 | 0 |
| AWRI796_0675 | NSE4 | -0.111 | 1 | 0 | AWRI796_2658 | URB2 | -0.126 | 1 | 0 |
| AWRI796_0829 | TVP23 | -0.111 | 1 | 0 | AWRI796_2863 | HSL1 | -0.126 | 1 | 0 |
| AWRI796_1682 | GPG1 | -0.111 | 1 | 0 | AWRI796_2871 | MBR1 | -0.126 | 1 | 0 |
| AWRI796_1773 | MPO1 | -0.111 | 1 | 0 | AWRI796_2969 | IRS4 | -0.126 | 1 | 0 |
| AWRI796_2938 | ATP7 | -0.111 | 1 | 0 | AWRI796_4516 | LEO1 | -0.126 | 1 | 0 |
| AWRI796_2951 | DID4 | -0.111 | 1 | 0 | AWRI796_0055 | SPO7 | -0.127 | 1 | 0 |
| AWRI796_4417 | DNL4 | -0.111 | 1 | 0 | AWRI796_1118 | RAD30 | -0.127 | 1 | 0 |
| AWRI796_4822 | POS5 | -0.111 | 1 | 0 | AWRI796_1293 | PRE1 | -0.127 | 1 | 0 |
| AWRI796_5227 | AWRI796_5227 | -0.111 | 1 | 0 | AWRI796_2809 | MRPL38 | -0.127 | 1 | 0 |
| AWRI796_0211 | ZTA1 | -0.112 | 1 | 0 | AWRI796_3003 | TRM2 | -0.127 | 1 | 0 |
| AWRI796_0456 | GRX1 | -0.112 | 1 | 0 | AWRI796_3251 | RPS31 | -0.127 | 1 | 0 |
| AWRI796_0725 | FAD1 | -0.112 | 1 | 0 | AWRI796_4596 | RCN2 | -0.127 | 1 | 0 |
| AWRI796_1186 | PLM2 | -0.112 | 1 | 0 | AWRI796_4833 | SPT14 | -0.127 | 1 | 0 |
| AWRI796_1258 | VMA3 | -0.112 | 1 | 0 | AWRI796_0585 | SHR3 | -0.128 | 1 | 0 |
| AWRI796_2739 | TTI2 | -0.112 | 1 | 0 | AWRI796_1509 | SPB4 | -0.128 | 1 | 0 |
| AWRI796_3863 | RCE1 | -0.112 | 1 | 0 | AWRI796_2685 | HAM1 | -0.128 | 1 | 0 |
| AWRI796_4757 | APM1 | -0.112 | 1 | 0 | AWRI796_3296 | MSC3 | -0.128 | 1 | 0 |
| AWRI796_2800 | RPL17A | -0.113 | 1 | 0 | AWRI796_3429 | ECM19 | -0.128 | 1 | 0 |
| AWRI796_4857 | ATG5 | -0.113 | 1 | 0 | AWRI796_4515 | GCY1 | -0.128 | 1 | 0 |
| AWRI796_4991 | ICL2 | -0.113 | 1 | 0 | AWRI796_4801 | PUS1 | -0.128 | 1 | 0 |
| AWRI796_0112 | UBP13 | -0.114 | 1 | 0 | AWRI796_0125 | SEC17 | -0.129 | 1 | 0 |
| AWRI796_1078 | BCS1 | -0.114 | 1 | 0 | AWRI796_0736 | PRP9 | -0.129 | 1 | 0 |
| AWRI796_1675 | CWC23 | -0.114 | 1 | 0 | AWRI796_0809 | AIM7 | -0.129 | 1 | 0 |
| AWRI796_3432 | ATP10 | -0.114 | 1 | 0 | AWRI796_1108 | TRS120 | -0.129 | 1 | 0 |
| AWRI796_3984 | SUII | -0.114 | 1 | 0 | AWRI796_2578 | DLS1 | -0.129 | 1 | 0 |
| AWRI796_4139 | OCA2 | -0.114 | 1 | 0 | AWRI796_2805 | TPO5 | -0.129 | 1 | 0 |
| AWRI796_4860 | NOP53 | -0.114 | 1 |  | AWRI796_2812 | MCD4 | -0.129 | 1 | 0 |
| AWRI796_0404 AWRI796_1511 | MRPL37 LOC1 | -0.115 -0.115 | 1 1 | 0 | AWRI796_3808 AWRI796_4981 | MRE11 AEP3 | -0.129 -0.129 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{l o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_5032 | BRR1 | -0.129 | 1 | 0 | AWRI796_5010 | APL4 | -0.143 | 1 | 0 |
| AWRI796_5217 | DDI2 | -0.129 | 1 | 0 | AWRI796_1955 | CIR1 | -0.144 | 1 | 0 |
| AWRI796_0799 | DET1 | -0.13 | 1 | 0 | AWRI796_2012 | RNH70 | -0.144 | 1 | 0 |
| AWRI796_1040 | PEX3 | -0.13 | 1 | 0 | AWRI796_2570 | SMC3 | -0.144 | 1 | 0 |
| AWRI796_1165 | SNM1 | -0.13 | 1 | 0 | AWRI796_2775 | CBT1 | -0.144 | 1 | 0 |
| AWRI796_1276 | YEA6 | -0.13 | 1 | 0 | AWRI796_3302 | BUR2 | -0.144 | 1 | 0 |
| AWRI796_1576 | PDE1 | -0.13 | 1 | 0 | AWRI796_3683 | NPL6 | -0.144 | 1 | 0 |
| AWRI796_1966 | TOS2 | -0.13 | 1 | 0 | AWRI796_4164 | RCM1 | -0.144 | 1 | 0 |
| AWRI796_2287 | MCM10 | -0.13 | 1 | 0 | AWRI796_4613 | MET7 | -0.144 | 1 | 0 |
| AWRI796_3011 | PAM17 | -0.13 | 1 | 0 | AWRI796_4720 | PIP2 | -0.144 | 1 | 0 |
| AWRI796_3480 | SST2 | -0.13 | 1 | 0 | AWRI796_0814 | DOS2 | -0.145 | 1 | 0 |
| AWRI796_3969 | ORC5 | -0.13 | 1 | 0 | AWRI796_1063 | CNL1 | -0.145 | 1 | 0 |
| AWRI796_5266 | REP1 | -0.13 | 1 | 0 | AWRI796_2302 | RPL16A | -0.145 | 1 | 0 |
| AWRI796_0152 | APN2 | -0.131 | 1 | 0 | AWRI796_2336 | BMT5 | -0.145 | 1 | 0 |
| AWRI796_0563 | AIM6 | -0.131 | 1 | 0 | AWRI796_2614 | RRN7 | -0.145 | 1 | 0 |
| AWRI796_1147 | NHX1 | -0.131 | 1 | 0 | AWRI796_3132 | AAT2 | -0.145 | 1 | 0 |
| AWRI796_1401 | YCK3 | -0.131 | 1 | 0 | AWRI796_4830 | CBC2 | -0.145 | 1 | 0 |
| AWRI796_2013 | CAB4 | -0.131 | 1 | 0 | AWRI796_0926 | CAB5 | -0.146 | 1 | 0 |
| AWRI796_2947 | CAP1 | -0.131 | 1 | 0 | AWRI796_1125 | BNA7 | -0.146 | 1 | 0 |
| AWRI796_2958 | MEH1 | -0.131 | 1 | 0 | AWRI796_2410 | EPS1 | -0.146 | 1 | 0 |
| AWRI796_0222 | UBP14 | -0.132 | 1 | 0 | AWRI796_2953 | VPS1 | -0.146 | 1 | 0 |
| AWRI796_0649 | RDII | -0.132 | 1 | 0 | AWRI796_3401 | TAL1 | -0.146 | 1 | 0 |
| AWRI796_1578 | RTF1 | -0.132 | 1 | 0 | AWRI796_3512 | MDM1 | -0.146 | 1 | 0 |
| AWRI796_1763 | GET1 | -0.132 | 1 | 0 | AWRI796_4966 | ULP1 | -0.146 | 1 | 0 |
| AWRI796_2610 | MAD2 | -0.132 | 1 | 0 | AWRI796_4990 | HAL1 | -0.146 | 1 | 0 |
| AWRI796_2641 | YJR015W | -0.132 | 1 | 0 | AWRI796_1653 | PEX14 | -0.147 | 1 | 0 |
| AWRI796_2906 | DEF1 | -0.132 | 1 | 0 | AWRI796_1785 | PEX31 | -0.147 | 1 | 0 |
| AWRI796_3492 | PGA3 | -0.132 | 1 | 0 | AWRI796_3156 | OSW2 | -0.147 | 1 | 0 |
| AWRI796_3857 | PPA2 | -0.132 | 1 | 0 | AWRI796_4711 | MSC6 | -0.147 | 1 | 0 |
| AWRI796_4634 | RBL2 | -0.132 | 1 | 0 | AWRI796_0471 | NFS1 | -0.148 | 1 | 0 |
| AWRI796_0500 | RHB1 | -0.133 | 1 | 0 | AWRI796_0586 | YDL211C | -0.148 | 1 | 0 |
| AWRI796_5055 | YPR084W | -0.133 | 1 | 0 | AWRI796_0800 | DBF4 | -0.148 | 1 | 0 |
| AWRI796_1227 | AVT2 | -0.134 | 1 | 0 | AWRI796_0887 | CPR1 | -0.148 | 1 | 0 |
| AWRI796_1331 | RSM18 | -0.134 | 1 | 0 | AWRI796_2683 | YAE1 | -0.148 | 1 | 0 |
| AWRI796_1630 | TOS3 | -0.134 | 1 | 0 | AWRI796_3193 | GIS3 | -0.148 | 1 | 0 |
| AWRI796_2175 | UBA4 | -0.134 | 1 | 0 | AWRI796_3913 | MDJ2 | -0.148 | 1 | 0 |
| AWRI796_2462 | OPT1 | -0.134 | 1 | 0 | AWRI796_4324 | RFC4 | -0.148 | 1 | 0 |
| AWRI796_4776 | SU13 | -0.134 | 1 | 0 | AWRI796_4715 | HAP5 | -0.148 | 1 | 0 |
| AWRI796_5043 | MED1 | -0.134 | 1 | 0 | AWRI796_0062 | ERP1 | -0.149 | - 1 | 0 |
| AWRI796_0385 | ISW1 | -0.135 | 1 | 0 | AWRI796_0180 | YBR013C | -0.149 | 1 | 0 |
| AWRI796_0506 | RRP43 | -0.135 | 1 | 0 | AWRI796_1409 | RPS26B | -0.149 | 1 | 0 |
| AWRI796_4014 | SSB2 | -0.135 | 1 | 0 | AWRI796_3515 | CUE4 | -0.149 | 1 | 0 |
| AWRI796_5119 | RHO1 | -0.135 | 1 | 0 | AWRI796_3754 | MLH1 | -0.149 | 1 | 0 |
| AWRI796_0091 | ROX3 | -0.136 | 1 | 0 | AWRI796_4346 | NBA1 | -0.149 | 1 | 0 |
| AWRI796_0426 | CTP1 | -0.136 | 1 | 0 | AWRI796_4928 | VPS28 | -0.149 | 1 | 0 |
| AWRI796_1071 | YPR1 | -0.136 | 1 | 0 | AWRI796_5052 | GRS2 | -0.149 | 1 | 0 |
| AWRI796_1114 | ERD1 | -0.136 | 1 | 0 | AWRI796_0084 | RTG3 | -0.15 | 1 | 0 |
| AWRI796_3485 | GAB1 | -0.136 | 1 | 0 | AWRI796_0553 | CDC50 | -0.15 | 1 | 0 |
| AWRI796_3536 | FPR3 | -0.136 | 1 | 0 | AWRI796_0785 | LYS14 | -0.15 | 1 | 0 |
| AWRI796_3735 | YMR147W | -0.136 | 1 | 0 | AWRI796_1043 | IRC3 | -0.15 | 1 | 0 |
| AWRI796_0204 | ATP3 | -0.137 | 1 | 0 | AWRI796_2662 | SSC1 | -0.15 | 1 | 0 |
| AWRI796_0386 | RRT2 | -0.137 | 1 | 0 | AWRI796_3337 | SEC22 | -0.15 | 1 | 0 |
| AWRI796_0614 | YDL177C | -0.137 | 1 | 0 | AWRI796_3370 | ATG39 | -0.15 | 1 | 0 |
| AWRI796_1012 | SUR2 | -0.137 | 1 | 0 | AWRI796_3704 | FOL3 | -0.15 | 1 | 0 |
| AWRI796_1029 | OMS1 | -0.137 | 1 | 0 | AWRI796_3977 | MRPL17 | -0.15 | 1 | 0 |
| AWRI796_1749 | YGL039W | -0.137 | 1 | 0 | AWRI796_5090 | ANT1 | -0.15 | 1 | 0 |
| AWRI796_2010 | TAF1 | -0.137 | 1 | 0 | AWRI796_0590 | GLE1 | -0.151 | 1 | 0 |
| AWRI796_3456 | SPP382 | -0.137 | 1 | 0 | AWRI796_1442 | CCA1 | -0.151 | 1 | 0 |
| AWRI796_3834 | PET111 | -0.137 | 1 | 0 | AWRI796_3651 | BUB2 | -0.151 | 1 | 0 |
| AWRI796_4313 | YOL107W | -0.137 | 1 | 0 | AWRI796_4502 | RGS2 | -0.151 | 1 | 0 |
| AWRI796_4523 | ORT1 | -0.137 | 1 | 0 | AWRI796_5244 | YNL284C-B | -0.151 | 1 | 0 |
| AWRI796_4561 | ALE1 | -0.137 | 1 | 0 | AWRI796_0405 | SDH8 | -0.152 | 1 | 0 |
| AWRI796_0138 | POL12 | -0.138 | 1 | 0 | AWRI796_0876 | PEX7 | -0.152 | 1 | 0 |
| AWRI796_0440 | KAR4 | -0.138 | 1 | 0 | AWRI796_1234 | HAT2 | -0.152 | 1 | 0 |
| AWRI796_4119 | EOS1 | -0.138 | 1 | 0 | AWRI796_2586 | ZAP1 | -0.152 | 1 | 0 |
| AWRI796_4211 | CPR8 | -0.138 | 1 | 0 | AWRI796_4447 | CKB2 | -0.152 | 1 | 0 |
| AWRI796_4691 | VMA4 | -0.138 | 1 | 0 | AWRI796_4560 | MED4 | -0.152 | 1 | 0 |
| AWRI796-4767 | GAL4 | -0.138 | 1 | 0 | AWRI796_4929 | CWC27 | -0.152 | 1 | 0 |
| AWRI796_5041 | HOS1 | -0.138 | 1 | 0 | AWRI796_4975 | TAF3 | -0.152 | 1 | 0 |
| AWRI796_0221 | MUM2 | -0.139 | 1 | 0 | AWRI796_0414 | PAF1 | -0.153 | 1 | 0 |
| AWRI796_0531 | SED4 | -0.139 | 1 | 0 | AWRI796_0648 | ARF2 | -0.153 | 1 | 0 |
| AWRI796_0997 | RRP45 | -0.139 | 1 | 0 | AWRI796_3546 | RPS1B | -0.153 | 1 | 0 |
| AWRI796_1153 | STP1 | -0.139 | 1 | 0 | AWRI796_4422 | TIR2 | -0.153 | 1 | 0 |
| AWRI796_1623 | RPS26A | -0.139 | 1 | 0 | AWRI796_0021 | PTA1 | -0.154 | 1 | 0 |
| AWRI796_1690 | TAF6 | -0.139 | 1 | 0 | AWRI796_0109 | RPS8A | -0.154 | 1 | 0 |
| AWRI796-2645 | REC107 | -0.139 | 1 | 0 | AWRI796_0813 | OCA6 | -0.154 | 1 | 0 |
| AWRI796_2698 | EMC2 | -0.139 | 1 | 0 | AWRI796_0839 | BMH2 | -0.154 | 1 | 0 |
| AWRI796_1129 | NPL3 | -0.14 | 1 | 0 | AWRI796_1041 | UBX5 | -0.154 | 1 | 0 |
| AWRI796_1676 | SOH1 | -0.14 | 1 | 0 | AWRI796_2923 | TTII | -0.154 | 1 | 0 |
| AWRI796_3681 | YTA12 | -0.14 | 1 | 0 | AWRI796_3426 | VAC14 | -0.154 | 1 | 0 |
| AWRI796_4347 | NUF2 | -0.14 | 1 | 0 | AWRI796_5182 | YNL284C-B | -0.154 | , | 0 |
| AWRI796_4419 | SGT2 | -0.14 | 1 | 0 | AWRI796_0073 | YAR028W | -0.155 | 1 | 0 |
| AWRI796_0769 | PSF1 | -0.141 | 1 | 0 | AWRI796_0153 | POP8 | -0.155 | 1 | 0 |
| AWRI796_2453 | THI13 | -0.141 | 1 | 0 | AWRI796_0537 | ERS1 | -0.155 | , | 0 |
| AWRI796_2486 | RPL17B | -0.141 | 1 | 0 | AWRI796_1080 | ATP17 | -0.155 | 1 | 0 |
| AWRI796_3590 | UBX2 | -0.141 | 1 | 0 | AWRI796_1742 | RPT6 | -0.155 | 1 | 0 |
| AWRI796_0417 | MRPL27 | -0.142 | 1 | 0 | AWRI796_1754 | RPL24A | -0.155 | , | 0 |
| AWRI796_0481 | CDC10 | -0.142 | 1 | 0 | AWRI796_2505 | FBP26 | -0.155 | 1 | 0 |
| AWRI796_0874 | MTQ2 | -0.142 | 1 | 0 | AWRI796_2831 | SDH3 | -0.155 | 1 | 0 |
| AWRI796_1285 | FMP52 | -0.142 | 1 | 0 | AWRI796_2885 | YKL077W | -0.155 | , | 0 |
| AWRI796_1906 | RPL24B | -0.142 | 1 | 0 | AWRI796_3328 | YLR257W | -0.155 | , | 0 |
| AWRI796_2588 | TIM54 | -0.142 | 1 | 0 | AWRI796_3385 | RPS25B | -0.155 | 1 | 0 |
| AWRI796_3717 | SAS2 | -0.142 | 1 | 0 | AWRI796_3625 | MSS1 | -0.155 | 1 | 0 |
| AWRI796_3729 | RIM11 | -0.142 | 1 | 0 | AWRI796_3920 | YNL320W | -0.155 | 1 | 0 |
| AWRI796_4512 | RPT5 | -0.142 | 1 | 0 | AWRI796_4191 | ATG3 | -0.155 | 1 | 0 |
| AWRI796_4672 | SNU66 | -0.142 | 1 | 0 | AWRI796_5072 | RPN7 | -0.155 | 1 | 0 |
| AWRI796_4970 | SWI1 | -0.142 | 1 | 0 | AWRI796_2205 | DCD1 | -0.156 | 1 | 0 |
| AWRI796_0959 | PRP42 | -0.143 |  | 0 | AWRI796_2246 | PTH1 | -0.156 | 1 | 0 |
| AWRI796_2152 | NAM8 | -0.143 | 1 | 0 | AWRI796_2691 | CDC11 | -0.156 | , | 0 |
| AWRI796_2196 | wSS1 | -0.143 | 1 | 0 | AWRI796_4404 | MDM12 | -0.156 | 1 | 0 |
| AWRI796_2297 | TPM2 | -0.143 | , | 0 | AWRI796_0328 | FZO1 | -0.157 | 1 | 0 |
| AWRI796_2422 | MSL1 | -0.143 | 1 | 0 | AWRI796-0701 | RXT3 | -0.157 | 1 | 0 |
| AWRI796_3372 | SPH1 | -0.143 | 1 | 0 | AWRI796_1190 | GMC1 | -0.157 | 1 | 0 |
| AWRI796_3392 | GAS2 | -0.143 | 1 | 0 | AWRI796_1359 | ICP55 | -0.157 | 1 | 0 |
| AWRI796_3459 | MAG2 | -0.143 | 1 | 0 | AWRI796_3317 | CDD1 | -0.157 | 1 | 0 |
| AWRI796_3610 AWRI796_4692 | ADI1 MRS2 | -0.143 -0.143 | 1 1 | 0 0 | AWRI796_3450 AWRI796_474 | CDC73 CDC21 | -0.157 -0.157 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_5093 | SPN1 | -0.157 | 1 | 0 | AWRI796_2343 | YIL089W | -0.174 | 1 | 0 |
| AWRI796_0882 | KGD2 | -0.158 | 1 | 0 | AWRI796_2845 | SSH4 | -0.174 | 1 | 0 |
| AWRI796_1644 | SUT1 | -0.158 | 1 | 0 | AWRI796_3350 | YLR287C | -0.174 | 1 | 0 |
| AWRI796_1802 | THG1 | -0.158 | 1 | 0 | AWRI796_4795 | SAR1 | -0.174 | 1 | 0 |
| AWRI796_3056 | JLP1 | -0.158 | 1 | 0 | AWRI796_0177 | HHF1 | -0.175 | 1 | 0 |
| AWRI796_4056 | PGA1 | -0.158 | 1 | 0 | AWRI796_1170 | KRE2 | -0.175 | 1 | 0 |
| AWRI796_0973 | PAM1 | -0.159 | 1 | 0 | AWRI796_1253 | HYP2 | -0.175 | 1 | 0 |
| AWRI796_2329 | SLM1 | -0.159 | 1 | 0 | AWRI796_1389 | SWI4 | -0.175 | 1 | 0 |
| AWRI796_3384 | MID2 | -0.159 | 1 | 0 | AWRI796_1413 | GDII | -0.175 | 1 | 0 |
| AWRI796_3691 | YMR099C | -0.159 | 1 | 0 | AWRI796_2917 | NFU1 | -0.175 | 1 | 0 |
| AWRI796_4159 | YNL035C | -0.159 | 1 | 0 | AWRI796_4088 | NCS2 | -0.175 | 1 | 0 |
| AWRI796_4759 | YPL257W | -0.159 | 1 | 0 | AWRI796_4171 | HHT2 | -0.175 | 1 | 0 |
| AWRI796_0016 | GEM1 | -0.16 | 1 | 0 | AWRI796_0298 | MRPS9 | -0.176 | 1 | 0 |
| AWRI796_0990 | MSW1 | -0.16 | 1 | 0 | AWRI796_0360 | HPC2 | -0.176 | 1 | 0 |
| AWRI796_1443 | RPH1 | -0.16 | , | 0 | AWRI796_1094 | YDR391C | -0.176 | 1 | 0 |
| AWRI796_2255 | AIM18 | -0.16 | 1 | 0 | AWRI796_1272 | UBC8 | -0.176 | 1 | 0 |
| AWRI796_2900 | FBA1 | -0.16 | 1 | 0 | AWRI796_2522 | MRS3 | -0.176 | 1 | 0 |
| AWRI796_3441 | DUS4 | -0.161 | 1 | 0 | AWRI796_2727 | IBA57 | -0.176 | 1 | 0 |
| AWRI796_3773 | MRPS17 | -0.161 | 1 | 0 | AWRI796_3631 | RSF1 | -0.176 | 1 | 0 |
| AWRI796_1117 | RPL12B | -0.162 | 1 | 0 | AWRI796_3701 | HFD1 | -0.176 | 1 | 0 |
| AWRI796_1184 | SEC20 | -0.162 | 1 | 0 | AWRI796_4291 | HRT1 | -0.176 | 1 | 0 |
| AWRI796_1207 | APA2 | -0.162 | 1 | 0 | AWRI796_4785 | CET1 | -0.176 | 1 | 0 |
| AWRI796_1212 | STL1 | -0.162 | 1 | 0 | AWRI796_0061 | NUP60 | -0.177 | 1 | 0 |
| AWRI796_1642 | YRB30 | -0.162 | 1 | 0 | AWRI796_1194 | SDH7 | -0.177 | 1 | 0 |
| AWRI796_1778 | RPN14 | -0.162 | 1 | 0 | AWRI796_2684 | RFC2 | -0.177 | 1 | 0 |
| AWRI796_1877 | SHY1 | -0.162 | 1 | 0 | AWRI796_2820 | SRP102 | -0.177 | 1 | 0 |
| AWRI796_2296 | REV7 | -0.162 | 1 | 0 | AWRI796_3100 | MMM1 | -0.177 | 1 | 0 |
| AWRI796_4177 | YNL010W | -0.162 | 1 | 0 | AWRI796_0213 | RPS11B | -0.178 | 1 | 0 |
| AWRI796_4360 | GPM3 | -0.162 | 1 | 0 | AWRI796_2677 | YJR061W | -0.178 | 1 | 0 |
| AWRI796_4632 | GPN2 | -0.162 | 1 | 0 | AWRI796_2706 | YJR096W | -0.178 | 1 | 0 |
| AWRI796_0316 | ARL1 | -0.163 | 1 | 0 | AWRI796_2761 | YKL222C | -0.178 | 1 | 0 |
| AWRI796_2210 | PEX28 | -0.163 | 1 | 0 | AWRI796_2878 | SRX1 | -0.178 | 1 | 0 |
| AWRI796_2634 | SUI2 | -0.163 | 1 | 0 | AWRI796_2937 | HCS1 | -0.178 | 1 | 0 |
| AWRI796_2703 | FIP1 | -0.163 | 1 | 0 | AWRI796_4276 | SPT20 | -0.178 | 1 | 0 |
| AWRI796_3167 | PET309 | -0.163 | 1 | 0 | AWRI796_4922 | YPL071C | -0.178 | 1 | 0 |
| AWRI796_3518 | VPS9 | -0.163 | 1 | 0 | AWRI796_0985 | DIN7 | -0.179 | 1 | 0 |
| AWRI796_3876 | HSH155 | -0.163 | 1 | 0 | AWRI796_1328 | CAJ1 | -0.179 | 1 | 0 |
| AWRI796_3910 | AAD14 | -0.163 | 1 | 0 | AWRI796_1804 | RPS25A | -0.179 | 1 | 0 |
| AWRI796_4803 | SRP72 | -0.163 | 1 | 0 | AWRI796_3178 | SIC1 | -0.179 | 1 | 0 |
| AWRI796_1516 | YFR006W | -0.164 | 1 | 0 | AWRI796_3393 | YLR345W | -0.179 | 1 | 0 |
| AWRI796_4114 | TCB2 | -0.164 | 1 | 0 | AWRI796_5120 | MRP2 | -0.179 | 1 | 0 |
| AWRI796_4874 | TBF1 | -0.164 | 1 | 0 | AWRI796_5149 | ARR3 | -0.179 | 1 | 0 |
| AWRI796_0754 | MED2 | -0.165 | 1 | 0 | AWRI796_1733 | YBP2 | -0.18 | 1 | 0 |
| AWRI796_0965 | AMD2 | -0.165 | 1 | 0 | AWRI796_1810 | TIM21 | -0.18 | 1 | 0 |
| AWRI796_1232 | PCM1 | -0.165 | 1 | 0 | AWRI796_1822 | UFD1 | -0.18 | 1 | 0 |
| AWRI796_1433 | YER158C | -0.165 | 1 | 0 | AWRI796_0460 | RRP7 | -0.181 | 1 | 0 |
| AWRI796_1834 | COX18 | -0.165 | 1 | 0 | AWRI796_0976 | CHL4 | -0.181 | 1 | 0 |
| AWRI796_2345 | AIM19 | -0.165 | 1 | 0 | AWRI796_1651 | CDC43 | -0.181 | 1 | 0 |
| AWRI796_2535 | NCA3 | -0.165 | 1 | 0 | AWRI796_2280 | COA1 | -0.181 | 1 | 0 |
| AWRI796_3161 | REX2 | -0.165 | 1 | 0 | AWRI796_2347 | SDS3 | -0.181 | 1 | 0 |
| AWRI796_4448 | GLO4 | -0.165 | 1 | 0 | AWRI796_2574 | YJL070C | -0.181 | 1 | 0 |
| AWRI796_0423 | APM3 | -0.166 | 1 | 0 | AWRI796_2875 | MIF2 | -0.181 | 1 | 0 |
| AWRI796_1694 | RMD9 | -0.166 | 1 | 0 | AWRI796_4971 | HST2 | -0.181 | 1 | 0 |
| AWRI796_1859 | PRP31 | -0.166 | 1 | 0 | AWRI796_0254 | PHO5 | -0.182 | 1 | 0 |
| AWRI796_2056 | APM2 | -0.166 | 1 | 0 | AWRI796_1960 | SLI1 | -0.182 | 1 | 0 |
| AWRI796_2194 | IGO2 | -0.166 | 1 | 0 | AWRI796_2827 | RPT1 | -0.182 | 1 | 0 |
| AWRI796_4462 | SLD7 | -0.166 | 1 | 0 | AWRI796_4377 | PRE6 | -0.182 | 1 | 0 |
| AWRI796_4499 | OST2 | -0.166 | 1 | 0 | AWRI796_4432 | SFM1 | -0.182 | 1 | 0 |
| AWRI796-0739 | MRX9 | -0.167 | 1 | 0 | AWRI796-4477 | RTS2 | -0.182 | 1 | 0 |
| AWRI796_3055 | YLL058W | -0.167 | 1 | 0 | AWRI796_5023 | MCM16 | -0.182 | 1 | 0 |
| AWRI796_3192 | NYV1 | -0.167 | 1 | 0 | AWRI796_0191 | SCO2 | -0.183 | 1 | 0 |
| AWRI796_3343 | DBP9 | -0.167 | 1 | 0 | AWRI796_1417 | MAG1 | -0.183 | 1 | 0 |
| AWRI796_3481 | RIF2 | -0.167 | 1 | 0 | AWRI796_1506 | SEC4 | -0.183 | 1 | 0 |
| AWRI796_4008 | RAP1 | -0.167 | 1 | 0 | AWRI796_1607 | YPT32 | -0.183 | 1 | 0 |
| AWRI796_0909 | UBC1 | -0.168 | 1 | 0 | AWRI796_2446 | YIR035C | -0.183 | 1 | 0 |
| AWRI796_1670 | PCL10 | -0.168 | 1 | 0 | AWRI796_3131 | SED5 | -0.183 | 1 | 0 |
| AWRI796_1784 | CUL3 | -0.168 | 1 | 0 | AWRI796_3736 | OSW5 | -0.183 | 1 | 0 |
| AWRI796_1882 | COG2 | -0.168 | 1 | 0 | AWRI796_5197 | cos3 | -0.183 | 1 | 0 |
| AWRI796_1922 | PUS6 | -0.168 | 1 | 0 | AWRI796_0644 | BPL1 | -0.184 | 1 | 0 |
| AWRI796_3238 | SPE4 | -0.168 | 1 | 0 | AWRI796_0773 | YDR018C | -0.184 | 1 | 0 |
| AWRI796-4469 | ALG8 | -0.168 | 1 | 0 | AWRI796_1520 | UBP6 | -0.184 | 1 | 0 |
| AWRI796_4819 | YPL191C | -0.168 | 1 | 0 | AWRI796_1521 | MIC19 | -0.184 | 1 | 0 |
| AWRI796_5003 | AGC1 | -0.168 | 1 | 0 | AWRI796_3574 | RCF1 | -0.184 | 1 | 0 |
| AWRI796_0338 | NTC20 | -0.169 | 1 | 0 | AWRI796_3873 | YKU70 | -0.184 | 1 | 0 |
| AWRI796_1027 | RAD34 | -0.169 | 1 | 0 | AWRI796_4548 | PET123 | -0.184 | 1 | 0 |
| AWRI796_1856 | CTT1 | -0.169 | 1 | 0 | AWRI796_4569 | GSP2 | -0.184 | 1 | 0 |
| AWRI796_2249 | LNP1 | -0.169 | 1 | 0 | AWRI796_0458 | MXR2 | -0.185 | 1 | 0 |
| AWRI796_2635 | MHO1 | -0.17 | 1 | 0 | AWRI796_1357A | YER076C | -0.185 | 1 | 0 |
| AWRI796_2699 | BIR1 | -0.17 | 1 | 0 | AWRI796_1661 | MRF1 | -0.185 | , | 0 |
| AWRI796_2869 | YJU2 | -0.17 | 1 | 0 | AWRI796_2191 | ARP1 | -0.185 | 1 | 0 |
| AWRI796_3756 | ALD3 | -0.17 | 1 | 0 | AWRI796_2406 | DOT5 | -0.185 | , | 0 |
| AWRI796_4297 | TRM13 | -0.17 | 1 | 0 | AWRI796_2512 | IDS2 | -0.185 | 1 | 0 |
| AWRI796_0049 | NTG1 | -0.171 | 1 | 0 | AWRI796_2550 | SAP185 | -0.185 | 1 | 0 |
| AWRI796_0189 | POA1 | -0.171 | 1 | 0 | AWRI796_3720 | YMR130W | -0.185 | , | 0 |
| AWRI796_0380 | THI2 | -0.171 | 1 | 0 | AWRI796_4398 | IRC10 | -0.185 | 1 | 0 |
| AWRI796_1150 | PFA5 | -0.171 | 1 | 0 | AWRI796_2126 | FYV4 | -0.186 | 1 | 0 |
| AWRI796_2835 | APL2 | -0.171 | 1 | 0 | AWRI796_4944 | VPS16 | -0.186 | , | 0 |
| AWRI796_3730 | SIP5 | -0.171 | 1 | 0 | AWRI796_0476 | ILV6 | -0.187 | 1 | 0 |
| AWRI796_4354 | APM4 | -0.171 | 1 | 0 | AWRI796_0523 | CTR86 | -0.187 | 1 | 0 |
| AWRI796_4740 | PHR1 | -0.171 | 1 | 0 | AWRI796_1517 | YFH7 | -0.187 | , | 0 |
| AWRI796_5104 | YPR148C | -0.171 | 1 | 0 | AWRI796_1841 | ENV11 | -0.187 | , | 0 |
| AWRI796_1582 | DOC1 | -0.172 | 1 | 0 | AWRI796_2530 | LSM1 | -0.187 | 1 | 0 |
| AWRI796_1947 | YPP1 | -0.172 | 1 | 0 | AWRI796_0094 | MRP21 | -0.188 | 1 | 0 |
| AWRI796_2371 | PCL7 | -0.172 | 1 | 0 | AWRI796_0124 | PIN4 | -0.188 | 1 | 0 |
| AWRI796_2742 | ном6 | -0.172 | 1 | 0 | AWRI796_0384 | GPX2 | -0.188 | 1 | 0 |
| AWRI796_4309 | MDY2 | -0.172 | 1 | 0 | AWRI796_3646 | CSM3 | -0.188 | 1 | 0 |
| AWRI796_0099 | BOI1 | -0.173 | 1 | 0 | AWRI796_3809 | YMR226C | -0.188 | 1 | 0 |
| AWRI796_0297 | ADH5 | -0.173 | 1 | 0 | AWRI796_4026 | YNL194C | -0.188 | 1 | 0 |
| AWRI796_0517 | IMG1 | -0.173 | 1 | 0 | AWRI796_0681 | BUG1 | -0.189 | , | 0 |
| AWRI796_0704 | YET3 | -0.173 | 1 | 0 | AWRI796_0906 | HMO1 | -0.189 | 1 | 0 |
| AWRI796_1321 | YEN1 | -0.173 | , | 0 | AWRI796_1106 | MRP20 | -0.189 | 1 | 0 |
| AWRI796_2186 | EPT1 | -0.173 | 1 | 0 | AWRI796_1188 | LPP1 | -0.189 | 1 | 0 |
| AWRI796_2536 | ASF1 | -0.173 | 1 | 0 | AWRI796_2534 | PH086 | -0.189 | 1 | 0 |
| AWRI796_2549 | CHS6 | -0.173 | 1 | 0 | AWRI796_2676 | CBF1 | -0.189 | 1 | 0 |
| AWRI796_3568 | YML037C | -0.173 | 1 | 0 | AWRI796_2929 | PAN3 | -0.189 | 1 | 0 |
| AWRI796_0678 AWRI796_161 | POL3 PRP3 | -0.174 -0.174 | 1 1 | 0 0 | AWRI796_3711 AWRI796_610 | ADE17 HES1 | -0.189 -0.189 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{l o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_5012 | NTO1 | -0.189 | 1 | 0 | AWRI796_3453 | RPN13 | -0.202 | 1 | 0 |
| AWRI796_1042 | GPI8 | -0.19 | 1 | 0 | AWRI796_3483 | PDP3 | -0.202 | 1 | 0 |
| AWRI796_1398 | SCS2 | -0.19 | 1 | 0 | AWRI796_4845 | YPL162C | -0.202 | 1 | 0 |
| AWRI796_1654 | NUT1 | -0.19 | 1 | 0 | AWRI796_0080 | MIX23 | -0.203 | 1 | 0 |
| AWRI796_1772 | SCL1 | -0.19 | 1 | 0 | AWRI796_0334 | MBA1 | -0.203 | 1 | 0 |
| AWRI796_1836 | VHT1 | -0.19 | 1 | 0 | AWRI796_1317 | PHM8 | -0.203 | 1 | 0 |
| AWRI796_1932 | RNR4 | -0.19 | 1 | 0 | AWRI796_1702 | USE1 | -0.203 | 1 | 0 |
| AWRI796_2385 | CST6 | -0.19 | 1 | 0 | AWRI796_3287 | PNP1 | -0.203 | 1 | 0 |
| AWRI796_2444 | MGA2 | -0.19 | 1 | 0 | AWRI796_3288 | CLB4 | -0.203 | 1 | 0 |
| AWRI796_4410 | PFA4 | -0.19 | 1 | 0 | AWRI796_3923 | ATP11 | -0.203 | 1 | 0 |
| AWRI796_4427 | ERP4 | -0.19 | 1 | 0 | AWRI796_3976 | TEX1 | -0.203 | 1 | 0 |
| AWRI796_4501 | VAM3 | -0.19 | 1 | 0 | AWRI796_4440 | HMS1 | -0.203 | 1 | 0 |
| AWRI796_0398 | RGD1 | -0.191 | 1 | 0 | AWRI796_4568 | SER1 | -0.203 | 1 | 0 |
| AWRI796_0703 | AHK1 | -0.191 | 1 | 0 | AWRI796_5054 | MDM36 | -0.203 | 1 | 0 |
| AWRI796_0794 | RPC11 | -0.191 | 1 | 0 | AWRI796_0349 | DER1 | -0.204 | 1 | 0 |
| AWRI796_1879 | SPT6 | -0.191 | 1 | 0 | AWRI796_1992 | PUP2 | -0.204 | 1 | 0 |
| AWRI796_1920 | TRS65 | -0.191 | 1 | 0 | AWRI796_1996 | MTM1 | -0.204 | 1 | 0 |
| AWRI796_2816 | KDX1 | -0.191 | 1 | 0 | AWRI796_3748 | HLJ1 | -0.204 | 1 | 0 |
| AWRI796_4226 | PET494 | -0.191 | 1 | 0 | AWRI796_4772 | SRP68 | -0.204 | 1 | 0 |
| AWRI796_5039 | UBA3 | -0.191 | 1 | 0 | AWRI796_4924 | BTS1 | -0.204 | 1 | 0 |
| AWRI796_0194 | YPK3 | -0.192 | 1 | 0 | AWRI796_5136 | ATG13 | -0.204 | 1 | 0 |
| AWRI796_0268 | ALG1 | -0.192 | 1 | 0 | AWRI796_0469 | KCC4 | -0.205 | 1 | 0 |
| AWRI796_0818 | SNF11 | -0.192 | 1 | 0 | AWRI796_0755 | ATP16 | -0.205 | 1 | 0 |
| AWRI796_0920 | SLY1 | -0.192 | 1 | 0 | AWRI796_1291 | YER010C | -0.205 | 1 | 0 |
| AWRI796_1574 | RMR1 | -0.192 | 1 | 0 | AWRI796_0549 | YCR090C | -0.206 | 1 | 0 |
| AWRI796_3472 | SIR3 | -0.192 | 1 | 0 | AWRI796_0695 | SUB2 | -0.206 | 1 | 0 |
| AWRI796_4429 | ROD1 | -0.192 | 1 | 0 | AWRI796_2653 | PET191 | -0.206 | 1 | 0 |
| AWRI796_1156 | PKH3 | -0.193 | 1 | 0 | AWRI796_3824 | RPL20A | -0.206 | 1 | 0 |
| AWRI796_2383 | NOT3 | -0.193 | 1 | 0 | AWRI796_3872 | RIT1 | -0.206 | 1 | 0 |
| AWRI796_3571 | SRC1 | -0.193 | 1 | 0 | AWRI796_4396 | ESC8 | -0.206 | 1 | 0 |
| AWRI796_3667 | IRC21 | -0.193 | 1 | 0 | AWRI796_0019 | YAL044W-A | -0.207 | 1 | 0 |
| AWRI796_4524 | YOR131C | -0.193 | 1 | 0 | AWRI796_0228 | ECM2 | -0.207 | 1 | 0 |
| AWRI796_0048 | TPD3 | -0.194 | 1 | 0 | AWRI796_0894 | CWC15 | -0.207 | 1 | 0 |
| AWRI796_0098 | YBL086C | -0.194 | 1 | 0 | AWRI796_1339 | PET117 | -0.207 | 1 | 0 |
| AWRI796_0206 | FAT1 | -0.194 | 1 | 0 | AWRI796_1815 | KSS1 | -0.207 | 1 | 0 |
| AWRI796_2572 | PSF2 | -0.194 | 1 | 0 | AWRI796_3110 | SSL1 | -0.207 | 1 | 0 |
| AWRI796_3224 | ACE2 | -0.194 | 1 | 0 | AWRI796_4881 | VPS30 | -0.207 | 1 | 0 |
| AWRI796_3305 | CDC42 | -0.194 | 1 | 0 | AWRI796_4926 | YPL067C | -0.207 | 1 | 0 |
| AWRI796_3655 | SAM37 | -0.194 | 1 | 0 | AWRI796_1320 | GLN3 | -0.208 | 1 | 0 |
| AWRI796_4217 | SOL1 | -0.194 | 1 | 0 | AWRI796_2365 | SNP1 | -0.208 | 1 | 0 |
| AWRI796_4662 | TIM18 | -0.194 | 1 | 0 | AWRI796_2555 | SRS2 | -0.208 | 1 | 0 |
| AWRI796_5018 | ERV2 | -0.194 | 1 | 0 | AWRI796_2560 | TRL1 | -0.208 | 1 | 0 |
| AWRI796_1592 | SHE10 | -0.195 | 1 | 0 | AWRI796_3771 | HSC82 | -0.208 | 1 | 0 |
| AWRI796_1845 | PEX8 | -0.195 | 1 | 0 | AWRI796_4449 | CUE5 | -0.208 | 1 | 0 |
| AWRI796_2689 | MOG1 | -0.195 | 1 | 0 | AWRI796_4843 | MLH3 | -0.208 | 1 | 0 |
| AWRI796_3533 | BET5 | -0.195 | 1 | 0 | AWRI796_0643 | CRD1 | -0.209 | 1 | 0 |
| AWRI796_4104 | OCA1 | -0.195 | 1 | 0 | AWRI796_0726 | MTF2 | -0.209 | 1 | 0 |
| AWRI796_4658 | RPS 10A | -0.195 | 1 | 0 | AWRI796_1247 | YEF1 | -0.209 | 1 | 0 |
| AWRI796_5053 | DIB1 | -0.195 | 1 | 0 | AWRI796_1729 | MRH4 | -0.209 | 1 | 0 |
| AWRI796_0319 | PEX32 | -0.196 | 1 | 0 | AWRI796_3323 | SYM1 | -0.209 | 1 | 0 |
| AWRI796_0884 | CTH1 | -0.196 | 1 | 0 | AWRI796_4189 | SWM2 | -0.209 | 1 | 0 |
| AWRI796_1025 | SSF2 | -0.196 | 1 | 0 | AWRI796_4916 | RPL21B | -0.209 | 1 | 0 |
| AWRI796_1181 | VPS3 | -0.196 | 1 | 0 | AWRI796_0492 | YCR016W | -0.21 | 1 | 0 |
| AWRI796_1379 | UBC6 | -0.196 | 1 | 0 | AWRI796_0683 | RPN6 | -0.21 | 1 | 0 |
| AWRI796_2630 | MRX12 | -0.196 | 1 | 0 | AWRI796_1600 | FRA2 | -0.21 | 1 | 0 |
| AWRI796_3437 | BDF1 | -0.196 | 1 | 0 | AWRI796_2143 | NMD2 | -0.21 | 1 | 0 |
| AWRI796_3605 | TAF4 | -0.196 | 1 | 0 | AWRI796_2215 | LAM1 | -0.21 | 1 | 0 |
| AWRI796_3624 | UBC7 | -0.196 | 1 | 0 | AWRI796_4162 | ARK1 | -0.21 | 1 | 0 |
| AWRI796_3777 | GYL1 | -0.196 | 1 | 0 | AWRI796_5148 | ARR2 | -0.21 | 1 | 0 |
| AWRI796_4972 | CIP1 | -0.196 | 1 | 0 | AWRI796_0057 | ERP2 | -0.211 | 1 | 0 |
| AWRI796_0682 | SNU23 | -0.197 | 1 | 0 | AWRI796_3215 | SRN2 | -0.211 | 1 | 0 |
| AWRI796_1157 | TLG1 | -0.197 | 1 | 0 | AWRI796_3451 | YLR419W | -0.211 | 1 | 0 |
| AWRI796_1346 | VHR2 | -0.197 | 1 | 0 | AWRI796_3556 | YML053C | -0.211 | 1 | 0 |
| AWRI796_1807 | POP6 | -0.197 | 1 | 0 | AWRI796_2263 | SKN7 | -0.212 | 1 | 0 |
| AWRI796_2121 | COX6 | -0.197 | 1 | 0 | AWRI796_2448 | GTT1 | -0.212 | 1 | 0 |
| AWRI796_2557 | DPB11 | -0.197 | 1 | 0 | AWRI796_2615 | PET130 | -0.212 | 1 | 0 |
| AWRI796_2649 | YJR030C | -0.197 | 1 | 0 | AWRI796_2728 | RPS5 | -0.212 | 1 | 0 |
| AWRI796_2955 | OSH6 | -0.197 | 1 | 0 | AWRI796_2926 | TFA1 | -0.212 | 1 | 0 |
| AWRI796_2994 | PET10 | -0.197 | 1 | 0 | AWRI796_3256 | IDP2 | -0.212 | 1 | 0 |
| AWRI796_4035 | MRPL19 | -0.197 | 1 | 0 | AWRI796_3577 | YOX1 | -0.212 | , | 0 |
| AWRI796_0560 | LRG1 | -0.198 | 1 | 0 | AWRI796_4098 | INP52 | -0.212 | 1 | 0 |
| AWRI796_1179 | MZM1 | -0.198 | 1 | 0 | AWRI796_4185 | DOM34 | -0.212 | 1 | 0 |
| AWRI796_1570 | FZF1 | -0.198 | 1 | 0 | AWRI796_0246 | TEC1 | -0.213 | 1 | 0 |
| AWRI796_2200 | YHR138C | -0.198 | 1 | 0 | AWRI796_0542 | AHC2 | -0.213 | , | 0 |
| AWRI796_3648 | FAR3 | -0.198 | 1 | 0 | AWRI796_1357B | YER076C | -0.213 | 1 | 0 |
| AWRI796-3760 | DDR48 | -0.198 | 1 | 0 | AWRI796_1468 | EMP47 | -0.213 | 1 | 0 |
| AWRI796_4367 | RRT8 | -0.198 | 1 | 0 | AWRI796_2413 | YIL001W | -0.213 | 1 | 0 |
| AWRI796_4933 | GRX5 | -0.198 | 1 | 0 | AWRI796_3075 | IRC19 | -0.213 | 1 | 0 |
| AWRI796_0232 | BAP2 | -0.199 | 1 | 0 | AWRI796_4987 | PDH1 | -0.213 | 1 | 0 |
| AWRI796_0576 | FMP45 | -0.199 | 1 | 0 | AWRI796_0479 | PGS1 | -0.214 | 1 | 0 |
| AWRI796_2377 | AGE2 | -0.199 | 1 | 0 | AWRI796_0702 | BRE1 | -0.214 | 1 | 0 |
| AWRI796_3957 | BOR1 | -0.199 | 1 | 0 | AWRI796_0854 | TMA64 | -0.214 | , | 0 |
| AWRI796_4588 | NPT1 | -0.199 | 1 | 0 | AWRI796_0897 | SEC5 | -0.214 | 1 | 0 |
| AWRI796_4593 | RUD3 | -0.199 | 1 | 0 | AWRI796_1907 | YGR149W | -0.214 | , | 0 |
| AWRI796_0251 | RFC5 | -0.2 | 1 | 0 | AWRI796_1956 | SER2 | -0.214 | , | 0 |
| AWRI796_0719 | PBP4 | -0.2 | 1 | 0 | AWRI796_1976 | YHB1 | -0.214 | 1 | 0 |
| AWRI796_1549 | ERJ5 | -0.2 |  |  | AWRI796_2061 | YLF2 | -0.214 | , | 0 |
| AWRI796_1816 | BUD9 | -0.2 | 1 | 0 | AWRI796_3409 | GRX8 | -0.214 | 1 | 0 |
| AWRI796_2857 | SLD2 | -0.2 | 1 | 0 | AWRI796_4532 | ARP8 | -0.214 | 1 | 0 |
| AWRI796_3928 | STB1 | -0.2 | , | 0 | AWRI796_4539 | SMP3 | -0.214 | , | 0 |
| AWRI796_3966 | PDR17 | -0.2 | 1 | 0 | AWRI796-4939 | OAZ1 | -0.214 | , | 0 |
| AWRI796_0632 | CLB3 | -0.201 | 1 | 0 | AWRI796_5040 | ISA2 | -0.214 | 1 | 0 |
| AWRI796_0873 | HPR1 | -0.201 | 1 | 0 | AWRI796_5075 | DBF20 | -0.214 | 1 | 0 |
| AWRI796_3640 | YET2 | -0.201 | 1 | 0 | AWRI796_0361 | YBP1 | -0.215 | 1 | 0 |
| AWRI796_3686 | CTF13 | -0.201 | 1 | 0 | AWRI796_0898 | TAF10 | -0.215 | 1 | 0 |
| AWRI796_3725 | GID8 | -0.201 | 1 | 0 | AWRI796_3715 | STO1 | -0.215 | 1 | 0 |
| AWRI796_3779 | ICY1 | -0.201 | 1 | 0 | AWRI796_3975 | RTC4 | -0.215 | 1 | 0 |
| AWRI796_4336 | ATG19 | -0.201 | 1 | 0 | AWRI796_4229 | YNR048W | -0.215 | 1 | 0 |
| AWRI796-4496 | KTR1 | -0.201 | 1 | 0 | AWRI796-4437 | STII | -0.215 | , | 0 |
| AWRI796_5100 | KAR3 | -0.201 | 1 | 0 | AWRI796_0350 | MCM7 | -0.216 | 1 | 0 |
| AWRI796_5125 | YPR172W | -0.201 | 1 | 0 | AWRI796_2168 | GRE3 | -0.216 | 1 | 0 |
| AWRI796_0575 | HBT1 | -0.202 | 1 | 0 | AWRI796-2609 | BET4 | -0.216 | 1 | 0 |
| AWRI796_1338 | HMF1 | -0.202 | 1 | 0 | AWRI796_3202 | LCL2 | -0.216 | 1 | 0 |
| AWRI796_1372 | MET6 | -0.202 | 1 | 0 | AWRI796_0026 | CDC19 | -0.217 | 1 | 0 |
| AWRI796_1432 | COG3 | -0.202 | , |  | AWRI796-0618 | PAR32 | -0.217 | 1 | 0 |
| AWRI796_2639 AWRI796_2913 | YJR012C PRI2 | -0.202 -0.202 | 1 1 | 0 0 | AWRI796_3446 AWRI796_4120 | BER1 TPM1 | -0.217 -0.217 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_4597 | MCT1 | -0.217 | 1 | 0 | AWRI796_4976 | RET3 | -0.237 | 1 | 0 |
| AWRI796_0486 | RVS161 | -0.218 | 1 | 0 | AWRI796_0927 | CBS2 | -0.238 | 1 | 0 |
| AWRI796_1122 | CAD1 | -0.218 | 1 | 0 | AWRI796_2380 | GVP36 | -0.238 | 1 | 0 |
| AWRI796_1290 | NTF2 | -0.218 | 1 | 0 | AWRI796_2855 | KTI12 | -0.238 | 1 | 0 |
| AWRI796_1848 | TWF1 | -0.218 | 1 | 0 | AWRI796_3531 | YML079W | -0.238 | 1 | 0 |
| AWRI796_2334 | FMC1 | -0.218 | 1 | 0 | AWRI796_3643 | MCM1 | -0.238 | 1 | 0 |
| AWRI796_2509 | DAS1 | -0.218 | 1 | 0 | AWRI796_3995 | PDR16 | -0.238 | 1 | 0 |
| AWRI796_3234 | PuT1 | -0.218 | 1 | 0 | AWRI796_4303 | RRI2 | -0.238 | 1 | 0 |
| AWRI796_0741 | DIA3 | -0.219 | 1 | 0 | AWRI796_0352 | LDH1 | -0.239 | 1 | 0 |
| AWRI796_2248 | CTF8 | -0.219 | 1 | 0 | AWRI796_2941 | ARC19 | -0.239 | 1 | 0 |
| AWRI796_2565 | ARP4 | -0.219 | 1 | 0 | AWRI796_3440 | SEII | -0.239 | 1 | 0 |
| AWRI796_2647 | MDE1 | -0.219 | 1 | 0 | AWRI796_0602 | NUS1 | -0.24 | 1 | 0 |
| AWRI796_3262 | SAM1 | -0.219 | 1 | 0 | AWRI796_0621 | UGX2 | -0.24 | 1 | 0 |
| AWRI796_0179 | IPP1 | -0.22 | 1 | 0 | AWRI796_1048 | MRPS28 | -0.24 | 1 | 0 |
| AWRI796_0853 | MRPL1 | -0.22 | 1 | 0 | AWRI796_2757 | YJR154W | -0.24 | 1 | 0 |
| AWRI796_1024 | TFB1 | -0.22 | 1 | 0 | AWRI796_3357 | ATP14 | -0.24 | 1 | 0 |
| AWRI796_2006 | HUA1 | -0.22 | 1 | 0 | AWRI796_3980 | MPA43 | -0.24 | 1 | 0 |
| AWRI796_2066 | YAP3 | -0.22 | 1 | 0 | AWRI796_4222 | YNR040W | -0.24 | 1 | 0 |
| AWRI796_2310 | AYR1 | -0.22 | 1 | 0 | AWRI796_0961 | MRPL7 | -0.241 | 1 | 0 |
| AWRI796_3108 | CMS1 | -0.22 | 1 | 0 | AWRI796_1028 | IPK1 | -0.241 | 1 | 0 |
| AWRI796_4073 | EAF7 | -0.22 | 1 | 0 | AWRI796_3947 | SEC21 | -0.241 | 1 | 0 |
| AWRI796_4973 | MRPS16 | -0.22 | 1 | 0 | AWRI796_4326 | YPQ1 | -0.241 | 1 | 0 |
| AWRI796_5086 | AXL1 | -0.22 | 1 | 0 | AWRI796_4675 | RPL20B | -0.241 | 1 | 0 |
| AWRI796_0880 | SWI5 | -0.221 | 1 | 0 | AWRI796_4899 | INA17 | -0.241 | 1 | 0 |
| AWRI796_0928 | RKM2 | -0.221 | 1 | 0 | AWRI796_1067 | ESC2 | -0.242 | 1 | 0 |
| AWRI796_2231 | ATG7 | -0.221 | 1 | 0 | AWRI796_1167 | DIG2 | -0.242 | 1 | 0 |
| AWRI796_2467 | YJL206C | -0.221 | 1 | 0 | AWRI796_1914 | MTR3 | -0.242 | 1 | 0 |
| AWRI796_2596 | AIM22 | -0.221 | 1 | 0 | AWRI796_2213 | SPO16 | -0.242 | 1 | 0 |
| AWRI796_4332 | AWRI796_4332 | -0.221 | 1 | 0 | AWRI796_2850 | SBA1 | -0.242 | 1 | 0 |
| AWRI796_2468 | RCY1 | -0.222 | 1 | 0 | AWRI796_4125 | MLF3 | -0.242 | 1 | 0 |
| AWRI796_2694 | AIM24 | -0.222 | 1 | 0 | AWRI796_4932 | MFM1 | -0.242 | 1 | 0 |
| AWRI796_0054 | MDM10 | -0.223 | 1 | 0 | AWRI796_0950 | HTA1 | -0.243 | 1 | 0 |
| AWRI796_0690 | NUR1 | -0.223 | 1 | 0 | AWRI796_0558 | YCR101C | -0.244 | 1 | 0 |
| AWRI796_1957 | TRX2 | -0.223 | 1 | 0 | AWRI796_1590 | EMC4 | -0.244 | 1 | 0 |
| AWRI796_2421 | PRII | -0.223 | 1 | 0 | AWRI796_1765 | JAC1 | -0.244 | 1 | 0 |
| AWRI796_2942 | PRP40 | -0.223 | 1 | 0 | AWRI796_1797 | UGA1 | -0.244 | 1 | 0 |
| AWRI796_3275 | NMT1 | -0.223 | 1 | 0 | AWRI796_2028 | Cos8 | -0.244 | 1 | 0 |
| AWRI796_4118 | PMS1 | -0.223 | 1 | 0 | AWRI796_2695 | EAF6 | -0.244 | 1 | 0 |
| AWRI796_0095 | AVT5 | -0.224 | 1 | 0 | AWRI796_3471 | RPS1A | -0.244 | 1 | 0 |
| AWRI796_1133 | GP119 | -0.224 | 1 | 0 | AWRI796_4072 | NAM9 | -0.244 | 1 | 0 |
| AWRI796_1649 | ARII | -0.224 | 1 | 0 | AWRI796_4979 | TFC8 | -0.244 | 1 | 0 |
| AWRI796_1665 | FLC3 | -0.224 | 1 | 0 | AWRI796_0803 | EMC10 | -0.245 | 1 | 0 |
| AWRI796_2270 | AWRI796_2270 | -0.224 | 1 | 0 | AWRI796_3425 | SWC7 | -0.245 | 1 | 0 |
| AWRI796_2888 | LHS1 | -0.224 | 1 | 0 | AWRI796_4259 | MAN2 | -0.245 | 1 | 0 |
| AWRI796_3314 | ARV1 | -0.224 | 1 | 0 | AWRI796_4679 | FAA1 | -0.245 | 1 | 0 |
| AWRI796_3524 | UFO1 | -0.224 | 1 | 0 | AWRI796_4846 | BEM4 | -0.245 | 1 | 0 |
| AWRI796_1499 | IES1 | -0.225 | 1 | 0 | AWRI796_0706 | BDF2 | -0.246 | 1 | 0 |
| AWRI796_3672 | CTF18 | -0.225 | 1 | 0 | AWRI796_1135 | LRS4 | -0.246 | 1 | 0 |
| AWRI796_4522 | AFI1 | -0.225 | 1 | 0 | AWRI796_1544 | CDC26 | -0.246 | 1 | 0 |
| AWRI796_0011 | PEX22 | -0.226 | 1 | 0 | AWRI796_1971 | DIE2 | -0.246 | 1 | 0 |
| AWRI796_1693 | YGL108C | -0.226 | 1 | 0 | AWRI796_2381 | APQ12 | -0.246 | 1 | 0 |
| AWRI796_3731 | RPL13B | -0.226 | 1 | 0 | AWRI796_2902 | TOA2 | -0.246 | 1 | 0 |
| AWRI796_4557 | LCB4 | -0.226 | 1 | 0 | AWRI796_2983 | DID2 | -0.246 | 1 | 0 |
| AWRI796_4580 | BFR1 | -0.226 | 1 | 0 | AWRI796_3595 | YAP1 | -0.246 | 1 | 0 |
| AWRI796_4985 | HAT1 | -0.226 | 1 | 0 | AWRI796_3627 | PEX12 | -0.246 | 1 | 0 |
| AWRI796_0596 | MGT1 | -0.227 | 1 | 0 | AWRI796_0220 | YBR056W | -0.247 | 1 | 0 |
| AWRI796_1187 | SAM2 | -0.227 | 1 | 0 | AWRI796_2435 | INA22 | -0.247 | 1 | 0 |
| AWRI796_1455 | FMP10 | -0.227 | 1 | 0 | AWRI796_2872 | BUD2 | -0.247 | 1 | 0 |
| AWRI796_3082 | PAU17 | -0.227 | 1 | 0 | AWRI796_3722 | JLP2 | -0.247 | 1 | 0 |
| AWRI796_0487 | ADY2 | -0.228 | 1 | 0 | AWRI796_0064 | RFA1 | -0.248 | 1 | 0 |
| AWRI796_0761 | RCR2 | -0.228 | 1 | 0 | AWRI796_0313 | CSH1 | -0.248 | 1 | 0 |
| AWRI796_1747 | YGL041W-A | -0.228 | 1 | 0 | AWRI796_1490 | EPL1 | -0.248 | 1 | 0 |
| AWRI796_2337 | PRK1 | -0.228 | 1 | 0 | AWRI796_2853 | RAD27 | -0.248 | 1 | 0 |
| AWRI796_3352 | GUF1 | -0.228 | 1 | 0 | AWRI796_3126 | IRC25 | -0.248 | 1 | 0 |
| AWRI796_3361 | EXG1 | -0.228 | 1 |  | AWRI796_3366 | CDA1 | -0.248 | 1 | 0 |
| AWRI796_3520 | GIM5 | -0.228 | 1 | 0 | AWRI796_4788 | YPL225W | -0.248 | 1 | 0 |
| AWRI796_4794 | PCL8 | -0.228 | 1 | 0 | AWRI796_0282 | ATG14 | -0.249 | 1 | 0 |
| AWRI796_1547 | OSW7 | -0.229 | 1 | 0 | AWRI796_0721 | LHP1 | -0.249 | 1 | 0 |
| AWRI796_3996 | ELA1 | -0.229 | 1 | 0 | AWRI796_0816 | PAA1 | -0.249 | 1 | 0 |
| AWRI796_5007 | CCL1 | -0.229 | 1 | 0 | AWRI796_1031 | MCM21 | -0.249 | 1 | 0 |
| AWRI796_1991 | GCN5 | -0.23 | 1 | 0 | AWRI796_1980 | PEX21 | -0.249 | 1 | 0 |
| AWRI796_3848 | AWRI796_3848 | -0.23 | 1 | 0 | AWRI796_3572 | RAD52 | -0.249 | 1 | 0 |
| AWRI796_4055 | ASI2 | -0.23 | 1 | 0 | AWRI796_3618 | SOK2 | -0.249 | 1 | 0 |
| AWRI796_4798 | CBP3 | -0.23 | 1 | 0 | AWRI796_4307 | SKM1 | -0.249 | 1 | 0 |
| AWRI796_4982 | LSP1 | -0.23 | 1 | 0 | AWRI796_4687 | SNC2 | -0.249 | 1 | 0 |
| AWRI796_2898 | MSN4 | -0.231 | , | 0 | AWRI796_2429 | MET28 | -0.25 | 1 | 0 |
| AWRI796_4225 | AGA1 | -0.231 | 1 | 0 | AWRI796_3412 | ARC18 | -0.25 | 1 | 0 |
| AWRI796_1552 | YFR045W | -0.232 | 1 | 0 | AWRI796_5088 | YLH47 | -0.25 | 1 | 0 |
| AWRI796_3566 | VPS71 | -0.232 | 1 | 0 | AWRI796_3547 | MFT1 | -0.251 | 1 | 0 |
| AWRI796_4601 | ISU2 | -0.232 | 1 | 0 | AWRI796_4105 | RAS2 | -0.251 | 1 | 0 |
| AWRI796_1010 | HDA2 | -0.233 | 1 | 0 | AWRI796_4286 | CDC33 | -0.251 | 1 | 0 |
| AWRI796_2430 | YAP5 | -0.233 | 1 | 0 | AWRI796_4879 | RNY1 | -0.251 | 1 | 0 |
| AWRI796_2601 | NSP1 | -0.233 | 1 | 0 | AWRI796_1746 | DST1 | -0.252 | 1 | 0 |
| AWRI796_2711 | VPS25 | -0.233 | 1 | 0 | AWRI796_1934 | TIM13 | -0.252 | 1 | 0 |
| AWRI796_3636 | MIH1 | -0.233 | 1 | 0 | AWRI796_4878 | SPC29 | -0.252 | 1 | 0 |
| AWRI796_3744 | AIM36 | -0.233 | 1 | 0 | AWRI796_0709 | PEX19 | -0.253 | 1 | 0 |
| AWRI796_4510 | TRS33 | -0.233 | 1 | 0 | AWRI796_0820 | PPH3 | -0.253 | 1 | 0 |
| AWRI796_1639 | SUA5 | -0.234 | , | 0 | AWRI796_1019 | YDR306C | -0.253 | 1 | 0 |
| AWRI796_1908 | CCM1 | -0.234 | 1 | 0 | AWRI796_3656 | RNA14 | -0.253 | 1 | 0 |
| AWRI796_3355 | SEC72 | -0.235 | 1 | 0 | AWRI796_4145 | YNL050C | -0.253 | 1 | 0 |
| AWRI796_3597 | TRM12 | -0.235 | , | 0 | AWRI796_4194 | CSE2 | -0.253 | 1 | 0 |
| AWRI796_4681 | GNT1 | -0.235 | 1 | 0 | AWRI796_4723 | RAD17 | -0.253 | 1 | 0 |
| AWRI796_0348 | BEM1 | -0.236 | 1 | 0 | AWRI796_5188 | PHO12 | -0.253 | 1 | 0 |
| AWRI796_1604 | SKI8 | -0.236 | 1 | 0 | AWRI796_0922 | HST4 | -0.254 | 1 | 0 |
| AWRI796_1838 | YGR067C | -0.236 | 1 | 0 | AWRI796_1739 | ERV14 | -0.254 | 1 | 0 |
| AWRI796_1939 | BUB1 | -0.236 | 1 | 0 | AWRI796_2173 | CTM1 | -0.254 | 1 | 0 |
| AWRI796_2372 | DFG10 | -0.236 | 1 | 0 | AWRI796_5001 | RLF2 | -0.254 | 1 | 0 |
| AWRI796_2795 | ASH1 | -0.236 | 1 | 0 | AWRI796_1223 | DSF1 | -0.256 | 1 | 0 |
| AWRI796_2892 | YKL069W | -0.236 | 1 | 0 | AWRI796_1296 | FAA2 | -0.256 | 1 | 0 |
| AWRI796_2989 | YKR041W | -0.236 | 1 | 0 | AWRI796_1444 | ADK2 | -0.256 | 1 | 0 |
| AWRI796_3621 | STB4 | -0.236 | 1 | 0 | AWRI796_2599 | YJL043W | -0.256 | 1 | 0 |
| AWRI796_3946 | CAF40 | -0.236 | , | 0 | AWRI796_3358 | YLR297W | -0.256 | 1 | 0 |
| AWRI796_4386 | MDM38 | -0.236 | 1 | 0 | AWRI796_3382 | NMA1 | -0.256 | 1 | 0 |
| AWRI796_4962 | SKS1 | -0.236 | 1 | 0 | AWRI796_3768 | SSO2 | -0.256 | 1 | 0 |
| AWRI796_0397 | YBR259W | -0.237 | 1 | 0 | AWRI796_4076 | FYV6 | -0.256 | 1 | 0 |
| AWRI796_1173 AWRI796_4323 | VPS60 HMI1 | -0.237 -0.237 | 1 1 | 0 | AWRI796_4651 AWRI796_0680 | RDL2 GET3 | -0.256 -0.257 | 1 | 0 |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_1558 | RPN12 | -0.257 | 1 | 0 | AWRI796_4940 | ARL3 | -0.277 | 1 |  |
| AWRI796_2423 | DSN1 | -0.257 | 1 | 0 | AWRI796_0429 | PCA1 | -0.278 | 1 |  |
| AWRI796_2744 | YJR141W | -0.257 | 1 | 0 | AWRI796_0777 | CIS1 | -0.278 | 1 |  |
| AWRI796_4019 | SPS19 | -0.257 | 1 | 0 | AWRI796_0915 | PLP1 | -0.278 | 1 |  |
| AWRI796_4535 | ELG1 | -0.257 | 1 | 0 | AWRI796_2539 | GZF3 | -0.278 | 1 |  |
| AWRI796_5031 | TFB4 | -0.257 | 1 | 0 | AWRI796_5147 | ARR1 | -0.278 | 1 |  |
| AWRI796_1460 | YER187W | -0.258 | 1 | 0 | AWRI796_0579 | YDL218W | -0.279 | 1 |  |
| AWRI796_1825 | YGR053C | -0.258 | 1 | 0 | AWRI796_0689 | RAM1 | -0.279 | 1 |  |
| AWRI796_1911 | CYS4 | -0.258 | 1 | 0 | AWRI796_0762 | RAD57 | -0.279 | 1 |  |
| AWRI796_4436 | BUB3 | -0.258 | 1 | 0 | AWRI796_3930 | MCK1 | -0.279 | 1 |  |
| AWRI796_1158 | SDC1 | -0.259 | 1 | 0 | AWRI796_4619 | APC5 | -0.279 | 1 |  |
| AWRI796_1659 | TIP20 | -0.259 | 1 | 0 | AWRI796_4635 | PNT1 | -0.279 | 1 |  |
| AWRI796_0427 | vba2 | -0.26 | 1 | 0 | AWRI796_5249 | SNO2 | -0.279 | 1 |  |
| AWRI796_0543 | TRX3 | -0.26 | 1 | 0 | AWRI796_4444 | PEP12 | -0.28 | 1 |  |
| AWRI796_1261 | RIP1 | -0.26 | 1 | 0 | AWRI796_5094 | MSS18 | -0.28 | 1 |  |
| AWRI796_1424 | PEA2 | -0.26 | 1 | 0 | AWRI796_1472 | OTU1 | -0.281 | 1 |  |
| AWRI796_2408 | NAS2 | -0.26 | 1 | 0 | AWRI796_1480 | MOB2 | -0.281 | 1 |  |
| AWRI796_3601 | YPT7 | -0.26 | 1 | 0 | AWRI796_2849 | VPH2 | -0.281 | 1 |  |
| AWRI796_0636 | ATG9 | -0.261 | 1 | 0 | AWRI796_3289 | ATG38 | -0.281 | 1 |  |
| AWRI796_0951 | ADK1 | -0.261 | 1 | 0 | AWRI796_4154 | YNL040W | -0.281 | 1 |  |
| AWRI796_2035 | EFM1 | -0.261 | 1 | 0 | AWRI796_4157 | IDH1 | -0.281 | 1 |  |
| AWRI796_2273 | YIL165C | -0.261 | 1 | 0 | AWRI796_4748 | KAR9 | -0.281 | 1 |  |
| AWRI796_2484 | ATP12 | -0.261 | 1 | 0 | AWRI796_1303 | SRB4 | -0.282 | 1 |  |
| AWRI796_3170 | XYL2 | -0.261 | 1 | 0 | AWRI796_2402 | BAR1 | -0.282 | 1 |  |
| AWRI796_3383 | CHS5 | -0.261 | 1 | 0 | AWRI796_2737 | SGM1 | -0.282 | 1 |  |
| AWRI796_4395 | TLG2 | -0.261 | 1 | 0 | AWRI796_4148 | SLM2 | -0.282 | 1 |  |
| AWRI796_4542 | ATG40 | -0.261 | 1 | 0 | AWRI796_4712 | GDS1 | -0.282 | 1 |  |
| AWRI796_4544 | SLP1 | -0.261 | 1 | 0 | AWRI796_1662 | GP110 | -0.283 | 1 |  |
| AWRI796_0879 | TAF12 | -0.262 | 1 | 0 | AWRI796_2591 | IRC8 | -0.283 | 1 |  |
| AWRI796_1215 | FDC1 | -0.262 | 1 | 0 | AWRI796_4176 | YNL011C | -0.283 | 1 |  |
| AWRI796_0430 | PH089 | -0.263 | 1 | 0 | AWRI796_4633 | DSE3 | -0.283 | 1 |  |
| AWRI796_3924 | DAL82 | -0.263 | 1 | 0 | AWRI796_4831 | CUP9 | -0.283 | 1 |  |
| AWRI796_0267 | CMD1 | -0.264 | 1 | 0 | AWRI796_0447 | POF1 | -0.284 | 1 |  |
| AWRI796_1311 | CHZ1 | -0.264 | 1 | 0 | AWRI796_3630 | FAR8 | -0.284 | 1 |  |
| AWRI796_3776 | SPG5 | -0.264 | 1 | 0 | AWRI796_2147 | LRP1 | -0.285 | 1 |  |
| AWRI796_4263 | CSS3 | -0.264 | 1 | 0 | AWRI796_3069 | SDH2 | -0.285 | 1 |  |
| AWRI796_4428 | PET127 | -0.264 | 1 | 0 | AWRI796_5231 | FEX1 | -0.285 | 1 |  |
| AWRI796_4480 | DIA2 | -0.264 | 1 | 0 | AWRI796_0015 | AIM2 | -0.286 | 1 |  |
| AWRI796_4892 | YPL107W | -0.264 | 1 | 0 | AWRI796_2469 | PRP21 | -0.286 | 1 |  |
| AWRI796_1990 | NOP19 | -0.265 | 1 | 0 | AWRI796_4707 | MNE1 | -0.286 | 1 |  |
| AWRI796_3421 | CTF3 | -0.265 | 1 | 0 | AWRI796_0660 | YDL121C | -0.287 | 1 |  |
| AWRI796_3494 | PHO84 | -0.265 | 1 | 0 | AWRI796_0749 | SLX5 | -0.287 | 1 |  |
| AWRI796_0165 | PDR3 | -0.266 | 1 | 0 | AWRI796_1334 | PIC2 | -0.287 | 1 |  |
| AWRI796_0564 | PHO13 | -0.266 | 1 | 0 | AWRI796_1878 | DAM1 | -0.287 | 1 |  |
| AWRI796_0692 | LUC7 | -0.266 | 1 | 0 | AWRI796_4017 | RTT106 | -0.287 | 1 |  |
| AWRI796_1185 | LCD1 | -0.266 | 1 | 0 | AWRI796_0913 | SAS4 | -0.288 | 1 |  |
| AWRI796_5085 | TH122 | -0.266 | 1 | 0 | AWRI796_3184 | ARP6 | -0.288 | 1 |  |
| AWRI796_0815 | DOA4 | -0.267 | 1 | 0 | AWRI796_3191 | SUL2 | -0.288 | 1 |  |
| AWRI796_1872 | VOA1 | -0.267 | 1 | 0 | AWRI796_3205 | REX3 | -0.288 | 1 |  |
| AWRI796_2520 | GLG2 | -0.267 | 1 | 0 | AWRI796_3247 | MAS1 | -0.288 | 1 |  |
| AWRI796_5207 | cos3 | -0.267 | 1 | 0 | AWRI796_5121 | MET16 | -0.288 | 1 |  |
| AWRI796_0462 | BIK1 | -0.268 | 1 | 0 | AWRI796_5131 | HDA3 | -0.288 |  |  |
| AWRI796_0931 | RAV2 | -0.268 | 1 | 0 | AWRI796_4274 | GRE2 | -0.289 | 1 |  |
| AWRI796_0964 | SNU56 | -0.268 | 1 | 0 | AWRI796_4927 | RGL1 | -0.289 | 1 |  |
| AWRI796_1579 | TAD1 | -0.268 | 1 | 0 | AWRI796_0656 | PCL2 | -0.29 | 1 |  |
| AWRI796_2127 | VMA22 | -0.268 | 1 | 0 | AWRI796_0591 | YDL206W | -0.291 | 1 |  |
| AWRI796_2441 | DCG1 | -0.268 | 1 | 0 | AWRI796_3766 | YMR181C | -0.291 | 1 |  |
| AWRI796_3152 | YLR050C | -0.268 | 1 | 0 | AWRI796_0290 | YBR137W | -0.292 | 1 |  |
| AWRI796_3548 | PIF1 | -0.268 | 1 | 0 | AWRI796_0631 | CMR1 | -0.292 | 1 |  |
| AWRI796_3709 | SHH3 | -0.268 | 1 | 0 | AWRI796_1456 | FAU1 | -0.292 | 1 |  |
| AWRI796_4493 | ARF3 | -0.268 | 1 | 0 | AWRI796_1814 | ORM1 | -0.292 | 1 |  |
| AWRI796_0972 | YDR249C | -0.269 | 1 | 0 | AWRI796_1954 | MVB12 | -0.292 | 1 |  |
| AWRI796_1076 | FRQ1 | -0.269 | 1 | 0 | AWRI796_3661 | UBX4 | -0.292 | 1 |  |
| AWRI796_2062 | OTU2 | -0.269 | 1 | 0 | AWRI796_4824 | UIP4 | -0.292 | 1 |  |
| AWRI796_3745 | MRPS8 | -0.269 | 1 | 0 | AWRI796_1921 | YGR168C | -0.293 | 1 |  |
| AWRI796_4763 | VIK1 | -0.269 | 1 | 0 | AWRI796_3080 | ISA1 | -0.293 | 1 |  |
| AWRI796_0717 | PSA1 | -0.27 | 1 | 0 | AWRI796_3486 | Cos3 | -0.293 | 1 |  |
| AWRI796_0851 | PDS1 | -0.27 | 1 | 0 | AWRI796_5165 | AWRI796_5165 | -0.293 | 1 |  |
| AWRI796_1415 | EMP65 | -0.27 | 1 | 0 | AWRI796_1721 | MPS2 | -0.294 | 1 |  |
| AWRI796_2589 | PEP8 | -0.27 | 1 | 0 | AWRI796_4445 | CYC2 | -0.294 | 1 |  |
| AWRI796_2681 | ARP3 | -0.27 | 1 | 0 | AWRI796_5127 | YPR174C | -0.294 | 1 |  |
| AWRI796_3417 | PSY3 | -0.27 | 1 | 0 | AWRI796_0356 | AME1 | -0.295 | 1 |  |
| AWRI796_4029 | DUG3 | -0.27 | 1 | 0 | AWRI796_1515 | SAD1 | -0.295 | 1 |  |
| AWRI796_4062 | INN1 | -0.27 | 1 | 0 | AWRI796_4660 | UAF30 | -0.295 | 1 |  |
| AWRI796_4335 | ATG34 | -0.27 | 1 | 0 | AWRI796_5122 | NUT2 | -0.295 | 1 |  |
| AWRI796_5132 | AOS1 | -0.27 | 1 | 0 | AWRI796_0413 | DPB3 | -0.296 | 1 |  |
| AWRI796_0265 | IML3 | -0.271 | 1 | 0 | AWRI796_1191 | GIN4 | -0.296 | 1 |  |
| AWRI796_1716 | YGL082W | -0.271 | 1 | 0 | AWRI796_2087 | YSC83 | -0.296 | 1 |  |
| AWRI796_3093 | EMC6 | -0.271 | 1 | 0 | AWRI796_2315 | RPI1 | -0.296 | 1 |  |
| AWRI796_3490 | RSC9 | -0.271 | 1 | 0 | AWRI796_3196 | HRT3 | -0.296 | 1 |  |
| AWRI796_4080 | NRK1 | -0.271 | 1 | 0 | AWRI796_4506 | YOR111W | -0.296 | 1 |  |
| AWRI796_1159 | UGO1 | -0.272 | 1 | 0 | AWRI796_5179 | YLR410W-B | -0.296 | 1 |  |
| AWRI796_2846 | SRP21 | -0.272 | 1 | 0 | AWRI796_0304 | SPP381 | -0.297 | 1 |  |
| AWRI796_3592 | RAD33 | -0.272 | 1 | 0 | AWRI796_2084 | SPO13 | -0.298 | 1 |  |
| AWRI796_3770 | RTP1 | -0.272 | 1 | 0 | AWRI796_3781 | VTI1 | -0.298 | 1 |  |
| AWRI796_4083 | SPC98 | -0.272 | 1 | 0 | AWRI796_3813 | PEP5 | -0.298 | 1 |  |
| AWRI796_0679 | DUN1 | -0.273 | 1 | 0 | AWRI796_0302 | TBS1 | -0.299 | 1 |  |
| AWRI796_0120 | PTC3 | -0.274 | 1 | 0 | AWRI796_2071 | HSE1 | -0.299 | 1 |  |
| AWRI796_1064 | GGA1 | -0.274 | 1 | 0 | AWRI796_2401 | SNL1 | -0.299 |  |  |
| AWRI796_1618 | DSD1 | -0.274 | 1 | 0 | AWRI796_3146 | TRX1 | -0.299 | 1 |  |
| AWRI796_2285 | YIL152W | -0.274 | 1 | 0 | AWRI796_0145 | YBL028C | -0.3 | 1 |  |
| AWRI796_0952 | SIR4 | -0.275 | 1 | 0 | AWRI796_0827 | STN1 | -0.3 | 1 |  |
| AWRI796_3295 | COA4 | -0.275 | 1 | 0 | AWRI796_0929 | VPS64 | -0.3 | 1 |  |
| AWRI796_3880 | HER2 | -0.275 | 1 | 0 | AWRI796_1777 | COG7 | -0.3 | 1 |  |
| AWRI796_4278 | PSF3 | -0.275 | 1 | 0 | AWRI796_1916 | RTS3 | -0.3 | 1 |  |
| AWRI796_4678 | COT1 | -0.275 | 1 | 0 | AWRI796_2354 | SER33 | -0.3 | 1 |  |
| AWRI796_5245 | YOL103W-B | -0.275 | 1 | 0 | AWRI796_0677 | QRI1 | -0.302 | 1 |  |
| AWRI796_1002 | YDR286C | -0.276 | 1 | 0 | AWRI796_2724 | ILM1 | -0.302 | 1 |  |
| AWRI796_2651 | CPR7 | -0.276 | 1 | 0 | AWRI796_3197 | CHA4 | -0.302 | 1 |  |
| AWRI796_2723 | STE24 | -0.276 | 1 | 0 | AWRI796_4984 | SNF8 | -0.302 | 1 |  |
| AWRI796_0284 | SHE3 | -0.277 | , | 0 | AWRI796_1594 | мTC3 | -0.303 | 1 |  |
| AWRI796_0442 | PBN1 | -0.277 | 1 | 0 | AWRI796_1710 | LIF1 | -0.303 | 1 |  |
| AWRI796_0757 | NHP10 | -0.277 | 1 | 0 | AWRI796_2198 | SPL2 | -0.303 | 1 |  |
| AWRI796_3484 | NBP1 | -0.277 | 1 | 0 | AWRI796_3088 | AWRI796_3088 | -0.303 | 1 |  |
| AWRI796_3629 | TAP42 | -0.277 | 1 | 0 | AWRI796_4786 | ALG5 | -0.303 | 1 |  |
| AWRI796_4096 AWRI796_443 | YNL108C SHE4 | -0.277 -0.277 | 1 1 | 0 0 | AWRI796_3462 AWRI796_3916 | $\stackrel{\text { ATG23 }}{\text { FIG4 }}$ | -0.304 -0.304 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\mathbf{1 o g}_{2}$ Fold Change | Adj. $p$-value | Sc |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_4534 | THI80 | -0.304 | 1 | 0 | AWRI796_5037 | YPR063C | -0.332 | 1 |  |
| AWRI796_4773 | IQG1 | -0.304 | 1 | 0 | AWRI796_2910 | ELM1 | -0.333 | 1 |  |
| AWRI796_0003 | FLO5 | -0.305 | 1 | 0 | AWRI796_4371 | PEX15 | -0.334 | 1 |  |
| AWRI796_2858 | YKL107W | -0.305 | 1 | 0 | AWRI796_0554 | OCA4 | -0.335 | 1 |  |
| AWRI796_3339 | CMG1 | -0.305 | 1 | 0 | AWRI796_1414 | RTR1 | -0.335 | 1 |  |
| AWRI796_0396 | POP4 | -0.306 | 1 | 0 | AWRI796_3059 | YLL054C | -0.335 | 1 |  |
| AWRI796_2593 | CHM7 | -0.306 | 1 | 0 | AWRI796_3379 | CWC24 | -0.335 | 1 |  |
| AWRI796_2814 | PIR3 | -0.306 | 1 | 0 | AWRI796_0670 | TMA17 | -0.336 | 1 |  |
| AWRI796_4365 | GAL11 | -0.306 | 1 | 0 | AWRI796_1755 | CGR1 | -0.336 | 1 |  |
| AWRI796_4587 | PTP2 | -0.306 | 1 | 0 | AWRI796_1931 | OKP1 | -0.336 | 1 |  |
| AWRI796_4758 | THI21 | -0.307 | 1 | 0 | AWRI796_4081 | TEP1 | -0.336 | 1 |  |
| AWRI796_0315 | EXO5 | -0.308 | 1 | 0 | AWRI796_4179 | ASI3 | -0.336 | 1 |  |
| AWRI796_0443 | LRE1 | -0.308 | 1 | 0 | AWRI796_4190 | VPS27 | -0.336 | 1 |  |
| AWRI796_0638 | RPN5 | -0.308 | 1 | 0 | AWRI796_1898 | CBF2 | -0.337 | 1 |  |
| AWRI796_1062 | SPC110 | -0.308 | 1 | 0 | AWRI796_4540 | MRPL23 | -0.337 | 1 |  |
| AWRI796_4439 | DFG16 | -0.308 | 1 | 0 | AWRI796_4643 | RIM20 | -0.337 | 1 |  |
| AWRI796_0945 | MFB1 | -0.309 | 1 | 0 | AWRI796_2519 | TIF2 | -0.338 | 1 |  |
| AWRI796_2856 | HAP4 | -0.309 | 1 | 0 | AWRI796_2074 | NEM1 | -0.339 | 1 |  |
| AWRI796_3898 | ELP6 | -0.309 | 1 | 0 | AWRI796_1513 | YPI1 | -0.34 | 1 |  |
| AWRI796_4153 | COG6 | -0.309 | 1 | 0 | AWRI796_0017 | SPC72 | -0.341 | 1 |  |
| AWRI796_5084 | CLB5 | -0.309 | 1 | 0 | AWRI796_1072 | XRS2 | -0.341 | 1 |  |
| AWRI796_0234 | ALG14 | -0.31 | 1 | 0 | AWRI796_2959 | RSC4 | -0.341 | 1 |  |
| AWRI796_2503 | FAR1 | -0.31 | 1 | 0 | AWRI796_5112 | CUR1 | -0.341 | 1 |  |
| AWRI796_4373 | NGL1 | -0.31 | 1 | 0 | AWRI796_0999 | MRX10 | -0.342 | 1 |  |
| AWRI796_0509 | BUD5 | -0.311 | 1 | 0 | AWRI796_1979 | KEL2 | -0.342 | 1 |  |
| AWRI796_2542 | IME2 | -0.311 | 1 | 0 | AWRI796_2632 | APL1 | -0.342 | 1 |  |
| AWRI796_2769 | YRA2 | -0.311 | 1 | 0 | AWRI796_2864 | YPF1 | -0.342 | 1 |  |
| AWRI796_2791 | HYM1 | -0.311 | 1 | 0 | AWRI796_4401 | HTZ1 | -0.342 | 1 |  |
| AWRI796_4961 | AWRI796_4961 | -0.311 | 1 | 0 | AWRI796_4476 | SKI7 | -0.342 | 1 |  |
| AWRI796_2886 | YKL075C | -0.312 | 1 | 0 | AWRI796_1267 | EAF5 | -0.344 | 1 |  |
| AWRI796_2924 | IXR1 | -0.312 | 1 | 0 | AWRI796_3363 | MET17 | -0.344 | 1 |  |
| AWRI796_3491 | ERG13 | -0.312 | 1 | 0 | AWRI796_4127 | RNH201 | -0.344 | 1 |  |
| AWRI796_3965 | IST1 | -0.312 | 1 | 0 | AWRI796_4607 | MGE1 | -0.344 | 1 |  |
| AWRI796_4242 | YNR061C | -0.312 | 1 | 0 | AWRI796_0933 | MSC2 | -0.345 | 1 |  |
| AWRI796_4351 | INP54 | -0.312 | 1 | 0 | AWRI796_3641 | ARA2 | -0.345 | 1 |  |
| AWRI796_4800 | LEA1 | -0.312 | 1 | 0 | AWRI796_4059 | CUZ1 | -0.345 | 1 |  |
| AWRI796_1196 | SLF1 | -0.313 | 1 | 0 | AWRI796_4317 | TPT1 | -0.346 | 1 |  |
| AWRI796_5092 | NAT3 | -0.313 | 1 | 0 | AWRI796_2070 | LAG1 | -0.347 | 1 |  |
| AWRI796_0335 | PCH2 | -0.314 | 1 | 0 | AWRI796_2418 | IST3 | -0.347 | 1 |  |
| AWRI796_3585 | YML018C | -0.314 | 1 | 0 | AWRI796_3960 | SEC2 | -0.347 | 1 |  |
| AWRI796_4812 | YPL199C | -0.314 | 1 | 0 | AWRI796_4572 | IES4 | -0.347 | 1 |  |
| AWRI796_1361 | AIM9 | -0.315 | 1 | 0 | AWRI796_3541 | ITT1 | -0.348 | 1 |  |
| AWRI796_3359 | YHC1 | -0.315 | 1 | 0 | AWRI796_0490 | POL4 | -0.349 | 1 |  |
| AWRI796_4853 | RAD53 | -0.315 | 1 | 0 | AWRI796_1022 | GIC2 | -0.349 | 1 |  |
| AWRI796_0308 | SLI15 | -0.316 | 1 | 0 | AWRI796_1648 | RCK1 | -0.349 | 1 |  |
| AWRI796_4708 | MEK1 | -0.316 | 1 | 0 | AWRI796_0115 | KIP1 | -0.35 | 1 |  |
| AWRI796_4728 | NUD1 | -0.316 | 1 | 0 | AWRI796_1021 | SRB7 | -0.35 | 1 |  |
| AWRI796_0437 | MRC1 | -0.317 | 1 | 0 | AWRI796_1689 | SLD3 | -0.35 | 1 |  |
| AWRI796_0784 | MRH1 | -0.317 | 1 | 0 | AWRI796_1783 | SWC4 | -0.35 | 1 |  |
| AWRI796_1712 | MAD1 | -0.317 | 1 | 0 | AWRI796_3181 | SRL2 | -0.35 | 1 |  |
| AWRI796_1803 | YGR026W | -0.317 | 1 | 0 | AWRI796_3307 | EST1 | -0.35 | 1 |  |
| AWRI796_4277 | PEX11 | -0.317 | 1 | 0 | AWRI796_3563 | PRP39 | -0.35 | 1 |  |
| AWRI796_4528 | IDH2 | -0.317 | 1 | 0 | AWRI796_4012 | VID27 | -0.35 | 1 |  |
| AWRI796_4722 | SCP1 | -0.317 | 1 | 0 | AWRI796_2206 | CRP1 | -0.351 | 1 |  |
| AWRI796_1318 | KRE29 | -0.318 | 1 | 0 | AWRI796_2356 | HOP1 | -0.351 | 1 |  |
| AWRI796_2272 | YIL166C | -0.318 | 1 | 0 | AWRI796_3716 | DLT1 | -0.351 | 1 |  |
| AWRI796_0744 | RPN4 | -0.319 | 1 | 0 | AWRI796_3962 | ALP1 | -0.351 | 1 |  |
| AWRI796_1447 | RAD24 | -0.319 | 1 | 0 | AWRI796_4126 | MSK1 | -0.351 | 1 |  |
| AWRI796_2972 | NTR2 | -0.319 | 1 | 0 | AWRI796_1149 | HEH2 | $-0.352$ | 1 |  |
| AWRI796_3102 | ORC3 | -0.319 | 1 | 0 | AWRI796_2824 | DBR1 | -0.352 | 1 |  |
| AWRI796_3671 | VPS20 | -0.319 | 1 | 0 | AWRI796_3151 | YLR049C | -0.352 | 1 |  |
| AWRI796_0763 | MAF1 | -0.32 | 1 | 0 | AWRI796_3326 | NDL1 | -0.352 | 1 |  |
| AWRI796_4030 | YNL190W | -0.32 | 1 | 0 | AWRI796_4087 | том70 | -0.352 | 1 |  |
| AWRI796_4362 | PSH1 | -0.32 | 1 | 0 | AWRI796_4628 | HNT3 | -0.352 | 1 |  |
| AWRI796_5105 | NCE102 | -0.32 | 1 | 0 | AWRI796_4863 | FRK1 | -0.352 | 1 |  |
| AWRI796_5183 | YOL103W-B | -0.32 | 1 | 0 | AWRI796_1453 | DMC1 | -0.353 | 1 |  |
| AWRI796_0050 | SYN8 | $-0.321$ | 1 | 0 | AWRI796_3057 | YLL056C | -0.353 | 1 |  |
| AWRI796_0842 | STE5 | -0.321 | 1 | 0 | AWRI796_3576 | TSA1 | -0.353 | 1 |  |
| AWRI796_2842 | PGM1 | -0.321 | 1 | 0 | AWRI796_0420 | YBR285W | -0.354 | 1 |  |
| AWRI796_2979 | SET3 | -0.321 | 1 | 0 | AWRI796_0731 | BSC1 | -0.354 | 1 |  |
| AWRI796-3751 | MSS 11 | -0.321 | 1 | 0 | AWRI796_3523 | RPM2 | -0.354 | 1 |  |
| AWRI796_4042 | TDA7 | -0.321 | 1 | 0 | AWRI796_0241 | ECM33 | -0.355 | 1 |  |
| AWRI796_4591 | SAS5 | -0.321 | 1 | 0 | AWRI796_0902 | YDR170W-A | -0.355 | 1 |  |
| AWRI796_0609 | YDL183C | -0.322 | 1 | 0 | AWRI796_1171 | VPS52 | -0.355 | 1 |  |
| AWRI796_2832 | TGL1 | -0.322 | 1 | 0 | AWRI796_1880 | YGR117C | -0.355 | 1 |  |
| AWRI796_0823 | SHU2 | -0.323 | 1 | 0 | AWRI796_2584 | BIT61 | -0.355 | 1 |  |
| AWRI796_2708 | YUH1 | -0.323 | 1 | 0 | AWRI796_1536 | ECO1 | -0.356 | 1 |  |
| AWRI796_2931 | YKL023W | -0.323 | 1 | 0 | AWRI796_3639 | SUB1 | -0.356 | 1 |  |
| AWRI796_3239 | SMD3 | -0.323 | 1 | 0 | AWRI796_4861 | KES1 | -0.356 | 1 |  |
| AWRI796_3805 | YMR221C | -0.323 | 1 | 0 | AWRI796_3538 | COG8 | -0.357 | 1 |  |
| AWRI796_5253 | RDS1 | -0.323 | 1 | 0 | AWRI796_0930 | SPC19 | -0.359 | 1 |  |
| AWRI796_1718 | KXD1 | -0.325 | 1 | 0 | AWRI796_0233 | TAT1 | -0.36 | 1 |  |
| AWRI796_3331 | LCB5 | -0.325 | 1 | 0 | AWRI796_1627 | STR3 | -0.36 | 1 |  |
| AWRI796_4252 | YNR071C | -0.325 | 1 | 0 | AWRI796_1817 | MTE1 | -0.36 | 1 |  |
| AWRI796_4836 | COX10 | -0.325 | 1 | 0 | AWRI796_3603 | MIX17 | -0.36 | 1 |  |
| AWRI796_5045 | NOT5 | -0.325 | 1 | 0 | AWRI796_2498 | JJJ2 | -0.361 | 1 |  |
| AWRI796_1193 | SmT3 | -0.326 | 1 | 0 | AWRI796_4116 | END3 | -0.361 | 1 |  |
| AWRI796-4144 | COG5 | -0.326 | 1 | 0 | AWRI796_1408 | COM2 | -0.362 | 1 |  |
| AWRI796_0291 | YBR138C | -0.327 | 1 | 0 | AWRI796_1732 | DUO1 | -0.362 | 1 |  |
| AWRI796_1435 | SPT2 | -0.327 | 1 | 0 | AWRI796_3014 | ВЕТ3 | -0.362 | 1 |  |
| AWRI796_2661 | VPS55 | -0.327 | 1 | 0 | AWRI796_0100 | CDC27 | -0.363 | 1 |  |
| AWRI796_3623 | MAC1 | -0.327 | 1 | 0 | AWRI796_1634 | BUD13 | -0.365 | 1 |  |
| AWRI796_4611 | YOR238W | -0.327 | 1 | 0 | AWRI796_3999 | CNM67 | -0.365 | 1 |  |
| AWRI796_0408 | HSM3 | -0.328 | 1 | 0 | AWRI796_4590 | STE4 | -0.365 | 1 |  |
| AWRI796_0142 | SHE1 | -0.329 | 1 | 0 | AWRI796_0459 | STE50 | -0.366 | 1 |  |
| AWRI796_2266 | CRG1 | -0.329 | 1 | 0 | AWRI796_2667 | ISY1 | -0.366 | 1 |  |
| AWRI796_2830 | MRP8 | -0.329 | 1 | 0 | AWRI796_4160 | YNL034W | -0.366 | 1 |  |
| AWRI796_4992 | REC8 | -0.329 | 1 | 0 | AWRI796_4709 | TFB6 | -0.366 | 1 |  |
| AWRI796_0258 | MMS4 | -0.33 | 1 | 0 | AWRI796_0860 | INO2 | -0.367 | 1 |  |
| AWRI796_1017 | RSC3 | -0.33 | 1 | 0 | AWRI796_2394 | YIL024C | -0.367 | 1 |  |
| AWRI796_1518 | FAR7 | -0.33 | 1 | 0 | AWRI796_2787 | SDS22 | -0.367 | 1 |  |
| AWRI796_2571 | JEM1 | -0.33 | 1 | 0 | AWRI796_4479 | ATX2 | -0.367 | 1 |  |
| AWRI796_2957 | MRPL13 | -0.33 | 1 | 0 | AWRI796_4577 | SLK19 | -0.367 | 1 |  |
| AWRI796_3743 | TPP1 | -0.33 | 1 | 0 | AWRI796_0630 | YDL157C | -0.368 | 1 |  |
| AWRI796_4167 | SSN8 | -0.33 | 1 | 0 | AWRI796_1671 | ITC1 | -0.368 | 1 |  |
| AWRI796_0281 AWRI796_3703 | VMA2 MED11 | -0.331 -0.332 | 1 1 | 0 | AWRI796_2620 AWRI796_1844 |  | -0.368 -0.369 | 1 |  |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score | AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $p$-value | Score |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| AWRI796_3504 | СTK3 | -0.369 | 1 | 0 | AWRI796_0911 | NVJ3 | -0.411 | 1 | 0 |
| AWRI796_0037 | SAW1 | -0.37 | 1 | 0 | AWRI796_1394 | SLX8 | -0.411 | 1 | 0 |
| AWRI796_1865 | ESP1 | -0.37 | 1 | 0 | AWRI796_3933 | YPT11 | -0.411 | 1 | 0 |
| AWRI796_2638 | YJR011C | -0.37 | 1 | 0 | AWRI796_1383 | RTT105 | -0.413 | 1 | 0 |
| AWRI796_2836 | OCT1 | -0.37 | 1 | 0 | AWRI796_2335 | FYV10 | -0.414 | 1 | 0 |
| AWRI796_1488 | STE2 | -0.371 | 1 | 0 | AWRI796_2524 | AIM23 | -0.414 | 1 | 0 |
| AWRI796_2267 | YHR210C | -0.371 | 1 | 0 | AWRI796_1101 | HPT1 | -0.415 | 1 | 0 |
| AWRI796_0123 | SAS3 | -0.372 | 1 | 0 | AWRI796_0994 | BSC2 | -0.416 | 1 | 0 |
| AWRI796_4090 | MLS1 | -0.372 | 1 | 0 | AWRI796_3778 | MRPL24 | -0.416 | 1 | 0 |
| AWRI796_4475 | UFE1 | -0.372 | 1 | 0 | AWRI796_4011 | RRG9 | -0.417 | 1 | 0 |
| AWRI796_1345 | THO1 | -0.373 | 1 | 0 | AWRI796_0555 | GIT1 | -0.418 | 1 | 0 |
| AWRI796_4389 | IFM1 | -0.373 | 1 | 0 | AWRI796_2890 | YKL071W | -0.418 | 1 | 0 |
| AWRI796_4680 | HSH49 | -0.373 | 1 | 0 | AWRI796_0981 | YAP6 | -0.42 | 1 | 0 |
| AWRI796_2784 | YкT6 | -0.374 | 1 | 0 | AWRI796_0674 | PHO2 | -0.421 | 0.981777 | 0 |
| AWRI796_3604 | MVP1 | -0.375 | 1 | 0 | AWRI796_0912 | SCC2 | -0.421 | 1 | 0 |
| AWRI796_3705 | YMR114C | -0.375 | 1 | 0 | AWRI796_2187 | NDT80 | -0.421 | 1 | 0 |
| AWRI796_0975 | MET32 | -0.377 | 1 | 0 | AWRI796_3659 | KAR5 | -0.421 | 1 | 0 |
| AWRI796_4100 | MET4 | -0.377 | 1 | 0 | AWRI796_3418 | FBP1 | -0.422 | 1 | 0 |
| AWRI796_4955 | SVL3 | -0.377 | 1 | 0 | AWRI796_5144 | YPR196W | -0.423 | 1 | 0 |
| AWRI796_5087 | CTR1 | -0.377 | 1 | 0 | AWRI796_2558 | SIP4 | -0.424 | 1 | 0 |
| AWRI796_0318 | POP7 | -0.378 | 1 | 0 | AWRI796_4312 | INO4 | -0.424 | 1 | 0 |
| AWRI796_1313 | FIR1 | -0.378 | 1 | 0 | AWRI796_4295 | YGK3 | -0.425 | 0.816423 | 0 |
| AWRI796_3002 | RHO4 | -0.378 | 1 | 0 | AWRI796_1203 | AGE1 | -0.426 | 0.748436 | 0 |
| AWRI796_4036 | NPR1 | -0.378 | 1 | 0 | AWRI796_2455 | AGP3 | -0.426 | 1 | 0 |
| AWRI796_4875 | HHO1 | -0.378 | 1 | 0 | AWRI796_4245 | YNR064C | -0.426 | 1 | 0 |
| AWRI796_2179 | COX23 | -0.379 | 1 | 0 | AWRI796_2939 | PUT3 | -0.427 | 1 | 0 |
| AWRI796_2292 | NDC80 | -0.379 | 1 | 0 | AWRI796_1805 | MSP1 | -0.428 | 0.709651 | 0 |
| AWRI796_4867 | GIP3 | -0.379 | 1 | 0 | AWRI796_2511 | MRX5 | -0.428 | 1 | 0 |
| AWRI796_1089 | MUS81 | -0.38 | 1 | 0 | AWRI796_3229 | TIS11 | -0.429 | 1 | 0 |
| AWRI796_1390 | LSM4 | -0.38 | 1 | 0 | AWRI796_3248 | SHH4 | -0.43 | 0.920426 | 0 |
| AWRI796_5095 | CTF4 | -0.38 | 1 | 0 | AWRI796_0582 | GDH2 | -0.431 | 0.468841 | 0 |
| AWRI796_1360 | YER079W | -0.381 | 1 | 0 | AWRI796_1123 | SNX41 | -0.432 | 0.838525 | 0 |
| AWRI796_3246 | RNH203 | -0.381 | 1 | 0 | AWRI796_4078 | том22 | -0.432 | 0.929287 | 0 |
| AWRI796_3769 | ADD37 | -0.381 | 1 | 0 | AWRI796_4563 | MPC54 | -0.432 | 1 | 0 |
| AWRI796_1136 | DOT1 | -0.382 | 1 | 0 | AWRI796_3332 | YPT6 | -0.434 | 0.71729 | 0 |
| AWRI796_3190 | GEP5 | -0.382 | 1 | 0 | AWRI796_2033 | YHL042W | -0.435 | 1 | 0 |
| AWRI796_3028 | DAD2 | -0.383 | 1 | 0 | AWRI796_3607 | AWRI796_3607 | -0.435 | 1 | 0 |
| AWRI796_1850 | TOM20 | -0.384 | 1 | 0 | AWRI796_3408 | NMD4 | -0.436 | 1 | 0 |
| AWRI796_3038 | PTR2 | -0.385 | 1 | 0 | AWRI796_5267 | REP2 | -0.438 | 0.715224 | 0 |
| AWRI796_3347 | ECII | -0.385 | 1 | 0 | AWRI796_1504 | SMC1 | -0.439 | 0.665738 | 0 |
| AWRI796_4937 | LEE1 | -0.385 | 1 | 0 | AWRI796_3036 | SRL3 | -0.439 | 1 | 0 |
| AWRI796_0655 | VCX1 | -0.386 | 1 | 0 | AWRI796_0329 | DTR1 | -0.441 |  | 0 |
| AWRI796_2815 | YKL162C | -0.386 | 1 | 0 | AWRI796_3368 | IMH1 | -0.441 | 0.534392 | 0 |
| AWRI796_0924 | MSS116 | -0.387 | 1 | 0 | AWRI796_0333 | YBR184W | -0.444 | 1 | 0 |
| AWRI796_1821 | TFC4 | -0.387 | 1 | 0 | AWRI796_2962 | YKR011C | -0.444 | 0.699282 | 0 |
| AWRI796_1830 | PEF1 | -0.387 | 1 | 0 | AWRI796_5000 | DSS4 | -0.445 | 1 | 0 |
| AWRI796_3788 | INP1 | -0.387 | 1 | 0 | AWRI796_3364 | ACO1 | -0.446 | 0.535651 | 0 |
| AWRI796_2915 | SPC42 | -0.388 | 1 | 0 | AWRI796_1985 | BRF1 | -0.447 | 0.428319 | 0 |
| AWRI796_3666 | ABF2 | -0.388 | 1 | 0 | AWRI796_3086 | SPA2 | -0.448 | 0.278208 | 0 |
| AWRI796_4292 | YOL131W | -0.388 | 1 | 0 | AWRI796_2475 | CDC6 | -0.449 | 0.877099 | 0 |
| AWRI796_0331 | SMP1 | -0.389 | 1 | 0 | AWRI796_2481 | ATG36 | -0.449 | 0.828033 | 0 |
| AWRI796_0646 | SCM3 | -0.389 | 1 | 0 | AWRI796_2617 | MPS3 | -0.449 | 0.621808 | 0 |
| AWRI796_1735 | RAD6 | -0.389 | 1 | 0 | AWRI796_3076 | YLL032C | -0.451 | 0.467757 | 0 |
| AWRI796_2303 | CSM2 | -0.389 | 1 | 0 | AWRI796_0210 | GIP1 | -0.452 | 0.670663 | 0 |
| AWRI796_2561 | EXO70 | -0.389 | 1 | 0 | AWRI796_1322 | MXR1 | -0.452 | 0.417917 | 0 |
| AWRI796_3252 | UPS2 | -0.389 | 1 | 0 | AWRI796_0790 | RSM10 | -0.453 | 0.253784 | 0 |
| AWRI796_3415 | VID22 | -0.389 | 1 | 0 | AWRI796_3154 | IES3 | -0.453 | 1 | 0 |
| AWRI796_1026 | PIB1 | -0.39 | 1 | 0 | AWRI796_4923 | MUK1 | -0.453 | 0.323065 | 0 |
| AWRI796_0283 | OPY1 | -0.391 | 1 | 0 | AWRI796_4631 | RPN8 | -0.454 | 0.378139 | 0 |
| AWRI796_0198 | EDS1 | -0.392 | 1 | 0 | AWRI796_1633 | SAE2 | -0.456 |  | 0 |
| AWRI796_2241 | SSP1 | -0.392 | 1 | 0 | AWRI796_3137 | RSC58 | -0.456 | 0.486132 | 0 |
| AWRI796_2274 | NIT1 | -0.392 | 1 | 0 | AWRI796_4240 | MNT4 | -0.456 | 0.266345 | 0 |
| AWRI796_2786 | MST1 | -0.392 | 1 | 0 | AWRI796_3660 | Sov1 | -0.457 | 0.286351 | 0 |
| AWRI796_3263 | VTA1 | -0.392 | 1 | 0 | AWRI796_1910 | GTO1 | -0.458 | 0.189786 | 0 |
| AWRI796-4505 | TFC7 | -0.392 | 1 | 0 | AWRI796-0337 | AWRI796_0337 | -0.46 | 1 | 0 |
| AWRI796_1857 | NNF2 | -0.393 | 1 | 0 | AWRI796_3814 | FUS2 | -0.46 | 0.934274 | 0 |
| AWRI796_2156 | YNG2 | -0.394 | 1 | 0 | AWRI796_3926 | SKP2 | $-0.46$ | 0.198533 | 0 |
| AWRI796_3599 | YML003W | -0.395 | 1 | 0 | AWRI796_3637 | MSN2 | -0.461 | 0.180551 | 0 |
| AWRI796_3708 | SPC24 | -0.395 | 1 | 0 | AWRI796_0850 | ALT2 | -0.462 | 0.27149 | 0 |
| AWRI796_3877 | ABZ2 | -0.396 | 1 | 0 | AWRI796_0847 | TRS85 | -0.463 | 0.158011 | 0 |
| AWRI796_3164 | PER33 | -0.398 | 1 | 0 | AWRI796_5194 | COS7 | -0.463 | 0.183422 | 0 |
| AWRI796_4850 | PRM4 | -0.398 | 1 | 0 | AWRI796_2545 | GSM1 | -0.465 | 0.114261 | 0 |
| AWRI796_0984 | YDR262W | -0.399 | 1 | 0 | AWRI796_4349 | RTG1 | -0.467 | 0.336 | 0 |
| AWRI796_1795 | YGR016W | -0.399 | 1 | 0 | AWRI796_0495 | PET18 | -0.47 | 0.189786 | 0 |
| AWRI796_2834 | CMC1 | -0.399 | 1 | 0 | AWRI796_0587 | UGA4 | -0.471 | 0.35127 | 0 |
| AWRI796_0846 | TMN2 | -0.401 | 1 | 0 | AWRI796_0673 | MSS2 | -0.473 | 0.16451 | 0 |
| AWRI796_1230 | CIN8 | -0.401 | 1 | 0 | AWRI796_0713 | RAD59 | -0.473 | 0.466597 | 0 |
| AWRI796_3340 | YCS4 | -0.401 | 1 | 0 | AWRI796_1086 | NKP1 | -0.473 | 0.129153 | 0 |
| AWRI796_0105 | ATG8 | -0.402 | 1 | 0 | AWRI796_0214 | REB1 | -0.474 | 0.050633 | 0 |
| AWRI796_0707 | CBS1 | -0.402 | 1 | 0 | AWRI796_3739 | YIM1 | -0.476 | 0.08006 | 0 |
| AWRI796_4250 | BSC5 | -0.402 | 1 | 0 | AWRI796_2037 | MUP3 | -0.477 | 0.105831 | 0 |
| AWRI796_4329 | HAL9 | -0.402 | 1 | 0 | AWRI796_4032 | KAR1 | -0.477 | 0.340527 | 0 |
| AWRI796_5225 | RSC30 | -0.402 | 1 | 0 | AWRI796_2909 | CSE4 | -0.48 | 0.072352 | 0 |
| AWRI796_2891 | YKL070W | -0.404 | 1 | 0 | AWRI796_4311 | ZEO1 | $-0.48$ | 0.14794 | 0 |
| AWRI796_3559 | AIM32 | -0.404 | 1 | 0 | AWRI796_2672 | HIT1 | -0.483 | 0.28633 | 0 |
| AWRI796_3687 | SNO1 | -0.404 | 1 | 0 | AWRI796_3023 | YKR078W | -0.484 | 0.328566 | 0 |
| AWRI796_4175 | SPO1 | -0.404 | 1 | 0 | AWRI796_0436 | VAC17 | -0.486 | 0.131206 | 0 |
| AWRI796_2358 | MAM33 | -0.405 | 1 | 0 | AWRI796_2980 | GMH1 | -0.486 | 0.632939 | 0 |
| AWRI796_3301 | YLR225C | -0.405 | 1 | 0 | AWRI796_4784 | YPL229W | -0.488 | 0.217029 | 0 |
| AWRI796_3596 | GIS4 | -0.405 | 1 | 0 | AWRI796_4790 | GRE1 | -0.489 | 0.319727 | 0 |
| AWRI796_3682 | YMR090w | -0.405 | 1 | 0 | AWRI796_1220 | YEL073C | -0.492 | 0.979922 | 0 |
| AWRI796_3726 | GAT2 | -0.405 | 1 | 0 | AWRI796_4423 | AUS1 | -0.492 | 0.061083 | 0 |
| AWRI796_0787 | EHD3 | -0.406 | 1 | 0 | AWRI796_2075 | GPA1 | -0.493 | 0.189159 | 0 |
| AWRI796_1731 | PYC1 | -0.406 | 1 | 0 | AWRI796_3698 | SPG4 | -0.493 | 0.044515 | -1 |
| AWRI796_0230 | AWRI796_0230 | -0.407 | 1 | 0 | AWRI796_1829 | LST7 | -0.494 | 0.125244 | 0 |
| AWRI796_1647 | YGL159W | -0.407 | 1 | 0 | AWRI796_1124 | RPN9 | -0.495 | 0.094225 | 0 |
| AWRI796_2393 | IRR1 | -0.407 | 1 | 0 | AWRI796_0770 | RAD61 | -0.496 | 0.087688 | 0 |
| AWRI796_0178 | HHT1 | -0.408 | 1 | 0 | AWRI796_1221 | RMD6 | -0.497 | 0.045503 | -1 |
| AWRI796_2439 | DAL4 | -0.408 | 1 | 0 | AWRI796_2123 | RSC30 | -0.497 | 0.01823 | -1 |
| AWRI796_4027 | YNL193W | -0.408 | 1 | 0 | AWRI796_5069 | COG4 | -0.497 | 0.039632 | -1 |
| AWRI796_2543 | SET4 | $-0.409$ | 1 | 0 | AWRI796_4345 | SDH5 | -0.499 | 0.027096 | -1 |
| AWRI796_2625 | CTK2 | -0.409 | 1 | 0 | AWRI796_4810 | AFT2 | -0.499 | 0.027096 | -1 |
| AWRI796_3764 | SPT21 | -0.409 | 1 | 0 | AWRI796_5184 | YNL284C-A | -0.501 | 0.664532 | 0 |
| AWRI796_0174 | UGA2 | -0.41 | 1 | 0 | AWRI796_2582 | BNA3 | -0.504 | 0.084086 | 0 |
| AWRI796_3584 | OST6 | -0.41 | 1 | 0 | AWRI796_2605 | SNX4 | -0.507 | 0.017166 | -1 |
| AWRI796_3881 AWRI796_455 | JNM1 SWT1 | -0.41 -0.41 | 1 1 | 0 | AWRI796_1567 AWRI796_2802 | ${ }_{\text {MNT2 }}$ | -0.511 -0.512 | 0.019525 0.349035 | -1 0 |


| AWRI796 Gene ID | Gene Name | $\log _{2}$ Fold Change | Adj. $\boldsymbol{p}$-value | Score |
| :---: | :---: | :---: | :---: | :---: |
| AWRI796_5163 | AWRI796_5163 | -0.512 | 0.151927 | 0 |
| AWRI796_2914 | PHD1 | -0.514 | 0.159962 | 0 |
| AWRI796_2660 | POL32 | -0.516 | 0.186218 | 0 |
| AWRI796_0910 | CSN9 | -0.518 | 0.133639 | 0 |
| AWRI796_3155 | YLR053C | -0.518 | 0.02508 | -1 |
| AWRI796_3135 | YLR030W | -0.519 | 0.052916 | 0 |
| AWRI796_4509 | YOR114W | -0.52 | 0.062835 | 0 |
| AWRI796_2489 | RFA3 | -0.524 | 0.018505 | -1 |
| AWRI796_2053 | SPO11 | -0.525 | 0.523722 | 0 |
| AWRI796_0212 | FMP23 | -0.527 | 0.020327 | -1 |
| AWRI796_0771 | HED1 | -0.527 | 0.523678 | 0 |
| AWRI796_2295 | AXL2 | -0.527 | 0.016379 | -1 |
| AWRI796_3207 | AHP1 | -0.528 | 0.551449 | 0 |
| AWRI796_3245 | ACS2 | -0.53 | 0.039159 | -1 |
| AWRI796_4706 | CIN1 | -0.53 | 0.01968 | -1 |
| AWRI796_4750 | ACM1 | -0.53 | 0.27149 | 0 |
| AWRI796_2357 | PCI8 | -0.534 | 0.137441 | 0 |
| AWRI796_1209 | KRE28 | -0.535 | 0.175397 | 0 |
| AWRI796_0027 | YAL037W | -0.536 | 0.015263 | -1 |
| AWRI796_3489 | MSC1 | -0.537 | 0.007361 | -1 |
| AWRI796_0998 | PHM6 | -0.538 | 0.006341 | -1 |
| AWRI796_1356 | PTP3 | -0.539 | 0.050633 | 0 |
| AWRI796_0435 | CHA1 | -0.54 | 0.007852 | 1 |
| AWRI796_0949 | HTB1 | -0.541 | 0.036087 | -1 |
| AWRI796_0185 | GAL7 | -0.543 | 0.045655 | -1 |
| AWRI796_4703 | REV1 | -0.543 | 0.045655 | -1 |
| AWRI796_4433 | YOR022C | -0.544 | 0.010209 | -1 |
| AWRI796_0530 | RAD18 | -0.552 | 0.037903 | -1 |
| AWRI796_4460 | ASE1 | -0.552 | 0.001968 | -1 |
| AWRI796_1189 | PSP1 | -0.555 | 0.001184 | -1 |
| AWRI796_5254 | AAD3 | -0.555 | 0.007255 | -1 |
| AWRI796_1216 | IRC4 | -0.56 | 0.18346 | 0 |
| AWRI796_0065 | SEN34 | -0.561 | 0.008701 | -1 |
| AWRI796_0252 | POL30 | -0.562 | 0.020552 | -1 |
| AWRI796_1819 | RME1 | -0.563 | 0.000825 | -1 |
| AWRI796_3882 | YMR295C | -0.566 | 0.00406 | -1 |
| AWRI796_2670 | BFA1 | -0.569 | 0.048402 | -1 |
| AWRI796_4296 | MDH2 | -0.57 | 0.016343 | -1 |
| AWRI796_0977 | RMD5 | -0.573 | 0.000825 | -1 |
| AWRI796_3619 | SPO20 | -0.579 | 1 | 0 |
| AWRI796_0218 | YRO2 | -0.587 | 0.0013 | -1 |
| AWRI796_3455 | ATG17 | -0.593 | 0.001116 | -1 |
| AWRI796_2217 | REC104 | -0.595 | 0.0706 | 0 |
| AWRI796_1001 | ZIP1 | -0.602 | 0.005723 | -1 |
| AWRI796_3746 | ATG16 | -0.602 | 0.005336 | -1 |
| AWRI796_4066 | YNL146W | -0.606 | 0.022802 | -1 |
| AWRI796_3693 | SRT1 | -0.612 | 0.057732 | 0 |
| AWRI796_1970 | AMA1 | -0.613 | 0.016832 | -1 |
| AWRI796_3109 | THI73 | -0.614 | 0.000125 | -1 |
| AWRI796_2214 | RTT107 | -0.615 | 0.00095 | -1 |
| AWRI796_1553 | CNN1 | -0.616 | 0.000731 | -1 |
| AWRI796_5178 | YOR343W-B | -0.617 | 0.005408 | -1 |
| AWRI796_1533 | PES4 | -0.628 | 0.065204 | 0 |
| AWRI796_3613 | YDR210W-B | -0.629 | 0.050633 | 0 |
| AWRI796_0155 | FUS3 | -0.643 | 0.015286 | -1 |
| AWRI796_2899 | BLI1 | -0.644 | 0.000351 | -1 |
| AWRI796_0593 | RTN2 | -0.663 | 0.000181 | -1 |
| AWRI796_3041 | PCK1 | -0.667 | 0.001633 | -1 |
| AWRI796_3375 | EST2 | -0.668 | $8.30 \mathrm{E}-05$ | -1 |
| AWRI796_3341 | PIG1 | -0.677 | 0.00095 | -1 |
| AWRI796_5180 | YOR192C-A | -0.679 | 0.042947 | -1 |
| AWRI796_0551 | MSH3 | -0.685 | 0.000351 | -1 |
| AWRI796_4576 | PEX27 | -0.696 | 0.000283 | -1 |
| AWRI796_1498 | HSP12 | -0.701 | 0.000163 | -1 |
| AWRI796_2646 | LSM8 | -0.721 | 0.000637 | -1 |
| AWRI796_3688 | SNZ1 | -0.721 | $7.00 \mathrm{E}-05$ | -1 |
| AWRI796_1279 | GIM4 | -0.723 | $4.30 \mathrm{E}-05$ | -1 |
| AWRI796_5177 | YOR343W-A | -0.723 | 0.009878 | -1 |
| AWRI796_1884 | YGR122W | -0.726 | $3.10 \mathrm{E}-05$ | -1 |
| AWRI796_1277 | VAB2 | -0.731 | 0.002214 | -1 |
| AWRI796_4667 | CPA1 | -0.731 | 0.000152 | -1 |
| AWRI796_4039 | RHO5 | -0.738 | 0.001026 | -1 |
| AWRI796_1347 | ICL1 | -0.74 | $4.90 \mathrm{E}-05$ | -1 |
| AWRI796_4261 | COS3 | -0.75 | 0.011501 | -1 |
| AWRI796_3206 | YLR108C | -0.752 | $7.00 \mathrm{E}-06$ | -1 |
| AWRI796_0666 | YDL114W | -0.769 | 0.005858 | -1 |
| AWRI796_4721 | YOR365C | -0.773 | 0.005408 | -1 |
| AWRI796_0235 | YBR071W | -0.8 | $6.40 \mathrm{E}-05$ | -1 |
| AWRI796_3670 | PDS5 | -0.82 | $1.30 \mathrm{E}-05$ | -1 |
| AWRI796_2705 | SFC1 | -0.823 | $1.20 \mathrm{E}-05$ | -1 |
| AWRI796_3058 | YCT1 | -0.831 | $5.60 \mathrm{E}-05$ | -1 |
| AWRI796_2032 | ECM34 | -0.833 | 0.008183 | -1 |
| AWRI796_4868 | ISU1 | -0.897 | $6.40 \mathrm{E}-05$ | -1 |
| AWRI796_0002 | SEO1 | -0.907 | 0.001633 | -1 |
| AWRI796_3144 | AFB1 | -0.911 | 0.004012 | -1 |
| AWRI796_3394 | CIS1 | -0.934 | $2.90 \mathrm{E}-05$ | -1 |
| AWRI796_5038 | ROX1 | -0.994 | 0.000366 | -1 |
| AWRI796_4438 | CIN5 | -0.996 | 0 | -1 |
| AWRI796_1508 | MSH4 | -1.018 | $6.40 \mathrm{E}-05$ | -1 |
| AWRI796_2704 | IME1 | -1.028 | $4.00 \mathrm{E}-06$ | -1 |
| AWRI796_0947 | YDR222W | -1.064 | 0 | -1 |
| AWRI796_0129 | ECM13 | -1.191 | 1.00E-06 | -1 |
| AWRI796_1837 | YGR066C | -1.217 | 0 | -1 |
| AWRI796_1077 <br> AWRI796 4158 | PHO92 <br> NCE103 | -1.495 -1.722 | $3.60 \mathrm{E}-05$ | -1 |

## Bibliography

Adams, A., Gottschling, D. E., Kaiser, C. A., and Stearns, T. (1998). Methods in Yeast Genetics: A Cold Spring Harbor Laboratory Course Manual, 1997 Edition. Cold Spring Harbor Laboratory Press, New York.

Albuquerque, P. and Casadevall, A. (2012). Quorum sensing in fungi - a review. Medical Mycology, 50(4):337-345.

Andreottola, G., Foladori, P., Nardelli, P., and Denicolo, A. (2005). Treatment of winery wastewater in a full-scale fixed bed biofilm reactor. Water Science and Technology, 51(1):71-79.

Antonangelo, A. T. B. F., Alonso, D. P., Ribolla, P. E. M., and Colombi, D. (2013). Microsatellite marker-based assessment of the biodiversity of native bioethanol yeast strains. Yeast, 30(8):307-317.

Azzolini, M., Fedrizzi, B., Tosi, E., Finato, F., Vagnoli, P., Scrinzi, C., and Zapparoli, G. (2012). Effects of Torulaspora delbrueckii and Saccharomyces cerevisiae mixed cultures on fermentation and aroma of Amarone wine. European Food Research and Technology, 235(2):303-313.

Barabási, A.-L. and Oltvai, Z. N. (2004). Network biology: understanding the cell's functional organization. Nature Reviews Genetics, 5(2):101-113.

Bardi, L., Crivelli, C., and Marzona, M. (1998). Esterase activity and release of ethyl esters of medium-chain fatty acids by Saccharomyces cerevisiae during anaerobic growth. Canadian Journal of Microbiology, 44(12):1171-1176.

Barrales, R. R., Jimenez, J., and Ibeas, J. I. (2008). Identification of novel activation mechanisms for FLO11 regulation in Saccharomyces cerevisiae. Genetics, 178(1):145156.

Bauer, F. F. and Pretorius, I. S. (2000). Yeast stress response and fermentation efficiency: how to survive the making of wine - a review. South African Journal for Enology and Viticulture, 21:27-51.

Beese, S. E., Negishi, T., Levin, D. E., Boulton, V., Wagle, M., and der Does, C. V. (2009). Identification of positive regulators of the yeast Fps1 glycerol channel. PLOS Genetics, 5(11):e1000738.

Bell, S.-J. and Henschke, P. A. (2005). Implications of nitrogen nutrition for grapes, fermentation and wine. Australian Journal of Grape and Wine Research, 11(3):242-295.

Binder, B. J., Sundstrom, J. F., Gardner, J. M., Jiranek, V., and Oliver, S. G. (2015). Quantifying two-dimensional filamentous and invasive growth spatial patterns in yeast colonies. PLOS Computational Biology, 11(2):e1004070.

Blackstone, E. and Roth, M. B. (2007). Suspended animation-like state protects mice from lethal hypoxia. Shock, 27(4):370-372.

Blanco, P., Orriols, I., and Losada, A. (2011). Survival of commercial yeasts in the winery environment and their prevalence during spontaneous fermentations. Journal of Industrial Microbiology and Biotechnology, 38(1):235-239.

Bojsen, R. K., Andersen, K. S., and Regenberg, B. (2012). Saccharomyces cerevisiae - a model to uncover molecular mechanisms for yeast biofilm biology. FEMS Immunology and Medical Microbiology, 65(2):169-182.

Bokulich, N. A., Ohta, M., Richardson, P. M., and Mills, D. A. (2013). Monitoring seasonal changes in winery-resident microbiota. PLOS ONE, 8(6):e66437.

Bokulich, N. A., Thorngate, J. H., Richardson, P. M., and Mills, D. A. (2014). Microbial biogeography of wine grapes is conditioned by cultivar, vintage, and climate. Proceedings of the National Academy of Sciences of the United States of America, 111(1):E139-E148.

Booher, R. N., Deshaies, R. J., and Kirschner, M. W. (1993). Properties of Saccharomyces cerevisiae wee1 and its differential regulation of p34 ${ }^{C D C 28}$ in response to $\mathrm{G}_{1}$ and $\mathrm{G}_{2}$ cyclins. The EMBO Journal, 12(9):3417-3426.

Borneman, A. R., Desany, B. A., Riches, D., Affourtit, J. P., Forgan, A. H., Pretorius, I. S., Egholm, M., and Chambers, P. J. (2011). Whole-genome comparison reveals novel genetic elements that characterize the genome of industrial strains of Saccharomyces cerevisiae. PLOS Genetics, 7(2):e1001287.

Borneman, A. R., Forgan, A. H., Kolouchova, R., Fraser, J. A., and Schmidt, S. A. (2016). Whole genome comparison reveals high levels of inbreeding and strain redundancy across the spectrum of commercial wine strains of Saccharomyces cerevisiae. G3: Genes, Genomes, Genetics, 6(4):957-971.

Borneman, A. R., Forgan, A. H., Pretorius, I. S., and Chambers, P. J. (2008). Comparative genome analysis of a Saccharomyces cerevisiae wine strain. FEMS Yeast Research, 8(7):1185-1195.

Braus, G. H., Grundmann, O., Brückner, S., and Mösch, H.-U. (2003). Amino acid starvation and Gcn4p regulate adhesive growth and FLO11 gene expression in Saccharomyces cerevisiae. Molecular Biology of the Cell, 14(10):4272-4284.

Brown, J. A., Sherlock, G., Myers, C. L., Burrows, N. M., Deng, C., Wu, H. I., McCann, K. E., Troyanskaya, O. G., and Brown, J. M. (2006). Global analysis of gene function in yeast by quantitative phenotypic profiling. Molecular Systems Biology, 2:2006.0001.

Brückner, S. and Mösch, H.-U. (2012). Choosing the right lifestyle: adhesion and development in Saccharomyces cerevisiae. FEMS Microbiology Reviews, 36(1):25-58.

Busturia, A. and Lagunas, R. (1986). Catabolite inactivation of the glucose transport system in Saccharomyces cerevisiae. Microbiology, 132(2):379-385.

Calderone, A., Castagnoli, L., and Cesareni, G. (2013). mentha: a resource for browsing integrated protein-interaction networks. Nature Methods, 10(8):690-691.

Campbell, K., Vowinckel, J., and Ralser, M. (2016). Cell-to-cell heterogeneity emerges as consequence of metabolic cooperation in a synthetic yeast community. Biotechnology Journal, 11(9):1169-1178.

Carmack, M., Moore, M. B., and Balis, M. E. (1950). The structure of the antihemorrhagic sodium bisulfite addition product of 2-Methyl-1,4-naphthoquinone (Menadione) ${ }^{1}$. Journal of the American Chemical Society, 72(2):844-847.

Carrozza, M. J., Florens, L., Swanson, S. K., Shia, W.-J., Anderson, S., Yates, J., Washburn, M. P., and Workman, J. L. (2005). Stable incorporation of sequence specific repressors Ash1 and Ume6 into the Rpd3L complex. Biochimica et Biophysica Acta (BBA) - Gene Structure and Expression, 1731(2):77-87.

Casalone, E., Barberio, C., Cappellini, L., and Polsinelli, M. (2005). Characterization of Saccharomyces cerevisiae natural populations for pseudohyphal growth and colony morphology. Research in Microbiology, 156(2):191-200.

Chant, J. and Pringle, J. R. (1995). Patterns of bud-site selection in the yeast Saccharomyces cerevisiae. The Journal of Cell Biology, 129(3):751-765.

Chavel, C. A., Caccamise, L. M., Li, B., and Cullen, P. J. (2014). Global Regulation of a Differentiation MAPK Pathway in Yeast. Genetics, 198(3):1309-1328.

Chen, H. and Fink, G. R. (2006). Feedback control of morphogenesis in fungi by aromatic alcohols. Genes $\mathcal{G}$ Development, 20(9):1150-1161.

Chen, H., Fujita, M., Feng, Q., Clardy, J., and Fink, G. R. (2004). Tyrosol is a quorumsensing molecule in Candida albicans. Proceedings of the National Academy of Sciences of the United States of America, 101(14):5048-5052.

Chen, L., Noorbakhsh, J., Adams, R. M., Samaniego-Evans, J., Agollah, G., Nevozhay, D., Kuzdzal-Fick, J., Mehta, P., and Balázsi, G. (2014). Two-dimensionality of yeast colony expansion accompanied by pattern formation. PLOS Computational Biology, 10(12):e1003979.

Christiaens, J. F., Franco, L. M., Cools, T. L., De Meester, L., Michiels, J., Wenseleers, T., Hassan, B. A., Yaksi, E., and Verstrepen, K. J. (2014). The fungal aroma gene ATF1 promotes dispersal of yeast cells through insect vectors. Cell Reports, 9(2):425-432.

Ciani, M., Comitini, F., Mannazzu, I., and Domizio, P. (2010). Controlled mixed culture fermentation: a new perspective on the use of non-Saccharomyces yeasts in winemaking. FEMS Yeast Research, 10(2):123-133.

Ciani, M., Mannazzu, I., Marinangeli, P., Clementi, F., and Martini, A. (2004). Contribution of winery-resident Saccharomyces cerevisiae strains to spontaneous grape must fermentation. Antonie van Leeuwenhoek, 85(2):159-164.

Clamens, T., Rosay, T., Crépin, A., Grandjean, T., Kentache, T., Hardouin, J., Bortolotti, P., Neidig, A., Mooij, M., Hillion, M., Vieillard, J., Cosette, P., Overhage, J., O’Gara, F., Bouffartigues, E., Dufour, A., Chevalier, S., Guery, B., Cornelis, P., Feuilloley, M. G. J., and Lesouhaitier, O. (2017). The aliphatic amidase AmiE is involved in regulation of Pseudomonas aeruginosa virulence. Scientific Reports, 7:41178.

Codon, A. C., Gasent-Ramirez, J. M., and Benitez, T. (1995). Factors which affect the frequency of sporulation and tetrad formation in Saccharomyces cerevisiae baker's yeasts. Applied and Environment Microbiology, 61(2):630-638.

Comitini, F., Gobbi, M., Domizio, P., Romani, C., Lencioni, L., Mannazzu, I., and Ciani, M. (2011). Selected non-Saccharomyces wine yeasts in controlled multistarter fermentations with Saccharomyces cerevisiae. Food Microbiology, 28(5):873-882.

Cook, J. G., Bardwell, L., and Thorner, J. (1997). Inhibitory and activating functions for MAPK Kss1 in the $S$. cerevisiae filamentous-growth signalling pathway. Nature, 390(6655):85-88.

Corbacho, I., Teixidó, F., Velázquez, R., Hernández, L. M., and Olivero, I. (2011). Standard YPD, even supplemented with extra nutrients, does not always compensate growth defects of Saccharomyces cerevisiae auxotrophic strains. Antonie van Leeuwenhoek, 99(3):591-600.

Cordente, A. G., Heinrich, A., Pretorius, I. S., and Swiegers, J. H. (2009). Isolation of sulfite reductase variants of a commercial wine yeast with significantly reduced hydrogen sulfide production. FEMS Yeast Research, 9(3):446-459.

Cordero-Bueso, G., Arroyo, T., Serrano, A., and Valero, E. (2011). Remanence and survival of commercial yeast in different ecological niches of the vineyard. FEMS Microbiology Ecology, 77(2):429-437.

Costanzo, M., Baryshnikova, A., Bellay, J., Kim, Y., Spear, E. D., Sevier, C. S., Ding, H., Koh, J. L., Toufighi, K., Mostafavi, S., Prinz, J., St. Onge, R. P., VanderSluis, B., Makhnevych, T., Vizeacoumar, F. J., Alizadeh, S., Bahr, S., Brost, R. L., Chen, Y., Cokol, M., Deshpande, R., Li, Z., Lin, Z.-Y., Liang, W., Marback, M., Paw, J., San

Luis, B.-J., Shuteriqi, E., Tong, A. H. Y., van Dyk, N., Wallace, I. M., Whitney, J. A., Weirauch, M. T., Zhong, G., Zhu, H., Houry, W. A., Brudno, M., Ragibizadeh, S., Papp, B., Pál, C., Roth, F. P., Giaever, G., Nislow, C., Troyanskaya, O. G., Bussey, H., Bader, G. D., Gingras, A.-C., Morris, Q. D., Kim, P. M., Kaiser, C. A., Myers, C. L., Andrews, B. J., and Boone, C. (2010). The genetic landscape of a cell. Science, 327(5964):425-431.

Costerton, J. W., Lewandowski, Z., Caldwell, D. E., Korber, D. R., and Lappin-Scott, H. M. (1995). Microbial biofilms. Annual Review of Microbiology, 49(1):711-745.

Cottier, F. and Mühlschlegel, F. A. (2011). Communication in fungi. International Journal of Microbiology, 2012:351832.

Cullen, P. J. and Sprague, G. F. (2000). Glucose depletion causes haploid invasive growth in yeast. Proceedings of the National Academy of Sciences of the United States of America, 97(25):13619-13624.

Cullen, P. J. and Sprague, G. F. (2002). The roles of bud-site-selection proteins during haploid invasive growth in yeast. Molecular Biology of the Cell, 13:2990-3004.

Cullen, P. J. and Sprague, G. F. (2012). The regulation of filamentous growth in yeast. Genetics, 190(1):23-49.

Cutler, N. S., Pan, X., Heitman, J., and Cardenas, M. E. (2001). The TOR signal transduction cascade controls cellular differentiation in response to nutrients. Molecular Biology of the Cell, 12(12):4103-4113.

Davis-Hanna, A., Piispanen, A. E., Stateva, L. I., and Hogan, D. A. (2008). Farnesol and dodecanol effects on the Candida albicans Ras1-cAMP signalling pathway and the regulation of morphogenesis. Molecular Microbiology, 67(1):47-62.

Dickinson, J. R. (1994). Irreversible formation of pseudohyphae by haploid Saccharomyces cerevisiae. FEMS Microbiology Letters, 119(1-2):99-103.

Dickinson, J. R. (1996). 'Fusel' alcohols induce hyphal-like extensions and pseudohyphal formation in yeasts. Microbiology, 142(6):1391-1397.

Dikicioglu, D., Dunn, W. B., Kell, D. B., Kirdar, B., and Oliver, S. G. (2012). Short- and long-term dynamic responses of the metabolic network and gene expression in yeast to a transient change in the nutrient environment. Molecular BioSystems, 8(6):1760-1774.

Dikicioglu, D., Karabekmez, E., Rash, B., Pir, P., Kirdar, B., and Oliver, S. G. (2011). How yeast re-programmes its transcriptional profile in response to different nutrient impulses. BMC Systems Biology, 5(1):148.

Divol, B., du Toit, M., and Duckitt, E. (2012). Surviving in the presence of sulphur dioxide: strategies developed by wine yeasts. Applied Microbiology and Biotechnology, 95(3):601-613.

Doeller, J. E., Isbell, T. S., Benavides, G., Koenitzer, J., Patel, H., Patel, R. P., Lancaster, J. R., Darley-Usmar, V. M., and Kraus, D. W. (2005). Polarographic measurement of hydrogen sulfide production and consumption by mammalian tissues. Analytical Biochemistry, 341(1):40-51.

Domitrovic, T., Kozlov, G., Freire, J. C. G., Masuda, C. A., Almeida, M. d. S., MonteroLomeli, M., Atella, G. C., Matta-Camacho, E., Gehring, K., and Kurtenbach, E. (2010). Structural and functional study of Yer067w, a new protein involved in yeast metabolism control and drug resistance. PLOS ONE, 5(6):e11163.

Dowell, R. D., Ryan, O., Jansen, A., Cheung, D., Agarwala, S., Danford, T., Bernstein, D. A., Rolfe, P. A., Heisler, L. E., Chin, B., Nislow, C., Giaever, G., Phillips, P. C., Fink, G. R., Gifford, D. K., and Boone, C. (2010). Genotype to phenotype: a complex problem. Science, 328(5977):469.

Elshorbagy, A. K., Valdivia-Garcia, M., Mattocks, D. A. L., Plummer, J. D., Orentreich, D. S., Orentreich, N., Refsum, H., and Perrone, C. E. (2013). Effect of taurine and N -acetylcysteine on methionine restriction-mediated adiposity resistance. Metabolism: Clinical \& Experimental, 62(4):509-517.

Finn, R. D., Coggill, P., Eberhardt, R. Y., Eddy, S. R., Mistry, J., Mitchell, A. L., Potter, S. C., Punta, M., Qureshi, M., Sangrador-Vegas, A., Salazar, G. A., Tate, J., and Bateman, A. (2016). The Pfam protein families database: towards a more sustainable future. Nucleic Acids Research, 44(D1):D279-D285.

Fleet, G. and Heard, G. (1993). Yeasts: growth during fermentation. In Fleet, G., editor, Wine Microbiology and Biotechnology, pages 27-75. Harwood Academic Publishers, Chur, Switzerland.

Francis, I. L. and Newton, J. L. (2005). Determining wine aroma from compositional data. Australian Journal of Grape and Wine Research, 11(2):114-126.

Furne, J., Saeed, A., and Levitt, M. D. (2008). Whole tissue hydrogen sulfide concentrations are orders of magnitude lower than presently accepted values. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 295(5):R1479-R1485.

Gardner, J. M., Poole, K., and Jiranek, V. (2002). Practical significance of relative assimilable nitrogen requirements of yeast: a preliminary study of fermentation performance and liberation of $\mathrm{H}_{2} \mathrm{~S}$. Australian Journal of Grape and Wine Research, 8(3):175-179.

Gasch, A. P., Spellman, P. T., Kao, C. M., Carmel-Harel, O., Eisen, M. B., Storz, G., Botstein, D., and Brown, P. O. (2000). Genomic expression programs in the response of yeast cells to environmental changes. Molecular Biology of the Cell, 11(12):4241-4257.

Gayevskiy, V. and Goddard, M. R. (2012). Geographic delineations of yeast communities and populations associated with vines and wines in New Zealand. The ISME Journal, 6(7):1281-1290.

Gietz, R. D. and Schiestl, R. H. (2007). High-efficiency yeast transformation using the LiAc/SS carrier DNA/PEG method. Nature Protocols, 2(1):31-34.

Gimeno, C. J., Ljungdahl, P. O., Styles, C. A., and Fink, G. R. (1992). Unipolar cell divisions in the yeast $S$. cerevisiae lead to filamentous growth: Regulation by starvation and RAS. Cell, 68(6):1077-1090.

Gladfelter, A. S., Kozubowski, L., Zyla, T. R., and Lew, D. J. (2005). Interplay between septin organization, cell cycle and cell shape in yeast. Journal of Cell Science, 118(8):16171628.

Gladfelter, A. S., Zyla, T. R., and Lew, D. J. (2004). Genetic interactions among regulators of septin organization. Eukaryotic Cell, 3(4):847-854.

Gobbi, M., Comitini, F., Domizio, P., Romani, C., Lencioni, L., Mannazzu, I., and Ciani, M. (2013). Lachancea thermotolerans and Saccharomyces cerevisiae in simultaneous and sequential co-fermentation: A strategy to enhance acidity and improve the overall quality of wine. Food Microbiology, 33(2):271-281.

Goddard, M. R., Anfang, N., Tang, R., Gardner, R. C., and Jun, C. (2010). A distinct population of Saccharomyces cerevisiae in New Zealand: evidence for local dispersal by insects and human-aided global dispersal in oak barrels. Environmental Microbiology, 12(1):63-73.

Gori, K., Knudsen, P. B., Nielsen, K. F., Arneborg, N., and Jespersen, L. (2011). Alcohol-based quorum sensing plays a role in adhesion and sliding motility of the yeast Debaryomyces hansenii. FEMS Yeast Research, 11(8):643-652.

Granek, J. A. and Magwene, P. M. (2010). Environmental and genetic determinants of colony morphology in yeast. PLOS Genetics, 6(1):e1000823.

Granek, J. A., Murray, D., Kayrkçi, Ö., and Magwene, P. M. (2013). The genetic architecture of biofilm formation in a clinical isolate of Saccharomyces cerevisiae. Genetics, 193(2):587-600.

Grüning, N.-M., Lehrach, H., and Ralser, M. (2010). Regulatory crosstalk of the metabolic network. Trends in Biochemical Sciences, 35(4):220-227.

Guo, B., Styles, C. A., Feng, Q., and Fink, G. R. (2000). A Saccharomyces gene family involved in invasive growth, cell-cell adhesion, and mating. Proceedings of the National Academy of Sciences of the United States of America, 97(22):12158-12163.

Hall, B., Durall, D. M., and Stanley, G. (2011). Population dynamics of Saccharomyces cerevisiae during spontaneous fermentation at a British Columbia winery. American Journal of Enology and Viticulture, 62(1):66-72.

Halme, A., Bumgarner, S., Styles, C., and Fink, G. R. (2004). Genetic and epigenetic regulation of the $F L O$ gene family generates cell-surface variation in yeast. Cell, 116(3):405-415.

Harashima, T. and Heitman, J. (2002). The G $\alpha$ protein Gpa2 controls yeast differentiation by interacting with Kelch repeat proteins that mimic $\mathrm{G} \beta$ subunits. Molecular Cell, 10(1):163-173.

Harkins, H. A., Pagé, N., Schenkman, L. R., De Virgilio, C., Shaw, S., Bussey, H., and Pringle, J. R. (2001). Bud8p and Bud9p, proteins that may mark the sites for bipolar budding in yeast. Molecular Biology of the Cell, 12(8):2497-2518.

Hasan, F., Xess, I., Wang, X., Jain, N., and Fries, B. C. (2009). Biofilm formation in clinical Candida isolates and its association with virulence. Microbes and Infection, 11(8-9):753-761.

Hazelwood, L. A., Daran, J.-M., van Maris, A. J. A., Pronk, J. T., and Dickinson, J. R. (2008). The Ehrlich pathway for fusel alcohol production: a century of research on Saccharomyces cerevisiae metabolism. Applied and Environmental Microbiology, 74(8):2259-2266.

He, X., Li, S., and Kaminskyj, S. G. W. (2014). Using Aspergillus nidulans to identify antifungal drug resistance mutations. Eukaryotic Cell, 13(2):288-294.

Henke, J. M. and Bassler, B. L. (2004). Bacterial social engagements. Trends in Cell Biology, 14(11):648-656.

Hess, D. C., Myers, C. L., Huttenhower, C., Hibbs, M. A., Hayes, A. P., Paw, J., Clore, J. J., Mendoza, R. M., Luis, B. S., Nislow, C., Giaever, G., Costanzo, M., Troyanskaya, O. G., and Caudy, A. A. (2009). Computationally driven, quantitative experiments discover genes required for mitochondrial biogenesis. PLOS Genetics, 5(3):e1000407.

Hine, C. and Mitchell, J. R. (2015). Calorie restriction and methionine restriction in control of endogenous hydrogen sulfide production by the transsulfuration pathway. Experimental Gerontology, 68:26-32.

Hinze, H. and Holzer, H. (1986). Analysis of the energy metabolism after incubation of Saccharomyces cerevisiae with sulfite or nitrite. Archives of Microbiology, 145(1):27-31.

Homoto, S. and Izawa, S. (2016). Effects of severe ethanol stress on septin-localization and morphology of Saccharomyces cerevisiae. In $14^{\text {th }}$ International Congress on Yeasts Program \& Abstracts, page 250.

Honigberg, S. M. (2011). Cell signals, cell contacts, and the organization of yeast communities. Eukaryotic Cell, 10(4):466-473.

Hope, E. A. and Dunham, M. J. (2014). Ploidy-regulated variation in biofilm-related phenotypes in natural isolates of Saccharomyces cerevisiae. G3: Genes, Genomes, Genetics, 4(9):1773-1786.

Hornby, J. M., Jensen, E. C., Lisec, A. D., Tasto, J. J., Jahnke, B., Shoemaker, R., Dussault, P., and Nickerson, K. W. (2001). Quorum sensing in the dimorphic fungus Candida albicans is mediated by farnesol. Applied and Environmental Microbiology, 67(7):2982-2992.

Hurles, M. E., Matisoo-Smith, E., Gray, R. D., and Penny, D. (2003). Untangling Oceanic settlement: the edge of the knowable. Trends in Ecology $\S \mathcal{E}$ Evolution, 18(10):531-540.

Hwang, G.-W., Furuchi, T., and Naganuma, A. (2007). Ubiquitin-conjugating enzyme Cdc34 mediates cadmium resistance in budding yeast through ubiquitination of the transcription factor Met4. Biochemical E Biophysical Research Communications, 363(3):873-878.

Iranon, N. N. and Miller, D. L. (2012). Interactions between oxygen homeostasis, food availability, and hydrogen sulfide signaling. Frontiers in Genetics, 3:257.

Iraqui, I., Vissers, S., André, B., and Urrestarazu, A. (1999). Transcriptional induction by aromatic amino acids in Saccharomyces cerevisiae. Molecular and Cellular Biology, 19(5):3360-3371.

Jia, X., He, W., Murchie, A. I. H., and Chen, D. (2011). The global transcriptional response of fission yeast to hydrogen sulfide. PLOS ONE, 6(12):e28275.

Jin, R., Dobry, C. J., McCown, P. J., and Kumar, A. (2008). Large-scale analysis of yeast filamentous growth by systematic gene disruption and overexpression. Molecular Biology of the Cell, 19(1):284-296.

Jiranek, V., Langridge, P., and Henschke, P. A. (1995). Regulation of hydrogen sulfide liberation in wine-producing Saccharomyces cerevisiae strains by assimilable nitrogen. Applied and Environmental Microbiology, 61(2):461-467.

John Hopkins School of Medicine (1999). Quick DAPI staining of yeast.
Johnson, C., Kweon, H. K., Sheidy, D., Shively, C. A., Mellacheruvu, D., Nesvizhskii, A. I., Andrews, P. C., and Kumar, A. (2014). The yeast Sks1p kinase signaling network regulates pseudohyphal growth and glucose response. PLOS Genetics, 10(3):e1004183.

Johnson, J. E. and Johnson, F. B. (2014). Methionine restriction activates the retrograde response and confers both stress tolerance and lifespan extension to yeast, mouse and human cells. PLOS ONE, 9(5):e97729.

Johnson, J. W., Fisher, J. F., and Mobashery, S. (2013). Bacterial cell-wall recycling. Annals of the New York Academy of Sciences, 1277(1):54-75.

Karunanithi, S., Joshi, J., Chavel, C., Birkaya, B., Grell, L., and Cullen, P. J. (2012). Regulation of mat responses by a differentiation MAPK pathway in Saccharomyces cerevisiae. PLOS ONE, 7(4):e32294.

Klis, F. M., Boorsma, A., and De Groot, P. W. J. (2006). Cell wall construction in Saccharomyces cerevisiae. Yeast, 23(3):185-202.

Knight, S., Klaere, S., Fedrizzi, B., Goddard, M. R., and Querol, A. (2015). Regional microbial signatures positively correlate with differential wine phenotypes: evidence for a microbial aspect to terroir. Scientific Reports, 5(1):14233.

Koh, J. L. Y., Ding, H., Costanzo, M., Baryshnikova, A., Toufighi, K., Bader, G. D., Myers, C. L., Andrews, B. J., and Boone, C. (2010). DRYGIN: a database of quantitative genetic interaction networks in yeast. Nucleic Acids Research, 38(Database issue):D502-D507.

Kron, S. J., Styles, C. A., and Fink, G. R. (1994). Symmetric cell division in pseudohyphae of the yeast Saccharomyces cerevisiae. Molecular Biology of the Cell, 5(9):1003-1022.

Kubota, S., Takeo, I., Kume, K., Kanai, M., Shitamukai, A., Mizunuma, M., Miyakawa, T., Shimoi, H., Iefuji, H., and Hirata, D. (2004). Effect of ethanol on cell growth of budding yeast: genes that are important for cell growth in the presence of ethanol. Bioscience, Biotechnology, and Biochemistry, 68(4):968-972.

Kuchin, S., Vyas, V. K., and Carlson, M. (2002). Snf1 protein kinase and the repressors Nrg1 and Nrg2 regulate FLO11, haploid invasive growth, and diploid pseudohyphal differentiation. Molecular and Cellular Biology, 22(12):3994-4000.

Kuthan, M., Devaux, F., Janderová, B., Slaninová, I., Jacq, C., and Palková, Z. (2003). Domestication of wild Saccharomyces cerevisiae is accompanied by changes in gene expression and colony morphology. Molecular Microbiology, 47(3):745-754.

Lafuente, M. J., Gancedo, C., Jauniaux, J.-C., and Gancedo, J. M. (2000). Mth1 receives the signal given by the glucose sensors Snf3 and Rgt2 in Saccharomyces cerevisiae. Molecular Microbiology, 35(1):161-172.

Lambrechts, M. and Bauer, F. (1996). Muc1, a mucin-like protein that is regulated by Mss10, is critical for pseudohyphal differentiation in yeast. Proceedings of the National Academy of Sciences of the United States of America, 93(16):8419-8424.

Law, C. W., Chen, Y., Shi, W., and Smyth, G. K. (2014). voom: precision weights unlock linear model analysis tools for RNA-seq read counts. Genome Biology, 15(2):R29.

Lees, E. K., Król, E., Grant, L., Shearer, K., Wyse, C., Moncur, E., Bykowska, A. S., Mody, N., Gettys, T. W., and Delibegovic, M. (2014). Methionine restriction restores a younger metabolic phenotype in adult mice with alterations in fibroblast growth factor 21. Aging Cell, 13(5):817-827.

Liao, Y., Smyth, G. K., and Shi, W. (2013). The Subread aligner: fast, accurate and scalable read mapping by seed-and-vote. Nucleic Acids Research, 41(10):e108.

Lilly, M., Bauer, F. F., Lambrechts, M. G., Swiegers, J. H., Cozzolino, D., and Pretorius, I. S. (2006). The effect of increased yeast alcohol acetyltransferase and esterase activity on the flavour profiles of wine and distillates. Yeast, 23(9):641-659.

Linderholm, A. L., Findleton, C. L., Kumar, G., Hong, Y., and Bisson, L. F. (2008). Identification of genes affecting hydrogen sulfide formation in Saccharomyces cerevisiae. Applied and Environmental Microbiology, 74(5):1418-1427.

Litzinger, S., Duckworth, A., Nitzsche, K., Risinger, C., Wittmann, V., and Mayer, C. (2010). Muropeptide rescue in Bacillus subtilis involves sequential hydrolysis by $\beta-N-$ acetylglucosaminidase and $N$-acetylmuramyl-L-alanine amidase. Journal of Bacteriology, 192(12):3132-3143.

Liu, H., Styles, C. A., and Fink, G. R. (1993). Elements of the yeast pheromone response pathway required for filamentous growth of diploids. Science, 262(5140):1741-1744.

Liu, H., Styles, C. A., and Fink, G. R. (1996). Saccharomyces cerevisiae S288C has a mutation in FLO8, a gene required for filamentous growth. Genetics, 144(3):967-978.

Liu, Z. and Butow, R. A. (2006). Mitochondrial retrograde signaling. Annual Review of Genetics, 40:159-185.

Lloyd, D. (2006). Hydrogen sulfide: clandestine microbial messenger? Trends in Microbiology, 14(10):456-462.

Lo, W. S. and Dranginis, A. M. (1998). The cell surface flocculin Flo11 is required for pseudohyphae formation and invasion by Saccharomyces cerevisiae. Molecular Biology of the Cell, 9(1):161-171.

Lõoke, M., Kristjuhan, K., and Kristjuhan, A. (2011). Extraction of genomic DNA from yeasts for PCR-based applications. BioTechniques, 50(5):325-328.

Lorenz, M. C., Cutler, N. S., and Heitman, J. (2000). Characterization of alcohol-induced filamentous growth in Saccharomyces cerevisiae. Molecular Biology of the Cell, 11(1):183199.

Lorenz, M. C. and Heitman, J. (1998). Regulators of pseudohyphal differentiation in Saccharomyces cerevisiae identified through multicopy suppressor analysis in ammonium permease mutant strains. Genetics, 150(4):1443-1457.

Luyten, K., Riou, C., and Blondin, B. (2002). The hexose transporters of Saccharomyces cerevisiae play different roles during enological fermentation. Yeast, 19(8):713-726.

Malandra, L., Wolfaardt, G., Zietsman, A., and Viljoen-Bloom, M. (2003). Microbiology of a biological contactor for winery wastewater treatment. Water Research, 37(17):41254134.

Mannheim, B. (1989). D-glucose/d-fructose. In Methods of Biochemical Analysis and Food Analysis, pages 50-55. Boehringer Mannheim.

Martineau, C. N., Beckerich, J. M., and Kabani, M. (2007). Flo11p-independent control of "mat" formation by Hsp70 molecular chaperones and nucleotide exchange factors in yeast. Genetics, 177(3):1679-1689.

Martineau, C. N., Melki, R., and Kabani, M. (2010). Swa2p-dependent clathrin dynamics is critical for Flo11p processing and 'Mat' formation in the yeast Saccharomyces cerevisiae. FEBS Letters, 584(6):1149-1155.

Martínez, A., Torello, S., and Kolter, R. (1999). Sliding motility in Mycobacteria. Journal of Bacteriology, 181(23):7331-7338.

Martínez, P., Pérez Rodríguez, L., and Benítez, T. (1997). Velum formation by flor yeasts isolated from sherry wine. American Journal of Enology and Viticulture, 48(1):55-62.

Martini, A. (1993). Origin and domestication of the wine yeast Saccharomyces cerevisiae. Journal of Wine Research, 4(3):165-176.

Martiniuk, J. T., Pacheco, B., Russell, G., Tong, S., Backstrom, I., and Measday, V. (2016). Impact of commercial strain use on Saccharomyces cerevisiae population structure and dynamics in Pinot Noir vineyards and spontaneous fermentations of a Canadian winery. PLOS ONE, 11(8):1-19.

Matsushita, M. and Fujikawa, H. (1990). Diffusion-limited growth in bacterial colony formation. Physica A: Statistical Mechanics and its Applications, 168(1):498-506.

McCarthy, D. J. and Smyth, G. K. (2009). Testing significance relative to a fold-change threshold is a TREAT. Bioinformatics, 25(6):765-771.

Miller, D. L. and Roth, M. B. (2007). Hydrogen sulfide increases thermotolerance and lifespan in Caenorhabditis elegans. Proceedings of the National Academy of Sciences of the United States of America, 104(51):20618-20622.

Miller, M. B. and Bassler, B. L. (2001). Quorum sensing in bacteria. Annual Review of Microbiology, 55(1):165-199.

Miller, R. A., Buehner, G., Chang, Y., Harper, J. M., Sigler, R., and Smith-Wheelock, M. (2005). Methionine-deficient diet extends mouse lifespan, slows immune and lens aging, alters glucose, T4, IGF-I and insulin levels, and increases hepatocyte MIF levels and stress resistance. Aging Cell, 4(3):119-125.

Mitchell, A., Chang, H.-Y., Daugherty, L., Fraser, M., Hunter, S., Lopez, R., McAnulla, C., McMenamin, C., Nuka, G., Pesseat, S., Sangrador-Vegas, A., Scheremetjew, M., Rato, C., Yong, S.-Y., Bateman, A., Punta, M., Attwood, T. K., Sigrist, C. J. A., Redaschi, N., Rivoire, C., Xenarios, I., Kahn, D., Guyot, D., Bork, P., Letunic, I., Gough, J., Oates, M., Haft, D., Huang, H., Natale, D. A., Wu, C. H., Orengo, C.,

Sillitoe, I., Mi, H., Thomas, P. D., and Finn, R. D. (2015). The InterPro protein families database: the classification resource after 15 years. Nucleic Acids Research, 43(Database issue):D213-D221.

Mortimer, R. and Polsinelli, M. (1999). On the origins of wine yeast. Research in Microbiology, 150(3):199-204.

Murray, D. B., Klevecz, R. R., and Lloyd, D. (2003). Generation and maintenance of synchrony in Saccharomyces cerevisiae continuous culture. Experimental Cell Research, 287(1):10-15.

Niederberger, P., Miozzari, G., and Hotte, R. (1981). Biological role of the general control of amino acid biosynthesis in Saccharomyces cerevisiae. Molecular and Cellular Biology, 1(7):584-593.

Ochiai, S., Yasumoto, S., Morohoshi, T., and Ikeda, T. (2014). AmiE, a novel Nacylhomoserine lactone acylase belonging to the amidase family, from the activatedsludge isolate Acinetobacter sp. strain Ooi24. Applied and Environmental Microbiology, 80(22):6919-6925.

Octavio, L. M., Gedeon, K., and Maheshri, N. (2009). Epigenetic and conventional regulation is distributed among activators of FLO11 allowing tuning of population-level heterogeneity in its expression. PLOS Genetics, 5(10):e1000673.

Oliveira, R., Lages, F., Silva-Graça, M., and Lucas, C. (2003). Fps1p channel is the mediator of the major part of glycerol passive diffusion in Saccharomyces cerevisiae: artefacts and re-definitions. Biochimica et Biophysica Acta (BBA) - Biomembranes, 1613(1):57-71.

Olson, K. R. (2012). Mitochondrial adaptations to utilize hydrogen sulfide for energy and signaling. Journal of Comparative Physiology B, 182(7):881-897.

Olson, K. R. and Whitfield, N. L. (2010). Hydrogen sulfide and oxygen sensing in the cardiovascular system. Antioxidants \& Redox Signaling, 12(10):1219-1234.

Olson, K. R., Whitfield, N. L., Bearden, S. E., St Leger, J., Nilson, E., Gao, Y., and Madden, J. A. (2010). Hypoxic pulmonary vasodilation: a paradigm shift with a hydrogen sulfide mechanism. American Journal of Physiology - Regulatory, Integrative and Comparative Physiology, 298(1):R51-R60.

O'Toole, G., Kaplan, H. B., and Kolter, R. (2000). Biofilm formation as microbial development. Annual Review of Microbiology, 54(1):49-79.

Palecek, S. P., Parikh, A. S., and Kron, S. J. (2000). Genetic analysis reveals that FLO11 upregulation and cell polarization independently regulate invasive growth in Saccharomyces cerevisiae. Genetics, 156(3):1005-1023.

Palecek, S. P., Parikh, A. S., and Kron, S. J. (2002). Sensing, signalling and integrating physical processes during Saccharomyces cerevisiae invasive and filamentous growth. Microbiology, 148(4):893-907.

Palková, Z., Janderová, B., Gabriel, J., Zikánová, B., Pospísek, M., and Forstová, J. (1997). Ammonia mediates communication between yeast colonies. Nature, 390(6659):532-536.

Palková, Z. and Váchová, L. (2006). Life within a community: benefit to yeast long-term survival. FEMS Microbiology Reviews, 30(5):806-824.

Palková, Z., Wilkinson, D., and Váchová, L. (2014). Aging and differentiation in yeast populations: elders with different properties and functions. FEMS Yeast Research, 14(1):96-108.

Palma, M., Madeira, S. C., Mendes-Ferreira, A., and Sá-Correia, I. (2012). Impact of assimilable nitrogen availability in glucose uptake kinetics in Saccharomyces cerevisiae during alcoholic fermentation. Microbial Cell Factories, 11:99.

Pan, X. and Heitman, J. (2002). Protein kinase A operates a molecular switch that governs yeast pseudohyphal differentiation. Molecular and Cellular Biology, 22(12):3981-3993.

Park, H. and Hwang, Y.-S. (2008). Genome-wide transcriptional responses to sulfite in Saccharomyces cerevisiae. Journal of Microbiology, 46(5):542-548.

Park, H.-O. and Bi, E. (2007). Central roles of small GTPases in the development of cell polarity in yeast and beyond. Microbiology and Molecular Biology Reviews, 71(1):48-96.

Parsek, M. R. and Singh, P. K. (2003). Bacterial biofilms: an emerging link to disease pathogenesis. Annual Reviews in Microbiology, 57(1):677-701.

Pinto, C., Pinho, D., Cardoso, R., Custódio, V., Fernandes, J., Sousa, S., Pinheiro, M., Egas, C., and Gomes, A. C. (2015). Wine fermentation microbiome: A landscape from different Portuguese wine appellations. Frontiers in Microbiology, 6:905.

Plaisance, E. P., Greenway, F. L., Boudreau, A., Hill, K. L., Johnson, W. D., Krajcik, R. A., Perrone, C. E., Orentreich, N., Cefalu, W. T., and Gettys, T. W. (2011). Dietary methionine restriction increases fat oxidation in obese adults with metabolic syndrome. The Journal of Clinical Endocrinology 8 Metabolism, 96(5):E836-E840.

Porman, A. M., Alby, K., Hirakawa, M. P., and Bennett, R. J. (2011). Discovery of a phenotypic switch regulating sexual mating in the opportunistic fungal pathogen Candida tropicalis. Proceedings of the National Academy of Sciences of the United States of America, 108(52):21158-21163.

Preibisch, S., Saalfeld, S., and Tomancak, P. (2009). Globally optimal stitching of tiled 3D microscopic image acquisitions. Bioinformatics, 25(11):1463-1465.

Pretorius, I. S., van der Westhuizen, T. J., and Augustyn, O. P. H. (1999). Yeast biodiversity in vineyards and wineries and its importance to the South African wine industry. South African Journal of Enology and Viticulture, 20(2):61-74.

Pruyne, D. and Bretscher, A. (2000). Polarization of cell growth in yeast. Journal of Cell Science, 113:365-375.

Querol, A., Barrio, E., and Ramón, D. (1994). Population dynamics of natural Saccharomyces strains during wine fermentation. International Journal of Food Microbiology, 21(4):315-323.

Ramage, G., Saville, S. P., Thomas, D. P., and López-Ribot, J. L. (2005). Candida biofilms: an update. Eukaryotic Cell, 4(4):633-638.

Rankine, B. C. and Pocock, K. F. (1969). Influence of yeast strain on binding of sulphur dioxide in wines, and on its formation during fermentation. Journal of the Science of Food and Agriculture, 20(2):104-109.

Recht, J., Martínez, A., Torello, S., and Kolter, R. (2000). Genetic analysis of sliding motility in Mycobacterium smegmatis. Journal of Bacteriology, 182(15):4348-4351.

Regenberg, B., Hanghøj, K. E., Andersen, K. S., and Boomsma, J. J. (2016). Clonal yeast biofilms can reap competitive advantages through cell differentiation without being obligatorily multicellular. Proceedings of the Royal Society B - Biological Sciences, 283(1842):20161303.

Rep, M., Krantz, M., Thevelein, J. M., and Hohmann, S. (2000). The transcriptional response of Saccharomyces cerevisiae to osmotic shock. The Journal of Biological Chemistry, 275(12):8290-8300.

Reynolds, T. B. (2006). The Opilp transcription factor affects expression of FLO11, mat formation, and invasive growth in Saccharomyces cerevisiae. Eukaryotic cell, $5(8): 1266-1275$.

Reynolds, T. B. and Fink, G. R. (2001). Bakers' yeast, a model for fungal biofilm formation. Science, 291(5505):878-881.

Reynolds, T. B., Jansen, A., Peng, X., and Fink, G. R. (2008). Mat formation in Saccharomyces cerevisiae requires nutrient and pH gradients. Eukaryotic Cell, 7(1):122130.

Ritchie, M. E., Phipson, B., Wu, D., Hu, Y., Law, C. W., Shi, W., and Smyth, G. K. (2015). limma powers differential expression analyses for RNA-sequencing and microarray studies. Nucleic Acids Research, 43(7):e47.

Roberts, R. L. and Fink, G. R. (1994). Elements of a single MAP kinase cascade in Saccharomyces cerevisiae mediate two developmental programs in the same cell type: mating and invasive growth. Genes $\mathfrak{E}$ Development, 8(24):2974-2985.

Robertson, L. S. and Fink, G. R. (1998). The three yeast A kinases have specific signaling functions in pseudohyphal growth. Proceedings of the National Academy of Sciences of the United States of America, 95(23):13783-13787.

Rodriguez, M. E., Orozco, H., Cantoral, J. M., Matallana, E., and Aranda, A. (2014). Acetyltransferase SAS2 and sirtuin SIR2, respectively, control flocculation and biofilm formation in wine yeast. FEMS Yeast Research, 14(6):845-857.

Rossouw, D., Bagheri, B., Setati, M. E., and Bauer, F. F. (2015). Co-flocculation of yeast species, a new mechanism to govern population dynamics in microbial ecosystems. PLOS ONE, 10(8):e0136249.

Rupp, S., Summers, E., Lo, H. J., Madhani, H., and Fink, G. (1999). MAP kinase and cAMP filamentation signaling pathways converge on the unusually large promoter of the yeast FLO11 gene. The EMBO Journal, 18(5):1257-1269.

Ryan, M., Bridge, P., Smith, D., and Jeffries, P. (2002). Phenotypic degeneration occurs during sector formation in Metarhizium anisopliae. Journal of Applied Microbiology, 93(1):163-168.

Ryan, O., Shapiro, R. S., Kurat, C. F., Mayhew, D., Baryshnikova, A., Chin, B., Lin, Z.-Y., Cox, M. J., Vizeacoumar, F., Cheung, D., Bahr, S., Tsui, K., Tebbji, F., Sellam, A., Istel, F., Schwarzmüller, T., Reynolds, T. B., Kuchler, K., Gifford, D. K., Whiteway, M., Giaever, G., Nislow, C., Costanzo, M., Gingras, A.-C., Mitra, R. D., Andrews, B., Fink, G. R., Cowen, L. E., and Boone, C. (2012). Global gene deletion analysis exploring yeast filamentous growth. Science, 337(6100):1353-1356.

Rytka, J. (1975). Positive selection of general amino acid permease mutants in Saccharomyces cerevisiae. Journal of Bacteriology, 121(2):562-570.

Saerens, S. M. G., Delvaux, F. R., Verstrepen, K. J., and Thevelein, J. M. (2010). Production and biological function of volatile esters in Saccharomyces cerevisiae. Microbial Biotechnology, 3(2):165-177.

Saerens, S. M. G., Verstrepen, K. J., Van Laere, S. D. M., Voet, A. R. D., Van Dijck, P., Delvaux, F. R., and Thevelein, J. M. (2006). The Saccharomyces cerevisiae EHT1 and EEB1 genes encode novel enzymes with medium-chain fatty acid ethyl ester synthesis and hydrolysis capacity. The Journal of Biological Chemistry, 281(7):4446-4456.

Sarode, N., Davis, S. E., Tams, R. N., and Reynolds, T. B. (2014). The Wsc1p cell wall signaling protein controls biofilm (mat) formation independently of Flo11p in Saccharomyces cerevisiae. G3: Genes, Genomes, Genetics, 4(2):199-207.

Sarode, N., Miracle, B., Peng, X., Ryan, O., and Reynolds, T. B. (2011). Vacuolar protein sorting genes regulate mat formation in Saccharomyces cerevisiae by Flo11p-dependent and -independent mechanisms. Eukaryotic Cell, 10(11):1516-1526.

Sato, T., Watanabe, T., Mikami, T., and Matsumoto, T. (2004). Farnesol, a morphogenetic autoregulatory substance in the dimorphic fungus Candida albicans, inhibits hyphae growth through suppression of a mitogen-activated protein kinase cascade. Biological and Pharmaceutical Bulletin, 27(5):751-752.

Saveanu, C., Bienvenu, D., Namane, A., Gleizes, P.-E., Gas, N., Jacquier, A., and FromontRacine, M. (2001). Nog2p, a putative GTPase associated with pre-60S subunits and required for late 60S maturation steps. The EMBO Journal, 20(22):6475-6484.

Schimz, K.-L. (1980). The effect of sulfite on the yeast Saccharomyces cerevisiae. Archives of Microbiology, 125(1-2):89-95.

Schimz, K.-L. and Holzer, H. (1979). Rapid decrease of ATP content in intact cells of Saccharomyces cerevisiae after incubation with low concentrations of sulfite. Archives of Microbiology, 121(3):225-229.

Schindelin, J., Arganda-Carreras, I., Frise, E., Kaynig, V., Longair, M., Pietzsch, T., Preibisch, S., Rueden, C., Saalfeld, S., Schmid, B., Tinevez, J.-Y., White, D. J., Hartenstein, V., Eliceiri, K., Tomancak, P., and Cardona, A. (2012). Fiji: an opensource platform for biological-image analysis. Nature Methods, 9(7):676-682.

Scholl, C. M., Morgan, S. C., Stone, M. L., Tantikachornkiat, M., Neuner, M., and Durall, D. M. (2016). Composition of Saccharomyces cerevisiae strains in spontaneous fermentations of Pinot Noir and Chardonnay. Australian Journal of Grape and Wine Research, 22(3):384-390.

Selvaraju, K., Gowsalya, R., Vijayakumar, R., and Nachiappan, V. (2016). MGL2/YMR210w encodes a monoacylglycerol lipase in Saccharomyces cerevisiae. FEBS Letters, 590(8):1174-1186.

Sengupta, N., Vinod, P. K., and Venkatesh, K. V. (2007). Crosstalk between cAMP-PKA and MAP kinase pathways is a key regulatory design necessary to regulate FLO11 expression. Biophysical Chemistry, 125(1):59-71.

Shannon, P., Markiel, A., Ozier, O., Baliga, N. S., Wang, J. T., Ramage, D., Amin, N., Schwikowski, B., and Ideker, T. (2003). Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome Research, 13(11):2498-2504.

Shively, C. A., Eckwahl, M. J., Dobry, C. J., Mellacheruvu, D., Nesvizhskii, A., and Kumar, A. (2013). Genetic networks inducing invasive growth in Saccharomyces cerevisiae identified through systematic genome-wide overexpression. Genetics, 193(4):1297-1310.

Sidari, R., Caridi, A., and Howell, K. S. (2014). Wild Saccharomyces cerevisiae strains display biofilm-like morphology in contact with polyphenols from grapes and wine. International Journal of Food Microbiology, 189:146-152.

Simpson-Lavy, K. J., Sajman, J., Zenvirth, D., and Brandeis, M. (2009). APC/CCdh1 specific degradation of Hsl1 and Clb 2 is required for proper stress responses of $S$. cerevisiae. Cell Cycle, 8(18):3006-3012.

Singh, A. and Sherman, F. (1974). Characteristics and relationships of mercury-resistant mutants and methionine auxotrophs of yeast. Journal of Bacteriology, 118(3):911-918.

Sohn, H.-Y., Murray, D. B., and Kuriyama, H. (2000). Ultradian oscillation of Saccharomyces cerevisiae during aerobic continuous culture: hydrogen sulphide mediates population synchrony. Yeast, 16(13):1185-1190.

Šťovíček, V., Váchová, L., Begany, M., Wilkinson, D., and Palková, Z. (2014). Global changes in gene expression associated with phenotypic switching of wild yeast. BMC Genomics, 15(1):1-16.

Šťovíček, V., Váchová, L., Kuthan, M., and Palková, Z. (2010). General factors important for the formation of structured biofilm-like yeast colonies. Fungal Genetics and Biology, 47(12):1012-1022.

Sperandio, V., Torres, A. G., and Kaper, J. B. (2002). Quorum sensing Escherichia coli regulators B and C (QseBC): a novel two-component regulatory system involved in the regulation of flagella and motility by quorum sensing in E. coli. Molecular Microbiology, 43(3):809-821.

Stefanini, I., Dapporto, L., Legras, J.-L., Calabretta, A., Di Paola, M., De Filippo, C., Viola, R., Capretti, P., Polsinelli, M., Turillazzi, S., and Cavalieri, D. (2012). Role of social wasps in Saccharomyces cerevisiae ecology and evolution. Proceedings of the National Academy of Sciences of the United States of America, 109(33):13398-13403.

Supek, F., Bošnjak, M., Škunca, N., and Šmuc, T. (2011). REVIGO summarizes and visualizes long lists of gene ontology terms. PLOS ONE, 6(7):e21800.

Swiegers, J. H., Bartowsky, E. J., Henschke, P. A., and Pretorius, I. S. (2005). Yeast and bacterial modulation of wine aroma and flavour. Australian Journal of Grape and Wine Research, 11(2):139-173.

Swiegers, J. H. and Pretorius, I. S. (2005). Yeast Modulation of Wine Flavor. In Laskin, A., Bennett, J., and Gadd, G., editors, Advances in Applied Microbiology, pages 131-175. Elsevier, New York, USA, vol. 57 edition.

Tamas, M. J., Luyten, K., Sutherland, F. C. W., Hernandez, A., Albertyn, J., Valadi, H., Li, H., Prior, B. A., Kilian, S. G., Ramos, J., Gustafsson, L., Thevelein, J. M., and Hohmann, S. (1999). Fps1p controls the accumulation and release of the compatible solute glycerol in yeast osmoregulation. Molecular Microbiology, 31(4):1087-1104.

Taylor, S., Wakem, M., Dijkman, G., Alsarraj, M., and Nguyen, M. (2015). A practical approach to RT-qPCR - publishing data that conform to the MIQE Guidelines. Technical report, Bio-Rad Laboratories, Inc., Hercule, CA.

Teixeira, M. C., Monteiro, P. T., Guerreiro, J. F., Gonçalves, J. P., Mira, N. P., dos Santos, S. C., Cabrito, T. R., Palma, M., Costa, C., Francisco, A. P., Madeira, S. C., Oliveira, A. L., Freitas, A. T., and Sá-Correia, I. (2014). The YEASTRACT database: an upgraded information system for the analysis of gene and genomic transcription regulation in Saccharomyces cerevisiae. Nucleic Acids Research, 42(Database issue):D161-D166.

Teste, M.-A., Duquenne, M., François, J. M., and Parrou, J.-L. (2009). Validation of reference genes for quantitative expression analysis by real-time RT-PCR in Saccharomyces cerevisiae. BMC Molecular Biology, 10:99.

Thévenaz, P. and Unser, M. (2007). User-friendly semiautomated assembly of accurate image mosaics in microscopy. Microscopy Research and Technique, 70(2):135-146.

Thomas, D. and Surdin-Kerjan, Y. (1997). Metabolism of sulfur amino acids in Saccharomyces cerevisiae. Microbiology and Molecular Biology Reviews, 61(4):503-532.

Thurston, P. A., Quain, D. E., and Tubb, R. S. (1982). Lipid metabolism and the regulation of volatile ester synthesis in Saccharomyces cerevisiae. Journal of the Institute of Brewing, 88(2):90-94.

Trapnell, C., Pachter, L., and Salzberg, S. L. (2009). TopHat: discovering splice junctions with RNA-Seq. Bioinformatics, 25(9):1105-1111.

Váchová, L., Štoví, V., Hlaváček, O., Chernyavskiy, O., Štěpánek, L., Kubínová, L., and Palková, Z. (2011). Flo11p, drug efflux pumps, and the extracellular matrix cooperate to form biofilm yeast colonies. Journal of Cell Biology, 194(5):679-687.

Valero, E., Cambon, B., Schuller, D., Casal, M., and Dequin, S. (2007). Biodiversity of Saccharomyces yeast strains from grape berries of wine-producing areas using starter commercial yeasts. FEMS Yeast Research, 7(2):317-329.

Valero, E., Schuller, D., Cambon, B., Casal, M., and Dequin, S. (2005). Dissemination and survival of commercial wine yeast in the vineyard: A large-scale, three-years study. FEMS Yeast Research, 5(10):959-969.

Van der Westhuizen, T. J., Augustyn, O. P. H., and Pretorius, I. S. (2000). Geographical distribution of indigenous Saccharomyces cerevisiae strains isolated from vineyards in the coastal regions of the Western Cape in South Africa. South African Journal of Enology and Viticulture, 21(1):3-9.

Van Mulders, S. E., Christianen, E., Saerens, S. M. G., Daenen, L., Verbelen, P. J., Willaert, R., Verstrepen, K. J., and Delvaux, F. R. (2009). Phenotypic diversity of Flo protein family-mediated adhesion in Saccharomyces cerevisiae. FEMS Yeast Research, 9(2):178-190.

Vandesompele, J., De Preter, K., Pattyn, F., Poppe, B., Van Roy, N., De Paepe, A., and Speleman, F. (2002). Accurate normalization of real-time quantitative RT-PCR
data by geometric averaging of multiple internal control genes. Genome Biology, $3(7)$ :research0034.1-research0034.11.

Verstrepen, K. J., Derdelinckx, G., Verachtert, H., and Delvaux, F. R. (2003). Yeast flocculation: what brewers should know. Applied Microbiology and Biotechnology, 61(3):197-205.

Vyas, V. K., Kuchin, S., Berkey, C. D., and Carlson, M. (2003). Snf1 kinases with different $\beta$-subunit isoforms play distinct roles in regulating haploid invasive growth. Molecular and Cellular Biology, 23(4):1341-1348.

Wach, A., Brachat, A., Pöhlmann, R., and Philippsen, P. (1994). New heterologous modules for classical or PCR-based gene disruptions in Saccharomyces cerevisiae. Yeast, 10(13):1793-1808.

Walker, M., Gardner, J., Vystavelova, A., McBryde, C., Lopes, M., and Jiranek, V. (2003). Application of the reuseable, KanMX selectable marker to industrial yeast: construction and evaluation of heterothallic wine strains of Saccharomyces cerevisiae, possessing minimal foreign dna sequences. FEMS Yeast Research, 4(3):339-347.

Wang, X. D., Bohlscheid, J. C., and Edwards, C. G. (2003). Fermentative activity and production of volatile compounds by Saccharomyces grown in synthetic grape juice media deficient in assimilable nitrogen and/or pantothenic acid. Journal of Applied Microbiology, 94(3):349-359.

White, H. E., Orlova, E. V., Chen, S., Wang, L., Ignatiou, A., Gowen, B., Stromer, T., Franzmann, T. M., Haslbeck, M., Buchner, J., and Saibil, H. R. (2006). Multiple distinct assemblies reveal conformational flexibility in the small heat shock protein Hsp26. Structure, 14(7):1197-1204.

Wiame, J.-M., Grenson, M., and Ars, H. N. (1985). Nitrogen catabolite repression in yeasts and filamentous fungi. Advances in Microbial Physiology, 26:1-88.

Winzeler, E. A., Shoemaker, D. D., Astromoff, A., Liang, H., Anderson, K., Andre, B., Bangham, R., Benito, R., Boeke, J. D., Bussey, H., Chu, A. M., Connelly, C., Davis, K., Dietrich, F., Dow, S. W., El Bakkoury, M., Foury, F., Friend, S. H., Gentalen, E., Giaever, G., Hegemann, J. H., Jones, T., Laub, M., Liao, H., Liebundguth, N., Lockhart, D. J., Lucau-Danila, A., Lussier, M., M’Rabet, N., Menard, P., Mittmann, M., Pai, C., Rebischung, C., Revuelta, J. L., Riles, L., Roberts, C. J., Ross-MacDonald, P., Scherens, B., Snyder, M., Sookhai-Mahadeo, S., Storms, R. K., Véronneau, S., Voet, M., Volckaert, G., Ward, T. R., Wysocki, R., Yen, G. S., Yu, K., Zimmermann, K., Philippsen, P., Johnston, M., and Davis, R. W. (1999). Functional characterization of the S. cerevisiae genome by gene deletion and parallel analysis. Science, 285(5429):901-906.

Wuster, A. and Babu, M. M. (2010). Transcriptional control of the quorum sensing response in yeast. Molecular BioSystems, 6(1):134-141.

Youk, H. and Lim, W. A. (2014). Secreting and sensing the same molecule allows cells to achieve versatile social behaviors. Science, 343(6171):1242782.

Young, M. D., Wakefield, M. J., Smyth, G. K., and Oshlack, A. (2010). Gene ontology analysis for RNA-seq: accounting for selection bias. Genome Biology, 11(2):R14.

Zara, G., Zara, S., Pinna, C., Marceddu, S., and Budroni, M. (2009). FLO11 gene length and transcriptional level affect biofilm-forming ability of wild flor strains of Saccharomyces cerevisiae. Microbiology, 155(12):3838-3846.

Zara, S., Bakalinsky, A. T., Zara, G., Pirino, G., Demontis, M. A., and Budroni, M. (2005). FLO11-based model for air-liquid interfacial biofilm formation by Saccharomyces cerevisiae. Applied and Environmental Microbiology, 71(6):2934-2939.

Zotenko, E., Mestre, J., O’Leary, D. P., and Przytycka, T. M. (2008). Why do hubs in the yeast protein interaction network tend to be essential: reexamining the connection between the network topology and essentiality. PLOS Computational Biology, 4(8):e1000140.

Zupan, J. and Raspor, P. (2010). Invasive growth of Saccharomyces cerevisiae depends on environmental triggers: a quantitative model. Yeast, 27(4):217-228.

