TRANSCRIPTIONAL RESPONSE OF O⁶- METHYLGUANINE METHYLTRANSFERASE DEFICIENT YEAST TO METHYL-N-NITRO-N-NITROSOGUANIDINE (MNNG)

by

Anoop Rao

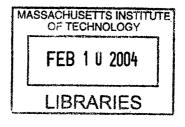
Submitted to the Biological Engineering Division, School of Engineering, Massachusetts Institute of Technology

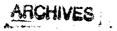
in partial fulfillment of the requirements for the degree of

Master of Science in Biological Engineering

at the

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Abstract

Damage to DNA can occur by means of endogenous biochemical processes or exogenous chemicals such as alkylating agents. If left unrepaired, alkylated bases, most notably, O⁶ Methylguanine (O⁶MeG) can be mutagenic and cytotoxic to the cell. Luckily, DNA methyltransferase (encoded by the gene MGT1 in yeast), repairs this damage. By using transcriptional profiling as a tool, an attempt to elucidate the role of MGT1 has been made. First, the basal expression profile of the *mgt1* was established. Then, the response of wild-type (WT) yeast and yeast lacking MGT1 (*mgt1*) to the alkylating agent, MNNG was studied using exponentially growing WT and *mgt1* cultures which were exposed to $30\mu g/ml$ of MNNG for 10 to 60 minutes.

Basal expression profile of yeast lacking *MGT1* showed up-regulation of *REV7*, a gene implicated in spontaneous mutagenesis. Response to MNNG was invoked immediately and was dramatic and widespread involving 30% of the genome in both WT and *mgt1*. Cell-cycle checkpoints, damage signal amplifiers, DNA repair genes (nucleotide excision repair, photoreactive repair, mismatch repair) and chromatin remodeling genes were induced. Genes involved in maintaining mitochondrial structure and mitochondrial genome were also induced. Intriguingly, *RPN4*, a key regulator of proteasomal system was found to be repressed. Environmental stress response genes were culled out to examine the effects of MNNG on WT and *mgt1*, more carefully.

Temporal gene expression profiles in WT and *mgt1* were informative in delineating differences in the distinct responses mounted by WT and *mgt1*. The magnitude of response in *mgt1* is more profound than in WT. The differences in the dynamic trends between the two suggest that *mgt1* initiates a coordinated response involving repression of transcription factors and subsequently, induction of RNA processing (35% of genes incrementally induced) and kinases involved in protein phosphorylation. In the WT, the response was restricted to a transient repression of fundamental biochemical processes. Interestingly, a gene whose repression is known to mimic apoptosis was found to be repressed in the WT. The overwhelming induction of ribosomal protein synthesis genes in both WT and *mgt1* in response to MNNG is an unexpected result that could signify a successful recovery following wide-spread cellular damage.

Thesis supervisor: Leona D Samson Title: Professor

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BACKGROUND

Genetic information in any cell is chemically stored in the form of deoxyribonucleic acid (DNA) and it essentially comprises a sequence of repeating nucleotides. Nucleotides in turn consist of a pentose sugar, a nitrogenous base and a variable number of phosphate groups stacked and aligned in an orderly fashion. Maintaining the physical and chemical integrity of the DNA structure is vital for its function. Unfortunately, however, errors can be introduced during replication, recombination and even repair. They can also be introduced via damage due to physical and chemical agents. Eventually, if errors remain uncorrected, it may lead to instability of the chemical structure and modification of the molecular structure. Such an alteration classifies as DNA damage and this may sometimes preclude the semiconservative replication of DNA, lead to cell cycle arrest and often, cell death. Another ominous outcome of unchecked DNA damage is the accumulation of mutations that can lead to cancer. (Figure 1)

APOPTOSIS

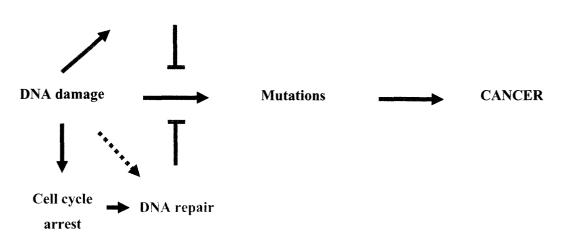


Figure 1: Unchecked DNA damage may lead to cancer.

The mechanism of damage to DNA

Spontaneous alterations

The nitrogenous bases, purines and pyrimidines, occasionally undergo a spontaneous alteration in their chemistry. The bases can lose their exocyclic amino group and undergo deamination. This modification increases the propensity for anomalous pairing of bases and an inappropriately incorporated base can introduce a transition or transversion mutation. In addition, instability of base pairing may also lead to replication arrest. Purines and pyrimidines can also be spontaneously hydrolyzed and lost. (Lindahl, 1993). Abasic sites that are produced can also lead to mutations during replication. (Loeb, 1986)

Unlike the fleeting deamination and hydrolysis reactions, oxidative damage to DNA is more elaborate and once initiated, results in a chain reaction. The cause of damage can be exogenous or endogenous. Exogenous sources of oxidative DNA damage include radiation, near UV light at 320 to 380nm and several drugs (Friedberg, 1995). Endogenously, redox reactions which ubiquitously occur in cells, are the major source of reactive oxygen species. Notable among them are the by-products of aerobic mitochondrial respiration. Singlet oxygen and hydrogen peroxide inflict damage via formation of hydroxyl radicals through metal catalyzed reactions. The intermediates and by-products of such reaction are independently capable of inflicting more damage on intracellular macromolecules. Fortunately, there are several cellular defense mechanisms help to mitigate the effect of these reactive oxygen species (ROS). These include antioxidant enzymes such as superoxide dismutase, glutathione peroxidase and other scavengers, Vitamin C and α tocopherol. Potentially unfavorable cellular responses triggered by the presence of ROS may include the inhibition of cell cycle progression, the initiation of apoptosis and the activation of a degradative process to replace macromolecules. Oxygen radicals are also known to induce chromosome breaks. In general, irrespective of the source and mechanism of alteration or damage, the most ominous outcome is typically a mismatch of base pairs during DNA synthesis. The most important oxidative base adduct, 8-oxoguanine can mispair and be mutagenic (Lindahl., 1993, Friedberg, 2002).

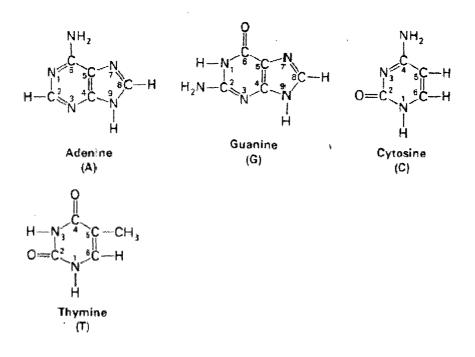


Figure 2: The nitrogenous bases; Purines (A,G) and Pyrimidines (C,T,U)

Environmental damage

Physical agents - Ionizing Radiation: Apart from spontaneous alterations and damage to DNA, physical and chemical agents in the environment inflict a substantial amount of damage. Exposure to ionizing radiation as a therapeutic, diagnostic or occupational hazard induces a variety of lesions by direct damage. Radiolysis of water generates reactive oxygen species that damage cellular macromolecules. Glutathione, a radioprotector, can counteract the damage at several tiers of radical production. Damage to bases, sugar moieties and direct induction of strand breaks can occur. Strand breaks are a special problem since mere DNA ligation may not be sufficient to repair the lesion. (Burrows, 1998). Ultraviolet (UV) radiation induces covalent linkage of adjacent pyrimidines producing cyclobutane pyrimidine dimers (CPD). These lesions distort the helix and lead to extensive bending of DNA, albeit variably. A less frequent lesion is the pyrimidine-pyrimidone (6-4) photoproduct that, like CPD's, distorts the helix (Ravanat, 2001). These physical distortions may result in an obligatory arrest of replication.

Chemical agents: Environmental exposure to chemicals included as food agents (Sugimura., 2002), inhalation of polluted air and ingestion of contaminated water are by far

the most common modes of encountering DNA damaging agents. Occupational hazards and therapeutic intervention, most notably by anti-cancer agents are responsible for most of the DNA damage in humans. The diverse class of chemicals known to cause DNA damage includes psoralens, benzo[a]pyrene, aflatoxins and nitroquinolones and alkylating agents. Historically, there has been an interest in examining the potential for food additives to be potent carcinogens. Most of the evidence has relied on demonstrating that electrophilic metabolites of the parent compound can forms DNA or protein adducts. Their metabolism is dependent on an inducible system of membrane proteins called the cytochrome P-450 system. Apart from this P-450 system, there are other enzymes that conjugate compounds to make them more water soluble and permit easy elimination from the system. They include acetyltransferases, glucoronyl transferases, adenosylating enzymes and methylating enzymes. In principle, the cell has several mechanisms of dealing with DNA damage but it is unfortunate, however, that metabolites can themselves be more harmful than the parent compounds.

Means of response to DNA damage

In essence, physical and chemical damage to DNA is a universal phenomenon across living systems. Damage by physical and chemical agents can lead to arrest of replication and transcription. Fortunately, there are sub-cellular systems that operate in a coordinated way to sense and respond to damage. Broadly, they can be classified as DNA repair mechanisms (specific set of events to eliminate the primary lesion) and DNA damage checkpoint mechanisms - accessory events that stall the cell cycle and permit the specific DNA repair mechanisms to act.

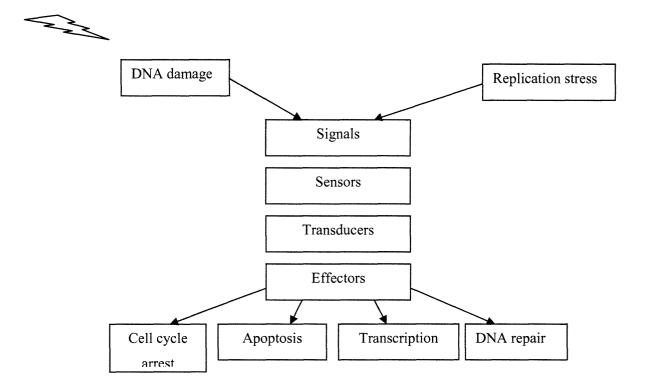


Figure 3: Causes and consequences of DNA damage.

An elaborate, overlapping set of enzymes, proteins and mechanisms deal with these deleterious lesions. Cells respond to DNA damage by delaying cell cycle progression and by increasing the expression of a few genes involved in the repair and tolerance of DNA damage (Friedberg et al,1995). Surveillance mechanisms in eukaryotic cells monitor and regulate the cell cycle and its progress. The cell-cycle checkpoints are activated by one or more signals and ultimately results in the inhibition of cell cycle progression. The checkpoint mechanism first detects damaged DNA and then generates a signal that arrests cells in the G₁/S or G₂/M phase of the cell cycle. It also slows down S phase (DNA synthesis). This mechanism is thought to prevent the replication of damaged templates and the segregation of broken chromosomes.

Consequences of unrepaired lesions

Despite the orchestrated response, however, the damage may not be mitigated. If lesions are not repaired, they would pose a problem by being mutagenic or lethal. In response to DNA damage the cell has four major routes of responses. Cell-cycle arrest provides the crucial time for repairing the damage. If the damage load is too profound for the cell to handle, it may undergo apoptosis (programmed cell death) to avoid the propagation of highly defective cells. The lesions may be fixed by DNA repair pathways or alternatively, the unrepaired lesions may generate sequence changes in the genome to be passed on as a mutation.

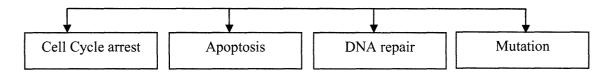


Figure 4: Outcomes of DNA damage

Overview of repair mechanisms

Photoreactivation by photolyases

UV light exposure generates 2 major classes of stable DNA lesions - cyclobutane pyrimidine dimers (CPDs) and 6-4 photoproducts (6-4 PD). Unless repaired, these lesions may lead to blockage of transcription, mutations, cell death and cancer. CPD's and 6-4 PD's are removed by two pathways: (i) nucleotide excision repair (NER); and (ii) photoreactivation. Some plants, bacteria, and yeast possess a photolyase that preferentially reverses the CPD's in the non-transcribed strand of active genes. DNA photolyases catalyze the light-dependent repair of pyrimidine dimers in DNA. (Carell, 2001). Photolyases bind tightly to CPDs and, on excitation by 340–400-nm light, catalyse the cleavage of the cyclobutane linkage between the adjacent pyrimidines and restore the monomeric bases without cutting the phosphodiester backbone of DNA.

In yeast, the Phr1 gene that codes for photolyase has been shown to be upregulated by several DNA-damaging agents such as UV radiation, 4NQO, MMS and MNNG (Sebastian et al, 1990). If Phr1 is unable to resolve cyclobutane linkages then it will also try to enhance the NER of CPDs. The photolyase enzyme functions as a model for proteins that interact with sites of DNA damage and have the potential to facilitate DNA-damage recognition by repair pathways. (Sebastian and Sancar, 1991)

Methylguanine methyltransferase

The methylguanine methyltransferase reverts O^6 -methylguanine to guanine by transferring the methyl group from DNA to a reactive cysteine group of the protein in an irreversible reaction. This covalent attachment of the alkyl group to the cysteine residue inactivates the enzyme. Alkylguanine methyl transferase is a suicide enzyme. The mechanism for this reaction is indicated in Figure 7.

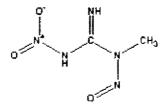


Figure 5: Alkylating agent, MNNG

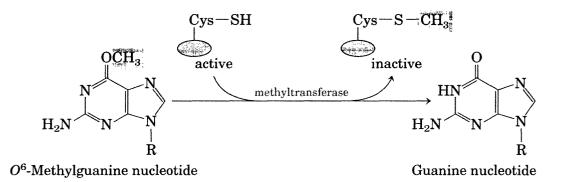


Figure 6: O⁶Mehyltguanine methyltransferase accepts the methyl group at its cysteine residue

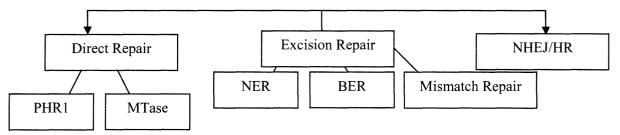


Figure 7: Overview of DNA repair mechanisms

Excision Repair

In contrast to direct repair there is cleavage of the sugar phosphate backbone in excision repair.

Base Excision Repair

Damage to DNA from deamination, oxidation and alkylation is mainly repaired by BER. In base excision repair, the DNA bases that are altered by small chemical modifications are replaced through the excision of only the damaged nucleotide (short patch BER) or through the removal of 2–13 nucleotides containing the damaged nucleotide (long-patch BER). DNA glycosylases initiate BER by excising damaged bases from DNA and generating abasic sites.

Nucleotide Excision Repair (NER)

In cases where the alteration involves the addition of large chemical additions or cross-links, the DNA bases are excised using the nucleotide excision repair where a short, single-stranded segment containing the damage is removed. NER helps in repair of bulky base adducts formed by UV radiation, various environmental mutagens, and certain chemotherapeutic agents. In NER. (Wood, 1997)

Mismatch Repair (MMR).

An important replication-associated correction function is provided by the postreplicative mismatch repair system. Base-base mismatches or loops of extra bases if left unrepaired, will generate point or frameshift mutations respectively. Misincorporation of noncomplementary bases by DNA polymerases is a major source of the occurrence of promutagenic base-pairing errors during DNA replication or repair. MMR is conserved from bacteria to humans. It identifies and corrects mispaired bases and 1–3-nucleotide loops that result from DNA polymerase errors during replication.

Double strand break. (DSB) repair

Double strand breaks are rare and two independent pathways handle them; homologous recombination (HR) and non-homologous end joining (NHEJ). Homologous recombination uses extensive homology to code DNA and maintain accuracy. Nonhomologous end joining involves a coordinated rejoining of the broken ends and uses no or extremely limited regions of homology as a template for repair. Consequently, this process is inaccurate and the deletions of a few nucleotides are introduced at the site of the DSB. HR and NHEJ are important in all eukaryotes and HR is more important in rapidly dividing cells and NHEJ is more important in quiescent or terminally differentiated cells. HR is important for meiosis or the repair of inter-strand cross-links, while NHEJ is required for joining of DNA fragments while generating the diversity of the immune system.

Mechanism of damage by alkylation

Alkylating agents are electrophilic compounds with affinity for nucleophilic centers in organic macromolecules. They are probably the broadest class of chemicals that have the potential to cause profound damage to DNA. Alkylating agents are classified as monofunctional or bifunctional depending on the number of reactive groups, and therefore, the ability to react with multiple sites within DNA. Alkylating agents attack nitrogen and oxygen at various sites within nitrogenous bases with different reactivity's. Apart from these veritable hot spots within nitrogenous bases, alkylating agents can react with oxygen in the phosphodiester linkage to form a phosphotriester.

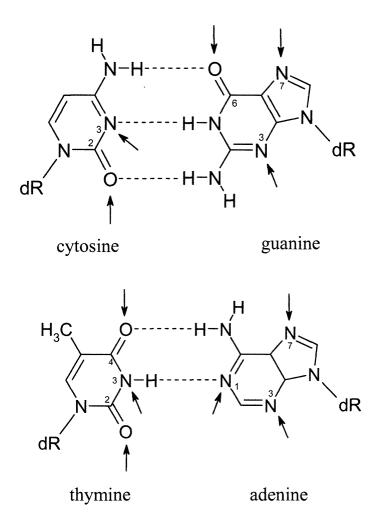


Figure 8: Sites within the nitrogenous bases susceptible to alkylation damage.

By virtue of its ability to reach several nucleophilic sites within the nitrogenous bases, inter and intra-strand cross links can occur as a consequence of exposure to bifunctional alkylating agents. The covalent link sustains this anomaly and prevents strand separation (if there is an inter-strand crosslink) leading to a complete block of replication and transcription.

Damage to DNA bases

Alkylating agents are structurally diverse group of chemicals that cause a wide range of biological effects including cell death, mutation and cancer. DNA damaged by these agents contains widely different amounts of 12 alkylated purines/pyrimidines and two

phosphotriester isomers. They are used in anticancer therapy and are also found in cigarette smoke.

Lesions caused by alkylation

Attack in O⁶ position of guanine leads to the formation of the adduct, O⁶ Methylguanine (O⁶ MeG). This is a relatively minor lesion compared to O⁴Methylthymine (O⁴MeT), but potentially the most deleterious lesion if left unrepaired in the system. Other potentially harmful lesions include 3 Methyl Adenine (3MeA). If the O⁶ MeG lesion remains unrepaired, then it permits G→A transition mutation following 2 rounds of replication. This happens in both eukaryotes and prokaryotes. Recombination and cell death that may ensue but both need a functional MMR system.

In *E.coli*, it has been shown that the miscoding alkylation adducts on the template strand would lead to anomalous base pairs upon replication. Provocation of mismatch repair by such lesions would result in a futile turnover of the newly synthesized strand because the offending adduct is not removed from the template DNA, a process that could lead to cell death. Luckily, the O^6 methylguanine MTase protein is able to counter this effect by irreversibly and covalently binding to the methyl group and plucking it off the base. Since the cysteine which is methylated is not regenerated at all, the capacity for repair of O^6 -methylguanine is limited by the number of molecules of the MTase available within the cell.

Alkyltransferases across systems

Methyltransferase belongs to a class of proteins, the alkyltransferases. There are close to a 100 alkyltransferases but the structure of only 3 three family members: the Ada-C protein from *Escherichia coli* (Moore et al 1994), the human alkyltransferase (hAGT) (Daniels, 2000), and *Pyrococcus kodakaraensis* (Hashimoto 1999) are known. The protein is non-enzymatic in nature and therefore the protection by alkyltransferase depends on the regulation of its synthesis and degradation.

Structure and function of Yeast methyltransferase (MGT1)

Repair of O⁶-MeG in yeast extracts was shown to be performed by a 25-kilodalton protein Methyl transfer was accompanied by the formation of S-methylcysteine. The *S. cerevisiae* MGT1 codes for a 188 amino acid protein. About half of the MGT1 protein has

homology with four bacterial MTases and also the human DNA MTase. (Xiaoand Samson 1992)

Exponentially growing yeast cultures have about 150 molecules of MTase in each cell. The yeast MTase has a half-life of about 4 min at 37°C. Synthesis of the yeast DNA MTase is not inducible by sublethal exposures to alkylating agent. The substrates for yeast MTase include O⁶ MeG and O⁴MeT. Unlike this, the human MTase is very specific for O⁶MeG.

Spontaneous mutations

Mutations are defined as spontaneous when they arise in cells that are not actively exposed to exogenous, xenobiotic mutagens. Spontaneous mutations occur due to either uncorrected DNA replication errors, or endogenous metabolites that cause lesions on DNA. Oxidative damage and alkylation damage are the 2 major sources of endogenous DNA damage. It results as a consequence of cellular metabolism and failure to correct this damage due to genetic defects results in significantly increased spontaneous mutation rates. Spontaneous mutations have been studied earlier using several systems including *MGT1* deletions in yeast. *MGT1* deleted mutants were shown to have an increased spontaneous mutation rate suggesting an endogenous source of DNA methylation damage. (Xiao and Samson, 1993).

Alkylation due to endogenous processes

S-adenosyl methionine (SAM) a cellular methylase co-factor has a reactive methyl group and is responsible for enzymatic methylation of DNA, RNA and proteins. Under physiological conditions, SAM has been shown to non-enzymatically methylate DNA to form 3-Methyl adenine and O⁶MeG (Rydberg and Lindahl 1982). Endogenous processes might include the 'aberrant' methylation of guanine by *S*-adenosylmethionine and the endogenous nitrosation of compounds containing primary amino groups and their subsequent breakdown to methylating species (Sedgwick, 1997). *n*nitrosoglycocholic acid has been shown to be able to methylate DNA *in vitro* and *in vivo* (Shuker and Margison, 1997).

Saccharomyces cerevisiae as a model system to study genome-wide expression.

The baker's yeast *S. cerevisiae* is an informative model organism in traditional genetic studies. It also presents an ideal model genome for large-scale functional analysis. Relative to other eukaryotes, *S. cerevisiae* has a compact genome. Approximately, 70% of its total (non-ribosomal DNA) genetic complement is protein-coding sequence. Encompassing 16 chromosomes, the 12-megabase (Mb) yeast genome is predicted to encode about 6,200 genes, with 1 gene per 2 kb of genomic sequence. (Goffeau, 1996).*S. cerevisiae* is an informative predictor of human gene function; nearly 50% of human genes implicated in heritable diseases have yeast homologues. (Bassett, 1996, 1997. Venter. 2001).

Since its development in the mid-1990s (Schena, 1995, Chee, et al 1996), the DNA microarray has emerged as the pre-eminent tool for functional genomics. The ability to analyse thousands of DNA samples simultaneously by hybridization-based assay has provided a popular method for analysing the relative levels of mRNA transcripts on a genome-wide scale. Typically, DNA microarrays have been used to identify genes, the expression of which is either induced or repressed during specific cellular responses. For example, DeRisi (DeRisi *et al.* 1997) used DNA microarrays to monitor relative changes in mRNA levels during the shift from anaerobic fermentation to aerobic respiration in yeast. Microarrays have also been used to identify genes differentially expressed during sporulation (Chu et al 1998), as well as genes periodically expressed during the cell cycle (Cho. et al 1998, Spellman, 1998). Jelinsky and Samson (1999) used oligonucleotide arrays to identify over 400 genes that are either induced or repressed in response to the DNA-damaging, alkylating agent methyl methanesulphonate (MMS). These and other microarray-based studies have identified genes that putatively function in common regulatory pathways; such pathways are also being delineated by transcriptional profiling of strains mutated for key regulatory components.

Affymetrix has used the genomic sequence of the budding yeast Saccharomyces cerevisiae to design and synthesize high-density oligonucleotide arrays for monitoring the expression levels of nearly all yeast genes. This direct and highly parallel approach involves the hybridization of total mRNA populations to a set of four arrays that contain a total of more than 260,000 specifically chosen oligonucleotides synthesized in situ using light-directed combinatorial chemistry.

Transcriptional response of *Saccharomyces cerevisiae* wild type and DNA methyltransferase mutants.

Materials and Methods

Yeast strains and growth conditions

To study the genome-wide transcriptional response of Saccharomyces cerevisiae upon exposure to MNNG two strains were obtained from Research Genetics, Carlsbad, CA. The wild-type (WT) BY4741 (MAT a his $3\Delta 1$ leu $2\Delta 0$ met $15\Delta 0$ ura $3\Delta 0$) and the methylguanine methyltransferase lacking strain, BY4741 mgt 1Δ (mgt1). The mgt 1Δ strain was originally created using a PCR based gene deletion strategy (Baudin et al., 1993 and Wach et al., 1994). This gene deletion is viable since MGT1 is a non-essential gene. The cells were grown and maintained on YPD (10 g yeast extract, 20 g peptone, 20 g dextrose, 20 g agar/liter) containing 200µg/ml of G418 (Geneticin, Sigma Chemicals).

N-Methyl-N'-Nitro-N-Nitrosoguanidine

A 1% stock solution of DNA damaging agent, N-Methyl-N'-Nitro-N-Nitrosoguanidine (MNNG) was prepared and stored in amber tubes away from light. This stock was used for all the experiments. First, the phenotypes of the strains were established using a gradient plate assay. Briefly, equal number of BY4741 and BY4741 *mgt1* Δ cells were plated in YPD+G418 plates which had MNNG in concentrations of 0 µg/ml, 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml and 25 µg/ml. The agar was allowed to settle at an angle in the plates. This permitted variable exposure of the cells to a fixed concentration of MNNG. Experiments were performed in duplicate. Colony formation was observed after 3 days of growth at 30°C.

Growth Curve

Single colonies of yeast were picked from YPD+G418 plates to inoculate 5 ml of YPD culture in a test-tube that was rotated overnight at 250 rpm at 30°C. 100µl of each strain was inoculated in 150 ml of YPD+G418 rotating at 300 rpm, at 30°C. OD and cell counts were taken over time to follow growth in cell number. Growth curves were plotted for BY4741 and BY4741 *mgt1* Δ .

MNNG-induced cell killing

The difference in the MNNG-induced cell killing between BY4741 and BY4741 *mgt1* was studied. One colony of wild-type (WT) and MTase lacking mutant (*mgt1*), was picked and grown in 2 separate test-tubes with 5ml YPD (with G418), overnight. Then, 100 μ l was transferred into 150 ml of media (with G418) in a 250 ml flask. This was grown for 12 hours at 30 °C after which 10 ml of culture was transferred into four 15ml tubes. To this 150 μ l of 1% MNNG stock was added to establish the final concentration of MNNG at 30 μ g/ml. After incubating them for 0, 20, 40 and 60 minutes, the test-tubes were centrifuged. The supernatant was discarded and the cells were re-suspended in 10 ml of distilled water. Over a series of dilutions, the re-suspended cells were plated onto YPD agar plates with G418. Colonies were counted after 3 days of incubation at 30 °C.

Cell preparation for Microarray Analysis

Single colonies of WT and *mgt1* were picked from YPD plates to inoculate 5 ml of YPD culture. They were incubated at 250 rpm at 30°C, overnight. 100 μ l of each strain was inoculated in 150 ml of YPD+G418 media in a flask rotating at 300 rpm maintained at 30°C. The cells were grown to mid-log phase (OD = 0.8). The cultures were split into 3 volumes of

50 ml before being exposed to MNNG (30 μ g/ml) for a variable length of time as shown in Table 1. The control samples were mock-treated with same amount of double distilled water. (DDW). After exposure for the appropriate length of time, the cells were spun down in 50 ml tubes centrifuged at 8000 rpm. The cells were snap-frozen and stored at -80°C.

Table 1: Experimental design of oligonucleotide expression study.

The number of BY4741 and BY4741 mgt1 Δ samples that were treated with double distilled water (DDW) or MNNG.

	Control		Treated with 30 μg/ml MNNG				
	(DDW)				e u je je slože je privlet	ana ang saring sar	
		10 min	20 min	30 min	40 min	50 min	60 min
WT	3	3	3	3	3	3	3
mgt1	3	3	3	3	3	3	3

Total RNA preparation

Total RNA was extracted from the frozen cells using the enzymatic lysis protocol (Qiagen RNEasy Mini Protocol – Standard Version) as detailed in the Appendix of Protocols. Briefly, the cells were incubated for 20-30 minutes (with gentle shaking, every 5 minutes) with 2 ml of buffer made from Sorbitol (1M), EDTA (0.1M) β mercaptoethanol (0.1%) and 50 U of lyticase (Sigma) per 1x10⁷ cells. The cells were then centrifuged to pellet the spheroplasts. In a series of steps the cell wall was lysed and the lysate was made to pass across a silica-gel membrane to trap the RNA. Finally, RNAse free water was used to elute the RNA out before estimating the concentration using a spectrophotometer. 260/280 absorbance readings were measured for total RNA. A ratio of 260/280 ratios between 1.8 to 2.1 was considered acceptable. If the ratio was below 1.8 (indicates possible contamination) or above 2.1

(indicates presence of degraded RNA truncated cRNA transcripts, and/or excess free nucleotides), the total-RNA process was repeated.

Pre-hybridization quality control

Forty-two samples of total RNA from the different experimental groups (Table 1) was isolated and stored at -20°C. The samples were also tested using the Agilent 2100 Bioanalyser system. This permits rapid visualization of RNA sample quality and quantity. A rRNA ratio of 28S/18S close to 2 implies minimal degradation of RNA, a prerequisite for efficient reverse transcription, cDNA synthesis and in-vitro transcription and to ensure the highest quality RNA hybridization to the gene expression microarrays. The steps for cRNA synthesis from total RNA is illustrated in Figure 9 and details are included in the Appendix.

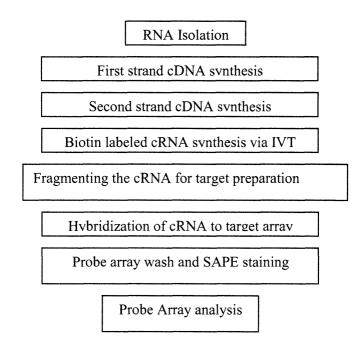


Figure 9: Steps in cRNA preparation and hybridization to GeneChip.

GeneChip® hybridizations and Image analysis.

Fragmented cRNA samples were hybridized to GeneChip® arrays containing the complete yeast genome for a total of 42 arrays (YG-S98 arrays, Affymetrix, CA). The GeneChip® Yeast Genome S98 Array contains probe sets for approximately 6,400 *S. cerevisiae* (S288C strain) genes identified in the Saccharomyces Genome Database (December 1998). This array also contains approximately 600 additional probe sets representing putative open reading frames (ORFs) identified by SAGE analysis, mitochondrial proteins, TY proteins, plasmids, and a small number of ORFs for strains other than S288C.

Scanning was carried out at the MIT Biopolymers Laboratory after hybridizing fragmented cRNA at a concentration of 0.05 ug/µl to GeneChip®s in 200µl of Affy buffer (100 mM MES, 1 M NaCl, 20 mM EDTA, 0.01% Tween 20) with GeneChip® eukaryotic hybridization controls (GeneChip® Eukaryotic Hybridization Controls Kit, Affymetrix, CA) in the presence of 0.1 mg/ml herring sperm DNA and 0.5 mg/ml acetylated BSA at 40 °C for 16 h with constant rotation. Arrays were rinsed after hybridization with 200 µl of stringent wash buffer (100 mM MES, 0.1 M NaCl, 0.01% Tween 20) followed by a non-stringent wash (6XSSPE, 0.01% Tween 20). 20XSSPE had the following composition (3 M NaCl, 0.2 M NaH₂PO₄, 0.02 M EDTA). Staining was done with 2 ug/ml streptavidin–phycoerytherin and 1 mg/ml acetylated BSA in 6×SSPE-T. Arrays were scanned by a HP G2500A GeneArray scanner.

Data analysis

A total of 42 hybridizations were performed and the scanned images from Micorarray Suite 5.0 were stored for computational analysis that was performed using Spotfire, MS Excel and S-plus Array analyzer.

Data Normalization

The .cel files generated after scanning using the Affymetrix suite were used for this analysis. All the 42 .cel files from the control and the experimental groups were analyzed simultaneously.

The variation between high-density oligonucleotide arrays was reduced by normalizing the data. The <u>Robust Multichip Average</u> (RMA) algorithm was used to adjust the background and perform quantile normalization. The expression results for each ORF/gene were represented as logarithm (to base 2) of the expression value. The software package RMAExpress 0.2 alpha 1 version for Windows was used for this purpose. RMAExpress combines the 16-20 probe pair intensities for a given gene to define a measure of expression that represents the amount of the corresponding mRNA species. The normalization takes only perfect matches into account and the mismatch probe cells are not used for calculation the signal intensity/measure of expression.

Analysis of RMA output files

The output of the RMAExpress, in the form of \log_2 values of expression, was exported to MS Excel. For further analysis, average expression value from 3 biological replicates (Table 1), for each time point was computed. Average expression values derived from all the arrays were compared with the average expression of untreated WT to get an expression ratio (ER). This

blanket comparison to compute ER ensures that all the data are compared to an unambiguous baseline. The comparisons were represented as \log_2 of expression ratio's (\log_2 ER).

Post-normalization cut-off

A $\log_2 \text{ER}$ for a gene/ORF > 1 indicates average fold change induction factor of 2 for that particular gene/ORF. Analogously, a $\log_2 \text{ER} < -1$ indicates an average fold change repression factor of 2. If $\log_2 \text{ER's}$ were between 1 and -1, they were classified as not significant (NS). For the purpose of visualization, the $\log_2 \text{ER's}$ across all treatment time-points for both WT and *mgt1* were exported and visualized in Spotfire's functional genomics module.

RESULTS

MNNG gradient plate

The phenotype of the WT and *mgt1* strains, in response to MNNG, was ascertained using gradient plates (Figure 10). Upon exposure to increasing concentrations of MNNG, fewer colonies of *mgt1* survived when compared to WT.

0 μg/ml MNNG	00.00	WT BY4741
	0.00.0	BY4741 mgt1 Δ
5 μg/ml MNNG		WT BY4741
	🍓 🙆 🐮 🔅	BY4741 mgtl Δ
10 µg/ml MNNG		WT BY4741
10 μg/ini MiNNO		BY4741 mgt1 Δ
15 μg/ml MNNG		WT BY4741
		BY4741 mgt1 Δ
20 μg/ml MNNG	$\mathbf{O} \cdot \mathbf{O} \cdot \mathbf{O}$	WT BY4741
		BY4741 mgt1 Δ
25 μg/ml MNNG		WT BY4741
		BY4741 mgt1 Δ
	MNNG Exposure	

Figure 10: MNNG gradient plate assay for Wild-type BY4741 (WT) and BY4741 *mgt1* Δ .

The agar was allowed to settle at an angle in the plates. This permitted variable exposure of the cells to a fixed concentration of MNNG. The same numbers of cells were inoculated on the surface of agar plates with increasing concentrations of MNNG (5-

 25μ g/ml). The cells were grown at 30°C for 3 days before being observed and photographed. The increased sensitivity of *mgt1* to killing by MNNG can be attributed to the lack of MTase.

MNNG-induced cell killing

MNNG-induced cell killing in cultures was compared between WT and *mgt1*. Exposure to MNNG at 30 μ g/ml cause significantly more killing in *mgt1* than in the WT. The lack of MTase and the inability to repair alkylation induced repair in the *mgt1* imparts this difference.

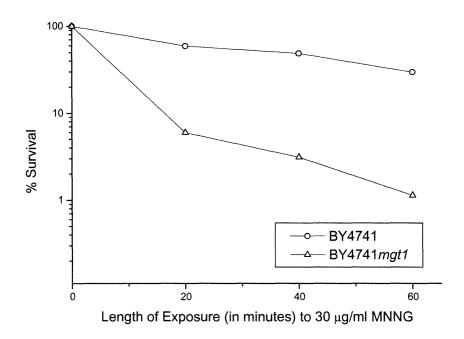


Figure 11: MNNG-induced killing in wild-type (WT) and MTase deficient yeast (*mgt1*).

WT and *mgt1* cells were picked and grown separately in 5ml YPD (with G418), overnight. Then, 100µl was transferred into 150 ml of media (with G418) in a 250 ml flask. After growth for 12 hours at 30 °C, 10 ml of culture was transferred to four 15ml tubes. To each, 150 μ l of 1% MNNG stock was added to establish the final concentration of MNNG at 30 μ g/ml. After incubating them for 0, 20, 40 and 60 minutes, the test-tubes were centrifuged. The supernatant was discarded and the cells were re-suspended in 10 ml of distilled water. Over a series of dilutions, the re-suspended cells were plated onto YPD agar plates with G418. Colonies were counted after 3 days of incubation at 30 °C. The colony count, for each duration of exposure (0, 20, 40 or 60 minutes), was compared to the colony count at time point 0. This was expressed as the percent survival (% survival) for that duration. The % survival plot for increasing length of exposure to MNNG, for WT and *mgt1*, is shown in Figure 11. *mgt1* was more sensitive to MNNG than WT. In addition, increasing the length of exposure to MNNG killed more *mgt1* cells than WT.

Total RNA extraction from exponentially growing cells.

WT or *mgt1* cells were grown to mid-log phase (OD = 0.8) as described earlier. The cultures were split into 3 volumes of 50 ml before being exposed to MNNG (30 μ g/ml) for a variable length of time as shown in Table 1. The control samples were mock-treated with same amount of double distilled water. After exposure for the appropriate length of time, the cells were spun down in 50 ml tubes centrifuged at 8000 rpm. The cells were snap-frozen and stored at -80°C before total RNA extraction using the Qiagen RNEasy protocol.

Pre hybridization quality control of total RNA samples

A few of the total RNA samples were tested for their quality using the Agilent Bioanalyzer system. Lane 1 in figure 12 shows the ladder. Lane 2 in Figure 12 depicts a sample that had a good 28s:18s ratio (1.84).

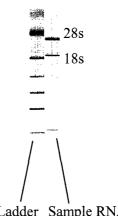


Figure 12: Pre-hybridization quality control gel of total RNA sample. This sample was from exponentially growing wild-type (WT) cells treated with 30µg/ml of MNNG for 40 minutes.

Ladder Sample RNA

The total RNA samples from the different experimental groups were tested using the Agilent 2100 Bioanalyzer system. This system permits rapid visualization and quality control of the RNA sample. The rRNA ratio (28S/18S) was between 1.61-1.87 in the tested samples. Quality of RNA is a prerequisite for efficient in vitro-transcription reaction.

Post-hybridization quality control.

After hybridization to the target Affymetrix YGS98 array, the quality of the arrays was judged by the following factors; percent present calls, presence of spiked control cRNA, background values and noise. All these quality control standards were met satisfactorily (summarized in Table 2). The hybridization efficiency was judged by the percentage of absent and present calls. On an average, the present calls were > 74% before normalization. Hybridization controls, BioB, bioC, and bioD represent genes in the biotin synthesis pathway of E. coli. Cre is the recombinase gene from P1 bacteriophage. The GeneChip Eukaryotic Hybridization Control Kit contains 20x Eukaryotic Hybridization controls composed of a mixture of biotin-labeled cRNA transcripts of bioB, bioC, bioD, and cre, prepared in staggered concentrations (1.5 pM, 5 pM, 25 pM, and 100 pM for *bioB*, *bioC*, *bioD*, and *cre*, respectively).

The 20x Eukaryotic hybridization controls are spiked into the hybridization cocktail, independent of RNA sample preparation, and are thus used to evaluate sample hybridization efficiency to gene expression arrays. *BioB* is at the level of assay sensitivity and should be called "Present" at least 50% of the time. *BioC, bioD,* and *cre* should always be called "Present" with increasing Signal values, reflecting their relative concentrations. The 20x Eukaryotic Hybridization Controls can be used to indirectly assess RNA sample quality among replicates. The overall intensity for a degraded RNA sample, or a sample that has not been properly amplified and labeled, will be lower when compared to a normal replicate sample.

Controls that were spiked-in were detected as expected (BioB-90%, BioC, D, Cre -100%). Their relative intensities were also in accordance with expectations (BioB < BioC < BioD < Cre). Ideally, the BioB control cRNA is spiked in at the detection threshold (1.5 pM) and should receive 'present' detection call in approximately 50 percent of all samples. BioB was present in 90% of the samples. Average background values ideally range from 20 to 100 for arrays scanned with GeneArray® Arrays. In our data, the average background value was about 60. Noise is a measure of the pixel-to-pixel variation of probe cells on a GeneChip array. The two main factors that contribute to noise - electrical noise of the GeneArray Scanner and sample quality. The datasets had an average noise of 1.4.

Parameters	Outcome		
Percent present calls	> 74%		
Spiked controls	As expected, BioB < BioC < BioD < Cre		
Background value	60 (Normal range 20-100)		
Noise (Q)	1.4		

 Table 2: Parameters of post-hybridization quality control.

Four parameters; percent present calls, presence of spike-in controls in the appropriate order, low background value and the presence of noise were assessed and found to be favorable.

RMA normalization

The data from 42 arrays were normalized using RMA method of normalization (Bolstad, 2003). The benefit of RMA normalization is depicted in Figure 13. Probe-set intensities from six arrays (three replicates each, from 2 experimental groups) are shown before (Figure 13A) and after (Figure 13B) normalization. After normalization, the variation between the arrays was minimized dramatically. S-plus's Array analyzer module was used to create and compare these plots directly from the Affymetrix .cel files obtained upon scanning.

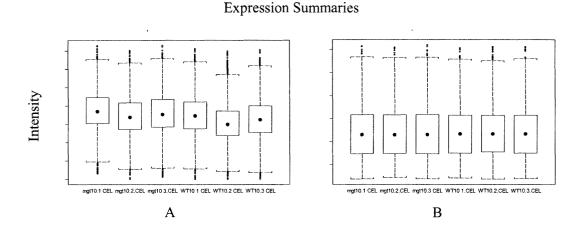


Figure 13: Box plots of intensities before (A) and after (B) RMA quantile normalization.

The intensities for six sample Affymetrix .cel files (3 WT and 3 mgt) are plotted on log_2 scale before (A) and after RMA quantile normalization. The Affymetrix .cel file intensities were imported to S-plus Arrayanalyzer module and RMA quantile normalization was performed. The normalization of the intensities reduces the variation between the samples and thus helps in making comparisons between disparate sets of oligonucleotide arrays.

Variability between the replicates

The variability between the replicates was assessed by computing the R^2 value between the \log_2 of RMA-normalized intensities (Table 3).

Table 3B

Table 3A

	WT1	WT2	WT3
WT1	1	0.94	0.96
WT2	0.94	1	0.95
WT3	0.96	0.95	1

	mgt1	mgt2	mgt3
mgt1	1	0.97	0.94
mgt2	0.97	1	0.93
mgt3	0.94	0.93	1

Table 3: R² values of WT (3A) and *mgt1* (3B) replicates

 R^2 value for the intensity plots for comparing the replicate arrays from the wild-type (WT) (3A) and the methylguanine methyltransferase mutant (*mgt1*) (3B). The samples used here included triplicate untreated WT and untreated *mgt1* arrays.

Computation of log₂ Expression Ratio

Mean gene expression profiles from all experimental groups were compared to mean expression from untreated WT. This uniform denominator allows comparisons to be made between the experimental groups. The numerator was either mean expression from triplicate arrays at a given time point or mean expression across all the arrays in WT or *mgt1* (18 each, representing 3 for each of the 6 time-points). To delineate genes of importance, the log₂ expression ratio (log₂ER) was used to classify genes. A log₂ ER > 1 indicates average fold change induction factor of 2 for that particular gene. Analogously, a log₂ ER < -1 indicates an average fold change repression factor of 2. If log₂ ER's were between 1 and -1, they were classified as not significant (NS). The log₂ ER's across all treatment time-points for both WT and *mgt1* were exported and visualized in Spotfire's functional genomics module. The expression ratios were the basis of making comparisons between the experimental groups in this study.

Comparison with the phenotypic database

We also studied the expression profile in the context of the phenotypic database (<u>http://genomicphenotyping.mit.edu</u>) which includes information on sensitivity of 4800 yeast gene deletion strains to MMS. These deletions strains are of those genes that are nonessential. It was shown earlier that several of these genes are important for cellular recovery after mutagen exposure. In addition, it was observed that transcriptional responsiveness to these mutagens was not predictive of contribution of a gene to the recovery from the damage.

Basal gene expression profile in methylguanine methyltransferase deficient mutant (mgt1).

The basal gene expression profile of a gene in the O^oMeG methylguanine methyltransferase deficient mutant (*mgt1*) was assessed by computing a ratio of mean expression in *mgt1* (for that gene

from triplicate arrays) to mean expression in WT for the same gene (from triplicate arrays). If the expression ratio (ER) for any gene/ORF was > 2, then that gene was classified as being up-regulated and if the ratio was < 0.5, then it was classified as down-regulated. A plot of the gene expression ratio's for *mgt1* versus WT for the entire gene population is shown in Fig 14. In the examination of *mgt1* expression profile, 148/9275 (1.6%) genes were found to be up-regulated (maximum fold change was 14.8x) and 92 genes (<1%) were found to be down-regulated (maximum fold change was 95x).

Genes up-regulated in basal mgt1

A subset of these genes that were up-regulated in basal *mgt1* expression, listed by function, is shown in Table 4A (Appendix of Tables). Genes that were up-regulated but can otherwise be a part of the environmental stress response are indicated in table 4B. Notable among the genes upregulated in the basal *mgt1* are those involved in detoxification and drug transport (*YER185W*, *YOR378W*, *YHL047C*, *YEL065W*), amino-acid biosynthesis (*BAT1*, *LEU1*) and transport (*BAP3*, *ALP1*). Other important genes included metabolism (*CHA1*) genes, genes involved in cell cycle control (*BAT1*, *BUB1*, *CKA1*), and transcription (*CKA1*, *TFG1*, *GAL80*, *GCN5*, *CBP2*, *RNA15*). Cell cytoskeleton and mitochondrial biogenesis (*SMP2*, *DCG1*, *GIC1*, *Q0183*) and *REV7*, a subunit of DNA polymerase-zeta (Pol-zeta) were also induced.

Genes down-regulated in basal mgt1

A subset of these genes that were down-regulated in basal *mgt1* has been ordered by function and is shown in Table 5A. Sixty-five of them had no known function and have not been shown. Genes that were down-regulated but is otherwise a part of the environmental stress response are indicated in table 5B. Among the genes that are repressed were those involved in amino acid

(*MET14, CYS3*, and *BAS1*) and carbohydrate metabolism (*SUC2, MIG2, HXT1, HXT3 and HXT4*) and transcription (*NFS1, CPR6 and MIG2*).

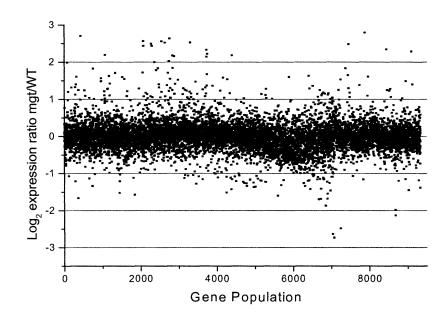


Figure 14: Expression ratio plot for yeast methylguanine methyltransferase mutant (*mgt1*).

Expression values (triplicate) of *mgt1* were compared to wild-type (WT) yeast expression and \log_2 transformed. Points above the y-axis grid line 1 indicate genes that are up-regulated in *mgt1*. Points below the y-axis grid line of -1 indicate genes that are down-regulated in *mgt1*.

Principal Component Analysis of experimental groups

The data from different experimental groups were also analyzed using Principal component analysis (PCA) in Matlab v6.0. Three untreated WT arrays 3 untreated *mgt1* datasets were compared with 6 datasets each from WT and *mgt1* treated with MNNG. Each WT and *mgt1* dataset included the mean expression from triplicate arrays. The PCA plot (Figure 15) shows 4 distinct clusters of data representing the untreated WT, untreated *mgt1*, treated WT and treated *mgt1*.

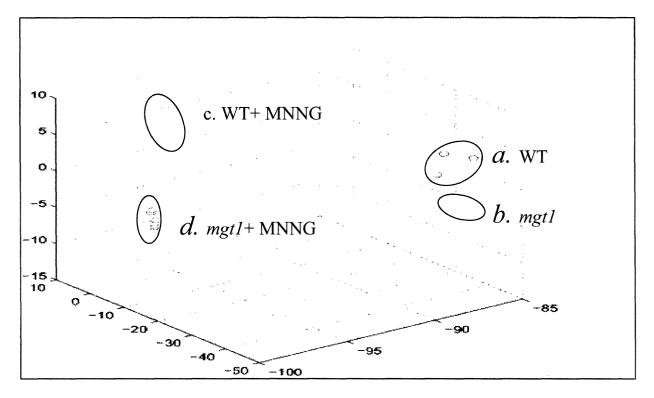


Figure 15: Principal component analysis of the experimental groups.

Three wild-type (WT) arrays (a) and 3 methylguanine methyltransferase mutants (mgt1) (b) were compared with 6 datasets (each representing the mean from triplicate arrays) from WT treated with alkylating agent, MNNG (c) and 6 datasets (each representing the mean from triplicate arrays) from mgt1 treated with alkylating agent, MNNG.

Effect of MNNG on transcriptional profile - Cluster Analysis

The \log_2 expression ratio's (ER's) were calculated for different experimental groups and exported to Spotfire. Hierarchical clustering (using Wards Method) of \log_2 ER's was used to generate a qualitative picture of the effect of MNNG on yeast. This heat map was generated using the data from 39 arrays (3 arrays were used as baseline for comparison).

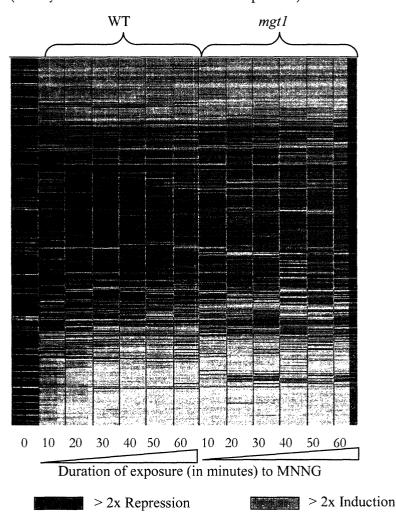


Figure 16: Heat map of the expression ratio from wild-type (WT) and Mtase mutant (mgt1). Log₂ expression ratio (log₂ER) was calculated for 9335 probe-sets by dividing the mean expression (from triplicates) for each probe-set by the mean expression for the same probe-set in the untreated WT (WT0). The first column of data represents the basal expression in mgt1. The other columns of data represent the mean expression value of triplicate arrays where yeast strains, either WT or mgt1, that was exposed to MNNG for variable length of time (10-60 minutes). This indicates that the genome is very responsive to the treatment with MNNG.

Temporal effects of gene categories

The temporal effects of MNNG on the yeast strains on a genome-wide scale were examined using the average expression profile for the treated WT (Figure 17A) and *mgt1* (Figure 17B). About 1200-1400 genes are induced or repressed upon treatment with MNNG in both WT and *mgt1*.

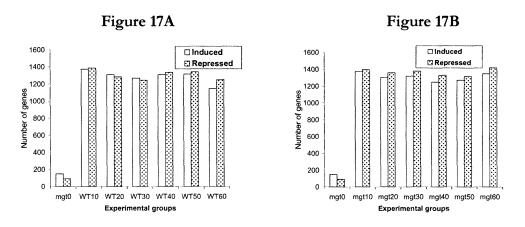


Figure 17A: Genes responsive to treatment with MNNG in the wild-type (WT) yeast.

The number of genes that are either induced or repressed in the WT yeast upon exposure to MNNG for varying lengths of time (10-60 minutes, WT10 through WT60) is shown. The untreated *mgt1* (*mgt0*) serves as a comparison.

Figure 17B: Genes responsive to treatment with MNNG in the methylguanine methyltransferase (*mgt1*) yeast.

The number of genes that are either induced or repressed in the methylguanine methyltransferase mutant (*mgt1*) yeast, upon exposure to MNNG for varying lengths of time (10-60 minutes, mgt10 through mgt60) is shown. The untreated *mgt1* (*mgt*0) category serves as a comparison.

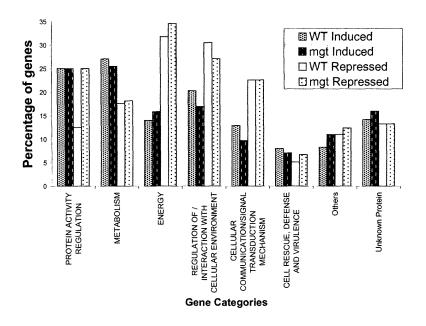


Figure 18: Gene expression responsiveness for some functional categories.

Average gene expression ratios for each gene within a particular functional category were compared across the experimental groups. The percentages of genes within a particular category, that are induced or repressed upon treatment with MNNG are indicated.

The expression profiles from entire categories of genes were examined to study the effect of MNNG on them and in particular if the gene expression was different between WT and *mgt1*. Mean fold induction and fold repression for each ORF/gene, across all the WT and *mgt1* arrays was calculated. In each category, the percentage of genes that were responsive upon MNNG treatment is shown in Figure 18. To calculate this, data from 18 WT and 18 *mgt1* arrays was used.

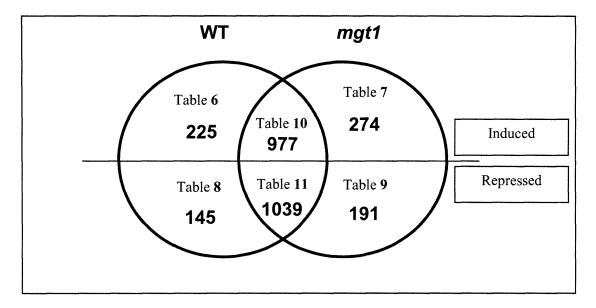


Figure 19: Venn-diagram of gene expression responsiveness in wild-type (WT) and methylguanine methyltransferase deficient yeast (*mgt1*) upon treatment with MNNG.

Genes that had a fold change (FC) > 2 that were either induced or repressed in WT and/or *mgt1* are represented using the Venn-diagram. This representation allows examination of effects that are unique to WT or *mgt1* or common both, upon exposure to MNNG. Gene expression response, induction or repression, that is specific to WT and *mgt1* can therefore be distinguished from a response that is found in both WT and *mgt1*. The upper-middle panel in the Venn diagram represents genes that are induced in both WT and *mgt1* (977 genes) as a common response to MNNG exposure. Alternatively, genes that are induced only in MNNG treated WT (225), or only in MNNG treated *mgt1* (274) are represented by the non-overlapping segments of the 2 circles. The lower-middle panel in the Venn diagram represents genes as a common response to MNNG treated WT (145), or only in MNNG treated *mgt1* (191) are represented by the non-overlapping segments of the 2 circles in the lower panel.

Genes induced specifically in WT upon treatment with MNNG

The upper-left panel in the Venn diagram (Figure 19) illustrates the response that can be attributed to WT strain upon exposure to MNNG. Upon MNNG-treatment, a total of 225 ORF's were specifically induced only in the WT. Since the only difference between WT and *mgt1* is the lack of MTase because of the deletion, it could be postulated that these genes are induced in the WT because of MNNG's effect in the presence of MTase. A total of 127 genes had a known function (listed in Tables 6A and 6B). Table 6B includes genes that are a part of the ESR. Table 6A includes

17 (17%) genes that are essential (highlighted in red). Interestingly 12 (12%) of the induced genes were involved in protein biosynthesis. Three DNA repair genes UNG1, SIR2 and RAD52 were also induced. Two mitochondrial genes, RIM1 and ERV1, were found to be induced. Table 7B includes 30 genes that are a part of the ESR. This included 12 genes (40%) that are otherwise essential in yeast (highlighted in red).

Genes that are induced specifically in mgt1 upon treatment with MNNG

There were 274 genes in this category. 103 of them had a known function and are listed in Table 7A and 7B. Table 7A includes 87 known genes that are induced in the *mgt1* upon MNNG treatment. Of them, 20 (22%) were essential genes. Notable among them were DNA repair genes *PRI2* and *CCE1* and several mitochondrial associated genes (*MRS11 TIM8, CCE1, COQ3, IDH2* and *DIC1*). In contrast to WT, only 3 protein synthesis genes were found to be specifically induced in *mgt1*. Interestingly, *SW16*, a substrate of Rad53 in the G(1)/S DNA damage checkpoint was activated. The homothallic switching (HO) endonuclease, which creates a site-specific double-strand break (DSB) in the genome at the mating-type (MAT) locus, was also induced. Table 7B includes 16 genes with known function that are induced in *mgt1* and are a part of the ESR. Nine (56%) were found to be essential.

Genes repressed in WT upon MNNG treatment

A total of 145 genes were repressed exclusively in WT. Table 8A lists 70 genes with known function that are repressed exclusively in WT upon MNNG treatment. This included 7 essential genes (10%). Six genes (*SUM1, DOT6, ESC1, ISW2, NGG1 and SET3*) involved in chromatin silencing and histone modification were repressed. Two DNA repair genes (RAD16 and RAD28)

were repressed. Table 8B lists 10 ESR genes that are repressed in WT. Only 1 gene was found to be essential.

Genes repressed in *mgt1* upon MNNG treatment

A total of 191 genes were repressed exclusively in *mgt1*. Table 9A lists 70 genes with known function that are repressed exclusively in *mgt1* upon MNNG treatment. This includes 14 essential genes (20%). Three genes (*SNF11*, *SPT10*, *TBF1*) involved in chromatin remodeling were repressed. *CKS1*, a cyclin-dependent kinase regulatory subunit, was also repressed. Table 9B lists 3 ESR genes that are repressed in *mgt1*.

Genes induced upon treatment with MNNG in both WT and mgt1

In contrast to a damage induced response exclusive to WT or *mgt1*, there were several genes that were induced upon treatment with MNNG in both WT and *mgt1*. This overlapping response indicated in the upper-middle panel of Figure 19 included 977 genes that were induced in both WT and *mgt1*. Of them, 127 genes were included as ESR genes. The function of 282 genes was not known. The remaining 568 genes, whose function was known and those that were not a part of the ESR are listed by function in Table 10A. 121 (21%) of these are essential genes. Briefly, the genes that were induced upon treatment with MNNG, and were not a part of ESR, included those involved in maintaining cellular structure and function. Primarily, these included genes involved in cell wall organization, ergosterol biosynthesis, amino acid metabolism, mitochondrial organization and biogenesis. A few other genes of interest included chromatin silencing genes (*APC5*, *ISW1*, *ORC3*, *MRC1*, *ORC5*, *NNT1*, *SWD1*, *SWD3*) genes involved in DNA damage response (*HUG1*, *DUN1*, *PCL2*), DNA recombination (CDC9), DNA repair (*HAM1*, *MSH1*, *RAD18*, *RHC18*, *POL1*), DNA replication (*POL5*, *RNR3*, *RNR4*, *RNR1*), DNA topological change (TOF1) and

DNA unwinding (*CDC46, HFM1, MCM2*). Specific DNA repair genes included those involved in nucleotide excision repair (*RFA 1, RFA2, RFA3, CDC2, POL30* and *DPB2*). Interestingly, 68 genes (11%) of the genes induced in both WT and *mgt1* were involved in protein synthesis. Table 10B lists 127 ESR genes that are induced upon treatment with MNNG in both WT and *mgt1*. Interestingly, 57 (44%) of these are essential genes. Eleven genes are involved in ubiquitin-dependent protein catabolism.

Genes repressed upon treatment with MNNG in both WT and mgt1

A total of 1039 genes were repressed in both WT and *mgt1*. Of them, 545 had a known function and are shown in Tables 11A and 11B. Table 11A includes genes that were repressed in both WT and *mgt1* and are not a part of the ESR. These included 75 genes (13%) that were essential. Notable among them were genes involved in cell wall organization, fatty acid metabolism, G1/S cell cycle transition genes, mRNA splicing, methionine biosynthesis and mitochondrial organization. The largest category of genes that were affected was involved in transcription and its regulation. About 43 genes (7%) of the genes belonged to this category. Interestingly several DNA repair genes were repressed. These included genes involved in DNA recombination and repair (*HEX3, SLX8, IXR31, NSE*) DNA replication (*RRM3, TAH11,RIM4*) DSB repair (*YKU80, SIR4, LRP1, FYV6*) nucleotide excision repair (*TFB3, DPB11, RAD4*). Table 11B includes 60 ESR genes with known function that are repressed in both WT and *mgt1* upon treatment with MNNG.

DNA damage response and repair genes

The DNA damage response and repair genes were of additional interest and were therefore examined as a separate class. The mean expression profile of the DNA damage response and repair genes is indicative of DNA repair pathways are likely to be activated in WT and *mgt1* in response to MNNG. A total of 133 genes were pooled into this category based on Affymetrix annotations that are derived from the SGD annotations. Twenty five genes were induced (Table 12A) and 20 genes were repressed (Table 12B). More than half the induced genes are essential or are sensitive upon deletion (Table 12A). 80 genes did not have an appreciable fold change to be classified as induction or repression. A total of 8 of the DNA repair and replication genes were classified as ESR genes (Table 12C).

Temporal effects of individual genes

To further elucidate the differences between WT and *mgt*,1 the temporal profiles of individual genes were examined. Mean expression profiles at 6 time points for WT (3 arrays per time point) and 6 time points for *mgt*1 (3 arrays per time point) were used. The temporal profile of a gene indicates a change in its mean expression upon increasing length of exposure to MNNG. The change was judged by 2 methods; a) the slope of the expression and b) the net fold change. The net fold-change can be defined as the ratio of expression at the 60th minute (\exp_{60}) to expression at the 10th minute (\exp_{10}) after exposure to MNNG. All genes that had an \exp_{60}/\exp_{10} ratio >2 were classified as induced and \exp_{60}/\exp_{10} ratio < 0.5 were classified as repressed. The Venn diagram in Figure 20 summarizes the differences and similarities in the responses between WT and *mgt*1. The upper panel represents genes that are incrementally induced starting at the first time of exposure (10th minute). The lower panel represents genes that are repressed over time, starting at the first time point. There are unique and shared responses by the WT and *mgt*1 to MNNG.

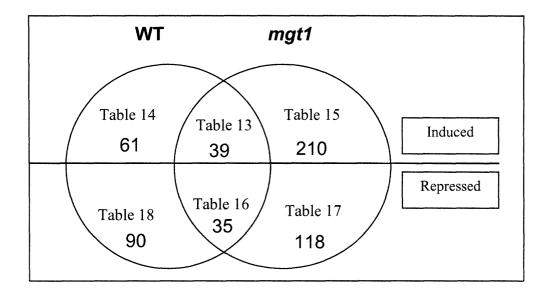


Figure 20: Venn-diagram of genes that are incrementally induced or repressed upon increasing length of exposure to MNNG.

The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60th minute to mean expression at the 10th minute. A cut-off of FC>2 (for induction) and FC<0.5 (for repression) was used to select genes that have been included in this representation.

Genes induced over time

When all such profiles were examined, the expression of 60 genes was found to have an incremental induction over time in the WT. Similarly, 210 genes in *mgt1* were found to increase upon increasing the length of exposure to MNNG. The incremental response of 39 genes was common to WT and *mgt1*. Induced genes that were known to have a function are represented in Table 13. In the WT, only 2 (out of 24 genes with known function, 8%) were essential. In contrast, 34 (out of 79 genes with known function, 43%) were found to be essential genes. In the WT, DNA damage effectors *HUG1* and *RNR3* were incrementally induced with increasing length of exposure to MNNG. In contrast to WT (61), there were more genes in *mgt1* (210) that were responsive. These

genes are involved in ribosomal RNA processing, mRNA processing and transcription were found to be incrementally induced. Several other ESR genes were also found to be a part of pre-rRNA processing and ribosomal protein synthesis. Overall, there were about 28 genes (35%) involved in mRNA, rRNA, tRNA and ribosomal function, that were incrementally induced in *mgt1* upon exposure to MNNG over time. 20 (out of 52 genes) fitted a profile of a dramatic initial repression (after 10 minutes of exposure to MNNG) followed by a steady increment towards the basal levels. In contrast, 7 genes were consistently induced. The reflex response by 20 genes is likely to represent a response that follows the perturbation. The 7 genes that are incrementally induced over and above basal levels are likely to represent processes that are integrated with damage response and recovery.

Genes repressed over time

Ninety genes were repressed exclusively in WT. In contrast 118 genes were repressed in *mgt1*. Only 35 genes were seemed to be repressed in both WT and *mgt1*. Repressed genes that were known to have a function are represented in Table 14. The corresponding sets of genes that belong to ESR are also listed.

In the WT, only 1 gene (out of 18) was found to be essential. Notable among them was the homothallic switching (HO) endonuclease, which creates a site-specific double-strand break (DSB) in the genome at the mating-type (MAT) locus. This gene was listed earlier as a gene that was induced in *mgt1* but not in WT. Closer examination of the profile revealed that there is an instantaneous induction of HO after the first exposure to MNNG in both WT and *mgt1*. While this induction is sustained in the *mgt1* (hence the mean $\log_2 ER>2$), there is a decline in the induction over time in the WT (therefore, explaining its classification as "repression").

Genes that were repressed in *mgt1* includes 6 genes (out of 47) that are essential. Notable among them are genes involved in protein folding, methionine metabolism and translation. 18 (out of 47)

genes) fitted a profile of a dramatic initial induction (after 10 minutes of exposure to MNNG) followed by a decline. In contrast, 13 genes were consistently repressed beyond the basal levels. The reflex response by 18 genes is likely to represent a response that follows the perturbation. The 13 genes that are incrementally repressed below basal levels are likely to represent processes that are integrated with damage response and recovery. The differential response between WT and *mgt1* can provide valuable insight into the differences in the mechanism of response to MNNG in the presence and absence of MTase.

DISCUSSION

Several authors have studied the genome-wide transcriptional effects of chemical and physical agents on yeast using microarrays. The yeast transcriptome response to MMS (Jelinsky and Samson 1999) and MNNG (Jelinsky et al 2000) have yielded valuable data on how the yeast adapts to these alkylating agents. Specifically, these studies explored the transcriptional response of S. cerevisiae to a wide range of chemical and physical damaging agents in an attempt to delineate the response of each ORF to these agents. Agarwal et al 2003, studied the genome-wide effects of antifungal agents on yeast in an attempt to characterize their mechanism of action. Several other microarray-based studies have examined the effect of single gene deletions on yeast transcriptome. For example, Ohkuni et al 2003, studied the genome-wide expression in the Deltanap1 cells in order to study the transcriptional control of NAP1, a nucleosomal assembly protein. Fry et al 2003, studied the effect of SGS1 deletion on transcriptional profile in yeast because of its homology with human genes involved in Werner and Blooms syndrome. Gasch et al 2001, studied basal expression profile in MEC1, DUN1 and CRT1 deficient yeast and their transcriptional changes in response to MMS. The study uncovered the role of MEC1, the human ATR homolog in yeast. It was also concluded that MEC1 was an integral part of controlling the environmental stress response. A literature survey yielded no genome-wide expression profile studies where deletion strains of DNA repair genes were used. The current study is the first report of the transcriptional responsiveness where a known DNA repair deficient (O^6 methylguanine methyltransferase deficient strain, *mgt1*) has been studied. While undertaking this study, the goals were two-fold. The first was to study the effects of deletion of mgt1 on the yeast transcriptome. The second was to study the effect of alkylation induced transcriptional changes over time in the WT and mgt1 and to examine the differences between them.

MNNG specific response genes enriched by culling out genes involved in environmental stress response (ESR).

In response to environmental perturbations, S. cerevisiae cells elicit rapid transcriptional reprogramming involving both activation and repression of gene expression. Some of these transcriptional changes represent responses that are common to chemical and physical stresses. Removing these ESR genes from the observed response, will help to enrich the set of genes that are specific to MNNG treatment and/or presence or absence of MTase. This was achieved by comparing the expression profile in the current study with ESR dataset from Gasch et al 2000 to identify ESR genes that might confound interpretation of the data. In the second tier of comparison, phenotypic sensitivity information of veast deletion strains from (http://genomicphenotyping.mit.edu) was incorporated along with expression.

Deletion of *MGT1* induces dramatic basal transcription changes, activates cell cycle checkpoints, transcription factors and a gene involved in spontaneous mutagenesis.

MGT1 is involved in direct repair of O⁶ Methylguanine and O⁴Methylthymine lesions. Genes that are induced upon deletion of MGT1 are likely to be involved in a) a direct interaction with MGT1 or b) a downstream effect of a lack of MGT1. A direct interaction can follow from the argument that MGT1 normally, represses these genes and removing MGT1 induces them. Alternatively, lack of MGT1 can lead to increased spontaneous mutations and DNA damage and genes induced might be a part of the downstream cellular processes that are involved in handling this damage. It was interesting to note the up-regulation of 148 genes upon the deletion of one single gene (MGT1). The deletion appears to up-regulate a gene involved in spontaneous mutagenesis and several genes that are transcription factors and 2 others that are involved in cell cycle control. The 7-fold up-regulation of REV7, a subunit of DNA polymerase-zeta (Pol-zeta, Pol ζ) is important in the context of spontaneous mutations. The other subunit of pol-zeta, is REV3 (which was not up-regulated). REV7 is the processivity factor for REV3 and complex together, to get involved in translesion (TLS) synthesis, a mechanism that probably helps cells cope with DNA lesions that have escaped the efficient DNA repair systems. TLS is invoked when there is a replication blocking lesion that the normal polymerases are not able to copy past. O⁶Methylguanine (O^oMeG) is a mutagenic lesion and is not considered as a replication blocking lesion. It is likely, therefore, that the endogenous lesion leading to the up-regulation of REV7, is probably not because of O⁶ MeG. At the same time that TLS helps to copy past the lesion, it has potentially mutagenic consequences making it responsible for the majority of spontaneous mutations (Friedberg 1995). Increase in spontaneous mutations in mgt1 has been observed earlier (Xiao and Samson 1992). The same study found that wild-type mutation rate was restored when the mgt1 mutant was transformed with a functional MGT1. The seven-fold induction of REV7 in this context may suggest a downstream effect of the deletion of MGT1 rather than via O⁶ MeG. Cell cycle control genes, BUB1 and CKA1 were up-regulated. BUB1 is a protein kinase and serves as a mitotic spindle checkpoint. CKA1 is the alpha unit of protein kinase CK2 and is known to be involved in DNA damage response and cell-cycle control. Among the transcription factors that were up-regulated GCN5 has two tiers of significance. First, Gcn5p plays a role in controlling the expression of 5 % of the yeast genome (Holstege et al, 1998). Secondly, GCN5, a histone acetyl transferase allows efficient access of the repair machinery to chromosomal DNA damage either indirectly via influencing transcription or directly via modifying chromatin structure. Gcn5 functions before or during the DNA repair process. An earlier report suggested that Gcn5 is recruited upstream of the damaged area by a hitherto unknown DNA damage sensor (Teng et al, 2002). Overall, it appears as though the deletion of MGT1 is leads to increased DNA damage good reason why cell cycle checkpoints are upregulated. Simultaneous up-regulation of a key component of the translesion synthesis suggests the role of error-prone damage tolerance mechanisms in response to possible replication blocking lesions. Up-regulation of *GCN5*, a gene that aids DNA repair and controls expression of 5% of the yeast genome is indeed remarkable.

Cellular response to MNNG in WT and mgt1

About 30% of the yeast genome (as represented on the Affymetrix GeneChip Array YGS98) was responsive to treatment with MNNG (Figure 16). As the heat map in Figure 16 indicates, response to most of the damage that was inflicted by MNNG was initiated in the first 10 minutes of exposure. Thereafter, the total number of responsive genes did not change dramatically. Evaluation of the genome-wide response across the length of time might lead us to miss changes in a subset of genes that might be instrumental in understanding the response to MNNG. Therefore, in order to dissect the transcriptional response further, genes belonging to several functional sub-categories were examined. This, however, did not yield any substantial change in the responsiveness in gene expression over time, to MNNG (Figure 17A and 17B).

MNNG induced damage activates cell-cycle checkpoint cascade, DNA damage signal amplifiers and downstream effectors

As the cells respond to an adverse condition such as exposure to MNNG, several cellular responses are mounted by WT and *mgt1*. The Venn diagram (Figure 19) indicates that a majority (977 genes, 66%) of this response was common to both WT and *mgt1*. The response that is shared by WT and the *mgt1* is indicative of cellular processes that are common to both strains in response to MNNG. Among the shared response are genes that serve as a part of S-phase checkpoint. The checkpoint regulatory mechanism has an important role in maintaining the integrity of the genome and results in a temporary cessation of DNA replication. Eukaryotic cells activate checkpoint

pathways that arrest cell cycle progression and induce the expression of genes that are required for DNA repair. This checkpoint machinery consists of proteins that recognize DNA damage and initiate the signaling response. The identification of the damage also needs to be amplified in order to recruit other mediators of DNA damage response. MRC1 and TOF1 are DNA damage signal amplifiers. TOF1 and MRC1 were induced in both WT and mgt1. Upon damage to DNA, TOF1 gets activated and forms a part of a replication-pausing complex. TOF1, located at the arrested forks activates checkpoint cascades, leading to repair of the damaged DNA. Recently, it was demonstrated that Tof1 and Mrc1 interact directly with the damaged DNA (Katou et al 2003). It has also been postulated that Tof1p links Mec1p with Rad53p (Foss, 2001). This is an interesting finding in the context that MEC1 and RAD53 is an indispensable component of DNA damage response. Rad53 and Mec1 are protein kinases required for DNA replication and recovery from DNA damage in S. cerevisiae. DNA damage during S phase slows down the rates of replication fork elongation (Tercero and Diffley, 2001) and triggers a Rad53/Mec1-dependent block. As a result, DNA damage leads to an abrupt decrease in DNA synthesis (Paulovich and Hartwell, 1995). In addition, Mec1 and Rad53 are required to prevent DNA damage-induced collapse of replication forks (Tercero and Diffley 2001), via their ability to phosphorylate replication and repair proteins at stalled replication forks. The essential function of Mec1 and Rad53 in S. cerevisiae is to promote deoxyribonucleotide triphosphate (dNTP) production during S phase to coincide with DNA replication. This is achieved via phosphorylation and subsequent degradation of Sml1 (Zhao et al., 2001), an inhibitor of ribonucleotide reductase (RNR). Ribonucleotide reductase (RNR) catalyzes the rate limiting step in the production of deoxyribonucleotides needed for DNA synthesis. Its synthesis is tightly regulated at the level of transcription. It is cell-cycle regulated and provides a metabolic state that facilitates DNA replicational repair processes. Dun1, a protein kinase, controls inducibility of RNR1, 2 and 3 in response to DNA damage and replication blocks. RNR genes in yeast form a regulon that is coordinately regulated by protein phosphorylation in response to DNA damage.

In our dataset, the $\log_2 \text{ER}$ for *MEC1* and *RAD53* was not induced more than 2 fold. It is likely that this is because they are kinases and hence present transiently. *DUN1* and *HUG1* are DNA damage response genes down-stream of *MEC1* and *RAD53* and were induced. *HUG1* (hydroxyurea and **U**V and **g**amma radiation induced) is a component of the *MEC1*-mediated checkpoint response to DNA damage and leads to replication arrest. The *HUG1* gene was identified as a component of the DNA-damage checkpoint response using deletion and overexpression mutants of *S. cerevisiae* (Kaplun 2000). DNA damage-specific induction of *HUG1* is independent of the cell cycle stage. *HUG1* induction also increased with increasing exposure to MNNG in both WT and *mgt1*. Its induction response to MNNG is therefore consistent with its role in DNA damage response.

MNNG induced damage activates chromatin silencing.

Mec1 is the central transducer of these stress-response signals (Zhou and Elledge 2000). Both Rad53 and Mec1 are key proteins involved in the response to replication blocks and they act together with a novel regulator of Rad53, Mrc1. The DNA damage response pathway has been linked to the control of chromatin organization. In response to DNA damage, certain proteins that are normally relocalize to silence telomeric chromatin (Martin et al. 1999, Mills et al. 1999). This relocation is dependent on Mec1 (Craven and Petes 2000). In the current data, 6 genes involved in chromatin silencing are induced and 3 of them are also known to be essential. This chromatinmediated maintenance of transcriptional inactivation is in accordance with expectations.

MNNG induced damage activates genes involved in DNA replication and repair.

DNA repair mechanisms are by far the most important components of the cellular response that gets induced upon damage to DNA by MNNG. DNA polymerase alpha (POL1) is an essential gene required for initiation of replication and lagging-strand synthesis. It was also found to be a part of the ESR. The MCM2 is a part of the Mcm2-Mcm7 protein complex that forms a DNA helicase that unwinds the DNA ahead of the replication fork (Labib and Diffley, 2001). Additionally, all the essential subunits of replication protein A (RPA) were induced. RPA is a single-stranded DNA binding protein (SSB) involved in DNA replication, recombination and repair (Kim C et al 1992). It has been recently shown that RPA facilitates telomerase action (Schramke, 2004). Proliferating cell nuclear antigen (PCNA), encoded by the POL30 gene, is essential for DNA replication (in association with RFC) and DNA repair. PCNA is a ring-shaped DNA polymerase accessory protein that can encircle duplex DNA. PCNA interacts with Pol eta to permit efficient lesion bypass. Another notable gene that was induced in response to MNNG was HAM1. It is known that overexpression of the yeast HAM1 gene prevents 6-N-hydroxylaminopurine mutagenesis in E. coli (Kozmin et al 1998) suggesting that it might play a protective role in MNNG induced damage. HAM1 controls 6-N-hydroxylaminopurine (HAP) sensitivity and mutagenesis in S. cerevisiae. The HAM1 protein protects the cell from HAP, either on the level of deoxynucleoside triphosphate or the DNA level by a yet unidentified set of reactions (Noskov, 1996). It was intriguing to note that HAM1 deletion phenotype was not sensitive to MMS

Repair of MNNG induced mitochondrial DNA damage

CDC9 gene encodes a DNA ligase protein that is targeted to both the nucleus and the mitochondria and this yeast rely upon a single DNA ligase, Cdc9p, to carry out mitochondrial DNA replication and recovery from both spontaneous and induced mitochondrial DNA damage

(Donahue 2001). *MSH1* is a DNA-binding protein in yeast mitochondria that recognizes nucleotide mismatches in DNA and plays a role in mitochondrial mutation avoidance. *MSH1* protein is targeted to the mitochondria where its mitochondrial-targeting sequence is removed (Chi and Kolodner, 1994). Taken together, the induction of *CDC9* and MSH1 appears to be a part of a program to repair damage to mitochondrial DNA.

MNNG induced damage activates ubiquitin mediated protein catabolism

Twenty genes involved in protein ubiquitination and ubiquitin mediated protein catabolism were induced (*RPT1*, *DOA1*, *RPN2*, *RPN1*, *PRE9*, *SCL1*, *RPN9*, *UFD2*, *RPN7*, *RPT5*, *PRE8*). Among them, *DOA1* is thought to encode a regulatory component of the proteasome pathway, which involves ubiquitin (Ub)-dependent protein degradation (Ghislain, 1996).

MNNG induced damage activates protein synthesis genes

The yeast ribosomal proteins (RPs) of are encoded by more than 100 genes. These are among the most transcriptionally active genes in the yeast genome. It consumes a prodigious amount of the cell's resources and, consequently, is tightly regulated. Interestingly, 68 genes (11%) of the genes induced in both WT and *mgt1* were involved in ribosomal protein synthesis. This is in contrast to earlier observations where protein synthesis genes were found to be repressed upon exposure to MMS (Jelinsky et al 1999) and osmotic stress (Rep, 2000). Notable among these include *RAP1*, a multifunctional transcription factor that has a BRCT domain. The BRCT domain is found predominantly in proteins involved in cell cycle checkpoint functions responsive to DNA damage. *RAP1* is essential for cell viability and can function as either an activator or a repressor of transcription, depending upon the context of its binding site. *RAP1* was incidentally found to be repressed and it is likely that repression of RAP1 is responsible for induction of the 68 ribosomal protein synthesis genes.

In an earlier study MAG1, 3-methyladenine DNA glycosylase, an integral component of the base excision repair pathway, was shown to be induced upon damage to DNA by MMS. It was also shown that MAG1 and MGT1 have a common upstream regulatory sequence. In this dataset, MAG1 was not found to be induced more than 2-fold.

Ubiquitin-proteasome regulator, RPN4, is repressed upon MNNG treatment.

Intracellular proteolysis in yeast occurs mainly via the ubiquitin-proteasome system. Expression of this system is under the control of the transcription factor, Rpn4p (Mannhaupt G et al, 1999). It has been shown earlier that alkylating agent MMS resulted in activation of genes that are involved in ubiquitin and 26S proteasome-dependent protein degradation. Rpn4p is a major transcription regulator that acts by binding to proteasome-associated control element (PACE) with a unique upstream activating sequence (5'-GGTGGCAAA-3'). This binding either stimulated or inhibited transcription. In this dataset, however, *RPN4* was found to be repressed 4.5 times.

Genes involved in non-homologous end joining (NHEJ), recombination and some elements of nucleotide excision repair are repressed in MNNG exposed yeast cells.

Among the genes repressed in both WT and *mgt1* are those involved in DSB repair via NHEJ. (*YKU80, SIR4, LRP1, FYV6*). The components of the non-homologous end joining (NHEJ) repair pathway were repressed 2-3.5 fold. Additionally, few other genes involved in recombination and replication were also repressed. *HEX3* and *SLX8* have DNA binding activity and are implicated in recombination repair. *SLX8* is required to resolve recombination intermediates that arise in response to DNA damage. The *RAD4* gene of yeast is required DNA binding and for

the incision of damaged DNA during nucleotide excision repair (NER) (Owsianik 2002). *TFB2* is a transcription/repair factor (TFIIH) subunit that is a transcription initiation factor required for NER.

Finally, two discrete set of genes, the "WT-specific MNNG-damage signature" and "*mgt1*-specific MNNG-damage signature" was created. These include uniquely up-regulated in the WT or *mgt1* upon exposure to MNNG. This signature may help define new candidates for involvement in cellular responses to MNNG in a wild-type and upon O⁶ methylguanine methyltransferase deletion.

MNNG induces genes involved in mRNA turnover and protein synthesis in WT

Since the only difference between WT and mgt1 is the lack of MTase, it could be postulated that the set of transcripts are specifically induced in WT are because of MNNG's effect in the WT MTase background. Expression of 7 genes involved in mRNA splicing (MSL1), cleavage (*PT11*) and catabolism (*NMD4*, *PUB1*), specifically in the WT is indicative of more mRNA turnover. There were 3 others that were classified as a part of ESR. Accordingly, there were 18 protein synthesis genes (6 were ESR genes) that were induced. It is likely that the overwhelming induction of protein synthesis genes is representative of a recovery response after the initial insult. More protein synthesis genes are induced in the WT as opposed to mgt, probably because it is able to recover faster (than the mgt1). Mitochondrial DNA damage response was exemplified by induction of *RIM1*. This has single stranded binding (SSB) activity and is involved in mitochondrial genome maintenance. *RIM1* forms an essential component of the yeast mtDNA replication apparatus (Van Dyck, 1992). *ERV1* gene is essential for cell viability and for the biogenesis of functional mitochondria.

Repression of chromatin remodeling genes following MNNG induced damage

While the genes that are specifically induced in the WT upon MNNG damage are involved in fundamental metabolic processes, the genes that are repressed include 5 chromatin remodeling and histone modification genes (of 18). In addition, *RPI1*, a repressor of the ras-cAMP pathway and *UBP10*, a deubiquitinating enzyme are repressed. Loss of *UBP10* function is known to lead to partial impairment of silencing at telomeres. A study of ubp10 deletion revealed that it mimicked oxidative damage by intracellular accumulation of reactive oxygen species and eventually leading to DNA fragmentation and phosphatidylserine externalization, which happen to be the 2 markers of apoptosis (Orlandi, 2003).

MNNG induces mitochondrial damage in mgt1

It appears as though the lack of MTase in *mgt1* results in increased damage to mitochondria. This was reflected in the responsiveness of several mitochondrial proteins that were induced specifically in *mgt1*. These genes are involved in fundamental biochemical processes in the mitochondria. *MRS11* and *TIM8* are protein transporters in the mitochondria. *CCE1* is involved in DNA recombination and is also present in the inner-mitochondrial membrane. *COQ3* is involved in ubiquinone biosynthesis, and is a component of the inner mitochondrial membrane. *IDH2* is involved in the TCA cycle and also localizes to the inner mitochondrial membrane. *DIC1* is involved in dicarboxylic transport across the mitochondrial membrane. There were only 3 protein synthesis genes

MNNG induced damage activates multifunctional transcription factor SWI6, in mgt1

SW16 is a transcription factor involved in controlling genes involved in cell wall biogenesis and architecture. It is also a key component of G1/S checkpoint. When a cell detects damaged DNA, Rad53 checkpoint kinase activity is dramatically increased, which ultimately leads to changes in DNA replication, repair, and cell division. *SW16*, a substrate of Rad53 in the G(1)/S DNA damage checkpoint was activated in *mgt1* indicating that there is more DNA damage in *mgt1*. *SW16* enhances the expression level of the recombination genes in meiosis in a dosage-dependent manner, which results in an effect on the frequency of meiotic recombination (Leem 1998). Another gene involved in recombination is *CCE1*.

Ho endonuclease introduces a site-specific double strand break (DSB) in the mating type (*MAT*) gene of yeast and its expression is tightly regulated. This endonuclease is known to be induced for a short duration and quickly degraded via the ubiquitin-26 S proteasome system (Kaplun, L et al 2000). Taken together, it appears as though *mgt1* has a propensity to undergo more mitochondrial damage and DNA recombination repair.

An exaggerated response of *mgt1*-specific MNNG-damage was limited to genes that seem to be involved in remodeling of the cell cytoskeleton, translation and signal transduction activity.

Role of environmental stress response genes

The environmental stress response, ESR is a stereotypical pattern of changes in the expression of approximately 900 genes evoked by a large variety of environmental stresses, including heat shock, osmotic shock, DTT, nitrogen starvation, and peroxide. Many of the genes in this program are induced in response to stressful environments and therefore may play a critical role of maintaining internal homeostasis. As expected, the ESR was rapidly initiated in wild-type and *mgt1* cells responding to MNNG, and it was sustained through the entire course of the experiment. From Gasch et al 2000, a total of 95 microarray hybridization experiments were used to deduce the environmental stress response genes that were found to be responsive in this study. Approximately 48% of the genes found in the ESR were also induced/repressed upon treatment with MNNG. Approximately 78% of these ESR genes were common to the response by WT and *mgt1*. This overlap is very suggestive of cellular responses that are common to processes that help the cell survive and achieve internal homeostasis.

In an earlier study Gasch et al 2000 reported the presence of a DNA damage signature cluster comprising nine genes including the ribonucleotide reductase subunits RNR2 and RNR4, the DNA-damage repair genes RAD51 and RAD54, the DNA-damage activated kinase DUN1, the DNA-damage-inducible mitochondrial nuclease DIN7, PLM2, which has homology to the forkhead associated-domain found in several transcription factors and kinases, and two uncharacterized ORFs (YER004W and YBR070C). A total of 4 genes from the 9 from their cluster (DUN1, PLM2 RNR4, and the ORF YBR070C) were found to be induced in the current study.

Temporal response to MNNG.

A comparison of temporal expression profiles of genes incrementally induced or repressed in WT and *mgt1* revealed interesting trends. Overall, there were more genes that showed induction or repression in the *mgt1* (210 induced, 118 repressed) than WT (61 induced, 90 repressed). There were a few genes that showed trends (39 induced, 35 repressed) that were shared between WT and *mgt1*. This result indicates that the perturbation in the *mgt1* is more profound than in the WT.

In the WT there is a reflex repression of several fundamental biochemical processes when the cells are first exposed to MNNG. These processes include glucose metabolism, lipid signaling pathways, fatty acid metabolism, electron transport system and the glyoxylate cycle. The repression is transient and is eased as the cell tries to recover from the perturbation. Almost simultaneously, there is a reflex induction of processes involved in maintaining the cell wall structure and function. Their induction wanes over time. Other genes that follow this pattern are involved in phosphatidylethanolamine and serine biosynthesis and threonine catabolism. Other interesting genes in this category included, *TLC1* which encodes the RNA subunit of telomerase (Singer, 1994) and HO endonuclease. The components of the DNA damage response pathway are known to degrade HO endonuclease via the ubiquitin 26s proteasome system (Kaplun L). This could explain the waning of "induction" over time. These responses are likely to be related to processes that are involved in damage recovery. A few genes were consistently induced after the initial exposure to MNNG. These responses need to be distinguished from the ones that are observed above. These responses are sustained as long as the cells are exposed to MNNG. Therefore, these are likely to be critical and related to processes that are directly related to the damage caused by MNNG or its downstream processes. To exemplify, GTT2 codes for a glutathione transferase and its deletion strain is also found to be very sensitive to MMS. In addition to its role as an antioxidant, glutathione has several physiological functions, such as detoxification of various cytotoxic compounds, acting as a co-factor for enzymes, protection of proteins' SH groups. Upon invasion by xenobiotics, glutathione-S-conjugates are formed by glutathione S-transferase and the conjugates or their degraded compounds are exported from the cytoplasm by some transporters. In S. cerevisiae, two glutathione S-transferase genes (GTT1 and GTT2) have been identified (Choi 1998). and glutathione-S-conjugates are transported into the vacuole by the YCF1 gene product, which is an ATP-binding-cassette transporter on the vacuolar membrane (Li, 1996). Induction of GSH synthesis in yeast has been shown to protect the mitochondrial DNA (mtDNA) from oxidative damage (Keiichi, 2001).

The damage by MNNG is more profound in *mgt1* than WT. Unlike the WT, the initial exposure to MNNG represses genes that are more likely to be transcriptional factors. After the initial repression these genes were incrementally induced and tended to approach WT levels. By virtue of affecting transcription factors, their influence on the expression profile is more pronounced than what is apparent. Other genes in this category included ones involved in RNA processing and kinases involved in protein phosphorylation. It was very intriguing to find RAD28 in this category of genes. It is a homolog of the Cockayne syndrome A (CSA) gene. CSA patients exhibit severe developmental and neurological abnormalities. In contrast genes that were induced as

a reflex response and waned over time included those involved in copper and lipid transport, glucan, sulfur and methionine metabolism. An interesting class of genes here were 5 genes involved in translation initiation, elongation and regulation. The temporal responsiveness in *mgt1* was striking on several other counts. About 35% of the induced genes were involved in ribosomal function and 43% of all the genes induced were found to be essential.

Overall, the propensity for damage to macromolecules and cellular processes is much more in the *mgt1* than the WT. Given that *mgt1* is not able to repair O⁶Methylguanine and O⁴Methylthymine, it can be postulated that the profound damage in *mgt1* could be because of these lesions itself or due to downstream processes. The repression of transcription factors followed by the induction of ribosomal and RNA components is an interesting finding that suggests that the recovery after damage is coordinated at the transcriptional level. This is unlike the WT that can repair the O⁶MeG lesion to a greater extent than the *mgt1*. In the WT, the reprogramming involves a transient repression of genes restricted to fundamental metabolic processes indicating that the damage is limited compared to *mgt1*.

Summary

In conclusion, the transcriptional changes precipitated by deleting MTase in yeast are indicative of DNA damage induction, cell cycle checkpoint activation and eventually, damage tolerance via *REV7*. This finding of error-prone translesion bypass polymerase activity correlates well with an earlier result where increased spontaneous mutagenesis was demonstrated in MTase deficient yeast. The effect of alkylating agent MNNG on yeast is dramatic and about 30% of the genome is instantly responsive. The initial insult with MNNG is rapidly followed by a repression of major metabolic processes but an induction of genes involved in maintaining cell wall structure and function. Other processes that try to maintain homeostasis after the initial insult with MNNG set in early and are sustained. A reflex response orchestrated by cell-cycle checkpoints serve to stall the cell-cycle and provide sufficient time to repair the DNA. This was evidenced by induction of DNA damage sensors, signal amplifiers and effectors. Nucleotide excision repair genes were the predominant class of repair proteins induced.

While most of the response to DNA damage is shared by the wild-type and *mgt1*, a fraction of the genes respond differentially and they include individual components of DNA repair systems. It appears as though the lack of MTase in *mgt1* leads to increased damage in mitochondria and a program that increases the transcription of genes pre-mRNA processing, mRNA splicing and ribosomal biogenesis. Damage due to alkylation does not limit itself to genetic material in the nucleus. It affects organelles such as mitochondria which appear to be very sensitive.

In the WT treated with MNNG, double-strand break repair was induced along with uracil DNA glycosylase (UNG1). There was more protein synthesis and transport across the subcellular organelles. In contrast, in *mgt*1, there was more mismatch repair (*MSH2*), and mitochondrial repair genes. The induction, over increasing length of exposure to MNNG, of 30 genes involved in pre-

RNA processing, mRNA splicing and ribosome maintenance could be attributed to the induction of *SW16*, a transcriptional co-activator.

Culling out environmental stress responsive genes (ESR genes) from the current study permitted a study of gene expression attributes specific to WT or *mgt1*. Five out of the 9 genes identified as the DNA damage cluster by Gasch et al 2000 were found to be induced upon MNNG exposure. These genes included *DUN1*, *PLM2*, *RNR4* and the ORF of yet unknown function, *YBR070C*.

It appears that the MNNG induced damage is not limited to the DNA alone. Other macromolecular processes are affected considerably. An equal dose of MNNG imparts more damage in mgt1 than the WT. While the O⁶Methylguanine lesion is successfully repaired by the MTase in WT, lack of MTase in mgt1 is not able to do so. With more O⁶Methylguanine in the genome, the mgt1 cells are killed faster than WT. The transcriptional changes that accompany imply that the cellular processes in mgt1 sustain more damage. Hence the transcriptional responsiveness is more elaborate than in the WT. As a rule, the fundamental metabolic processes (glucose metabolism, amino acid metabolism and fatty acid metabolism) are transiently repressed in order to cope up with this stress and cell wall synthesis genes are induced in both WT and mgt1.

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Appendix of Tables

Table 4: A subset of the genes that are up-regulated in basal mgtl.

A total of 148 genes upregulated (log₂ER>2) in basal mgtl. The function for 57 of them was known and is shown in Table 4A. Table 4B shows $\frac{http://genomicphenotyping.mit.edu}{http://genomicphenotyping.mit.edu}$. Sensitivity score can range for 0-30. A score of > 2 implies sensitivity to MMS. Essential genes are genes that upregulated in basal mgt/ but are a part of the environmental stress response (ESR). The corresponding fold changes upon treatment in WT and mgtl are shown for reference. The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from highlighted in red.

ORFGeneFunction $mgr1$ SensitivitivitivitionVMR165CSMP2aerobic respuration:2.35 \mathbb{P} VMR165CSMP2aerobic respuration:2.35 \mathbb{P} VR031CDAL7allantion catabolism3.35 \mathbb{P} VHR061CGIC1axial budding2.15 \mathbb{P} VHR051CBIO2biotin biosynthesis2.18 \mathbb{P} VHR208WBAT1branched chan family AA biosynthesis2.18 \mathbb{P} VFR013WIOC3chromatin modeling3.03 \mathbb{P} \mathbb{P} VFR058WPET117cytochrome c oxidase biogenesis2.18 \mathbb{P} \mathbb{P} VFR058WPET117cytorhome c oxidase biogenesis2.26 \mathbb{P} \mathbb{P} VIL046_ex2BET1ER to Golgi transport2.46 \mathbb{P} \mathbb{P} VR051WGAL80galactose metabolism2.32 \mathbb{P} \mathbb{P} VIL047CRNLAnsiinterne acetylation2.36 \mathbb{P} \mathbb{P} VIL051WGAU5Interne transport2.38 \mathbb{P} \mathbb{P} VIL047CARN2Interne biosynthesis2.13 \mathbb{P} \mathbb{P} VIL138CLEU1intorne itansport2.38 \mathbb{P} \mathbb{P} VIL138CLEU1intorne itansport2.38 \mathbb{P} \mathbb{P} VIL138CREV7RNA cleavage2.13 \mathbb{P} \mathbb{P} VIL138CREV7RNA cleavage2.13 \mathbb{P} \mathbb{P} VIL139CREV7 <th></th> <th></th> <th></th> <th>Basal</th> <th></th>				Basal	
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PET117 cytochrome c oxidase biogenesis 2.26 BET1 ER to Golgi transport 2.64 PDC6 ethanol metabolism 2.46 FDH1 formate catabolism 2.32 FDH1 formate catabolism 2.43 FDH1 formate catabolism 2.43 GAL80 galactose metabolism 2.43 GAL80 galactose metabolism 2.43 ARN2 inscience acetylation 3.06 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 FDM2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 RAN2 iron-siderochrome transport 2.43 RAN2 iron-siderochrome transport 2.43 RMA15 metabolism 2.13 RNA15 mutagenesis 2.13 RNA15 mutagenesis 5.13 RNA15 mutagenesis 5.13 <tr< td=""><td>YFR013W</td><td>10C3</td><td>chromatin modeling</td><td>3.03</td><td>0</td></tr<>	YFR013W	10C3	chromatin modeling	3.03	0
BET1 ER to Golgi transport 2.64 PDC6 ethanol metabolism 2.46 FDH1 formate catabolism 2.32 FDH1 formate catabolism 2.33 GAL80 galactose metabolism 2.43 GAL80 galactose metabolism 2.43 GAL80 galactose metabolism 2.43 GAL80 galactose metabolism 2.43 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.38 IFW2 isotropic bud growth 2.38 TPM2 isotropic bud growth 2.38 ROG1 lipid metabolism 2.38 ROG1 ipid metabolism 2.13 RNA15 mNA cleavage 2.13 RNA15 mutagenesis 6.93 REV7 mutagenesis 6.30 DCG1 nitrogen metabolism 2.01 OPT2 oligopeptide transport 2.01 OPT2 oligopeptide transport 2.80	YER058W	PET117	cytochrome c oxidase biogenesis	2.26	0
PDC6 ethanol metabolism 2.46 FDH1 formate catabolism 2.32 FDH1 formate catabolism 2.32 GAL80 galactose metabolism 2.33 GAL80 palactose metabolism 2.48 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.38 ITPM2 isotropic bud growth 2.80 ITPM2 isotropic bud growth 2.80 ROG1 tipid metabolism 2.13 ROG1 tipid metabolism 3.05 RNA15 mRNA cleavage 2.13 RNA15 mutagenesis 6.93 REV7 mitrogen metabolism 2.01 DCG1 nitrogen metabolism 2.01 OPT2 oligopeptide transport 2.01 Phosphatidylethanolarmine biosynthesis 2.80	YIL004C_ex2	BET1	ER to Golgi transport	2.64	0
FDH1 formate catabolism 2.32 GAL80 galactose metabolism 2.43 GAL80 galactose metabolism 2.43 GCN5 histone acetylation 3.08 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.80 TPM2 isotropic bud growth 2.80 TPM2 isotropic bud growth 2.80 IEU1 teucine biosynthesis 2.13 ROG1 tipid metabolism 3.05 RNA15 mRNA cleavage 2.13 RNA15 mutagenesis 6.93 REV7 mitrogen metabolism 2.01 DCG1 nicogen metabolism 2.01 OPT2 oligopeptide transport 2.01 OPT2 oligopeptide transport 2.80	YGR087C	PDC6	ethanol metabolism	2.46	0
GAL80 galactose metabolism 2.43 GCN5 histone acetylation 3.08 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.38 TPM2 isotropic bud growth 2.38 TPM2 isotropic bud growth 2.80 TPM2 isotropic bud growth 2.80 ROG1 lipid metabolism 2.13 ROG1 inpreses 2.13 RNA15 mRNA cleavage 2.13 RNA15 mutagenesis 6.93 ROG1 nitrogen metabolism 2.01 OPT2 oligopeptide transport 3.57 CPT1 phosphatidylethanolarmine biosynthesis 2.80	YOR388C	FDH1	formate catabolism	2.32	ш
GCN5 histone acetylation 3.08 ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.38 IPM2 isotropic bud growth 2.38 TPM2 isotropic bud growth 2.38 ROG1 lipid metabolism 2.13 ROG1 lipid metabolism 3.05 RNA15 mRNA cleavage 2.13 ROG1 nitrogen metabolism 3.05 ROG1 nitrogen metabolism 2.13 ROG1 nitrogen metabolism 2.13 ROG1 nitrogen metabolism 2.13 REV7 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oligopeptide transport 3.57 Phosphatidylethanolarmine biosynthesis 2.80	YML051W	GAL80	galactose metabolism	2.43	0
ARN2 iron-siderochrome transport 2.48 SIT1 iron-siderochrome transport 2.38 TPM2 isotropic bud growth 2.38 LEU1 teucre brosynthesis 2.13 ROG1 lipid metabolism 3.05 RNA15 rnRNA cleavage 2.13 RV15 rnRNA cleavage 2.13 RC17 nutagenesis 2.13 REV7 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oligopeptide transport 3.57 PPT1 phosphatidylethanolarmine biosynthesis 2.80	YGR252W	GCN5	histone acetylation	3.08	7
SIT1 iron-siderochrome transport 2.38 TPM2 isotropic bud growth 2.80 LEU1 teucre brosynthesis 2.13 ROG1 lipid metabolism 3.05 RNA15 mRNA cleavage 2.13 RNA15 mRNA cleavage 2.13 RC01 inpid metabolism 3.05 RC17 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oligopeptide transport 3.57 EPT1 phosphatidylethanolarmine biosynthesis 2.80	YHL047C	ARN2	iron-siderochrome transport	2.48	0
TPM/2 isotropic bud growth 2.80 LEU1 leucre blosynthesis 2.13 ROG1 lipid metabolism 3.05 RNA15 mRNA cleavage 2.13 RNA15 mRNA cleavage 2.13 ROT mutagenesis 5.93 DCG1 nitrogen metabolism 2.01 DCG1 nitrogen metabolism 2.01 PCG1 phosphatidylethanolarmine biosynthesis 2.01	YEL065W	SIT1	iron-siderochrome transport	2.38	4
LEU1 Leucrne brosynthesis 2.13 ROG1 lipid metabolism 3.05 RNA15 mRNA cleavage 2.13 REV7 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oigopeptide transport 3.57 PT1 phosphatidylethanolarnine biosynthesis 2.80	YIL138C	TPM2	isotropic bud growth	2.80	0
ROG1 lipid metabolism 3.05 RNA15 mRNA cleavage 2.13 REV7 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oilgopeptide transport 3.57 OPT2 oilgopeptide transport 3.57 EPT1 phosphatidylethanolamine biosynthesis 2.80	YGL009C	LEU1	ieucine biosynthesis	2.13	نە
RNA15 mRNA cleavage 2.13 REV7 mutagenesis 6.93 DCG1 nitrogen metabolism 2.01 DCG1 oligopeptide transport 3.57 OPT2 oligopeptide transport 3.57 EPT1 phosphatidylethanolarnine biosynthesis 2.80	YGL144C	ROG1	lipid metabolism	3.05	0
REV7 mutagenesis 6.93 9 DCG1 nitrogen metabolism 2.01 9 OPT2 oligopeptide transport 3.57 9 EPT1 phosphatidylethanolarnine biosynthesis 2.80 9	YGL044C	RNA15	mRNA cleavage	2.13	ш
DCG1 nitrogen metabolism 2.01 OPT2 oligopeptide transport 3.57 EPT1 phosphatidylethanolarnine biosynthesis 2.80	YIL139C	REV7	mutagenesis	6.93	18
OPT2 oligopeptide transport 3.57 EPT1 phosphatidylethanolarnine biosynthesis 2.80	YIR030C	DCG1	nitrogen metabolism	2.01	2
EPT1 phosphatidylethanolamine biosynthesis 2.80	YPR194C	OPT2	oligopeptide transport	3.57	0
-	YHR123W_ex1	EPT1	phosphatidylethanolamine biosynthesis	2.80	0

			Basal	
ORF	Gene	Function	mgt1	Sensitivity
YHR123W_ex2	EPT1	phosphatidylethanolamine biosynthesis	2.96	0
VIL035C	CKA1	protein amino acid phosphorylation	2.13	12
YGR188C	BUB1	protein amino acid phosphorylation	2.38	15
YMR225C_ex2	MRPL44	protein biosynthesis	2.44	0
YER153C	PET122	protein biosynthesis	2.08	0
YHR189W	PTH1	protein biosynthesis	2.61	4
YHR060W	VMA22	protein complex assembly	2.63	13
YIL071C	PCI8	protein deneddylation	3.14	0
YGR218W	CRM1	protein-nucleus export	2.05	ш
УНL038C	CBP2	RNA splicing	6.50	9
YOR382W	FIT2	siderochrome transport	4.56	0
YOR383C	FIT3	siderochrome transport	2.02	0
YNL334C	SN02	thiamin biosynthesis	2.42	0
YNL333W	SNZ2	thiamin biosynthesis	2.08	0
YCL064C	CHA1	threonine catabolism	2.36	0
YHR124W	NDT80	transcription	2.89	0
YGR186W	TFG1	transcription initiation from Pol II promoter	2.03	ш
YNL270C	ALP1	transport	2.30	0
YDR046C	BAP3	transport	2.50	0
YEL003W	GIM4	tubulin folding	2.68	9
YPL276W	FDH2	NA	2.15	w
YGR090W	UTP22	NA	2.11	ш

			Basal	
ORF	Gene	Function	mgt1	Sensitivity
YHR093W	AHT1	NA	3.97	0
CEN8	CEN8	NA	12.70	0
YGL110C	CUE3	NA	2.30	0
YHR059W	FYV4	NA	2.42	0

Table 4B: ESR subset of genes that are up-regulated in mgt1

			Basal	
ORF	Gene	Function	mgt1	Sensitivity
YLR267W	BOP2	NA	2.27	0
YGR187C	HGH1	NA	3.26	4
YPL263C	KEL3	NA	2.92	0
YLR134W	PDC5	ethanol fermentation	5.60	5
YIL104C	SHQ1	snoRNA metabolism	5.08	ш

			Basal	
ORF	Gene	Function	mgt1	Sensitivity
YMR195W	ICY1	NA	2.21	0
YHR156C	LIN1	NA	2.32	0
YEL035C	UTR5	NA	4.89	0
YGR089W	NNF2	NA	10.02	4

Table 5: A subset of the genes that are down-regulated in basal mgtl.

A total of 89 genes down regulated (log2ER<0.5) in basal mgt1. The function for 24 of them was known and is shown in Table 5A. Table 5B shows genes that down-regulated in basal mgt1 but are a part of the environmental stress response (ESR). The corresponding fold changes upon treatment in WT and mgt1 are shown for reference. The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from http://genomicphenotyping.mit.edu. Sensitivity score can range for 0-30. A score of > 2 implies sensitivity to MMS. Essential genes are highlighted in red.

Table 5A

			Basal	
ORF	Gene	Function	mgt1	Sensitivity
YDL200C	MGT1	DNA dealkylation	-26.49	12
YGL209W	MIG2	glucose metabolism	-2.97	0
YHR094C	HXT1	hexose transport	-2.88	0
YDR345C	HXT3	hexose transport	-2.31	0
YKR099W	BAS1	histidine biosynthesis	-2.32	0
YGR142W	BTN2	intracellular protein transport	-3.17	0
YCL017C	NFS1	Iron-sulfur cluster assembly	-5.60	ш
YCL018W	LEU2	leucine biosynthesis	-126.12	μ
YCL050C	APA1	nucleotide metabolism	-2.10	9
YGL158W	RCK1	protein AA phosphorylation	-2.24	4
YLR216C	CPR6	protein folding	-2.19	4
YMR238W	DFG5	pseudohyphal growth	-2.02	0
YGR211W	ZPR1	regulation of cell cycle	-2.60	ш

	0	0	9	0	ш	0	0	0	2
	-2.27	-2.30	-2.16	-2.52	-6.66	-2.39	-2.02	-2.09	-2.73
retrograde (endosome to Golgi)	transport	sucrose catabolism	sulfate assimilation	sulfur amino acid metabolism	NA	NA	NA	NA	AA
	үрт6	SUC2	MET14	CYS3	ZPS1	FSH1	ICY2	PIN2	UBP11
	YLR262C	YIL162W	YKL001C	YAL012W	YOL154W	YHR049W	YPL250C	YOR104W	YKR098C

Table 5B

Gene
response to stress
AN

Table 6: Subset of genes that are specifically induced in WT upon MNNG treatment

A total of 225 genes were induced (log2ER>2) specifically in WT. The function for 127 of them was known and is shown in Table 6A. Table 6B shows genes that induced in WT but are a part of the environmental stress response (ESR). The corresponding fold changes upon treatment in other categories are shown for reference. The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from http://genomicphenotyping.mit.edu. Sensitivity score can range for 0-30. A score of > 2 implies sensitivity to MMS. Essential genes are highlighted in red.

			¥1	
ORF	Gene	Function	FC	Sens
YLR429W	CRN1	actin filament organization	2.18	0
YCR105W	ADH7	alcohol metabolism	2.06	0
VFL057C	NA	aldehyde metabolism	3.13	ω
YDL243C	AAD4	aldehyde metabolism	2.59	10
YIR027C	DAL1	allantoin catabolism	2.57	2
YBR085W	AAC3	ATP ADP exchange	3.12	0
YPR185W	APG13	autophagy	2.02	0
YNR058W	BIO3	biotin biosynthesis	2.34	0
YDR226W	ADK1	cell proliferation	2.13	2
YDR141C	DOP1	cellular morphogenesis	2.05	p.,
YJL072C	NA	DNA dependent DNA replication	2.24	'n
YML021C	UNG1	DNA repair	2.02	0
YDL042C	SIR2	DSB repair via NHEJ	2.07	4
YML032C	RAD52	DSB repair via NHEJ	2.32	23
YHR007C	ERG11	electron transport	2.02	w
YNR075W_1	COS10	endocytosis	2.46	0
YHR098C	SFB3	ER to Goigi transport	2.04	u)
YGR284C	ERV29	ER to Golgi transport	2.29	0
YGR166W	KRE11	ER to Golgi transport	2.25	0
YAR002C-A	ERP1	ER to Golgi transport	2.14	4
YLR208W	SEC13	ER-associated protein catabolism	2.04	a
YMR015C	ERG5	ergosterol biosynthesis	2.18	9
YHR044C	DOG1	glucose metabolism	2.17	0
YMR006C	PLB2	glycerophospholipid metabolism	2.71	0
YMR205C	PFK2	glycolysis	2.11	0
YJL099W	CHS6	Golgi to plasma membrane transport	2.25	0
YMR079W ex2	SEC14	Golgi to plasma membrane transport	2.41	0

			ž	
ORF	Gene	Function	с Г	Sens
YDR044W	HEM13	hene prosynthesis	2.67	ш
YER145C	FTR1	high affinity iron ion transport	2.15	0
YLR214W	FRE1	iron ion transport	2.03	0
YDL066W	10P1	isocitrate metabolism	2.11	7
YCR086W	CSM1	meiotic chromosome segregation	2.02	0
YKL 104C	GFA1	metabolism	2.04	ω
YLR180W	SAM1	methionine metabolism	2.98	0
YPL124W	SPC29	microtubule nucleation	2.11	ω
YDR488C	PAC11	microtubule-based process	2.40	0
YCR028C-A_ex2	RIM1	mitochondrial genome maintenance	2.34	0
YGR029W_ex2_alt	ERV1	mitochondrion organization and biogenesis	2.53	0
YCL055W	KAR4	mitosis	2.28	0
YDL008W	APC11	mitotic metaphase anaphase transition	2.16	ш
VDR180W	scc2	mitotic sister chromatid cohesion	2.24	ш
YLR363C	NMD4	mRNA catabolism, nonsense-mediated	2.35	0
YNL016W	PUB1	mRNA catabolism, nonsense-mediated	2.21	5
YGR156W	PT11	mRNA cleavage	2 39	IJ
YIR009W	MSL1	mRNA splicing	2.95	0
YOL 103W	ITR2	myo-inositol transport	2.18	0
YBR218C	PYC2	NADPH regeneration	2.03	5
YCL026C-A	FRM2	negative regulation of fatty acid metabolism	4.33	0
YDR451C	YHP1	negative regulation of transcription from Pol II promoter	2.80	2
YDL232W	OST4	N-linked glycosylation	2.48	0
YMR246W	FAA4	N-terminal protein myristoylation	2.15	0
YIL016W	SNL1	nuclear pore organization and biogenesis	2.02	2
YCR073C	SSK22	osmosensory signaling pathway	2.06	0
YOL028C	YAP7	positive regulation of transcription from Pol II promoter	2.25	0
YGR109C	CLB6	premeiotic DNA synthesis	2.03	0

ORF	Gene	Function	Ę	Sens
YMR142C_ex2	RPL13B	protein biosynthesis	2.50	0
YJL177W_ex1	RPL17B	protein biosynthesis	2.03	0
YBL027W_ex2	RPL19B	protein biosynthesis	2.11	0
YBR191W_ex2	RPL21A	protein biosynthesis	2.71	0
YOL127W_ex2	RPL25	protein biosynthesis	2.76	0
YMR194W_ex2	RPL36A	protein biosynthesis	2.21	0
YPR043W_ex2	RPL43A	protein biosynthesis	2.03	0
YPR043W_ex2	RPL43A	protein biosynthesis	2.02	0
YMR143W_ex2	RPS16A	protein biosynthesis	2.15	0
YOR096W_ex1	RPS7A	protein biosynthesis	2.28	0
YNL096C_ex1	RPS7B	protein biosynthesis	2.62	0
YNL096C_ex2	RPS7B	protein biosynthesis	2.75	0
YML019W	OST6	protein complex assembly	2.47	0
YDL141W	BPL1	urotein modification	513 13	ш
YMR300C	ADE4	purine base metabolism	2.09	0
YGR061C	ADE6	purine nucleotide biosynthesis	2.04	0
YCR059C	YIH1	regulation of amino acid metabolism	2.72	0
YML028W	TSA1	regulation of redox homeostasis	2.00	13
YPR052C	NHP6A	regulation of transcription from Pol II promoter	2.14	0
YMR179W	SPT21	regulation of transcription from Pol II promoter	2.01	19
YOR018W	ROD1	response to drug	2.22	10
YBR008C	FLR1	response to toxin	3.32	2
YCR106W	RDS1	response to xenobiotic stimulus	2.88	0
YNL287W	SEC21	retrograde (Golgi to ER) transport	2.20	u.
YHR114W	BZZ1	salinity response	2.03	0
YML049C	RSE1	spirceosome assembly	2.38	ш
YPL145C	KES1	steroid biosynthesis	2.42	0
YPR167C	MET16	sulfate assimilation	2.36	0
YMR260C	TIF11	translational unitiation	7.00	ш
YBR170C	NPL4	tRNA-nucleus export	2.20	12
YOL038W	PRE6	ubiquitin-dependent protein catabolism	2.48	ш
YER031C	YPT31	vesicle-mediated transport	2.03	2
YER143W	DDI1	vesicle-mediated transport	2.01	11
YGL263W	COS12	NA	3.40	0
YKL219W	COS9	NA	2.35	0
YDL178W	DLD2	NA	2.01	0
YGL083W	SCY1	NA	2.04	0
YGL259W	YPS5	NA	2.51	0
YLR466W_0	YRF1-4	NA	2.51	0
VDI 1710	0-1/10			

			WT	
	Gene	Function	л С	Sens
YGR136W	LSB1	NA	2.18	11
GR136W	LSB1	NA	2.06	11

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Table 6B: ESR subset of genes induced only in WT

			M	
ORF	Gene	Function	FC	Sensitivity
YLR062C	BUD28	bud site selection	2.01	0
YLR299W	ECM38	cell wall organization and biogenesis	2.28	0
YBR283C	SSH1	cotranslational membrane targeting	2.31	0
YJL014W	CCT3	cytoskeleton organization and biogenesis	2.14	ω
YJR064W	CCT5	cytoskeleton organization and biogenesis	2.24	ដេ
YNL256W	FOL1	folic acid and derivative biosynthesis	2.30	0
YLR017W	MEU1	glutamate biosynthesis	2.04	5
YMR217W	GUA1	GMP metabolism	2.08	0
YGR195W	SKI6	rnRNA catabolism	2.17	W
VHR065C	RRP3	mRNA splicing	2.10	ш
YIL079C	AIR1	mRNA-nucleus export	2.01	0
YPL037C	EGD1	nascent polypeptide association	2.19	0
YBR106W	PHO88	phosphate transport	2.06	0
YOR253W	NAT5	protein amino acid acetylation	2.01	0
YPR102C	RPL11A	protein biosvnthesis	2.30	w
YLR029C	RPL15A	prorein biosynthesis	2.54	ना
VNL067W	RPL9B	protein biosynthesis	2.04	0
YOR369C	RPS12	protein biosynthesis	2.15	0
YOR167C	RPS28A	protein biosynthesis	2.21	0
YLR264W	RPS28B	protein biosynthesis	2.20	0
YML106W	URA5	pyrimidine base biosynthesis	2.16	0
YLR397C	AFG2	response to drug	2.38	ш
YHR148W	IMP3	rRNA modification	2.33	цı
YMR235C	RNA1	rRNA-nucleus export	2.01	ω
YPR110C	RPC40	transcription from Pol III promoter	2.20	ω
YDR382W	RPP2B	translational elongation	2.04	0
YOR260W	GCD1	translational initiation	2.18	لب
YMR309C	NIP1	iransiational initiation	2.54	ιu
VDL167C	NRP1	NA	2.05	0
YLR221C	RSA3	NA	2.26	0

Table 7: A subset of the genes that are induced specifically in mgtl

induced in mgt1 but are a part of the environmental stress response (ESR). The corresponding fold changes upon treatment in other categories are shown for reference. The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from http://genomicphenotyping.mit.edu. Sensitivity score can A total of 274 genes were induced (log2ER>2) specifically in mgt1. The function for 87 of them was known and is shown in Table 7A. Table 7B shows genes that range for 0-30. A score of $> \hat{2}$ implies sensitivity to MMS. Essential genes are highlighted in red. There were 29 essential genes induced in *mgt*¹ 9 of which were induced in the ESR subset (Table 7B)

			ıngui	
ORF	Gene	Function	С Г	Sensitivity
YBR058c-a	TSC3	3-keto-sphinganine metabolism	2.13	0
YDL029W_ex2	ARP2	actin filament organization	2.08	0
YLR139C	SLS1	aerobic respiration	2.09	0
YHR011W	DIA4	aerobic respiration	2.12	15
YNR044W	AGA1	aggiutination during conjugation with cellular fusion	2.05	ιIJ
YKL008C	LAC1	aging	2.31	0
YLL048C	YBT1	bile acid transport	2.08	9
YIL003W	DRE3	cell growth and	2.02	0
YHR142W	CHS7	cell wall chitin biosynthesis	2.03	0
YCR089W	FIG2	cellular morphogenesis during conjugation with cellular	2.12	2
	t de transforme	fusion		
YBR093C	PH05	cellular response to phosphate starvation	3.21	0
YLR381W	CTF3	chromosome segregation	2.46	0
YGL028C	SCW11	cytokinesis, completion of separation	2.31	0
YLR348C	DIC1	dicarboxylic acid transport	3.43	0
YKL011C	CCE1	DNA recombination	2.14	10
YKL045W	PRI2	DNA repair synthesis	2.00	ш
YER073W	ALD5	electron transport	3.16	0
YNL272C	SEC2	exocytosis	2.28	ш
VJL167W	ERG20	farnesyl dipnosphate biosynthesis	2.06	LL.
YDL132W	CDC53	G1 S transition of mitotic cell cycle	2.21	ω
YLR182W	SWI6	G1 S-specific transcription in mitotic cell cycle	2.12	20
YDL227C	어	gene conversion at MAT locus	2.24	0
YPR160W	GPH1	glycogen catabolism	2.40	23
YHR092C	HXT4	hexose transport	2.62	0
YMR319C	FET4	intracellular copper ion transport	2.92	4
YNL188W	KAR1	karvogamy during conjugation with cellular fusion	2.24	w

			mgt1	
ORF	Gene	Function	FC	Sensitivity
LR382C	NAM2	feucyl-tRNA aminoacylation	2.40	0
/DL131W	LYS21	Iysine biosynthesis, aminoadipic pathway	2.59	0
/JR135w-a	TIM8	mitochondrial translocation	2.52	0
/HRU05C-A	MRS11	mitochondriai transiocation	2.11	ш
/HR152W	SP012	mitotic cell cycle	2.24	6
/GL116W	CDC20	mitotic metaphase anaphase transition	2.01	ш
/DR016C	DAD1	mitotic spindle assembly	2.34	ω
GL061C	DU01	mitotic spindle assembly	2.31	ш
/MR178W	NA	Mo-molybdopterin cofactor biosynthesis	2.03	0
1.R115W	CFT2	mRNA cleavage	2.06	ц,
'ER105C	NUP157	mRNA-hucieus export	2.13	ίΩ.
/JR131W	MNS1	N-linked glycosylation	2.05	0
KR061W	KTR2	N-linked glycosylation	2.45	4
/LR148W	PEP3	nonselective vesicle docking	2.32	17
PR018W	RLF2	nucleosome assembly	2.04	15
/GL119W	ABC1	oxidative phosphorylation, ubiguinone to cytochrome c	2.15	ш
rkL209C	STE6	pepticle pheromone export	2.81	ш
NR013C	PHO91	phosphate transport	2.21	0
/LR305C	ST14	phosphatidylethanolamine biosynthesis	2.11	ш
/LR386W	VAC14	phospholipid metabolism	2.01	7
OR181W	LAS17	polar budding	2.01	ш
/AL021C	CCR4	poly(A) tail shortening	2.05	17
OR270C	VPH1	polyphosphate metabolism	2.04	4
/BR015C	MNN2	protein amino acid glycosylation	2.16	0
GR092W	DBF2	protein amino acid phosphorylation	2.28	18
GL143C	MRF1	protein biosynthesis	2.29	0
GR084C	MRP13	protein biosynthesis	2.18	0

			mgt1	
ORF	Gene	Function	FC	Sensitivity
YDR237W	MRPL7	protein biosynthesis	2.09	0
YIL098C	FMC1	protein complex assembly	2.05	4
YJR099W	YUH1	protein deubiquitination	2.19	0
YDR390C	UBA2	protein sumoyiation	2.50	ш
YIL005W	EPS1	protein-ER retention	2.08	2
YGL238W	CSE1	protein-nucleus export	2.18	U)
YML097C	VPS9	protein-vacuolar targeting	2.52	7
YGL151W	NUT1	regulation of transcription from Pol II promoter	2.47	13
YMR267W	PPA2	respiratory gaseous exchange	2.19	0
YNL239W	LAP3	response to antibiotic	2.01	0
YMR092C	AIP1	response to osmotic stress	2.25	0
YHR136C	SPL2	response to temperature	2.01	0
YGL223C	COG1	retrograde (vesicle recycling within Golgi) transport	2.07	0
YGR116W	SPT6	RNA elongation from Pol II promoter	2.27	ш
YHR110W	ERP5	secretory pathway	2.02	5
YDR461W	MFA1	signal transduction during conjugation with cellular	2.03	0
		fusion		
YNL145W	MFA2	signal transduction during conjugation with cellular	2.35	0
		fusion		

			mgt1	
ORF	Gene	Function	С, Г	Sensitivity
YKL092C	BUD2	small GTPase mediated signal transduction	2.17	0
YKL120W	OAC1	sulfate transport	3.61	0
YJR130C	STR2	sulfur metabolism	2.05	0
YOR337W	TEA1	transcription	2.27	0
YGL049C	TIF4632	translational initiation	2.47	0
YNR055C	HOL1	transport	2.04	0
YOR136W	IDH2	tricarboxylic acid cycle	2.13	4
YGR119C	NUP57	tRNA-nucleus export	2.09	ш
YOL096C	coo3	ubiquinone biosynthesis	2.04	5
YFL004W	VTC2	vacuole fusion (non-autophagic)	2.18	0
YNL085W	MKT1	viral life cycle	2.01	0
YML132W_1	COS3	NA	2.16	0
YIL171W	HXT12	NA	2.04	0
YGL221C	NIF3	NA	2.00	0
YBR162C	TOS1	NA	2.03	0
YGL161C	YIP5	NA	2.05	0
YBR111C	YSA1	NA	2.24	2

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Table 7B : ESR subset of genes specifically induced in <i>mgt1</i> upon MNNG
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			mgt1	
ORF	Gene	Function	ñ	Sensitivity
YLR129W	DIP2	processing of 20S pre-rRNA	2.14	ш
YLR222C	UTP13	processing of 20S pre-rRNA	3.39	ω
YML093W	UTP14	processing of 20S pre-rRNA	2.30	ш
YKL144C	RPC25	transcription from Pol III promoter	2.27	ш
YGR083C	GCD2	translational initiation	2.13	ш
YBR079C	RPG1	translational initiation	2.09	ш
YKL035W	UGP1	UDP-glucose metabolism	2.31	ш
YNL182C	IPI3	NA	2.36	ш
YLR409C	UTP21	NA	2.29	ш

		Sensitivity	0		0	0	0	0	0	14
	mgt1	ñ	2.32		2.81	2.21	2.16	2.05	2.58	2.29
		Function	glucose 6-phosphate utilization	MAPKKK cascade (cell wall	biogenesis)	mismatch repair	phosphate transport	regulation of meiosis	NA	translational initiation
		Gene	PGM2		SDP1	MSH6	PHO90	DOT1	PUF6	FUN12
		ORF	YMR105C		YIL113W	YDR097C	YJL198W	YDR440W	YDR496C	YAL035W
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Table 8: A subset of the genes that are repressed specifically in WT

A total of 145 genes were induced (log2ER<0.5) specifically in WT. The function for 70 of them was known and is shown in Table 8A. Table 8B shows genes that induced in WT but are a part of the environmental stress response (ESR). The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from <u>http://genomicphenotyping.mit.edu</u>. Sensitivity score can range for 0-30. A score of > 2 implies sensitivity to MMS. Essential genes are highlighted in red. There were 8 essential genes repressed in WT, 1 of which were induced in the ESR subset (Table 8B)

ORF G YML129C CC YPR100W M YPL132W CC			-						
	Gene	Function	Ъ.	tivity	ORF	Gene	Function	Б	tivity
	COX14	aerobic respiration	-2.01	0	YOR078W	BUD21	processing of 20S pre-rRNA	-2.43	0
	MRPL51	aerobic respiration	-2.52	0	YJL186W	MNN5	protein amino acid glycosylation	-2.25	0
	COX11	aerobic respiration	-2.33	2	YOL016C	CMK2	protein amino acid phosphorylation	-2.41	0
	APG14	autophagy	-2.07	0	YNR037C	RSM19	protein biosynthesis	-2.01	0
YKR063C	LAS1	bud growth	-2.00	ιĿ	YPL013C	MRPS1	protein biosynthesis	-2.06	2
YNL192W CI	CHS1	budding	-2.24	0		9			
YDL179W PC	PCL9	cell cycle	-2.10	0	YGR174C	CBP4	protein complex assembly	-2.27	2
YOR304W IS	ISW2	chromatin modeling	-2.21	0	YBR083W	TEC1	pseudohyphal growth	-3.45	0
YDR310C SI	SUM1	chromatin silencing at HML and HMR (sensu Saccharomyces)	-2.24	5	YKL048C	ELM1	pseudohyphal growth	-2.05	11
YER088C Do	DOT6	chromatin silencing at ribosomal DNA (rDNA)	-2.35	7	YER040W	GLN3	regulation of nitrogen utilization	-2.12	0
YMR219W ES	ESC1	chromatin silencing at telomere	-2.14	0	YKL139W	CTK1	regulation of transcription from Pol II promoter	-2.26	18
YBR095C R	RXT2	conjugation with cellular fusion	-2.03	6	YJL006C	CTK2	regulation of transcription from Pol II promoter	-2.06	21
YDR030C R	RAD28	DNA repair	-2.80	4	YCR097W_ex2	HMRA1	regulation of transcription, mating-type specific	-2.54	0
YMR020W FP	FMS1	electron transport	-2.03	0	YDR423C	CAD1	response to cadmium ion	-2.12	0
YOR375C GI	GDH1	glutamate biosynthesis, using glutamate dehydrogenase	-2.17	0	YOR153W	PDR5	response to drug	-2.33	0
YDR176W NI	NGG1	histone acetylation	-2.04	4	YNL074C	MLF3	response to drug	-2.08	4
YKR029C St	SET3	histone deacetylation	-2.12	8	YOR075W	UFE1	retrograde (Golgi to ER) transport	-2.41	ω
YER075C P	PTP3	inactivation of MAPK (osmolarity sensing)	-2.27	0	YLR223C	IFH1	rRNA processing	-2.03	ш
YBR066C NI	NRG2	invasive growth	-2.02	0	YBR257W	POP4	rRNA processing	-2.11	ш
YOR354C M	MSC6	meiotic recombination	-2.20	0	VOL010W	RCL1	rRNA processing	2.33	ω
YIL144W	TID3	microtubule nucleation	-2.20	ω	YNL091W	NST1	salinity response	-2.64	0
YPR141C K	KAR3	mitosis	-2.02	18	YDL194W	SNF3	signal transduction	-2.13	0
LSR1_1 LS	LSR1	mRNA splicing	-2.65	0	YDR104C	SP071	spore wall assembly (sensu Saccharomyces)	-2.04	0
YCR033W SI	SNT1	negative regulation of meiosis	-2.09	10	YAR044W	0SH1	steroid biosynthesis	-2.01	0
YDR397C_ex2 N	NCB2	negative regulation of transcription from Pol II promoter	-2.11	0	YIL119C	RP11	thiamin biosynthesis	-2.61	0
YDR028C RI	REG1	negative regulation of transcription from Pol II promoter	-2.14	5	YOR194C	TOA1	transcription initiation from Pol II promoter	-2.20	ш
YLR231C BI	BNA5	nicotinamide adenine dinucleotide biosynthesis	-2.32	0	YAL001C_ex2	TFC3	transcription initiation from Pol III promoter	-2.46	0
YDR075W PF	PPH3	nitrogen metabolism	-2.12	19	YOR245C	DGA1	triacylglycerol biosynthesis	-2.07	0
YBR114W R	RAD16	nucleotide-excision repair, DNA damage recognition	-2.58	0	YLR304C	AC01	tricarboxylic acid cycle	-2.02	0
YKR093W P	PTR2	peptide transport	-2.24	9	YHL016C	DUR3	urea transport	-2.11	10
YGR138C TF	TP02	polyamine transport	-6.30	0	YDR202C	RAV2	vacuolar acidification	-2.19	0

OBE C				Sensi
	DIAD		د	uvity
YGR196C	FYV8	NA	-2.60	0
	RMD1 NA	NA	-2.18	0
	TPP1	NA	-2.04	0
YJR127C	ZMS1	NA	-2.11	2
YBR033W	EDS1	NA	-2.01	e

			WT	Sensi
ORF	Gene	Gene Function	БĊ	tivity
YJR122W	CAF17	NA	-2.03	9
YNL215W	IES2	NA	-2.29	7
YDL115C	IWR1	NA	-2.12	15
YAL011W	SWC1 NA	NA	-2.13	25

Table 8B: ESR Subset of genes that are repressed only in WT upon MNNG treatment

			Basal		mgt1	
	Gene	Function	mgt1	WT FC	Ð	Sensitivity
YOR173W C	DCS2	NA	1.01	-3.23	-1.89	0
YLR080W E	EMP46	ER to Golgi transport	-1.17	-2.26	-1.50	0
YML128C N	MSC1	meiotic recombination	-1.08	-2.35	-1.52	0
YMR304W L	UBP15	protein deubiquitination	-1.22	-2.12	-1.44	0
VNL186W L	UBP10	protein deubiquitination	-1.08	-2.08	-1.96	ш
YPR149W N	NCE102	protein secretion	-1.18	-2.10	-1.76	0
YMR271C U	URA10	pyrimidine base biosynthesis	-1.12	-2.17	-1.84	2
YFL014W H	HSP12	response to dessication	-1.00	-2.32	-1.73	4
YBR072W H	HSP26	response to stress	1.01	-2.66	-1.77	0
YNL015W P	PBI2	vacuole fusion (non-autophagic)	-1.08	-2.29	-1.74	0

Table 9: A subset of the genes that are repressed specifically in *mgt1*

A total of 191 genes were induced (log2ER<0.5) specifically in mgt1. The function for 70 of them was known and is shown in Table 9A. Table 9B shows genes that The information on phenotypic sensitivity of deletion strains of yeast to MMS was obtained from http://genomicphenotyping.mit.edu. Sensitivity score can range for induced in mgt1 but are a part of the environmental stress response (ESR). The corresponding fold changes upon treatment in other categories are shown for reference. 0-30. A score of > 2 implies sensitivity to MMS. Essential genes are highlighted in red. There were 14 essential genes repressed in mgtl.

			mgt1	
ORF	Gene	Function	л С	Sensitivity
YLR395C	COX8	aerobic respiration	-2.11	0
YDL067C	COX9	aerobic respiration	-2.54	0
YJR055W	HIT1	aerobic respiration	-2.18	0
YKL055C	OAR1	aerobic respiration	-2.20	28
YDR538W	PAD1	aromatic compound catabolism	-2.26	0
YKL106W	AAT1	asparagine biosynthesis from oxaloacetate	-2.29	4
YLR295C	ATP14	ATP synthesis coupled proton transport	-2.05	0
YBR039W	ATP3	ATP synthesis coupled proton transport	-2.05	ω
YCR068W	CVT17	autophagy	-2.19	0
YCR068W	CVT17	autophagy	-2.45	0
YIL155C	GUT2	carbohydrate metabolism	-2.10	0
YBR297W	MAL33	carbohydrate metabolism	-2.27	0
YBL101C	ECM21	cell wall organization and biogenesis	-2.61	0
YDR073W	SNF11	chromatin modeling	-2.54	0
YJL127C	SPT10	chromatin modeling	-2.01	26
YJR060W	CBF1	DNA replication and chromosome cycle	-2.26	6
YNL044W	YIP3	ER to Golgi transport	-2.01	0
		establishment and or maintenance of chromatin		
YDR143C	SAN1	architecture	-2.25	11
YNL161W	CBK1	exit from mitosis	-2.04	ω
YDL168W	SFA1	formaldehyde assimilation	-2.05	0
YIL135C	NA	G1 S transition of mitotic cell cycle	-2.14	0
YJL219W	HXT9	nexose transport	-2.71	ш
YFL041W	FET5	iron ion transport	-2.49	0
YER013W	PRP22	ianat formation. 5'-splice sue cleavage	-2.11	ш
YPL 128C	TBF1	ioss of chromatin silencing	-2.35	ω

			mgt1	
ORF	Gene	Function	Ъ С	Sensitivity
YJL146W	IDS2	meiosis	-2.06	0
YLR329W	REC102	meiotic recombination	-2.63	2
YDR502C	SAM2	methionine metabolism	-2.22	0
YOL060C	MAM3	mitochondrion organization and biogenesis	-2.35	0
YJR091C	JSN1	mRNA catabolism, deadenylation-dependent	-2.09	0
YPR042C	PUF2	mRNA catabolism, deadenylation-dependent	-2.34	0
YDL160C	DHH1	mRNA catabolism, nonsense-mediated	-2.80	15
YEL036C	ANP1	N-finked glycosylation	-2.08	0
YDR441C	APT2	nucleoside metabolism	-3.10	0
YLR005W	SSL1	nucleotide-excision repair	-2.27	ш
YDR019C	GCV1	one-carbon compound metabolism	-2.08	0
YOR298C-A	MBF1	positive regulation of transcription from Pol II promoter	-2.52	0
YBR101C	NA	protein biosynthesis	-3.32	16
YOR027W	STI1	protein folding	-2.13	6
YGL058W	RAD6	protein monoubiquitination	-2.18	7
YEL059C-A	SOM1	proteolysis and peptidolysis	-2.05	0
YOR128C	ADE2	purine base metabolism	-2.30	0
YBR135W	CKS'	regulation of cell cycle	-2.47	ш
YML010W	SPT5	regulation of transcription. DNA-dependent	-2.21	ш
YML010W	SPT5	regulation of transcription. DNA-dependent	-2.09	ш
YPL179W	РРQ1	regulation of translation	-2.51	0
YBL005W	PDR3	response to drug	-2.26	0
YLR006C	SSK1	response to hydrogen peroxide	-2.19	18
YLR037C	DAN2	response to stress	-2.12	2
YOR025W	HST3	short-chain fatty acid metabolism	-2.52	11

			ingu	
ORF	Gene	Function	5 C	Sensitivity
YBR213W	MET8	siroheme biosynthesis	-2.28	0
YDR403W	DIT1	spore wall assembly (sensu Saccharomyces)	-2.34	0
YGR055W	MUP1	sulfur amino acid transport	-2.96	0
YMR095C	SN01	thiamin biosynthesis	-2.07	0
YBR240C	THI2	thiamin biosynthesis	-2.03	5
YCR020C	PET18	thiamin metabolism	-2.22	0
YLR237W	THI7	thiamin transport	-2.14	0
YDR156W	RPA14	transcription from Pol I promoter	-2.13	0
YBL014C	RRN6	transcription from Pol I promoter	-2 03	u)
YPR168W	NUT2	transcription from Pol II promoter	-2.02	(۲,
YIL125W	KGD1	tricarboxylic acid cycle	-2.33	0
YNR034W	SOL1	tRNA processing	-2.41	0

			mgt1	
ORF	Gene	Function	л С	Sensitivity
YDR151C	CTH1	NA	-2.33	0
YNL245C	CWC25	NA	-2.80	ш
YDR373W	FRQ1	NA	-2.15	ω
YGR002C	GOD1	NA	-2.10	ш
YMR161W	HLJ1	NA	-2.40	0
	RDN37-			
RDN37-1_2	-	NA	-2.96	0
YMR266W	RSN1	NA	-2.11	0
YPL239W	YAR1	NA	-2.75	0
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Table 9B ESR subset of genes that are repressed specifically in mgtl upon MNNG treatment

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			Basal	WT	mgt1	Sens
ORF	Gene	Function	mgt1	5 C	FC	itivity
YJR059W PTK2	PTK2	polyamine transport	-1.06	-1.06 -1.98 -2.16	-2.16	2
		regulation of redox				4
YBL064C	NA	homeostasis	-1.08	-1.08 -1.73 -2.16	-2.16	
		vacuolar protein				0
YEL060C	PRB1	catabolism	-1.09	-1.09 -1.79	-2.11	

Table 10: Genes that are induced in WT and	mgt1 upon MNNG treatment	

This overlapping response indicated in the upper-middle panel of Figure 19 included 977 genes that were induced in both WT and mgt1. Of them, 127 genes were included as ESR genes. The function of 282 genes was not known and is not indicated in these tables. The remaining 568 genes, whose function was known and those that were not a part of the ESR are listed by function in Table 10A. 121 (21%) of these are essential genes.

Table 10A					
ORF					
YLR153C	AGene	acetyl-CoA biosFutaction	W.T.	mgtik	Sens
YKL013C	ARC19	actin cortical patch assembly	F ² C ³	FČ ⁶⁷	ίIJ
YCR088W	ABP1	actin cortical patch assembly	3.27	3.44	0
		actin cytoskeleton organization and			
YLR144C	ACF2	biogenesis	2.28	2.17	e
YBR234C	ARC40	actin filament organization	2.37	2.43	ω
YIL034C	CAP2	actin filament organization	2.87	3.67	2
YDL135C	RDI1	actin filament organization	2.14	2.09	0
YGR080W	TWF1	actin polymerization and or depolymerization	2.85	2.90	0
		adaptation to pheromone during conjugation			
YLR452C	SST2	with cellular fusion	2.36	3.08	0
YNL220W	ADE12	adenosine biosynthesis	2.92	2.50	7
YDR487C	RIB3	aerobic respiration	2.61	2.22	Lu
YIL070C	MAM33	aerobic respiration	2.02	2.39	4
		agglutination during conjugation with cellular			
YGL032C	AGA2	fusion	2.21	3.79	0
YBR145W	ADH5	alcohol metabolism	5.25	5.86	4
YMR318C	ADH6	alcohol metabolism	16.76	16.00	0
YFL056C	AAD6	aldehyde metabolism	5.82	2.08	e
YIR028W	DAL4	allantoin transport	3.14	2.87	2
YGL105W	ARC1	amino acid activation	2.74	2.49	0
YFR055W	NA	amino acid metabolism	14.64	13.62	0
YLL058W	NA	amino acid metabolism	3.58	3.05	0
YIL111W_ex2	COX5B	anaerobic respiration	2.06	2.70	0
YGL106W	MI C1	apical bud growth	2.53	2.20	21

Table 10A					
ORF	Gene	Function	FC WT	mgt1 FC	Sens
YNL298W	CLA4	apical bud growth	2.59	3.38	23
YJL071W	ARG2	arginine biosynthesis	2.33	2.87	0
YHR018C	ARG4	arginine biosynthesis	7.10	8.30	0
YER069W	ARG5.6	arginine biosynthesis	2.41	2.19	0
YDR127W	AR01	aromatic amino acid family biosynthesis	4.66	5.32	0
YDR035W	AR03	aromatic amino acid family biosynthesis	2.86	2.95	0
YGL202W	AR08	aromatic amino acid family metabolism	5.73	5.36	0
YLR088W	GAA1	attachment of GPI anchor to protein	2.86	2.97	ω
VHR188C	GP116	attachment of GPI anchor to protein	2.31	2.13	u
YIL109C	SEC24	autophagy	2.26	2.16	w
YDR309C	GIC2	axial budding	2.14	2.02	2
YDR135C	YCF1	bilirubin transport	2.87	2.85	0
YGL065C	ALG2	niosynthesis	2.29	2.16	u
YER090W	TRP2	biosynthesis	4.58	4.33	0
YJR016C	ILV3	pranched cnair famity amino acid biosynthesis	2.29	3.00	ш
YER086W	ILV1	branched chain family amino acid biosynthesis	4.21	4.46	21
YCL009C	9/1	branched chain family amino acid biosynthesis	2.65	2.28	0
YNR027W	BUD17	bud site selection	3.39	2.33	4
YOR301W	RAX1	bud site selection	3.37	3.02	4
YIL140W	AXL2	bud site selection	3.49	3.52	0
YGR041W	BUD9	bud site selection	2.02	2.27	0
YLR084C	RAX2	bud site selection	2.93	2.31	0
YEL031W	SPF1	calcium ion homeostasis	3.40	3.11	0
YOR087W	YVC1	cation homeostasis	4.21	3.56	5
YOR087W	YVC1	cation homeostasis	4.30	3.28	5
YHL003C	LAG1	cell aging (sensu Saccharomyces)	3.18	3.54	4
YDL127W	PCL2	cell cycle	2.19	2.24	0
YML058w-a	HUG1	cell cycle arrest	11.42	9.32	0
YDL101C	DUN1		6.55	7.72	18
		cell cycle dependent actin filament			
YDL226C	GCS1	reorganization	4.44	3.92	5
YKL101W	HSL1	cell morphogenesis checkpoint	2.44	2.45	7
YMR109W	MYO5	cell wall organization and biogenesis	3.05	2.62	9
YHL030W	ECM29	cell wall organization and biogenesis	5.92	5.64	4
YJL158C	CIS3	cell wall organization and biogenesis	4.78	4.50	0
YGL027C	CWH41	cell wall organization and biogenesis	3.27	3.92	0
				-	

Table 10A					<u> </u>	Table 10A					
							Gene	Function	W٦	mgt1	Sens
ORF						ORF			Ъ.	л С	
YHR143W	DGene	cell wall organiz Rigm of Workgenesis	W.TO	mgth	Seins	VEL055C	POL5	UNA dependent DNA replication	3.18	3.41	ω
YBR078W_ex1	ECM33	cell wall organization and biogenesis	_ි වේ	FČ ⁷⁸	0	YDL164C	CDC9	DNA recombination	3.70	3.95	ш
YBR078W_ex2	ECM33	cell wall organization and biogenesis	2.46	2.80	0	YLR383W	RHC18	DNA repair	2.29	3.54	ш
YMR062C	ECM40	cell wall organization and biogenesis	5.76	5.70	0	YCR066W	RAD18	DNA repair	2.55	2.61	30
YLR342W	FKS1	cell wall organization and biogenesis	3.41	3.78	0	YJR069C	HAM1	DNA repair	9.17	8.81	0
YOR109W	INP53	cell wall organization and biogenesis	2.38	2.16	0	YHR120W	MSH1	DNA repair	2.18	2.20	0
YGL178W_ex2	MPT5	cell wall organization and biogenesis	2.07	2.40	0	YGR180C	RNR4	DNA replication	3.14	3.06	6
YNL283C	WSC2	cell wall organization and biogenesis	6.04	7.23	0	YIL066C	RNR3	DNA replication	4.18	6.16	0
YOR249C	APC5	chromaun assembly disassembly	2.15	2.62	LU	YNL273W	TOF1	DNA topological change	4.95	6.19	15
YBR245C	ISW1	chromatin modeling	2.10	2.24	12	YLR274W	CDC46	ONA unwinding	4.83	5.30	ш
		chromatin sitencing at HML and HMR (sensu				YBL023C	MCM2	6uipuiwun ANCi	2.88	2.77	ш
YLL004W	ORC3	Saccharomyces)	2.10	2.12	iLI	YGL251C	HFM1	DNA unwinding	2.58	2.27	0
		chromatin silencing at HML and HMR (sensu				YOR067C	ALG8	dolichol-linked oligosaccharide biosynthesis	2.65	2.57	0
YNL261W	ORC5	Saccharomyces)	2.80	2.53	ш	YNR030W	ECM39	dolichol-linked oligosaccharide biosynthesis	4.31	4.29	0
And and a second s		chromatin silencing at HML and HMR (sensu				YBL082C	RHK1	dolichol-linked oligosaccharide biosynthesis	3.81	3.13	0
YCL061C	MRC1	Saccharomyces)	2.61	2.76	6	YOR074C_ex1	CDC21	dTMP biosynthesis	2.50	2.45	0
YLR285W	NNT1	chromatin silencing at ribosomal DNA (rDNA)	3.18	2.91	0	YOR074C_ex2	CDC21	dTMP biosynthesis	6.45	6.30	0
YAR003W	\$UWS	chromatin silencing at telomere	2.80	2.20	ω	YNL111C	CYB5	electron transport	2.69	2.33	4
YBR175W	SWD3	chromatin silencing at telomere	5.88	4.46	7	YJL204C	RCY1	endocytosis	2.16	2.18	15
YAL034W-A	MTW1	chromosome segregation	2.53	2.74	ш	YNR075W_0	COS10	endocytosis	3.33	2.53	0
YPR046W	MCM16	chromosome segregation	2.68	2.01	2	YNR075W_1	COS10	endocytosis	5.25	3.79	0
YOL058W	ARG1	citrulline metabolism	9.98	11.09	5	YBR080C	SEC18	ER to Golgi transport	2.55	2.58	ш
YAR031W	PRM9	conjugation with cellular fusion	4.23	3.14	0	YDL195W	SEC31	ER to Goigi transport	2.12	2.08	ω
YMR305C	SCW10	conjugation with cellular fusion	3.53	3.65	0	YDR407C	TRS120	ER to Golgi transport	2.31	2.27	ω
YNL259C	ATX1	copper ion transport	3.30	3.44	5	YBR254C	TRS20	ER to Golgi transport	2.46	2.59	ш
YCR075C	ERS1	cystine transport	2.04	2.39	0	YNL263C	VIF1	ER to Goigi transport	2.40	2.00	ω
YHR107C	CDC12	cytokinesis	2.47	2.04	ш.	YCL001W	RER1	ER to Golgi transport	2.18	2.02	4
YLR314C	CDC3	cytokinesis	212	7.76	ω	YAL007C	ERP2	ER to Golgi transport	6.14	7.08	0
YNL327W	EGT2	cytokinesis	2.18	2.63	12	YOR216C	RUD3	ER to Golgi transport	3.45	3.89	0
YNL233W	BNI4	cytokinesis	2.28	2.22	0	YCR067C	SED4	ER to Golgi transport	5.04	4.16	0
YDL117W	CYK3	cytokinesis	2.19	2.55	0	YOR115C	TRS33	ER to Golgi transport	2.93	3.08	0
YIL142W	CCT2	cytoskeleton organization and biogenesis	2.36	2.42	ιt _i	YNR026C	SEC12	ER-associated protein catabolism	3.75	3.37	0
YJL008C	CCT8	cytoskeleton organization and biogenesis	2.20	2 13	υ	YGR175C	ERG1	ergosterol biosynthesis	2.17	2.04	ш
YDR212W	1'CP1	cytoskeleton organization and biogenesis	2.74	2.30	ιIJ	YPL028W	ERG10	ergosterol biosynthesis	2.59	2.00	ιυ
YNL138W	SRV2	cytoskeleton organization and biogenesis	2.12	2.29	0	YML126C	ERG13	ergosterol biosynthesis	5.72	3.82	uл
YDL219W_ex1	DTD1	D-amino acid catabolism	11.36	9.61	0	YGR060W	ERG25	ergosterol biosynthesis	5.44	3.76	ω
YDL219W_ex2	DTD1	D-amino acid catabolism	7.55	7.00	0	YGL001C	ERG26	ergosterol biosynthesis	3.94	3.30	ш
YKL212W	SAC1	dephosphorylation	5.03	5.07	4	YLR100W	ERG27	ergosteroi biosynthesis	3.10	3.07	ω
YDR489W	NA	DNA dependent DNA replication	3.01	2.67	ш	YHR190W	ERG9	ergosterol biosvnthesis	2.47	2.57	ш

FunctionMTMTMTInstidine biosynthesis9.06Instidine biosynthesis9.06Instidine biosynthesis9.06Instidine biosynthesis1.824.40Instidine biosynthesis3.73Instidine biosynthesis3.73Instidine biosynthesis1.821.821.821.40Instidine biosynthesis3.73Instidine biosynthesis3.74Instidine biosynthesis3.74Instidue biosynthesis3.	Table 10A						Table 10A					
Observe Currents		T						Gene	Function	ł	mgt1	Sens
QRMSUnspectively long/fmemberWDMQDMQDMQDMQDMQDMQDMQDMQDMQDMQDMQDFIRS3explored long/memasE40251	ORF						ORF			ည်	С	
(F) (F) <td>YER044C</td> <td>EGene</td> <td>ergosterol biosyRumistion</td> <td>08.W</td> <td>mgth</td> <td>Sêns</td> <td>YER055C</td> <td>HIS1</td> <td>histidine biosynthesis</td> <td>90.6</td> <td>7.68</td> <td>0</td>	YER044C	EGene	ergosterol biosyRumistion	08.W	mgth	Sêns	YER055C	HIS1	histidine biosynthesis	90.6	7.68	0
FIGS endolse opponentiation 615 616 616 Wittington 145 Wittington 126 FIG2 epigerial biopynthus 234 236 7 7 236 237 236 FIG2 epigerial biopynthus 234 236 7 7 7 236 237 236 FIG3 epigerial biopynthus 631 7 7 7 7 236 <td>YLR056W</td> <td>ERG3</td> <td>ergosterol biosynthesis</td> <td>لۇر¹0</td> <td>E²⁵¹</td> <td>29</td> <td>YFR025C</td> <td>HIS2</td> <td>histidine biosynthesis</td> <td>4.40</td> <td>4.52</td> <td>0</td>	YLR056W	ERG3	ergosterol biosynthesis	ل ۇر ¹ 0	E ²⁵¹	29	YFR025C	HIS2	histidine biosynthesis	4.40	4.52	0
ERQ2ERQ2experiendeERQ3ERQ3experiendeERQ3ERQ3experiendeERQ3ERQ3experiendeERQ3E	YML008C	ERG6	ergosterol biosynthesis	6.15	6.18	25	YOR202W	HIS3	histidine biosynthesis	7.82	6.80	0
Image: Restant properties and sector sector sequences and sector sector sequences and sector sector sequences and sector sector sector sequences and sector sector sector sequences and sector sector sector sequences and sector sector sector sequences and sector sector sector sector sector sequences and sector sector sequences and sector sector sequences and sector sector sequences and sector sector sector sector sector sector sector sector sector sequences and sector sect	YMR202W	ERG2	ergosterol biosynthesis	5.24	3.97	23	YIL116W	HIS5	histidine biosynthesis	3.73	3.14	0
W EFG/23 Sequence Indeprintention 236 -70.2360/th FM:003 FM:003 FM:003 237 237 // EFG/43 Sequence Indeprintention C31 Numerologic Securitory Securitory Securitory Securitory Securitory Securitory Securitory Securitory Securitory Security Securit	YNL280C	ERG24	ergosterol biosynthesis	2.31	2.86	6	YGR191W	HP	histidine transport	2.34	2.48	ω
(1) (Fick) erganitation dependingation (13) (14) <	YMR208W	ERG12	ergosterol biosynthesis	2.55	2.26	0	YDL236W	PH013	histone dephosphorylation	5.93	5.83	0
	YGL012W	ERG4	ergosterol biosynthesis	13.68	13.96	0	YFL037W	TUB2	homologous chromosome segregation	3.71	3.39	ш
			of cell polarity				YML085C_ex2	TUB1	homologous chromosome segregation	2.88	3.14	0
(1) (1) <td>YGL019W</td> <td>CKB1</td> <td>Saccharomyces)</td> <td>2.20</td> <td>2.26</td> <td>10</td> <td>YML124C_ex2</td> <td>TUB3</td> <td>homologous chromosome segregation</td> <td>4.46</td> <td>3.88</td> <td>0</td>	YGL019W	CKB1	Saccharomyces)	2.20	2.26	10	YML124C_ex2	TUB3	homologous chromosome segregation	4.46	3.88	0
			of cell polarity				YLR113W	HOG1	hyperosmotic response	2.80	2.72	11
γ	YDL225W	SHS1	Saccharomyces)	2.63	2.86	0	YBR288C	APM3	intracellular protein transport	2.49	2.81	0
SH1Spectrate on the sectore of the secto	Martin Concerning and the second se		of cell polarity	ļ			YDR093W	DNF2	intracellular protein transport	3.13	3.23	0
E101fatt and endpaired, unstanted fath add5.686.340ViRit00WG.6A2intreendlar egrand, rensport4.264.26710Reventedbalm4.172.484ViL 122WNAintreendlar egrand, escade3.043.04710Reventedbalm1.172.321.22.21.42.042.172.172.172.0210Statembol2.342.312.301.0Nintreendlar egrand, escade2.312.342.0212.182.342.312.3201.0Nintreendlar egrand, escade2.312.342.0212.182.342.312.301.0Nintreendlar egrand, escade2.342.342.0213.142.342.311.0Nintreendlar egrand, escade2.342.342.0313.1414.1410.141.01.01.02.342.342.0413.1414.141.01.01.01.02.342.342.1113.141.01.01.01.01.02.342.342.1113.141.01.01.01.01.02.342.342.1113.1411.1410.121.01.01.01.02.342.342.1113.1411.1411.141.01.01.01.02.342.342.1113.1411.1411.141.01.01.01.02.34 <td>YLR313C</td> <td>SPH1</td> <td>Saccharomyces)</td> <td>3.26</td> <td>2.65</td> <td>0</td> <td>YDR093W</td> <td>DNF2</td> <td>intracellular protein transport</td> <td>2.62</td> <td>2.85</td> <td>0</td>	YLR313C	SPH1	Saccharomyces)	3.26	2.65	0	YDR093W	DNF2	intracellular protein transport	2.62	2.85	0
7ACB1data back alcoholic 4.7 4.26 4.2 YRR 2100/LNAintraediular signaling cascade 3.00 3.00 7DCD26Ele incontrocación tranço 4.11 2.29 2.2 2.7 2.7 2.7 2.7 2.7 7DCD26CDC26CS Transition or miciolic cell cycle 2.80 2.2 2.2 2.7 2.7 2.7 2.7 7DCD26CDC26CDC26CDC26CDC26CDC26 2.7 2.7 2.7 2.7 7DCD26CDC26CDC26CDC26CDC26CDC26 2.7 2.7 2.7 2.7 7DCD26CDC26CDC26CDC26CDC26CDC26CDC26 2.7 2.7 2.7 2.7 7DCD26DDC3DDC3CDC26CDC26CDC26CDC26 2.7 2.7 2.7 2.7 7DDC3DDC3DDC3CDC26CDC26CDC26 2.7 2.7 2.7 2.7 7DDC3DDC3DDC3DDC3DDC3DDC3 </td <td>YJL196C</td> <td>EL01</td> <td>fatty acid elongation, unsaturated fatty acid</td> <td>5.69</td> <td>6.36</td> <td>0</td> <td>YHR108W</td> <td>GGA2</td> <td>intracellular protein transport</td> <td>4.25</td> <td>4.01</td> <td>0</td>	YJL196C	EL01	fatty acid elongation, unsaturated fatty acid	5.69	6.36	0	YHR108W	GGA2	intracellular protein transport	4.25	4.01	0
CNC3 EN81 Intracendation transport 311 232 304 X CUC23 C1 servance of multic cell ordet 2.3 2.3 YUL32W GFZ Intra-odg transport 2.17 2.17 X CUC3 C1 servance of multic cell ordet 2.14 2.30 13 YUL14UC PGZ Intra-odg transport 2.18 2.71 2.78 Z CUE3 C2 M transferon fimilic cell ordet 2.14 2.30 13 YUL14UC POR3 Intra-odg transport 2.78 2.78 2.78 2.78 2.78 2.74 2.78 2.74 2.78 2.74	YGR037C	ACB1	fatty acid metabolism	4.77	4.26	4	YBR210W	NA	intracellular signaling cascade	3.00	2.64	4
1CLGKC1 Stansition of muchoc cell code2.22C1 <td>YOL158C</td> <td>ENB1</td> <td>ferric-enterobactin transport</td> <td>4.11</td> <td>2.59</td> <td>2</td> <td>YNL123W</td> <td>AN</td> <td>intracellular signaling cascade</td> <td>3.04</td> <td>2.73</td> <td>0</td>	YOL158C	ENB1	ferric-enterobactin transport	4.11	2.59	2	YNL123W	AN	intracellular signaling cascade	3.04	2.73	0
ShP4 G1 Stansilion of mitolic cell cycle 2.60 2.28 0 VDI 152/W AFF1 inite-Jody transport 2.64 // CBE2 C2 Wransilion of mitolic cell cycle 2.14 2.30 13 VOI 132/W Inite-Jody transport 2.76 2.78 .ucd EXCI Jucan metabolism 2.66 2.57 0 VRI17W MM17 Inon monostatis 2.76 2.76 V EXCI Jucan metabolism 2.66 2.37 0 VRI00W PRI MM17 Inon monostatis 2.76 76 V EXCI Jucantione biosynthesis 2.67 0 VRI00W NR NR 4.15 76 V EXCI Jucantione biosynthesis 2.43 7 VRI00W NR NR 4.15 76 V EVCI Jucantione biosynthesis 2.41 0 VRI00W NR NR 4.15 76 V EVCI JUCA NR NR Humbio Biograme Biosynthesis	VBR160W	CDC28	G ! S transition of mutotic cell cycle	2.92	2.72	w	YEL022W	GEA2	intra-Goigi transport	2.17	2.26	ш
	YGL229C	SAP4	G1 S transition of mitotic cell cycle	2.60	2.28	0	YDL192W	ARF1	intra-Golgi transport	2.54	2.62	0
$_{\rm exc}$ PM40GPP-menose biosynthesis 2.11 2.23 0 $V(L14,C$ $POR2$ in transport 4.26 2.24 V EX01glucan retabolism 2.66 2.57 0 $VMR17W$ $MM1$ in on ion monostasis 4.26 2.76 V GN1glucan retabolism 8.23 4.46 7.42 0 8.27 0 4.26 2.76 2.76 V GN1glucan retabolism 1.63 8.48 8 0 $VR08W$ RT 1.60 in transport 4.16 2.76 V GN1glucan retabolism 1.63 8.48 6 5.96 0 $VR08W$ RT 1.60 in grane diogram 4.16 2.24 V GU1glucan retabolism 2.24 2.28 4.80 4.80 4.80 2.24 2.28 2.24 2.24 V GN0glucan retabolism 2.36 4.70 1.72 retaine biosynthesis 2.24 2.24 V GN0glucan retabolism 2.32 2.49 0 V V 2.24 2.24 V GN0glucan retabolism 2.32 2.49 0 V V 0 0 0 2.24 V GN0glucan retabolism 2.31 0 V 0 0 0 0 0 0 V Glucan retabolism 2.24 2.2 2.49 0 0 0 0 0 0 0 0 <	YPR119W	CLB2	G2 M transition of mitotic cell cycle	2.14	2.30	13	YOR080W	DIA2	invasive growth	2.78	2.79	24
VEX(1)guorae featbolish2.66 2.57 0VMR177WMMTicon ion noneostasis4.241NPGMIguorae featbolish10.638.4437 $\sqrt{180,025}$ PR11iagong strand elongation2.767.427.43VGNU7guuthone matabolism10.638.4437 $\sqrt{180,035}$ ieading strand elongation2.767.45VGNU7guuthone matabolism10.638.447 $\sqrt{180,035}$ ieading strand elongation2.412.41VGU7guuthone matabolism2.242.247 $\sqrt{180,045}$ 1.75ieading strand elongation2.242.24VGU7guuthone matabolism2.242.242.490 $\sqrt{180,045}$ 1.75ieading strand elongation2.242.24VGPM3gycolysis2.490 $\sqrt{180,045}$ ATZImaganese ion homeostasis2.242.24VGPM3golu o tesma memorane transport2.16 $\sqrt{11,016}$ ATZImaganese ion homeostasis2.242.24VGPM3golu o tesma memorane transport2.16 $\sqrt{11,016}$ MRTMAPKKK stastedee2.242.24VGPM3GPM3ATM3RPM4ATM3MAPKKK stastedee2.242.242.24VGPM3GPM3ATM3RPM4MAPKKK stastedee2.242.242.24VGPM3GPM3GPM3RPM4RPM4RPM4RP	YER003C_ex2	PMI40	GDP-mannose biosynthesis	2.71	2.32	0	YIL114C	POR2	ion transport	4.28	3.04	0
PGMIpGMIgucose 6-phosphet utilization8.287.420 $v(ROBC.$ PR1lagging strand elorgation2.760GND1glucose metabolism10.636.4480 $v(RO108W$ R-C5i eading strand elorgation4.104.100G172glutathone metabolism10.636.4487 $v(RO108W$ R-C5i eading strand elorgation4.104.100G172glutathone metabolism2.113.547 $v(RO108W$ R-C5i eading strand elorgation4.104.100glucose metabolism2.122.2844 $v(RO108W$ R-R5i eading strand elorgation2.242.241glucosesglucosesta2.232.490 $v(RO130C$ ATX2manganese ion homostalsis2.242.241glucosesta2.232.490 $v(RO130C$ ATX2MAPKKK sestade2.242.242GP11glucosesta2.212.203.210 $v(RO130C$ ATX2manganese ion homostalsis2.242GP11glucosesta2.212.28 $v(RO130C$ ATX2MAPKKK sestade2.242.242GP11GP11GP11RD140C2.212.74 $v(RO130C$ 2.742.742GP11GP11GP11RD140C2.242.74 $v(RO130C$ 2.242.742GP11GP11GP11RD120CATX2AD20CAD30C <t< td=""><td>YLR300W</td><td>EXG1</td><td>glucan metabolism</td><td>2.66</td><td>2.57</td><td>0</td><td>YMR177W</td><td>MMT1</td><td>iron ion homeostasis</td><td>4.24</td><td>2.85</td><td>0</td></t<>	YLR300W	EXG1	glucan metabolism	2.66	2.57	0	YMR177W	MMT1	iron ion homeostasis	4.24	2.85	0
vGN01guocose metabolism1063 8.44 8 $v RR087W$ $R FC5$ $iacting strang clongation4.134.13vGSH2glutathione metabolism4.013.647V R108WNAleading strang clongation4.164.16cGUP1glucathione metabolism2.244.013.644.180V R1034CL VS1leading strang clongation4.154.16cBN02glucathione metabolism2.244.180V R115CL VS2leading strang clongations2.242.24rglucathises2.364.180V R115CL VS2leading strang clongations2.242.24rglucathises2.362.490V R116CR R1M R KK cascade2.242.24rSEC66.364 to totescule transport2.362.722.490V R116CR R1M R KK cascade2.342.34rR D154M R M KK cascade2.362.490V R R M R KK cascade2.342.34rR D154R D154M R M KK cascade2.342.342.342.342.34rR D154M R M R K cascade2.342.342.472.472.342.34rR D154R D154R D154R D154R D164R D10642.342$	YKL127W	PGM1	glucose 6-phosphate utilization	8.29	7.42	0	VIR008C	PRI1	lagging strand elongation	2.76	2.87	ພ
(GSH2guathione blosynthesis4.965.980VOR106WNAleucine blosynthesis4.404.15GT72guathione metabolism4.013.647YBR041WFAT1lipld transport4.154.16GUP1glycerol transport2.242.284VYR115CLYS1lysine blosynthesis, antinoadific pathway2.242.24VGN3glycolysis4.56 4.18 0VVR079CATX2magarese ion homeostasis6.392.34VGPK1glycolysis2.282.490VYR116CPRK1MAPKKK cascade2.362.34VGPU4SEC6Gold to desma memorane transport2.322.490VYR029W extNOTRDH54meiotic recombination2.332.32VGPU1GPU1GPU1GPU1RDH54meiotic recombination2.342.342.342.342.342.34VGPU1GPU1GPU1GPU1PRD50W extYCP1Methorane organization and biogenesis3.303.323.323.323.32VGPU1GPU1GPU1GPU1GPU1Methorane organization and biogenesis3.32 <td< td=""><td>YHR183W</td><td>GND1</td><td>glucose metabolism</td><td>10.63</td><td>8.44</td><td>80</td><td>YBI2087W</td><td>RFC5</td><td>teading strand elongation</td><td>4,13</td><td>3.81</td><td>ш</td></td<>	YHR183W	GND1	glucose metabolism	10.63	8.44	80	YBI2087W	RFC5	teading strand elongation	4,13	3.81	ш
GTZ2Gutatione metabolism4.01 3.64 7YBR04:W $FAT1$ Ipid transport 4.15 4.15 WGUP1glycerol transport2.242.284 $YR034C$ LYS1lysine biosynthesis, antroadipic pathway3.377WENO2glycolysis 4.60 4.67 E $YR034C$ LYS1lysine biosynthesis, antroadipic pathway2.242.32WGPM3glycolysis 2.52 2.49 0YR116CRTX2manganese ion homeostasis6.392.39SEC6solig to second transport 2.32 2.32 2.31 0YR039CMSC7manganese ion homeostasis2.312.34SEC6solig to vacuel transport 2.32 2.31 0 YR039CMSC7manganese ion homeostasis3.322.33SEC6solig to vacuel transport 2.34 2.34 0 YR038W_extRDH54metoic recombination2.342.33SEC6GP14GP14GP14RDH54metoic recombination 2.34 2.342.342.332.33SEC6GP14GP14/6GP14PRD54MSC7MSC7metoic recombination2.342.34SEC6GP14GP14GP164RDH54RDH54metoic recombination2.342.332.34SEC6GP14GP14GP140PRD54RDH54RDH542.342.342.34SEC7GP14GP14GP14RDH54RDH54R	YOL049W	GSH2	glutathione biosynthesis	4.96	5.98	0	YOR108W	NA	leucine biosynthesis	4.40	7.10	0
U_{V} <	YLL060C	GTT2	glutathione metabolism	4.01	3.64	7	YBR041W	FAT1	lipid transport	4.15	3.96	5
($($	YGL084C	GUP1	glycerol transport	2.24	2.28	4	YIR034C	LYS1	lysine biosynthesis, aminoadipic pathway	3.37	2.99	4
	YHR174W	EN02	glycolysis	4.60	4.67	LLI	YBR115C	LYS2	lysine biosynthesis, aminoadipic pathway	2.24	2.52	0
r PFK1gycotysis 2.52 2.49 0 $YKL16C$ PRR1MAPKKK cascade 2.56 2.56 r SEC6Golg to otasma membrane transport 2.38 2.72 $\tilde{r}YR073WRDH54meiotic recombination2.742.74rAPL6Golg to vacuole transport2.363.210YHR039CMSC7meiotic recombination2.342.32rGP11GP1anchor biosynthesis3.153.170YR028W_ex1YOP1membrane organization and biogenesis3.02rGP14GP1anchor biosynthesis3.153.170YR028W_ex1YOP1membrane organization and biogenesis3.172.490vHEM12heme biosynthesis2.742.260VIL123WSIM1membrane organization and biogenesis2.172.17vHEM2heme biosynthesis2.742.260VIL123WSIM1microtubule organization and biogenesis2.172.17vHEM4heme biosynthesis2.742.260VIL123WSIM1microtubule organization and biogenesis2.172.17vHEM4heme biosynthesis2.742.200VIL123WSIM1microtubule organization and biogenesis2.172.17vHEM4heme biosynthesis2.212.200VIL123WSIM1ii2.31<$	YOL056W	GPM3	glycolysis	4.59	4.18	0	YOR079C	ATX2	manganese ion homeostasis	6.39	5.30	0
SEC6Golg to olasma memorane transport 2.36 2.72 2.7 7 $Rentation$ 2.74 7 2.70 2.74 7 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.33 2.32 2.32 2.32 2.32 2.32 2.32 2.32 2.32 2.32 2.32 2.31 0 7 7 $membrane organization and biogenesis2.172.322.312.31077membrane organization and biogenesis2.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.322.312.32$	YGR240C	PFK1	glycolysis	2.52	2.49	0	YKL116C	PRR1	MAPKKK cascade	2.59	2.72	0
λ APL6Golg to vacuole transport 2.70 3.21 0 γ HR03GCMSC7meiotic recombination 2.33 2.33 κ GPI1GPI anchor biosynthesis 3.06 4.26 E γ PR028W_ex1 γ OP1membrane organization and biogenesis 3.02 3.02 κ GPI1GPI anchor biosynthesis 3.15 3.17 0 γ PR028W_ex2 γ OP1membrane organization and biogenesis 3.02 2.17 κ HEM12heme biosynthesis 2.47 2.49 0 γ HR123W γ M1microtubule cytoskeleton organization and biogenesis 2.17 κ HEM4heme biosynthesis 2.74 2.26 0 γ HR172W $SM1$ biogenesis 2.38 4.87 κ HEM4heme biosynthesis 2.37 2.56 0 γ HR172W $SPC97$ microtubule cytoskeleton organization and 2.38 κ HEM4heme biosynthesis 2.30 0 γ HR172W $SPC97$ microtubule cytoskeleton organization and 2.38 κ HIShigh affinity iron ion transport 2.20 2.30 0 γ HR172W $SPC97$ microtubule-based process 4.77 κ HIShistidine biosynthesis 3.86 2.99 2.00 γ L051C $MH1$ microtubule-based process 3.74 4.77 κ HIShistidine biosynthesis 3.16 3.07 4 γ DL198C γ HM1microtubule ance 3.26 7.74	YIL068C	SEC6	Goigi to plasma membrane transport	2.38	2.72	:6	YBR073W	RDH54	meiotic recombination	2.74	2.94	12
(0) (0) <	YGR261C	APL6	Golgi to vacuole transport	2.70	3.21	0	YHR039C	MSC7	meiotic recombination	2.33	2.37	б
C GP1GP1 anchor blosynthesis 3.15 3.17 0 $YPR028W_{eX2}$ $YOP1$ membrane organization and blogenesis 2.17 2.17 $MCD4$ GP1 anchor blosynthesis 2.74 2.49 0 $YIL123W$ $M1$ incotubule cytoskeleton organization and blogenesis 4.87 4.87 V HEM1heme blosynthesis 2.74 3.25 $\mathbb{C}YIL123WM1blogenesis4.872.88VHEM4heme blosynthesis2.743.25\mathbb{C}VYIL123WSM1blogenesis4.872.88VHEM4heme blosynthesis2.742.500VYIL123WSM1blogenesis4.772.38VFET3high affnity ion ion transport2.202.300VYIL241C_{EX2}CIN2microtubule-based process4.77VHIS7histidine blosynthesis3.852.99200VVL051CMF1microtubule-based process3.76HIS4histidine blosynthesis3.163.074YDL198CYHM1microtubule genome maintenance3.444.47$	YNL038W	GPI15	GPt anchor biosynthesis	3 06	4.26	u	YPR028W_ex1	YOP1	membrane organization and biogenesis	3.02	3.24	0
MCD4GP1 anchor biosynthesis 2.47 2.49 0 146 160 160 und cytoskeleton organization and 1.81 <th< td=""><td>YGR216C</td><td>GP11</td><td>GPI anchor biosynthesis</td><td>3.15</td><td>3.17</td><td>0</td><td>YPR028W_ex2</td><td>YOP1</td><td>membrane organization and biogenesis</td><td>2.17</td><td>2.59</td><td>0</td></th<>	YGR216C	GP11	GPI anchor biosynthesis	3.15	3.17	0	YPR028W_ex2	YOP1	membrane organization and biogenesis	2.17	2.59	0
v HEM12 heme blosvitthesis 2.74 3.25 E YIL123W SIM1 biogenesis 4.87 8.87 4.87 4.87 4.87 v HEM4 heme blosvitthesis 2.47 2.50 0 vHR172W SPC97 mcrotubule-based process 4.87 2.38 4.77 2.30 0 YPL241C_ex2 CIN2 microtubule-based process 4.77	YKL165C	MCD4	GPI anchor biosynthesis	2.47	2.49	0			microtubule cytoskeleton organization and			
V HEM4 heme biosynthesis 2.47 2.50 0 7HR172W SPC97 microaubule hareation 2.38 2.38 2.38 2.38 2.38 2.38 2.38 2.38 2.37 0 7HL241C_ex2 CIN2 microaubule-based process 2.38 4.77 7 <t< td=""><td>YDR047W</td><td>HEM12</td><td>heme biosynthesis</td><td>2.74</td><td>3.25</td><td>ω</td><td>YIL123W</td><td>SIM1</td><td>biogenesis</td><td>4.87</td><td>6.01</td><td>0</td></t<>	YDR047W	HEM12	heme biosynthesis	2.74	3.25	ω	YIL123W	SIM1	biogenesis	4.87	6.01	0
V FET3 high affinity iron ion transport 2.20 2.30 0 YPL241C_ex2 CIN2 microtubule-based process 4.77 i HIS7 histidine biosynthesis 3.85 2.99 20 YL051C MMF1 mitoconomial genome maintenance 3.26 HIS4 histidine biosynthesis 3.16 3.07 4 YDL198C YHM1 mitochondrial genome maintenance 13.44 14 14.44	YOR278W	HEM4	heme biosynthesis	2.47	2.50	0	YHR172W	SPC97	microtubule nucleation	2.38	2.42	ш
HIS7 histidine biosynthesis 3.85 2.99 20 7L051C MMF1 mitochonarial genome maintenance 3.26 HIS4 histidine biosynthesis 3.16 3.07 4 YDL198C YHM1 mitochondrial genome maintenance 13.44 14.44 <	YMR058W	FET3	high affinity iron ion transport	2.20	2.30	0	YPL241C_ex2	CIN2	microtubule-based process	4.77	5.26	0
HIS4 histidine biosynthesis 3.16 3.07 4 YDL198C YHM1 mitochondrial genome maintenance 13.44	YBR248C	HIS7	histidine biosynthesis	3.85	2.99	20	VIL051C	MMF1	initochonarial genome maintenance	3.26	3.14	ш
	YCL030C	HIS4	histidine biosynthesis	3.16	3.07	4	YDL198C	YHM1	mitochondrial genome maintenance	13.44	13.70	2

Function WT mgt1 Function 3.72 3.90 N-linked glycosylation 3.72 3.90 N-linked glycosylation 2.45 2.37 N-linked glycosylation 2.45 2.37 N-linked glycosylation 2.45 2.37 N-linked glycosylation 2.45 2.38 N-linked glycosylation 2.45 2.38 N-linked glycosylation 2.45 2.38 N-linked glycosylation 2.45 2.38 N-linked glycosylation 2.45 2.45 N-linked glycosylation 2.45 2.45 Nucleute vesicle coating 2.45 2.47 Nucleute vesicle coating 3.14 2.47 Nucleute and metabolism 3.71 3.35 nucleobase, nucleoside, nucleoside, nucleoside and 3.71 3.36 nucleobase, nucleoside, nucleoside, nucleoside and 3.71 3.26 nucleobase, nucleoside, nucleoside, nucleoside and 3.71 3.27 nucleoside metabolism nucleobase, nucleoside, nucleoside and 3.71 <	Table 10A						Table 10A					
No. Open No. No. <th></th> <th></th> <th></th> <th></th> <th></th> <th>4.1</th> <th></th> <th>Gene</th> <th>Function</th> <th>ΥT</th> <th>mgt1</th> <th>Sens</th>						4.1		Gene	Function	ΥT	mgt1	Sens
Name Number of the methoding Number of the methoding	ORF						ORF			С Ч	с Г	
RM <th>YCR028C-</th> <th>Gene</th> <th>Function</th> <th>WT</th> <th>mgt1</th> <th>Sens</th> <th>YPL227C</th> <th>ALG5</th> <th>N-linked glycosylation</th> <th>3.72</th> <th>3.90</th> <th>0</th>	YCR028C-	Gene	Function	WT	mgt1	Sens	YPL227C	ALG5	N-linked glycosylation	3.72	3.90	0
ukg number lengen ykg ukga ukga ukga ukga ykga	A_ex1	RIM1	mitochondrial genome maintenance	ائر الح	E ²¹²	0	YGR227W	DIE2	N-linked glycosylation	2.40	2.27	0
(N)0 (N)0 <th< td=""><td>YHR024C</td><td>MAS2</td><td>mitochondhal processing</td><td>5.14</td><td>5.84</td><td>œⁱ</td><td>YBR205W</td><td>KTR3</td><td>N-linked glycosylation</td><td>2.45</td><td>2.37</td><td>0</td></th<>	YHR024C	MAS2	mitochondhal processing	5.14	5.84	œ ⁱ	YBR205W	KTR3	N-linked glycosylation	2.45	2.37	0
(1),1) (1),1)<	YNL070W	TOM7	mitochondrial translocation	2.60	2.09	4	YBR205W	KTR3	N-linked glycosylation	2.22	2.14	0
0022 methonometal manyor 23 23 23 23 23 23 EW1 methonometal manyor 23 23 23 23 23 23 EW1 methonometal manyor 23	YIL134W	FLX1	mitochondrial transport	2.54	2.44	17	YGL226C-					
Q11 memolectore operation operation G12 C <thc< th=""> <thc< th=""> C <</thc<></thc<>	YOR222W	ODC2	mitochondrial transport	2.29	2.33	0	A_ex2	OST5	N-linked glycosylation	3.19	3.47	0
EW1 EW1 Immediational collogenesis 214 220 </td <td>YMR012W</td> <td>CLU1</td> <td>mitochondrion organization and biogenesis</td> <td>6.55</td> <td>6.11</td> <td>0</td> <td>VIL076W</td> <td>SEC28</td> <td>nonselective vesicle coating</td> <td>4.22</td> <td>4.25</td> <td>2</td>	YMR012W	CLU1	mitochondrion organization and biogenesis	6.55	6.11	0	VIL076W	SEC28	nonselective vesicle coating	4.22	4.25	2
MX003 Multical memolection agricultation and hologenesis 344 0 VLI Numerical period system 2.45 5.48 AK1 meson memolection agricultation 2.37 2.38 2.39 2.3 2.39 2.34	YGR029W	ERV1	mitochondrion organization and biogenesis	2.14	2.02	0	YDR164C	SEC1	nonselective vesicle fusion	2.31	2.21	ш
4.10 minasi 2.37 2.08 Voltition Voltition Current methoding 5.02 5.05 MOT MOT MOT MOT motion methoding 3.14 2.47 MOT MOT MOT MOT MOT MOT MOT MOT 3.12 2.38 5.43 MOT 3.14 3.47 MOT MOT MOT MOT MOT MOT MOT MOT 3.14 3.14 3.14 MOT MOT MOT MOT MOT MOT MOT 3.14 3.14 MOT MOT MOT MOT MOT MOT MOT 3.14 3.14 MOT MOT MOT MOT MOT MOT MOT 3.14 3.14 MOT MOT MOT MOT MOT MOT MOT MOT MOT 3.	YGL020C	MDM39	mitochondrion organization and biogenesis	3.88	4.44	0	YLR195C	NMT1	N-terminal peptidyl-glycine N-myristoylation	2.45	2.88	0
APM middle and black 2.23 2.04 7 NC01 mone currencementation 3.24 5.28 5 NC01 mone currencementation 3.24 5.28 5 NC01 mone currencementation 3.24 5.28 5 NC01 mone currencementation 3.24 0.00 NC01 mone currencementation 3.24 0.01 NC01 mone currencementation 2.06 2.86 5 0.02 NC01 mone same formation 2.01 2.06	YGL021W	ALK1	mitosis	2.37	2.03	0	YOR130C	ORT1	nuclear migration (sensu Saccharomyces)	5.02	5.96	0
WDD: molectrimonosome conferention 322 2.41 2.44 SMC2 molectrimonosome conjensition 3.25 2.35 2.41 2.44 SMC3 molectrimonosome sequention 3.25 2.48 2.44 2.44 SMC3 molectrimonosome sequention 2.75 2.44 2.44 2.44 SMC3 molectrimonosome sequention 2.75 2.44 2.44 2.44 SMC3 molectrimonosome sequention 2.75 2.44 2.45 2.44 Unit molectrimonosome sequention 2.75 2.44 2.45 2.44 SMC3 molectrimonosome sequention 2.45 2.74 2.74 2.74 SMC3 molectrimonosome sequention 2.45 2.74 2.74 2.74 SMD molectrimonosome sequention 2.45 2.74 2.74 2.74 SMD molectrimonosome sequention 2.74 2.75 2.74 2.74 SMD molectrimonosome sequention 2.75 2.74 2.74 <t< td=""><td>YHR129C</td><td>ARP1</td><td>mitotic anaphase B</td><td>2.23</td><td>2.08</td><td>7</td><td></td><td></td><td>le,</td><td></td><td></td><td></td></t<>	YHR129C	ARP1	mitotic anaphase B	2.23	2.08	7			le,			
SUCC Implementation 32 4.8 r Implementation 127 328 12 328 12 328 12 328 12 328 12 328 12 328 12 328 12 328 12 328 12 328 12 328 <t< td=""><td>YDL003W</td><td>MCD1</td><td>mitotic chromosome condensation</td><td>3.52</td><td>2.89</td><td>ιIJ</td><td>YKR091W</td><td>SRL3</td><td></td><td>3.14</td><td>2.47</td><td>2</td></t<>	YDL003W	MCD1	mitotic chromosome condensation	3.52	2.89	ιIJ	YKR091W	SRL3		3.14	2.47	2
SitC: motic state ritronance sequeption 21 23 4 Activation 371 356 RK1 motics state ritronance correan 21 34 402 RK1 motics state ritronance correan 21 34 402 RK1 motics state ritronance correan 21 276 276 RK1 motics state ritronance correan 24 34 402 SM2 PKN 245 24 24 24 SM3 FFKN PKN PKN PKN 242 24 MKN FFKN PKN PKN PKN PKN 242 24 MKN FFKN PKN PKN PKN PKN 242 24 MKN FFKN PKN PKN<	YFR031C	SMC2	mitotic chromosome condensation	3.22	4.58	۰L			nucleotide			
(R) (molic state) chroning contesion 272 355 (c) (c) <th< td=""><td>YFL008W</td><td>SMC1</td><td>mitolic chromosome segregation</td><td>2.67</td><td>2.94</td><td>ليا</td><td>YOR247W</td><td>SRL1</td><td></td><td>3.71</td><td>3.95</td><td>0</td></th<>	YFL008W	SMC1	mitolic chromosome segregation	2.67	2.94	ليا	YOR247W	SRL1		3.71	3.95	0
SMC3mitore same chromatic remain206 7 7 7 7 3 4 2 2 3 4 2 3 4 2 3 4 2 3 4 2 3 4 2 3 4 2 3 2 3 2 3 2 3 2 3 2 3 <th< td=""><td>VIL026C</td><td>IRR1</td><td>mitotic sister chromatid conesion</td><td>2.72</td><td>3.55</td><td>ш</td><td></td><td></td><td>de, nucleotide</td><td></td><td></td><td></td></th<>	VIL026C	IRR1	mitotic sister chromatid conesion	2.72	3.55	ш			de, nucleotide			
multi multi <th< td=""><td>YJL074C</td><td>SMC3</td><td>mitotic sister chromatid cohesion</td><td>2.08</td><td>2.58</td><td>Ψ</td><td>YOR247W</td><td>SRL1</td><td>nucleic acid metabolism</td><td>3.54</td><td>4.02</td><td>0</td></th<>	YJL074C	SMC3	mitotic sister chromatid cohesion	2.08	2.58	Ψ	YOR247W	SRL1	nucleic acid metabolism	3.54	4.02	0
104Sectontonees) 4.0 3.0 2.4 2.0 3.0 2.4 2.4 2.4 2.4 2.2 2.4 2.4 2.0 reflext element 2.4	www.weightign.go.go.go.go.go.go.go.go.go.go.go.go.go.		spindle assembly				YAL022C	FUN26	nucleoside transport	2.76	2.75	0
C.P1(FMA) riseage(2.8)(2.4)(2.4)(2.2)(2.1)(2.2.6)SHE3FMA locatization, intracellular(2.8)(2.7)(2.9) <t< td=""><td>YLR212C</td><td>TUB4</td><td>Saccharomyces)</td><td>4.09</td><td>3 98</td><td>u:</td><td>YDL102W</td><td>CDC2</td><td>nucleotide-excision repair</td><td>2.32</td><td>2.44</td><td>ш</td></t<>	YLR212C	TUB4	Saccharomyces)	4.09	3 98	u:	YDL102W	CDC2	nucleotide-excision repair	2.32	2.44	ш
SH23mRMA horalization, intracellular2362730 $YAR0R6C$ PCL30mcdenete-exoison repair4103.3.4SAD1mRMA splicing3.483.742.545.471 $YAR0N2$ RFA1mcdenete-exoison repair4.153.413.41SAD3mRMA splicing2.542.518 $YAR0N2$ RFA2hurdenete-exoison repair2.132.132.132.132.132.132.132.132.132.132.132.142.232.142.232.132.142.232.132.142.232.132.142.232.132.142.232.132.142.232.132.142.232.142.242.142.242.142.242.142.242.142.24 </td <td>YUR250C</td> <td>CLP1</td> <td>mRNA cleavage</td> <td>2.34</td> <td>2.45</td> <td>ω</td> <td>YPR175W</td> <td>0PB2</td> <td>nucleotide-excision repair</td> <td>2.11</td> <td>2.28</td> <td>ш</td>	YUR250C	CLP1	mRNA cleavage	2.34	2.45	ω	YPR175W	0PB2	nucleotide-excision repair	2.11	2.28	ш
SD1Introduction crasm348 3.74 5.74 $1.7400.$ RA10undendre-excision repair316413SMD2ImRNA splicing 2.84 2.84 2.61 2.63 2.61 2.63 2.61 2.03 2.43 2.33 2.61 2.22 2.31 2.33 2.32 2.31 2.32	YBR130C	SHE3	mRNA localization, intracellular	2.85	2.73	0	YRR088C	POL30	nucleolide-excision repair	4.05	3.42	ш
SMD2ImRNA solitongZ56Z56Z56Z56Z56Z56Z618VL173CWRFA2Incleatedecosion repair2222321ST01imRNA splicing263261890VL13FW, excRFA2incleatedecosion repair2232333MR31imRNA-nucleus export21323557VL138WMD11Onlineed exosion repair2333 <td< td=""><td>YFR005C</td><td>SAD1</td><td>mRNA splicing</td><td>3.48</td><td>3.74</td><td>ų.</td><td>YAR007C</td><td>RFA1</td><td>nucleotide-excision repair</td><td>3.96</td><td>4,13</td><td>ε</td></td<>	YFR005C	SAD1	mRNA splicing	3.48	3.74	ų.	YAR007C	RFA1	nucleotide-excision repair	3.96	4,13	ε
ST01mRNA splicing2.632.618VNL312W.ex2R.FA2nucleotide excision repair4.694.27MRS1mRNA-nucleus export4.222.19 F VL050WMDL1oligoperide transport2.292.132.00DBP5mRNA-nucleus export2.122.19 F VL050WPMT1O-linked gycosylation2.292.132.30NUP188mRNA-nucleus export2.132.855Y0039WPMT3O-linked gycosylation2.303.00NM1mNA-nucleus export2.132.922.420Y0039WPMT3O-linked gycosylation2.312.322.30NM1mon-inositio metabolism2.292.420Y0137WPMT3O-linked gycosylation2.152.0111.26NN1mon-inositio metabolism2.322.412Y1.45CPM13O-linked gycosylation2.152.0111.26NN1NADH metabolism2.362.112Y1.45CPM13O-linked gycosylation2.152.0111.26NN1NADH metabolism2.362.3430Y1.45CPM13O-linked gycosylation2.162.422.16NN1NADH metabolism2.262.112Y1.45CPM13Pmtorthenate biosynthesis11.5711.26AV11neutral amino add transport2.363.440Y1.45CPM13Pmtorthenate biosynthesis2.173.37AV11neutral amino add tr	YLR147C	SMD3	inRNA splicing	2.54	2.54	'n.	YJL173C	RFA3	nucleotide-excision repair	2.12	2.31	ш
MR51mRN splicing1826.190VR180WMD11oligoperide transport2.292.132.30DBFS $mRNA-nucleus export2.222.132.865VD035WPMT1O-linked glycosylation2.303.00NUP168mRNA-nucleus export2.132.865V10.035WPMT3O-linked glycosylation2.312.322.29NM1mRNA-nucleus export2.172.210VD033WPMT3O-linked glycosylation2.372.292.91NM1mRNA-nucleus export2.552.420VD033WPMT5O-linked glycosylation2.872.292.91NM1mRNA-nucleus export2.562.420VD033WPMT5O-linked glycosylation2.872.912.91NM1mV1-netabolism2.262.1120VL45CPAN6Pantotherate blycosylation2.912.711.166NV1NP1nescent polypeptide exsociation2.822.1420VL45CPAN6Pantotherate blycosylation2.912.712.91NV1neural amino acti transport2.822.1120VL45CPAN6Pantotherate blycosylation2.912.712.722.91NV1neural amino acti transport2.822.91VL45CPAN6PAN6Pantotherate blycosylation2.712.742.91NV1neural amino acti transport2.822.91VR53VVL45C$	YMR125W	ST01	mRNA splicing	2.63	2.61	8	YNL312W_ex2	RFA2	nucleotide-excision repair	4.69	4.27	0
DBFS $riktNahundeus enzort2.222.18ritritDelinked gycosylation2.803.003.00NuNumRN-nucleus export2.132.8557Yal.023CPMT3O-linked gycosylation2.322.822.92NAmRN-nucleus export2.172.212.21072.322.822.292.92SXM1mRN-nucleus export2.152.552.620YD.093WPMT5O-linked gycosylation2.312.322.29NN1myo-inostiol metabolism2.562.660YD.163WPMT5O-linked gycosylation2.312.122.01NN1myo-inostiol metabolism2.562.660YD.163WPMT5O-linked gycosylation2.172.122.01NN1myo-inostiol metabolism2.692.660YL145CPAN6Pantohenate blosynthesis1.1571.126NT109neutral anisoti2.363.410YL145CPAN6Pantohenate blosynthesis4.172.43NT109neutral anisoti2.363.420YL145CPAN6PAN64.172.122.16NT1109neutral anisoti2.863.410YL145CPAN6PAN64.174.172.44NT1109neutral anisoti2.863.42YR145KPAN6PAN64.172.167.123.37NT1101neutral anisoti2.81YL145CPANPAN2$	YIR021W	MRS1	mRNA splicing	4.82	6.19	0	YLR188W	MDL1	oligopeptide transport	2.29	2.13	e
NUP 188mRNA-nucleus export2.132.8655YAL023CPMT2Clinked glycosylation3.143.292NAmRNA-nucleus export2.172.210YOR321WPMT3Clinked glycosylation2.322.292.42SXM1mRNA-nucleus export2.562.620YD1093WPMT5Clinked glycosylation2.382.122.29SXM1mRNA-nucleus export2.562.620YD1093WPMT5Clinked glycosylation2.872.872.792.79NH11mvo-inositid metabolism2.292.420YD103WPMT5Clinked glycosylation2.872.872.712.712.712.71NT109negative regulation of DNA transposition2.863.440YL435CFMT6Panothernate biosynthesis1.1571.126NT110negative regulation of DNA transposition2.863.440YL435CFMT6Panothernate biosynthesis7.713.31NT110N-inked glycosylation2.863.440YL154KSNF4Pentolemente biosynthesis7.722.713.31AUTN-inked glycosylation2.863.440YL154KSNF4Pentolemente biosynthesis7.722.312.31NT110N-inked glycosylation2.863.440YL154KPHO1Pentolemente biosynthesis2.773.372.34NoN-inked glycosylation2.662.865.46FM </td <td>YOR046C</td> <td>0BP5</td> <td>mRNA-nucleus expori</td> <td>2.22</td> <td>2.19</td> <td>St.</td> <td>YDL095W</td> <td>PMT1</td> <td>O-linked glycosylation</td> <td>2.80</td> <td>3.00</td> <td>0</td>	YOR046C	0BP5	mRNA-nucleus expori	2.22	2.19	St.	YDL095W	PMT1	O-linked glycosylation	2.80	3.00	0
NAInfluencieus export 2.17 2.21 0 <	YML103C	NUP188	mRNA-nucleus export	2.13	2.85	5	YAL023C	PMT2	O-linked glycosylation	3.14	3.29	0
SMHmRNA-rucleus export2.552.620VDL03VWPMT50-linked glycosylation2.872.791INM1myo-inositol metabolism2.292.420VOR241WMET7one-carbon compound metabolism2.122.011NPY1NADH metabolism2.262.660VOR241WMET7one-carbon compound metabolism2.122.011BT11nascent polypeptide association2.362.660VIL145CPAN6pantothenate biosynthesis11.5711.262.44BT11nearabon of DNA transposition2.823.2430VIL145CPAN6pentoenate biosynthesis3.924.241AVT1neural amino add transport5.635.7000VIL15WSNF4pentoenate biosynthesis3.174.241AUT1Nuinked glycosynation2.863.440VIL15WSNF4pentosenate biosynthesis4.163.313.37AUC7N-linked glycosynation2.962.960VIL15WSNF4pentosenate biosynthesis2.173.373.37AUC7N-linked glycosynation2.962.962.962.96VIL15WSNF4pentosenate biosynthesis2.173.373.37AUC7N-linked glycosynation2.962.962.962.962.96YIL13WPH011pinovasion and biogenesis2.173.37AUC7N-linked glycosynation2.962.962.962	YNL253W	NA	mRNA-nucleus export	2.17	2.21	0	YOR321W	PMT3	O-linked glycosylation	2.32	2.29	0
IMMTmyo-inositol metabolism2.292.420VOR241WMET7one-carbon compound metabolism2.122.01NPY1NADH metabolism2.692.660 $VIL145C$ PAN6pantothenate biosynthesis11.5711.262.01BTT1nascent polypeptide association2.362.112 2.77 3.92 4.24 4.24RT109negative regulation of DNA transposition2.823.2430 $VIL145C$ $FAN6$ pantothenate biosynthesis3.92 4.24 AVT1neutral amino acid transport5.635.700 $VIL35C$ $TAL1$ pentosephagete bienome maturation 4.17 4.24 AUT1neutral amino acid transport5.635.700 $VIR35C$ $TAL1$ pentosephagete bienome maturation 4.16 4.24 AUC7N-linked glycosylation2.563.440 $VIR35C$ $FA17$ pentosephagete biosynthesis, prephenate 2.77 3.37 AUC7N-linked glycosylation2.96 2.66 2.56 2.32 E $VAR071W$ $PHO11$ phosphate metabolism 2.77 2.79 2.79 2.99 DPM1N-linked glycosylation 2.96 2.66 2.90 2.90 2.90 2.90 2.76 2.91 2.79 2.91 NoN-linked glycosylation 2.91 2.91 2.91 2.91 2.92 2.92 2.92 2.92 NoN-linked glycosylation 2.91 2.92 2.91 <td>YDR395W</td> <td>SXM1</td> <td>mRNA-nucleus export</td> <td>2.55</td> <td>2.62</td> <td>0</td> <td>YDL093W</td> <td>PMT5</td> <td>O-linked glycosylation</td> <td>2.87</td> <td>2.79</td> <td>0</td>	YDR395W	SXM1	mRNA-nucleus export	2.55	2.62	0	YDL093W	PMT5	O-linked glycosylation	2.87	2.79	0
NPY1NADH metabolism2.692.660VIL145CPAN6partotherate biosynthesis11.5711.56BTT1nascent polypeptide association2.362.1123.2430VBR176WECM31pantotherate biosynthesis3.924.244.24RT1109negative regulation of DNA transposition2.823.2430VLR354CTAL1pentotherate biosynthesis3.924.244.24AVT1neutral amino acid transport5.635.7000VLR354CTAL1pentose-phosphate shurt4.174.24AUT1neutral amino acid transport2.563.440VLR354CTAL1pentose-phosphate shurt4.164.24ALG7N-linked glycosylation2.563.440VLR155CPHA1pentose-phosphate shurt4.183.31ALG7N-linked glycosylation2.962.6877.81PHO11phonylatalinie9.573.37OST2N-linked glycosylation2.962.912.96PHO14PHO14phonsphate metabolism4.803.50ST3N-linked glycosylation3.373.2333.24PHO14Phonsphate dispond for biosynthesis2.172.372.13ALG7N-linked glycosylation2.962.962.962.962.962.962.962.972.992.96DPM1N-linked glycosylation3.373.233.233.242.902.772.912.91 <td< td=""><td>YHR046C</td><td>INM1</td><td>myo-inositol metabolism</td><td>2.29</td><td>2.42</td><td>0</td><td>YOR241W</td><td>MET7</td><td>one-carbon compound metabolism</td><td>2.12</td><td>2.01</td><td>2</td></td<>	YHR046C	INM1	myo-inositol metabolism	2.29	2.42	0	YOR241W	MET7	one-carbon compound metabolism	2.12	2.01	2
BTT1ascent polypeptide association2.362.1122.1423.924.244.24RTT109negative regulation of DNA transposition2.823.2430 $YLR354C$ TAL1pentose-phosphate shurt4.174.244.24AVT1neutral amino acid transport5.635.7000 $YLR354C$ TAL1pentose-phosphate shurt4.183.31AVT1neutral amino acid transport5.635.7000 $YR410C$ STE14pentose-phosphate shurt4.183.31ALG7N-linked glycosylation2.563.440 $YCL15W$ SNF4penvisione organization and biogenesis2.773.37ALG7N-linked glycosylation2.962.662.687YAR071WPHO11phosphate metabolism4.803.50DPM1N-linked glycosylation2.262.32EYML123CPHO84phosphate metabolism4.803.50ST3N-linked glycosylation3.373.233.240YML123CPHO84phosphate fransport2.772.19ST3N-linked glycosylation3.373.233.233.242.01phosphate fransport2.272.132.14ALG7N-linked glycosylation3.373.233YL133WCK11phosphate fransport2.872.132.13N-linked glycosylation3.373.2333.242.01phosphate fransport2.272.132.14 <tr< td=""><td>YGL067W</td><td>NPY1</td><td>NADH metabolism</td><td>2.69</td><td>2.66</td><td>0</td><td>YIL145C</td><td>PAN6</td><td>pantothenate biosynthesis</td><td>11.57</td><td>11.26</td><td>2</td></tr<>	YGL067W	NPY1	NADH metabolism	2.69	2.66	0	YIL145C	PAN6	pantothenate biosynthesis	11.57	11.26	2
RTT109neatrive regulation of DNA transposition2.82 3.24 30 YLR354CTAL1pentose-phosphale shunt 4.17 4.24 4.24 AVT1neutral amino acid transport 5.63 5.70 00YDR410CSTE14peptide pheromone maturation 4.18 3.31 3.37 MN11N-glycan processing 2.56 3.44 0YCL115WSNF4perovisome organization and biogenesis 2.77 3.37 3.37 $ALG7$ N-linked glycosylation 2.96 2.66 E $YNL316C$ PHA2perovisome organization and biogenesis 2.77 3.37 $DPM1$ N-linked glycosylation 2.96 2.66 E $YAR71W$ PHO11phonylatalinie $biosynthesis, prephenate2.762.49DPM1N-linked glycosylation2.962.69EYAR71WPHO11phonsphate transport2.772.752.49ST3N-linked glycosylation2.32EYAR71WPHO11phonsphate transport2.772.752.49ST3N-linked glycosylation3.373.233YL133WCK11phosphate transport2.242.01$	YDR252W	BTT1	nascent polypeptide association	2.36	2.11	2	YBR176W	ECM31	pantothenate biosynthesis	3.92	4.24	0
AVT1neutral amino acid transport5.635.7000VDR410CSTE14peptide pheromone maturation4.183.313.31MNN1N-linked glycosylation2.56 3.44 0VGL115WSNF4perovisome organization and biogenesis 2.77 3.37 3.23 3.226 2.96 2.96 2.96 2.96 2.96 2.96 2.97 2.75 2.49 2.46 2.75 2.49 2.46 2.75 2.49 2.75 2.49 3.50 <td>YLL002W</td> <td>RTT109</td> <td>negative regulation of DNA transposition</td> <td>2.82</td> <td>3.24</td> <td>30</td> <td>YLR354C</td> <td>TAL1</td> <td>pentose-phosphate shunt</td> <td>4.17</td> <td>4.24</td> <td>0</td>	YLL002W	RTT109	negative regulation of DNA transposition	2.82	3.24	30	YLR354C	TAL1	pentose-phosphate shunt	4.17	4.24	0
MN1N-glycan processing2.56 3.44 0YGL15WSNF4peroxisome organization and biogenesis2.77 3.37 3.37 $ALG7$ N-linked glycosylation 4.85 5.46 E $YAR071W$ PHO11phenylalanine biosynthesis, prephenate 2.75 2.49 $DPM1$ N-linked glycosylation 2.96 2.69 E $YAR071W$ PHO11phonylatanine biosynthesis, prephenate 2.75 2.49 0572 N-linked glycosylation 2.26 2.32 E $YAR071W$ PHO11phosphate metapolism 4.80 3.50 0572 N-linked glycosylation 3.06 2.90 E $YAR123C$ PHO84phosphate transport 2.75 2.49 0573 N-linked glycosylation 3.37 3.23 3.23 3.23 3.23 3.23 2.24 2.01 2.74 2.01	YJR001W	AVT1	neutral amino acid transport	5.63	5.70	0	YDR410C	STE14	peptide pheromone maturation	4.18	3.31	0
ALG7 N-Inreed glycosylation 3.46 5.46 5 3.46 5 3.46 5 3.46 5 3.46 5 3.46 5 3.46 2.45 2.45 2.45 2.45 2.45 2.45 2.45 2.45 2.45 2.46 PHA2 pathway biothylatine 2.75 2.49 2.46 2.45	YER001W	MNN1	N-glycan processing	2.56	3.44	0	YGL115W	SNF4	peroxisome organization and biogenesis	2.77	3.37	0
DPM1 N-linked glycosylation 2.96 2.69 E YNL316C PHA2 pathway 2.75 2.49 0.572 N-linked glycosylation 2.26 2.32 E YAR071W PHO11 phosphate metaoolism 4.80 3.50 3.50 5.13 N-linked glycosylation 2.37 3.30 5.30 YML123C PH084 phosphate transport 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.13 2.14 2.13 2.13 2.13 2.14 2.13 2.13 2.14 2.13 2.14 2.13 2.14 2.14 2.14 2.14 2.14 2.14 2.01	YBR243C	ALG7	N-linked glycosylation	4.85	5.48	111			lanine biosynthesis,			
OST2 N-linked glycosylation 2.26 2.32 E YAR071W PHO11 phosphate metabolism 4.80 3.50 3.50 STT3 N-linked glycosylation 3.06 2.90 E YML123C PH084 phosphate transport 2.27 2.13 2.13 2.14 2.14 2.14 2.14 2.13 2.13 2.13 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.14 2.01 <td< td=""><td>YPR183W</td><td>DPM1</td><td>N-linked glycosylation</td><td>2.96</td><td>2.69</td><td>ш</td><td>YNL316C</td><td>PHA2</td><td>pathway</td><td>2.75</td><td>2.49</td><td>0</td></td<>	YPR183W	DPM1	N-linked glycosylation	2.96	2.69	ш	YNL316C	PHA2	pathway	2.75	2.49	0
STT3 N-linked glycosylation 3.06 2.90 F YML123C PHO84 phosphate transport 2.27 2.13 CAX4 N-linked glycosylation 3.37 3.23 3 YLR133W CKI1 phosphatidylcholine biosynthesis 2.24 2.01	YOR103C	OST2	N-linked glycosylation	2.26	2.32	ш	YAR071W	PH011	phosphate metabolism	4.80	3.50	ш
CAX4 N-linked glycosylation 3.37 3.23 3 YLR133W CKI1 phosphatidylcholine biosynthesis 2.24 2.01	YGL022W	STT3	N-linked glycosylation	3.06	2.90	Ψ	YML123C	PHO84	phosphate transport	2.27	2.13	0
	YGR036C	CAX4	N-linked glycosylation	3.37	3.23	3	YLR133W	CKI1	phosphatidylcholine biosynthesis	2.24	2.01	8

Table 10A						Table 10A					
							Gene	Function	M	mgt1	Sens
ORF						ORF			л С	с Г	
YDL083C_ex2	ROBINE	protein biosynth Fam Ction	W.T2	mgth	Seins	YIL049W	DFG10	pseudohyphal growth	3.04	3.28	0
YDL083C_ex2	RPS16B	protein biosynthesis	r ² 62	F234	0	YJR147W	HMS2	pseudohyphal growth	3.13	3.43	0
YML024W_ex2	RPS17A	protein biosynthesis	2.31	2.15	0	YIR019C	MUC1	pseudohyphal growth	2.44	2.72	0
YML026C_ex2	RPS18B	protein biosynthesis	3.15	2.76	0	YJR105W	AD01	purine base metabolism	2.50	2.20	2
YNL302C_ex2	RPS19B	protein biosynthesis	3.00	2.45	0	YLR209C	PNP1	purine nucleoside catabolism	3.71	3.57	0
YJL136C_ex2	RPS21B	protein biosynthesis	2.55	2.30	0	YGL224C	SDT1	pyrimidine base metabolism	5.47	5.52	0
YJL136C_ex2	RPS21B	protein biosynthesis	2.03	2.02	0	YPL256C	CLN2	regulation of CDK activity	2.86	3.11	8
YLR367W_ex2	RPS22B	protein biosynthesis	6.10	6.72	0	YGR108W	CLB1	regulation of CDK activity	3.76	7.01	0
YER074W_ex2	RPS24A	protein biosynthesis	3.76	3.12	0	YLR103C	CDC45	regulation of cell cycle	4.31	4.14	ω
YHR021C_ex2	RPS27B	protein biosynthesis	2.81	2.46	0	YDR353W	TRR1	regulation of redox homeostasis	4.62	4.17	ω
YPL090C_ex2	RPS6A	protein biosynthesis	3.09	2.21	0	YIL010W	DOT5	regulation of redox homeostasis	3.81	3.39	9
YOR096W_ex2	RPS7A	protein biosynthesis	2.73	2.18	0			regulation of transcription from Pol II			
YBR173C	UMP1	protein catabolism	2.87	2.40	0	YPR052C	NHP6A		2.40	2.19	0
YGR105W	VMA21	protein complex assembly	2.30	2.42	11			regulation of transcription from Pol II			
YOR085W	OST3	protein complex assembly	3.02	2.56	0	YHL009C	YAP3	promoter	2.43	2.49	0
YKL119C	VPH2	protein complex assembly	2.39	2.43	0	YFL028C	CAF16	regulation of transcription, DNA-dependent	4.60	5.31	2
YFR010W	UBP6	protein deubiquitination	2.39	2.64	2	YGL030W_ex2	RPL30	regulation of translation	2.19	2.23	0
YDR304C	CPR5	protein folding	2.77	2.92	4	YGL195W	GCN1	regulation of translational elongation	3.72	3.72	9
YDR518W	EUG1	protein folding	2.61	2.57	0	YFR009W	GCN20	regulation of translational elongation	2.25	2.88	4
YOL088C	MPD2	protein folding	2.53	2.36	0	YBR048W_ex2	RPS11B	regulation of translational fidelity	2.91	2.54	0
YKL117W	SBA1	protein folding	3.07	2.79	0	YGR118W_ex1	RPS23A	regulation of translational fidelity	3.96	3.96	0
YMR214W	scJ1	protein folding	2.83	2.46	0	YPL081W_ex2	RPS9A	regulation of translational fidelity	3.06	2.34	0
YHR109W	CTM1	protein modification	2.10	2.55	0	YPL081W_ex2	RPS9A	regulation of translational fidelity	2.78	2.38	0
YMR275C	BUL1	protein monoubiquitination	3.80	3.24	7	YBR189W_ex2	RPS9B	regulation of translational fidelity	4.52	4.58	0
YLR024C	UBR2	protein monoubiquitination	2.22	2.15	0	YBR189W_ex2	RPS9B	regulation of translational fidelity	3.48	3.32	0
YGR082W	TOM20	protein targeting	3.00	3.63	ω	YOL090W	MSH2	removal of nonhomologous ends	6.66	8.13	5
YDR414C	ERD1	protein-ER retention	2.89	2.47	6	YPL163C	SVS1	response to chemical substance	3.19	3.68	2
YBL040C_ex2	ERD2	protein-ER retention	2.11	2.10	0	YDL166C	FAP7	response to oxidative stress	3.90	3.77	
YDR292C	SRP101	protein-ER targeting	2.37	2.52	iu)	YBR244W	GPX2	response to oxidative stress	4.18	4.50	15
VPL243W	SRP68	protein-ER targeting	3.31	3.37	цı			response to pheromone during conjugation			
YPL210C	SRP72	protein-ER targeting	2 15	2.38	u	YFLUZ6W	SIE2	with cellular fusion	3.05	4.44	4
YBL069W	AST1	protein-membrane targeting	2.28	2.04	0	YHR043C	DOG2	response to stress	3.22	2.98	0
YBL069W_alt	AST1	protein-membrane targeting	2.04	2.54	0	YER011W	TIR1	response to stress	5.61	5.06	0
YGL016W	KAP122	protein-nucleus import	5.27	4.29	10	YGR234W	YHB1	response to stress	7.20	8.04	0
YGL241W	KAP114	protein-nucleus import	2.58	3.11	0	YCR044C	PER1	response to unfolded protein	5.00	3.72	0
YNL246W_ex2	VPS75	protein-vacuolar targeting	4.29	4.12	0	YER089C	PTC2	response to unfolded protein	2.71	2.57	0
YDR144C	MKC7	proteolysis and peptidolysis	4.47	3.13	10	YDL145C	COP1	retrograde (Golgi to ER) transport	3.94	3.62	ы
YBL022C	PIM1	proteolysis and peptidolysis	2.15	2.10	0	VFR051C	RET2	retrograde (Golgi to ER) transport	3.30	2.89	ш
YCL057W	PRD1	proteolysis and peptidolysis	2.65	2.31	0	YPL010W	RET3	retrograde (Golgi to ER) transport	3.65	3.61	ш

Table 10A						Table 10A					
					2***		Gene	Function	٧T	mgt1	Sens
ORF						ORF			FC	Ъ	
YGL137W_ex2	SGenie	retrograde (GoldFunter ionsport	W42	mgth	Seins	YJL212C	OPT1	sulfur metabolism	2.75	3.57	0
YHL034C	SBP1	RNA metabolism	ل ^ت رأ	F ²⁰²	0			telomerase-dependent telomere			
YDL014W	10P1	RNA methylation	2.74	2.65	ω	YBR275C	RIF1	maintenance	2.13	2.28	8
YFL001W	DEG1	RNA processing	3.04	2.85	12			telomerase-dependent telomere			
YLR059C	REX2	RNA processing	2.51	2.15	5	YIL009C-A_ex1	EST3	maintenance	2.69	2.92	0
YGR276C	RNH70	RNA processing	2.41	2.67	0			telomerase-dependent telomere			
YJL133W	MRS3	RNA splicing	2.30	2.97	0	YIL009C-A_ex2	EST3		2.86	3.77	0
YML031W	NDC1	RNA-nucleus export	2.21	2.11	111			telomerase-dependent telomere			
YHR062C	RPP1	rRNA processing	2.41	2.02	Ψ	TLC1_0	TLC1		2.87	4.91	•
YOL080C	REX4	rRNA processing	2.49	2.69	4			telomerase-dependent telomere			
YMR285C	NGL2	rRNA processing	2.34	2.39	2	TLC1_1	п.с1	maintenance	3.28	6.08	0
YLR306W_ex2	UBC12	RUB1-protein conjugation	2.22	2.72	0	VOR143C	THI80	thiamin biosynthesis	2.10	2.28	ш
YER019W	ISC1	salinity response	3.11	2.76	10	YBR092C	PH03	thiamin transport	5.53	10.27	5
YDL018C	ERP3	secretory pathway	3.62	4.07	0	YER052C	HOM3	threonine metabolism	60.6	8.58	12
YIL074C	SER33	serine family amino acid biosynthesis	3.96	2.84	2	YDR158W	HOM2	threonine metabolism	8.15	7.21	0
YGR208W	SER2	serine family amino acid biosynthesis	3.91	2.43	0	YKL194C	MST1	threonyl-tRNA aminoacylation	2.49	2.60	0
VIR022W	SFC11	signat peolide processing	3.06	3.22	т,	YOR340C	RPA43	transcription from Pol I promoter	2.98	3.08	ш
YI ROBBW	SPC3	sional ventide processino	2.62	2.51	L.	YDR308C	SRB/	transcription from Pol II promoter	2.75	2.67	ω
VAN DESIAL	SPC3	simal rentide processing	230	2 30	ę	YIL128W	MET18	transcription from Pol II promoter	2.20	2.28	18
VER027M	ECO1	sister chromatid rohesion	7.85	3.06		YNL236W	SIN4	transcription from Pot It promoter	3.54	3.20	8
VPR069C	SPE3	snarmidina hinsvnthasis	3.08	2.79	0	YHR041C_ex2	SRB2	transcription from Pol II promoter	4.39	3.64	0
	21.01	sobinoolinid biosvothesis	2.70	2.45	4	VDR045C	RPC11	transcription from Pot III promoter	2.87	2.03	μ
YOR198C	BFR1	spindle assembly	4.18	3.93	0	YCR065W	HCM1	transcription initiation from Pol II promoter	3.10	2.20	0
VDI DAAC	DRD11	snirrensome assembly	3.25	02. C		VPL007C	TFC8	franscription initiation from Pol III promoter	2.04	2.61	ш
YDR260C	SWM1	spreadante accuración servicio saccharomyces)	2.59	2.12	6	YDL130W_ex1	RPP1B	translational elongation	2.66	2.49	0
YCR002C	CDC10	spore wall assembly (sensu Saccharomyces)	3.82	4.35	0	YDL130W_ex2	RPP1B	translational elongation	2.33	2.03	0
YER012W	PRE1	sporulation (sensu Saccharomyces)	2.85	2.5?	cu	YKL081W_ex1	TEF4	translational elongation	5.17	3.23	0
VGR253C	5dD4	sporulation (sensu Saccharomyces)	2.46	2.46	111	YKL081W_ex2	TEF4	translational elongation	4.53	3.40	0
YJL001W ex2	PRE3	sporulation (sensu Saccharomyces)	2.67	2.86	0	YJR047C	ANB1	translational initiation	2.82	2.07	0
YML052W	SUR7	sporulation (sensu Saccharomyces)	2.46	2.75	0	YOR306C	MCH5	transport	2.41	2.15	7
		SRP-dependent corranslational membrane				YPR058W	YMC1	transport	7.15	6.17	7
YML105C	SEC65	targeting, signal sequence recognition	2.07	2.22	ш	YPR021C	NA	transport	2.38	2.22	5
		SRP-gependent corranslational membrane				YOL119C	MCH4	transport	2.85	2.76	4
YOR254C	SEC63	targeting, translocation	2.73	3.25	IJ	YBR104W	YMC2	transport	7.03	9.14	4
		SRP-dependent cotranslational membrane				YBL089W	AVT5	transport	2.13	2.11	0
YBR171W	SEC66	targeting, translocation	3.02	2.79	0	YMR261C	TPS3	trehalose biosynthesis	2.57	2.66	0
YGR177C	ATF2	steroid metabolism	3.06	2.20	0	YDL112W	TRM3	tRNA methylation	2.01	2.30	0
YOL064C	MET22	sulfate assimilation	3.21	2.58	9	YHR163W	SOL3	tRNA processing	4.82	3.30	0
YJR137C	ECM17	sulfate assimilation	3.64	2.14	0	YER107C	GLE2	tRNA-hucteus export	2.68	2.45	ш
		-									

Table 10A						Table 10A					
	- -						Gene	Function	ΜT	mgt1	Sens
ORF						ORF			С С	Ъ С	
YGL092W	NGene	rRNA-nucleus e Franction	W.48	mgat	Sens	YDR261C	EXG2	NA	4.49	4.45	4
YDR354W	TRP4	tryptophan biosynthesis	ل ^و د5	د وی ا	12	YOL030W	GAS5	NA	2.40	2.63	4
YKL211C	TRP3	tryptophan biosynthesis	5.00	5.19	2	YJR118C	ILM1	NA	2.48	2.47	4
YGL026C	TRP5	tryptophan biosynthesis	4.26	4.33	0	YLR315W	NKP2	NA	2.92	2.29	4
YDR268W	MSW1	tryptophanyl-tRNA aminoacylation	3.10	3.89	0	YPL246C	QUT1	NA	2.60	2.58	4
YML094W_ex2	GIM5	tubulin folding	2.91	2.68	0	YOL093W	TRM10	NA	2.63	2.83	4
YBR166C	TYR1	tyrosine metabolism	4.44	5.32	3	YKR013W	PRY2	NA	4.34	4.89	2
YBR003W	COQ1	ubiquinone metabolism	2.09	2.34	4	YDR257C	RMS1	NA	3.18	2.64	2
YNR041C	C002	ubiquinone metabolism	4.13	4.29	0	YKL218C	SRY1	NA	2.51	2.16	2
YKL210W	UBA1	ubiguitin cycle	2.18	2.24	u.	YDL100C	ARR4	NA	2.78	2.50	0
YML092C	PRE8	ubiquitin-dependent protein catabolismi	3.37	2.68	u	YMR116C_ex1	ASC1	NA	4.12	2.77	0
YHR027C	RPN1	ubiquitin-dependent protein catabolism	2.41	2.20	ω	YMR116C_ex2	ASC1	NA	3.93	3.13	0
YIL075C	RPN2	ubiquitin-dependent protein catabolism	2.04	2.28	ш	YGR295C_0	cose	NA	2.01	2.05	0
YPR108W	RPN7	ubiauitin-dependent protein catabolism	2.33	2.06	Ψ.	YER060W	FCY21	NA	2.75	2.66	0
YDR427W	RPN9	ubiquitin-dependent protein catabolism	2.72	2.88	u	YOR280C	FSH3	NA	2.73	2.56	0
YKL145W	RPT1	ubiquitin-devendent protern catabolism	2.49	2.52	ш	YER057C	HMF1	NA	2.34	2.50	0
YOR117W	RPT5	ubiquitin-dependent protein catabolism	2.53	2.54	ų	YML056C_ex1	IMD4	NA	6.74	5.32	0
YGL011C	scl 1	ubiquitin-dependent protein catabolism	2.31	2.20	ω	YML056C_ex2	IMD4	NA	7.17	7.75	0
YKL213C	DOA1	ubiquitin-dependent protein catabolism	3.46	4.27	30	YFR024C-					
YGR135W	PRE9	ubiquitin-dependent protein catabolism	3.38	3.27	0	A_ex2	LSB3	NA	3.21	2.42	0
YDL190C	UFD2	ubiquitin-dependent protein catabolism	2.05	2.20	0	YDR033W	MRH1	NA	3.38	4.38	0
YPL244C	HUT1	UDP-galactose transport	3.80	3.86	0	YIL164C	NIT1	NA	3.13	2.40	0
YDL103C	QRI1	UDP-N-acetyiglucosamine biosynthesis	10.89	10.81	ىلە:	YLR351C	NIT3	NA	2.71	2.44	0
YEL051W	VMA8	vacuolar acidification	2.52	2.82	18	YGR038W	ORM1	NA	2.70	2.24	0
YGR020C	VMA7	vacuolar acidification	3.53	3.82	7	YHR179W	OYE2	NA	3.91	4.09	0
YLR043C	TRX1	vacuole fusion (non-autophagic)	2.47	2.71	æ	YBR233W	PBP2	NA	3.15	2.78	0
YPL019C	VTC3	vacuole fusion (non-autophagic)	2.59	2.69	0	YMR123W	PKR1	NA	2.68	2.53	0
YJL012C	VTC4	vacuole fusion (non-autophagic)	2.51	2.16	0	YDR501W	PLM2	NA	4.25	4.42	0
YBR164C	ARL1	vesicle-mediated transport	2.40	2.27	7	YKL128C	PMU1	NA	7.18	6.15	0
YEL053C	MAK10	virus-host interaction	2.35	2.42	4	YDL189W_ex2	RBS1	NA	2.45	2.62	0
YBR256C	RIB5	vitamin B2 biosynthesis	2.11	2.20	ш	YIL011W	TIR3	NA	3.42	3.37	0
YHR063C	PAN5	NA	4 4()	5.59	14.2	YER175C	TMT1	AN	3.28	4.62	0
YPR048W	TAH18	NA	2.16	2.14	ω	YGR221C	TOS2	NA	2.20	2.35	0
YHR047C	AAP1'	NA	3.74	3.90	10	YLR467W_2	YRF1-5	AN	2.88	2.37	0
YIL040W	APQ12	NA	2.11	2.30	0	YHR017W	YSC83	NA	2.59	2.76	0
YOL002C	PHO36	NA	4.98	4.25	7	YNR065C	YSN1	NA	3.01	2.30	0
YHR117W	TOM71	NA	2.17	2.45	7						
YER170W	ADK2	NA	2.29	2.18	9						
YIL027C	KRE27	NA	2.26	2.44	5						

ubset of genes that are induced	l in bo	duced in both WT and	and	Table					
genes that are induced upon	treat	upon treatment with	with	10B					
WT and mgf1. Interestingly, 5/ (44%) of these	/ (44%	0) of th	nese	YDR037W	KRS1	lysvi-tRNA aminoacylation	4.74	5.21	ш
				YPR145W	ASN1	metabolism	8.31	7.62	0
				YER043C	SAH1	methionine metabolism	2.76	2.23	ш
				YNL066W	SUN4	mitochondrion organization and biogenesis	4.04	3.29	0
	;	Э	ţţ	YGL213C	SKI8	mRNA catabolism	2.14	2.68	0
	FC	4 E	viti	YJL080C	SCP160	mRNA localization, intracellular	8.14	7.26	10
	τN	, 61	su	YMR308C	PSE1	mRNA-nucieus export	2.26	2.59	ш
	١	u	əS	YJR025C	BNA1	nicotinamide adenine dinucleotide biosynthesis	3.79	4.79	2
LUICHON				YGR019W	UGA1	nitrogen utilization	2.49	2.86	0
amino acid activation	2.82	2 48	w	YGL225W	VRG4	N-linked glycosylation	3.10	2.72	ω
amino acid activation	3.11	3.23	ω			nucleobase, nucleoside, nucleotide and nucleic			
amino acid activation	39.65	9.35	ш	YBR084W	MIS1	acid metabolism	6.28	6.61	7
amino acid metabolism	3.06	2.74	2	YJR143C	PMT4	O-linked glycosylation	5.56	5.32	പ
AMP biosynthesis	4.92	4.10	15	YPR074C	TKL1	pentose-phosphate shunt	5.55	4.13	2
anti-apoptosis	2.93	2.76	11	YL.R060W	FRS1	unenylalanyi-tRNA amirioacytation	7.34	6.62	ω
aromatic amino acid family biosynthesis	6.87	6.59	2	YFL022C	FRS2	phenylalanyi-tRNA aminoacylation	2.87	3.16	ш
aromatic amino acid family biosynthesis	11.26	9.64	4	YDR324C	UTP4	processing of 20S pre-rRNA	2.16	2.41	μ
asparagine biosynthesis	3.65	3.21	5	YGR128C	UTP8	processing of 20S pre-rRNA	2.22	2.25	ш
esparaginyi-tRNA aminoacytation	99.c	-3.86	ų	YDR300C	PR01	proline biosynthesis	2.27	2.22	0
base-excision repair, AP site formation	4.85	4.95	0	YHR013C	ARD1	protein amino acid acetylation	4.93	5.44	22
cell wall organization and biogenesis	11.35	8.29	0	YEL042W	GDA1	protein amino acid glycosylation	2.37	2.22	0
cell wall organization and biogenesis	5.71	6.11	4	YGR123C	PPT1	protein amino acid phosphorylation	3.39	2.78	6
celtular moronogenesis	3.52	3.89	ιώ	VPR102C	RPL11A	protein biosynthesis	2.20	2.03	u:
cytoskeleton organization and biogenesis	3.74	3.30	ω	YLR029C	RPL:5A	protein biosynthesis	2.49	2.02	ш
DNA repair synthesis	2.75	3.26	ω	YBL092W	RPI.32	protein biosynthesis	2.59	2.30	iu)
DNA replication	23.03	22.30	5	VOL040C	RPS15	protein biosynthesis	2.86	2.26	ω
ergosterol biosynthesis	3.01	2.49	0	YGL 189C	RPS26A	protein biosynthesis	2.23	2.09	ш
fatty acid biosynthesis	12.68	11.59	0	YJR123W	RPS5	protein biosynthesis	3.06	2.33	ы
GMP metabolism	3.15	3.19	0	YIL078W	THS1	protein biosynthesis	6.15	6.39	ш
GTP biosynthesis	3.20	2.95	υ	YGR085C	RPL11B	protein biosynthesis	2.16	2.49	0
histidine biosynthesis	2.69	2.77	0	YEL054C	RPL12A	protein biosynthesis	2.99	2.02	0
nistroyl-tRNA aminoacylation	4.99	4.96	ω	YMR242C	RPL20A	protein biosynthesis	2.71	2.32	0
hypusine biosynthesis from peptidyl-lysine	5.46	4.39	Ш	YGL031C	RPL24A	protein biosynthesis	2.34	2.25	0
Isoprenoid biosynthesis	5.10	3.46	ш	YHL033C	RPL8A	protein biosynthesis	3.17	2.64	0
lartat formation. 5'-splice site cleavage	2.23	2.30	ω	YLL045C	RPL8B	protein biosynthesis	2.37	2.14	0
ieucyi-tRNA aminoacytatior:	3.17	3.34	w	YLL045C	RPL8B	protein biosynthesis	3.62	3.37	0
				Transferration of the second sec					

ASN2 DED81

YHR019C

YBR249C YGR124W

0661

YML060W YEL040W YMR307W YMR212C YDL143W

UTR2

GAS1 EFR3

CC F4 POL1 RNR1

YNL102W YER070W

STM1 ARO2 AR04

YLR150W YGL148W

YML022W

ASP1 APT1

YGR185C YDR321W

YDR023W

PRP43 CDC60

YGL120C YPL160W

MVD1

YNR043W

DYS1

YHR068W

HTS1

SUR4 GUK1

PRS4

YBL068W VPR033C

1MD2

YHR216W

NCP1

YHR042W YLR372W YDR454C

and in both WT and that Table 10B: ESR subset of gmgtl.127 ESR genes thMNNG in both WT and are essential genes.

Gene

ORF

Table

10B

MES1 SES1 TYS1

YGR264C

					10B		
RPL9A	protein biosynthesis	2.90	3.37	0	YDR087C	RKP1	rRNA processing
RPS1A	protein biosynthesis	3.79	3.06	0	VGL097W	SRM1	rRNA-nucleus export
RPS1A	protein biosynthesis	2.73	2.54	0	YGR152C	RSR1	small GTPase mediated signal transduction
RPS1B	protein biosynthesis	3.23	3.08	0	YLR146C	SPE4	spermine biosynthesis
RPS26B	protein biosynthesis	3.48	3.43	0	YCR034W	FEN1	sphingolipid biosynthesis
RPS28A	protein biosynthesis	2.88	2.67	0	YIR026C	YVH1	sporulation (sensu Saccharomyces)
RPS29A	protein biosynthesis	2.23	2.35	0	YPL273W	SAM4	sulfur amino acid metabolism
RPL12B	protein biosynthesis	4.77	3.87	5	YHR025W	THR1	threonine metabolism
RPL12B	protein biosynthesis	4.35	3.84	5	YCR053W	THR4	threonine metabolism
RPS22A	protein biosynthesis	5.95	5.15	7	VPR010C	RPA135	transcription from Pol I promoter
RPL24B	protein biosynthesis	2.67	2.33	8	YNL248C	RPA49	transcription from Pol I promoter
CIC1	protein catabolism	2.45	2.41	ш	YIL021W	RPB3	transcription from Pol II promoter
ZU01	protein folding	4.50	4.47	2	YGL070C	RPB9	transcription from Pol II promoter
SRP102	protein-ER targeting	2.50	2.60	ш	YBR121C	GRS1	transcription termination
NTF2	protein-nucleus import	2.65	2.31	L	YLR340W	0ддя	translational elongation
SH01	pseudohyphal growth	2.39	2.68	0	YOL039W	RPP2A	translational elongation
PUS7	pseudouridine synthesis	3.95	3.85	0	YDR429C	TIF35	translational initiation
	pyrimictine deoxynbonucieoside triphosphate				YKR026C	GCN3	translational initiation
DUT1	catabolism	3.33	3.34	ω	YBR143C	SUP45	translational termination
DCD1	pyrimidine nucleotide metabolism	4.93	4.62	ω	YLR083C	EMP70	transport
FUR1	pyrimidine salvage	3.32	2.55	ω	YNL292W	PUS4	tRNA modification
PMA1	regulation of pH	2.53	2.15	w	70L097C	WRS ¹	iryptophanyl-tRNA aminoacviation
TSA2	regulation of redox homeostasis	5.84	9.75	0	YNL153C	GIM3	tubulin folding
RPS2	regulation of translational fidelity	2.14	2.05	ш	YHR026W	PPA1	vacuolar acidification
	ribosoniai large subunii assembly and				YKL080W	VMA5	vacuolar acidification
DBP9	maintenance	2.48	2.38	ω	YKL103C	LAP4	vacuolar protein catabolism
	ribosomal large subunit assembly and				YGR094W	VAS1	valyi-tRNA aminoacylation
SOT1	maintenance	2.36	2.09	U.J	YLR196W	1dMc	NA
NSA1	ribosomal large subunit biogenesis	2.09	2.24	ιυ	YDR091C	RLI1	TN
EMG	ribosome biogenesis	3.12	3,14	w	YDR516C	EMI2	NA
RRB1	abosome biogenesis	2.50	2.61	U.	YLR449W	FPR4	NA
GAR1	rRNA modification	4.92	4 30	ω	YMR215W	GAS3	NA
NOP58	rRNA modification	3.01	2.53	ιμ	YNL175C	NOP13	NA
SIK1	rRNA modification	3.40	4.00	111			
NID7							

ble					
B					
<u>1</u> C	RRP1	rRNA processing	2.80	2.78	נט
M2	SRM1	rRNA-nucleus export	3.74	3.48	ш
2C	RSR1	small GTPase mediated signal transduction	2.78	2.54	0
6C	SPE4	spermine biosynthesis	3.78	3.88	0
4W	FEN1	sphingolipid biosynthesis	7.58	7.23	0
2	YVH1	sporulation (sensu Saccharomyces)	4.16	3.78	0
3W	SAM4	sulfur amino acid metabolism	23.63	20.90	0
5W	THR1	threonine metabolism	8.31	8.29	12
ME	THR4	threonine metabolism	3.72	3.54	13
00	RPA135	transcription from Pol I promoter	2.50	2.56	ω
gC	RPA49	transcription from Pol I promoter	4.70	4.37	0
W	RPB3	transcription from Pol II promoter	2.10	2.24	ω
Ŋ	RPB9	transcription from Pol II promoter	2.59	2.31	19
10	GRS1	transcription termination	3.17	3.05	9
MO	0дду	translational elongation	2.26	2.14	ш
M6	RPP2A	translational elongation	2.81	2.35	4
30	TIF35	translational initiation	2.37	2.05	ιω
90	GCN3	translational initiation	2.88	2.99	9
3C	SUP45	translational termination	2.39	2.36	ш
30	EMP70	transport	3.42	3.10	0
2W	PUS4	tRNA modification	3.53	3.02	0
7C	WRS ¹	iryptophanyl-tRNA aminoacviation	4.82	4.35	ω
g	GIM3	tubulin folding	3.77	3.54	9
6W	PPA1	vacuolar acidification	2.48	2.47	4
MO	VMA5	vacuolar acidification	2.78	2.54	15
30	LAP4	vacuolar protein catabolism	2.55	2.74	0
94W	VAS1	valyi-tRNA aminoacylation	4.57	447	ш
6W	1dMc	NA	2.13	2.15	u
11	RLI1	ΨŇ	3.23	2.49	ш
60	EMI2	NA	2.40	2.37	0
9W	FPR4	NA	3.52	3.56	0
5W	GAS3	NA	5.52	7.08	0
50	NOP13	NA	2.69	2.72	2

<u>79</u>

and <i>mgt1</i>	
ooth WT	
epressed in l	tment.
renes r	IG trea
Table 11: C	NNM noqu

A total of 1039 genes were repressed in both WT and *mgt1*. Of them, 545 had a known function and are shown here. Table 11A includes genes that were repressed in both WT and *mgt1* and are not a part of the ESR. These included 75 genes (13%) that were essential. The largest category of genes that were affected was involved in transcription and its regulation. About 43 genes (7%) of the genes belonged to this category.

Table 11B includes the ESR subset of genes that are repressed in both WT and mgt

Table 11A		uoi	FC	ਹਤਾ	itivity
ORF	əuəĐ	Functi	TW	6ш	suəS
YAL054C	ACS1	acetyl-CoA biosynthesis	-18.63	-25.51	4
YBL015W	ACH1	acetyl-CoA metabolism	-6.48	-7.72	0
YDR208W	MSS4	actin cable assembly	-2.76	-2.69	ιĿ
YNL020C	ARK1	actin filament organization	-3.04	-3.05	0
YJL100W	LSB6	actin filament organization	-2.63	-2.42	0
YGL191W	COX13	aerobic respiration	3.85	-3.98	ш
YGL187C	COX4	aerobic respiration	-2 14	-2.17	51
YEL024W	RIP1	aerobic respiration	-2.88	-4.04	4
YMR256C	COX7	aerobic respiration	-2.62	-2.41	4
YNL052W	COX5A	aerobic respiration	-3.30	-5.35	0
YMR188C	MRPS17	aerobic respiration	-5.42	-3.81	0
YDR529C	QCR7	aerobic respiration	-2.20	-2.26	0
YFR033C	QCR6	aerobic respiration	-4.14	-4.16	0
YBL045C	COR1	aerobic respiration	-2.90	-2.56	0
YJL166W	QCR8	aerobic respiration	-2.59	-2.39	0
YDL174C	DLD1	aerobic respiration	-3.41	-3.06	0
YOL025W	LAG2	aging	-2.61	-2.43	0
YER024W	YAT2	alcohol metabolism	-8.95	-7.88	0
YAR035W	YAT1	alcohol metabolism	-27.04	-30.28	0
YJR155W	AAD10	aldehyde metabolism	-4.41	-5.53	0

NA amino acid biosynthesis -56.64 - SPS100 amino acid metabolism -76.93 - SPS100 amino acid metabolism -76.93 - MUP3 amino acid metabolism -3.91 - MUP3 amino acid metabolism -3.91 - MUP3 amonium transport -10.74 - MUP3 arginine tetabolism -2.75 - CAR2 arginine catabolism -2.22 - A ATP ADP exchange -5.35 - A ATP Synthesis - - - A ATP18 transport - - - A ATP Synthesis - - - - - A ATP18 transport -	Table 11A	e uəŋ	nu T ctio	FC	ີ່ວ∃ ງດີພ	sitiv ity
NA amino acid biosynthesis -56.64 SPS100 amino acid metabolism -76.93 SPS100 amino acid transport -77.63 MUP3 amonium transport -3.91 MEP1 amonium transport -3.01 MEP1 amonium transport -3.05 CAR1 arginine biosynthesis -2.75 CAR1 arginine catabolism -2.22 AC01 ATP Synthesis -0.10.28 AAC1 ATP synthesis -0.2.03 AAC1 ATP synthesis -14.10 A ATP18 transport -3.16 A ATP synthesis -4.10 A ATP synthesis -4.10 A ATP synthesis -4.10 A APG5 autophagic vacuole formon -3.16 A APG5 autophagic vacuole formon -3.16 A APG5 autophagic vacuole formon -4.10 B DD23 bud site selection -2.03 APG5 autophagic	ORF					
SPS 100 amino acid metabolism -76.93 MUP3 amino acid transport -3.91 MUP3 amino acid transport -3.01 MUP3 amino acid transport -3.01 MUP3 amino acid transport -3.05 MUP3 arginine biosynthesis -2.75 CAR1 arginine catabolism to ornithine -10.28 CAR1 arginine metabolism -2.22 AC01 ATP synthesis -5.35 AC1 ATP synthesis -10.28 AC1 ATP synthesis -14.10 AC1 ATP synthesis -3.16 AC1 ATP synthesis -4.10 AC3 autophagic vacuole formation -3.16 AC4 beta-16 glucan biosynthesis -4.10 APG3 autophagic vacuole formation -3.16 APG3 autophagic vacuole formation -3.16 APG3 autophagic vacuole formation -3.16 APG3 autophagic vacuole formation -4.10 APG3 autophagic vacuole formation -4.10 APG3 beta-16 glucan biosynthesis <t< td=""><td>YHR033W</td><td>NA</td><td>amino acid biosynthesis</td><td>-56.64</td><td>-43.69</td><td>0</td></t<>	YHR033W	NA	amino acid biosynthesis	-56.64	-43.69	0
MUP3 amino acid transport -3.91 MEP1 ammonium transport -10.74 CPA1 arginine biosynthesis -2.75 CAR2 arginine biosynthesis -2.75 CAR1 arginine biosynthesis -3.03 CAR1 arginine catabolism to ornithine -10.28 CAR1 arginine metabolism -2.22 AC1 ATP Synthesis -5.35 AC1 ATP Synthesis -5.35 AC1 ATP Synthesis -10.28 AC1 ATP Synthesis -5.35 AC1 ATP Synthesis -14.10 AC1 ATP Synthesis -14.10 AC1 ATP Synthesis -2.03 AC1 ATP Synthesis -3.16 AC1 ATP Synthesis -4.10 AC1 ATP Synthesis -5.92 AC1 ATP Synthesis -3.16 AC1 ATP Synthesis -4.10 AC1 beta-1.6 glucan biosynthesis -5.92 SOK1 camb-mediated signaling -5.92 AC4 canobydrate metabolism -5.67	rHR139C	SPS100	amino acid metabolism	-76.93	-53.29	0
MEP1 armonium transport -10.74 CPA1 arginine biosynthesis -2.75 CAR2 arginine biosynthesis -2.75 CAR1 arginine catabolism to ornithine -10.28 CAR1 arginine metabolism to ornithine -10.28 AC1 ATP Synthesis -5.35 AAC1 ATP Synthesis -5.35 AC1 ATP Synthesis -10.10 AC1 ATP Synthesis -5.35 AC1 ATP Synthesis -5.35 AC1 ATP Synthesis -10.10 AC1 ATP Synthesis -10.203 AC1 ATP Synthesis -10.10 ATP Synthesis -114.10 -114.10 APG5 autophagy -2.03 APG5 autophagic -2.03 APG5 autophagic -3.16 APG5 autophagic -2.03 APG5 autophagic -2.03 APG5 autophagic -2.03 APG5 autophagic -2.03 <t< td=""><td>YHL036W</td><td>MUP3</td><td>amino acid transport</td><td>-3.91</td><td>-7.01</td><td>4</td></t<>	YHL036W	MUP3	amino acid transport	-3.91	-7.01	4
CPA1 argnine blosynthesis -2.75 CAR2 argnine catabolism -2.75 CAR2 argnine catabolism -2.23 AC1 Argnine metabolism -2.22 AC1 ATP ADP exchange -5.35 AC1 ATP Synthesis -5.35 AC1 ATP synthesis -5.35 AC1 ATP synthesis -5.35 AC1 ATP synthesis -5.35 ATP synthesis -5.35 -5.35 ATP synthesis -5.35 -5.35 ATP synthesis -10.00 -14.10 ATP synthesis -14.10 -14.10 APG5 autophagic vacuole formation -3.16 APG5 autophagic vacuole formation -3.16 BUD23 bud site selection -2.43 BUD23 bud site selection -2.69 APG5 autophagic vacuole formation -3.16 BUD23 bud site selection -5.92 CAMP-mediated signaling -5.92 -4.12 APG8 carbohydrate metabolism -5.69 BUD23 bud site selec	YGR121C	MEP1	ammonium transport	-10.74	-11.93	0
CAR2 arginine catabolism to ornithine -8.23 CAR1 arginine metabolism to ornithine -10.28 AC1 ATP ADP exchange -5.35 AC1 ATP ADP exchange -5.35 AC1 ATP Synthesis coupled proton -2.23 INH1 transport -2.83 AC1 ATP synthesis coupled proton -3.16 INH1 transport -14.10 APG5 autopinagy -2.03 APG5 autopinagy -2.03 KNH1 beta-1.6 gucan biosynthesis -4.10 BUD23 bud site selection -3.16 BUD23 bud site selection -3.18 KNH1 beta-1.6 gucan biosynthesis -4.10 BUD23 bud site selection -2.69 SOK1 cambnydrate metabolism -5.92 APG2 cambnydrate metabolism -5.67 SOK1 cambnydrate metabolism -5.61 MET30 calton homeostasis -4.12 MET30 calton homeostasis -7.14 MET30 calton homeostasis -7.12 <	YOR303W	CPA1	arginine biosynthesis	-2.75	-2.64	0
CAR1 arginine catabolism to ornithine -10.28 ARC360 arginine metabolism -2.22 AAC1 ATP ADP exchange -5.35 AC ATP aDP exchange -5.35 AC1 ATP Synthesis coupled proton -2.23 INH1 transport -2.83 AC1 ATP synthesis coupled proton -3.16 INH1 transport -2.83 APG5 autophagic vacuole formation -3.16 APG5 autophagy -2.03 KNH1 beta-1.6 glucan biosynthesis -4.10 BUD23 bud site selection -3.16 BUD23 bud site selection -3.18 FXNH1 beta-1.6 glucan biosynthesis -4.10 BUD23 bud site selection -2.69 SOK1 cAMP-mediated signaling -6.08 FDE2 campohydrate metabolism -5.92 SOK1 campohydrate metabolism -5.67 MET30 calton homeostasis -4.12 MET30 calton homeostasis -4.12 MET30 cell cycle -5.03	YLR438W	CAR2	arginine catabolism	-8.23	-8.52	0
ARG80 arginine metabolism -2.22 AAC1 ATP ADP exchange -5.35 AC1 ATP ADP exchange -5.35 AC1 ATP synthesis coupled proton -5.35 INH1 transport -5.35 AFG9 autophagy -5.03 APG5 autophagy -14.10 APG3 autophagy -2.18 KNH1 beta-1.6 gucan biosynthesis -4.10 BUD23 bud site selection -3.16 BUD23 bud site selection -3.18 FDE2 cAMP-mediated signaling -6.08 SOK1 cAMP-mediated signaling -5.67 PDE2 cAMP-mediated signaling -5.67 SOK1 carbohydrate metabolism -5.67 MET30 calton homeostasis -4.12 MET30 cell cycle -5.67 NE carbohydrate metabolism -5.67 NE carbohydrate metabolism -5.67 NET30 cell cycle -2.08 REC2 carbohydrate metabolism -5.67 NE cell cycle <	YPL111W	CAR1	arginine catabolism to ornithine	-10.28	-10.03	0
AAC1 ATP ADP exchange -5.35 A ATP 18 synthesis -6.35 A ATP 18 synthesis -5.35 A ATP 18 synthesis -5.35 INH1 transport -2.83 - AFG5 autophagy -14.10 -14.10 APG3 autophagy -2.03 - KNH1 beta-1.6 gucan biosynthesis -4.10 - BUD23 bud site selection -3.16 - BUD23 bud site selection -3.18 - BUD23 bud site selection -3.18 - BUD23 bud site selection -2.03 - BUD23 bud site selection -2.18 - SOK1 carbohydrate metabolism -2.69 - BUD23 carbohydrate metabolism -5.67 - SAT4 carbohydrate metabolism -5.67 - BUD23 carbohydrate metabolism -5.67 - MET30 cell cycle -2.03 - - NA cell cycle <td>YMR042W</td> <td>ARG80</td> <td>arginine metabolism</td> <td>-2.22</td> <td>-2.72</td> <td>0</td>	YMR042W	ARG80	arginine metabolism	-2.22	-2.72	0
A ATP synthesis coupled proton 8.3 A ATP synthesis coupled proton 8.3 INH1 transport 8.16 APG5 autophagy 14.10 APG5 autophagy 3.16 APG5 autophagy 3.16 APG5 autophagy 3.03 APG5 autophagy 2.03 APG5 autophagy 2.03 APG5 autophagy 2.03 APG5 autophagy 2.03 BUD23 bud site selection 3.16 BUD23 bud site selection 2.03 SOK1 cAMP-mediated signaling -6.08 SOK1 carbohydrate metabolism 5.67 ALT carbohydrate metabolism 5.67 MET30 cation homeostasis 4.12 MET30 cation homeostasis 4.12 MET30 cation homeostasis 5.67 MET30 cell cycle 3.29 MET30 cell cycle 3.20 REC2 cell cycle 3.20 <	YMR056C	AAC1	ATP ADP exchange	-5.35	-6.24	0
A ATP18 transport -2.83 INH1 transport -14.10 APG5 autophagic vacuole formation -3.16 APG5 autophagy -3.16 KNH1 beta-1.6 glucan biosynthesis -4.10 APG5 autophagy -5.92 KNH1 beta-1.6 glucan biosynthesis -4.10 BUD23 bud site selection -2.18 PDE2 cAMP-mediated signaling -5.92 SOK1 cAMP-mediated signaling -5.67 AD7 carbohydrate metabolism -5.67 AD4 carbohydrate metabolism -5.67 SOK1 cAMP-mediated signaling -6.31 AD4 carbohydrate metabolism -5.67 AD5 carbohydrate metabolism -5.67 AD4 carbohydrate metabolism -5.67 AD5 carbohydrate metabolism -5.67 NET30 cel			ynthesis coupled			
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MET unophagic vacuole formation			ynthesis coupled	01 10	-10.02	c
AFCS autophagor vacuore formation -5.10 APG5 autophagy -2.03 KNH1 beta-1.6 glucan biosynthesis -4.10 BUD23 bud site selection -2.03 PDE2 cAMP-mediated signaling -5.92 SOK1 cAMP-mediated signaling -6.08 HOR2 carbohydrate metabolism -2.69 GL04 carbohydrate metabolism -5.67 MET30 call cycle -4.12 NA call cycle -5.67 NA call cycle -5.10 NA call cycle -3.20 REG2 call growth and or maintenance -3.21 KRE1 call growth and or maintenance -3.31 KRE1 cell wall organization and biogenesis -7.74 ECM13 cell wall organization and biogenesis -7.72 S1T4 cell wall organization and biogenesis -7.73 S1T4 cell wall organization and biogenesis -7.73 S1T4 cell wall organization and biogenesis -7.73 S114 cell wall organization and biogenesis -7.73 S	10L101W	1100		0.10	20.01-	
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KNH1 beta-1.6 glucan biosynthesis -4.10 BUD23 bud site selection -2.18 PDE2 cAMP-mediated signaling -5.92 SOK1 cAMP-mediated signaling -5.92 SOK1 cAMP-mediated signaling -5.02 SOK1 cAMP-mediated signaling -5.02 SOK1 cAMP-mediated signaling -5.03 AD23 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 NET30 cell cycle -4.12 NA calton homeostasis -4.12 NA cell cycle -5.31 NA cell cycle -5.31 REC2 cell cycle -5.38 REC3 pheromone -3.208 REC4 cell wold organization and biogenesis -7.74 REC3 cell wold organization and biogenesis -7.74 ECM3 cell wall organization and biogenesis -7.74 ECM3 cell wall organization and biogenesis -7.74 SIT4 cell wall organization and biogen	YPL149W	APG5	autophagy	-2.03	-2.03	4
BUD23 bud site selection -2.18 PDE2 cAMP-mediated signaling -5.92 SOK1 cAMP-mediated signaling -5.92 SOK1 carbohydrate metabolism -5.92 HOR2 carbohydrate metabolism -5.67 MET30 carbohydrate metabolism -5.67 NA carbohydrate metabolism -5.67 NET30 cell cycle -4.12 NA cell cycle -5.31 NA cell cycle -5.31 Cell cycle attom homeostasis -4.12 NA cell cycle -5.31 REG2 cell cycle -5.31 REG2 cell cycle -3.81 REG2 cell cycle -3.29 REG3 cell cycle -3.240 REGM3 cell wa	YDL049C	KNH1	beta-1,6 glucan biosynthesis	-4.10	-6.54	0
PDE2 CAMP-mediated signaling -5.92 SOK1 CAMP-mediated signaling -5.08 SOK1 carbohydrate metabolism -5.67 HOR2 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 NET30 cell cycle -4.12 NA cell cycle -5.31 NA cell cycle -5.31 NA cell cycle -5.31 REG2 cell cycle -5.31 REG2 cell cycle -5.31 REG2 cell cycle -3.29 REG2 cell cycle -3.29 REG2 cell cycle -3.29 REG2 cell wall organization and biogenesis -2.55 REG3 cell wall organization and biogenesis -7.74 REM3 cell wall organization and biogenesis -7.74 REM3 cell wall organization and biogenesis -2.72 REM3 cell wall organization and biogenesis -2.74 REM3 cell wall organization and biogenesis -2.73 REM3 cell wall organization and biogenesis	YCR047C	BUD23	bud site selection	-2.18	-2.25	æ
SOK1 cAMP-mediated signaling -6.08 HOR2 carbohydrate metabolism -5.67 GL04 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 MET30 calf cycle -5.67 NA cell cycle -5.31 NA cell cycle -5.31 NA cell cycle -5.31 REC3 cell cycle -5.31 REC4 cell cycle -5.31 REC2 cell cycle -5.31 REC3 cell cycle -3.208 REC4 cell cycle -3.205 REC3 cell wall organization and biogenesis -2.55 REC4 cell wall organization and biogenesis -2.74 REM3 cell wall organization and biogenesis -2.73 ECM13 cell wall organization and biogenesis -2.74 SIT4 cell wall organization and biogenesis -2.74 REV3 cell wall organization and biogenesis -2.74 REV3 cell wall organization and biogenesis -2.74 SIT4 cell wall organization and biogenesi	YOR360C	PDE2	cAMP-mediated signaling	-5.92	-5.59	6
HOR2 carbohydrate metabolism -2.69 GLO4 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 NA cali cycle -5.67 NA cell cycle -5.31 NA cell cycle -5.31 NA cell cycle -5.31 REG2 cell cycle arrest in response to -3.81 FAR3 pheromone -3.29 REG2 cell growth and or maintenance -3.81 KRE1 cell wall organization and biogenesis -2.55 ECM37 cell wall organization and biogenesis -2.72 ECM17 cell wall organization and biogenesis -2.74 ECM13 cell wall organization and biogenesis -2.74 SIT4 cell wall organization and biogenesis -2.73 FCM13 cell wall organization and biogenesis -2.74 FCM13 cell wall organization and biogenesis -2.74 FCM13 cell wall organization and biogenesis -2.73 FCM14 cell wall organization and biogenesis -2.73 FCM14 cell wall organization and biogenesis<	YDR006C	SOK1	cAMP-mediated signaling	-6.08	-3.82	0
GLO4 carbohydrate metabolism -5.67 SAT4 carbohydrate metabolism -5.67 SAT4 cation homeostasis -4.12 MET30 cell cycle -6.31 NA cell cycle -5.08 NA cell cycle -5.31 REG2 cell cycle arrest in response to -3.29 FAR3 pheromone -3.29 REG2 cell growth and or maintenance -3.81 KRE1 cell wall organization and biogenesis -2.55 ECM37 cell wall organization and biogenesis -2.74 ECM2 cell wall organization and biogenesis -2.72 ECM3 cell wall organization and biogenesis -2.74 FCM3 cell wall organization and biogenesis -2.73 FCM3 cell wall organization and biogenesis -2.74 FCM3 cell wall organization and biogenesis -2.74 FCM3 cell wall organization and biogenesis -2.73 FCM3 cell wall organization and biogenesis -2.74 FCM3 cell wall organization and biogenesis -2.73 FCM3 cell wall organiza	YER062C	HOR2	carbohydrate metabolism	-2.69	-2.92	0
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MET30 cell cycle -6.31 NA cell cycle -2.08 REG2 cell growth and or maintenance -3.29 REG2 cell wall organization and biogenesis -2.55 KRE1 cell wall organization and biogenesis -2.74 ECM37 cell wall organization and biogenesis -2.72 ECM27 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.73 FCM13 cell wall organization and biogenesis -2.74 FCM13 cell wall organization and biogenesis -2.75 FCM13 cell wall organization and biogenesis -2.74 FCM13 cell wall organization and biogenesis -2.75 FCM13 cell wall organization and biogenesis -2.73 FCM13 cell wall organization and biogenesis -2.73 FCM13 cell wall organization and biogenesis -2.73 FCM14 cell wall organization and biogenesis -2.33 FCM15 cell wall organization and biogenesis -3.33 FCM2 cell wall organization and biogenesis -7.23 FCS2 <td< td=""><td>YCR008W</td><td>SAT4</td><td>cation homeostasis</td><td>-4.12</td><td>-3.81</td><td>0</td></td<>	YCR008W	SAT4	cation homeostasis	-4.12	-3.81	0
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FAR3 pheromone -3.29 REG2 cell growth and or maintenance -3.81 KRE1 cell wall organization and biogenesis -2.55 ECM37 cell wall organization and biogenesis -2.40 ECM2 cell wall organization and biogenesis -7.74 ECM13 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 S1T4 cell wall organization and biogenesis -2.72 S1T4 cell wall organization and biogenesis -2.72 RCM13 cell wall organization and biogenesis -2.55 CSR2 cell wall organization and biogenesis -7.23 GSC2 cell wall organization and biogenesis -7.23			cycle arrest in response			
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KRE1 cell wall organization and biogenesis -2.55 ECM37 cell wall organization and biogenesis -2.40 ECM2 cell wall organization and biogenesis -7.74 ECM2 cell wall organization and biogenesis -7.74 ECM3 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 FCM13 cell wall organization and biogenesis -2.74 FCM14 cell wall organization and biogenesis -2.75 FCM15 cell wall organization and biogenesis -2.55 FCM2 cell wall organization and biogenesis -13.47 FCM2 cell wall organization and biogenesis -7.23 GSC2 cell wall organization and biogenesis -7.23	YBR050C	REG2	cell growth and or maintenance	-3.81	-3.35	0
ECM37 cell wall organization and biogenesis -2.40 ECM2 cell wall organization and biogenesis -7.74 ECM27 cell wall organization and biogenesis -7.74 ECM13 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.93.31 SIT4 cell wall organization and biogenesis -2.84 PIR3 cell wall organization and biogenesis -2.55 HLR1 cell wall organization and biogenesis -5.75 CSR2 cell wall organization and biogenesis -1.3.47 GSC2 cell wall organization and biogenesis -7.23	YNL322C	KRE1	cell wall organization and biogenesis	-2.55	-2.56	4
ECM2 cell wall organization and biogenesis -7.74 ECM27 cell wall organization and biogenesis -2.72 ECM13 cell wall organization and biogenesis -2.72 FCM13 cell wall organization and biogenesis -2.84 SIT4 cell wall organization and biogenesis -2.84 PIR3 cell wall organization and biogenesis -5.7 HLR1 cell wall organization and biogenesis -5.55 CSR2 cell wall organization and biogenesis -13.47 GSC2 cell wall organization and biogenesis -7.23	YIL146C	ECM37	cell wall organization and biogenesis	-2.40	-2.67	4
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	YGR032W	GSC2	cell wall organization and biogenesis	-7.23	-3.56	0

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FC WT		-23.93	-2.10		-3.63	-38.22	-2.97	-11.14	-3.24	-2.32	-2.78	-2.56	-3.90	-2.51	-11.46	-2.61		-2.66	-2.92		-2.33		-2.71		-3.41		-2.18		-2.50		-3.46	:	-27.10	-3.60	-2.95		-2.64	-2.19
n ctio Fun		lactate transport	lipid metabolism	mannosyl diphosphorylinositol	ceramide metabolism	MAPKKK cascade	meiosis	meiotic chromosome segregation	meiotic recombination	meiotic recombination	meiotic recombination	metal ion transport	metal ion transport	methionine biosynthesis	methionine biosynthesis	microtubule nucleation	mitochondrial magnesium ion	transport	mitochondrial transport	mitochondrion organization and	biogenesis	mitochondrion organization and		mitochondrion organization and		mitochondrion organization and	biogenesis	mitochondrion organization and		mitochondrion organization and		mitochondrion organization and	biogenesis	mitotic anaphase B	mitotic metaphase	mitotic metaphase anaphase	transition	mitotic metaphase anaphase
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Table 11A	ORF	YKL217W	YMR313C		YDR072C	YDL214C	YJR094C	YPL200W	YJR021C_ex1	YJR021C_ex2	YLR219W	YLL018C-A	YBR290W	YGL184C	YNL277W	YOR257W		YPL060W	YPL134C		YML091C		YGL219C		YOR147W		YOL027C		YPR083W		YBR179C		YJL116C	YOR058C	YBL084C		YKL022C	YFR036W
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ਹਰਾ	бш	-2.58	-2.32	-11.23	-23.63	-24.54	-6.04	-2.79	-3.97	-36.05	-4.83	-2.45	-3.29	-52.59	-4.37	-19.04	-2.20	-3.43	-3.60		-34.47	-2.67	-3.02	-3.02	-3.25	-3.30	-2.19	-8.64	-2.56	-4.48	-2.60	-12.99	-3.59	-4.92	-5.51	-6.19	-12.28	~~~~
FC	TW	-2.21	-2.10	-12.75	-15.85	-20.73	-4.84	-2.63	-8.28	-27.15	-3.73	-2.61	-3.85	-46.40	-4.51	-14.23	-2.27	-3.14	-4.21		-33.60	-2.49	-2.61	-2.34	-2.89	-3.03	-2.24	-7.67	-2.55	-5.38	-2.41	-13.28	-2.60	-4.31	-4.55	-5.63	-10 90	00.01
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ວງກ	6ш	-2.58	-2.32	-11.23	-23.63	-24.54	-6.04	-2.79	-3.97	-36.05	-4.83	-2.45	-3.29	-52.59	-4.37	-19.04	-2.20	-3.43	-3.60	-34.47	-2.67	-3.02	-3.02	-3.25	-3.30	-2.19	-8.64	-2.56	-4.48	-2.60	-12.99	-3.59	-4.92	-5.51	-6.19	-12.28
L FC	ΓW	-2.21	-2.10	-12.75	-15.85	-20.73	-4.84	-2.63	-8.28	-27.15	-3.73	-2.61	-3.85	-46.40	-4.51	-14.23	-2.27	-3.14	-4.21	-33.60	-2.49	-2.61	-2.34	-2.89	-3.03	-2.24	-7.67	-2.55	-5.38	-2.41	-13.28	-2.60	-4.31	-4.55	-5.63	-10.90
noit	bnuf	galactose metabolism	galactose metabolism	gluconeogenesis	gluconeogenesis	gluconeogenesis	glucose metabolism	glucose metabolism	glutamate biosynthesis	glutamate biosynthesis	glycerol metabolism	glycogen biosynthesis	glycogen biosynthesis	giyoxylate cycle	glyoxylate cycle	glyoxylate cycle	Golgi to endosome transport	Golgi to plasma membrane transport	Golgi to vacuole transport	G-protein signaling, coupled to cAMP nucleotide second messenger	heme biosynthesis	hexadecanal biosynthesis	nexose transport	hexose transport	high-affinity zinc ion transport	histone acetylation	histone methylation	hyperosmotic response	intracellular signaling cascade	invasive growth	invasive growth	iron ion transport	iron-siderochrome transport	iron-siderochrome transport	iron-sulfur cluster assembly	isocitrate metabolism
	əuəĐ	GAL4	GAL1	MDH2	PCK1	FBP1	MIG1	RGT1	CIT2	GDH3	GUT1	GLC8	GLG2	MLS1	NA	ICL1	ENT5	SNC2	PEP12	RGS2	HEM1	CEM1	HXT16	HXT10	ZRT1	SPT8	LGE1	НОТ1	GIS3	DFG16	NRG1	ISA1	FRE3	FRE4	ISU1	IDP2
Table 11A	ORF	YPL248C	YBR020W	YOL126C	YKR097W	YLR377C	YGL035C	YKL038W	YCR005C	YAL062W	YHL032C	YMR311C	YJL137C	YNL117W	YFL030W	YER065C	YDR153C	YOR327C	YOR036W	YOR107W	YDR232W	YER061C	YJR158W	YFL011W	YGL255W	YLR055C	YPL055C	YMR172W	YLR094C	YOR030W	YDR043C	YLL027W	YOR381W	YNR060W	YPL135W	YLR174W

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MRI prosphate/predictions bosynthesis 3.39 4.01 0 YR.020C SPT23 1 DPI3 prosphate/predictine bosynthesis 2.61 2.84 0 YR.020C SPT23 1 Ext1 prosphate/predictine bosynthesis 3.66 3.56 0 YR.020C SPT3 PR032W PDH1 NO2 prosphate/predictine bosynthesis 3.13 3.00 YR.020C SPT3 PDH1 PDC1 PDH1 PDC2 C SPT3 PDF1 PDF2 PDF1 PDF2 PDF1 PDF2 PDF1 PDF2 PDF1 PDF1 PDF1 PDF1 PDF1 PDF2 PDF1 PDF2 PDF1 PDF2 PDF1 PDF2 PDF1 PDF1 PDF2 PDF1 PDF1 PDF1 PDF1 PDF1 PDF1 PDF2	YBR296C	PHO89	phosphate transport	-6.26	-13.54	0			positive regulation of transcription			
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OP11 prospholipid biosynthesis 4.25 5.46 23 YER054C CIP2 C NOC4 prospholipid biosynthesis 3.23 3.14 0 YR0057C KSP1 YR0109C KH55 YR0109C KSP1 YR0109C YR01 YR0109C KS11 YR0109C YR1 YR0109C YR1 <	YOL011W	PLB3	phosphatidylserine catabolism	-6.47	-7.35	0						
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$NO2$ prospholyation -2.53 -4.01 0 $VHR082C$ $KSP1$ NA $ARG82$ phosphorylation -2.53 -2.65 4 $VDR247W$ NA $IUP2$ parametherance -2.53 -2.65 4 $VDL079C_{ext}$ $KK1$ $IVP0$ polyamine transport -2.14 -2.18 4 $VDL079C_{ext}$ $KK1$ $IVT1$ polyamine transport -3.72 -4.05 0 $VDL079C_{ext}$ $KK1$ III $PIX1$ polyamine transport -3.72 -4.05 0 $VDL079C_{ext}$ $KK1$ III $PIX1$ polyamine transport -3.72 -4.05 0 $VDL079C_{ext}$ $KK1$ III $PIX1$ positive regulation of irranscription -5.07 -5.38 0 $VDL079C_{ext}$ $KH12$ III $PIX1$ positive regulation of irranscription -5.07 -5.38 0 $VDL09C_{ext}$ $KH12$ $IIII$ $IVE1$ positive regulation of irranscription -3.258 -2.71 15 $VDL08C$ $VSI1$ $IIII1$ from Pol II ponoter -2.54 -2.71 15 $VDR405W$ $MRP20$ $IIII1$ from Pol II ponoter -2.56 -2.71 15 $VDR405W$ $MRP20$ $IIII11$ from Pol II ponoter -2.55 -2.71 15 $VDR405W$ $MRP20$ $IIII11$ from Pol II ponoter -2.55 -2.71 15 $VDR405W$ $MD11$ $IIII111$ from Pol II ponoter -2.5	YOL108C	IN04	phospholipid biosynthesis	-3.23	-3.14	0	YOL110W	SHR5	protein amino acid palmitoylation	-2.85	-3.34	4
AFG82 phosphorylation 2.53 2.65 4 VDR247W MA J_LP2 pasma mannenance 2.55 2.56 7 VD076_ex11 MRK1 TPO4 polyamine transport 2.14 2.18 4 VD070_ex1 MRK1 FIK1 polyamine transport 3.72 4.05 0 VD159U SF27 MRK1 alt PTK1 polyamine transport 3.72 4.05 0 VD159U SF27 MRK1 alt PTK1 polyamine transport 3.72 4.05 0 VD159U SF27 MRK1 alt PTK1 polyamine transport 3.72 4.05 0 VD159U SF7 YD109U YD139C YE7 alt positive regulation of transcription 3.35 3.36 E YD138C YB116 YD138C YB116 YD138C YD149C YB116 YD159C YD159C YD15 YD15 YD156C YD15 YD151 YD151C YD151C YD15	YDR123C	INO2	phospholipid biosynthesis	-4.03	-4.01	0	YHR082C	KSP1	protein amino acid phosphorylation	-2.35	-2.84	12
ULP2 Distruct maintenance 2.55 2.56 ε VPL028C SK31 TFO4 polyamine transport -2.14 -2.18 4 VDL75C_ex1 MKK1 IFO4 polyamine transport -2.14 -2.18 4 VDL75C_ex2 MKK1 IFO4 polyamine transport -3.72 -4.05 0 VDL75C_ex2 MK1 IFO4 polyamine transport -3.72 -4.05 0 VDL75C_ex2 MK1 IFO5 positive regulation of pycolysis -5.07 -5.38 0 VDL75C_ex2 MK1 IFO5 positive regulation of transcription -3.23 -3.36 P VDL75BC VGK3 MAC1 positive regulation of transcription -3.25 -3.36 P VDR405W MR21 MAC1 from Pol II promoter -3.25 -2.71 15 PDR-4 MR21 MAC1 from Pol II promoter -3.56 -2.71 15 PDR-45W MR16 MAC1 from Pol II promoter -	YDR173C	ARG82	phosphorylation	-2.53	-2.65	4	YDR247W	NA	protein amino acid phosphorylation	-6.07	-5.29	9
TPO4polyamine transport -2.14 -2.18 4 VDL079C_ex1MRK1PTK1polyamine transport -4.07 4.45 0VDL079C_ex2MRK1altPTK1polyamine transport -3.72 -4.05 0VDL079C_ex2MRK1altPTK1polyamine transport -3.72 -4.05 0VDL079C_ex2MRK1altPTK1positive regulation of glycolysis -5.07 -5.38 0VOL100WPKH2TYE7positive regulation of glycolysis -5.07 -5.38 0VOL102WRSM10PR43trom Pol II promoter -3.27 -3.38 EVDR041WRSM10mAC1trom Pol II promoter -2.54 -2.71 15VDR465WMRP16mAC1from Pol II promoter -2.54 -2.71 15VDR465WMRP16mAC1from Pol II promoter -2.54 -2.71 15VDR452WMRP16mAC1from Pol II promoter -2.54 -2.71 15VDR452WMRP16sMP1from Pol II promoter -2.54 -2.71 15VDR452WMRP16sMP1from Pol II promoter -2.54 -2.71 15VDR552WMD17sMP1from Pol II promoter -2.55 -2.71 5VLR106CMD17sMP1from Pol II promoter -2.55 -2.71 5VLR106CMD17sMP1from Pol II promoter -2.55 -2.71 5VLR106CMD14 </td <td>YIL031W</td> <td>ULP2</td> <td>plasmid maintenance</td> <td>2.55</td> <td>2.56</td> <td>:11</td> <td>YPL026C</td> <td>SKS1</td> <td>protein amino acid phosphorylation</td> <td>-20.99</td> <td>-18.47</td> <td>0</td>	YIL031W	ULP2	plasmid maintenance	2.55	2.56	:11	YPL026C	SKS1	protein amino acid phosphorylation	-20.99	-18.47	0
FTK1polyamine transport 4.07 4.45 0YDL 159WSTE7altFTK1polyamine transport 3.72 4.05 0YDL 079C_eX2MRK1YCLaltpositiveregulationof 5.07 5.38 0YCL 128CYGK3YCLTYE7positiveregulationof gluconeogenesis 2.53 2.53 2.53 2.53 2.59 0YCL 128CYGK3YGK3TYE7positiveregulationof gluconeogenesis 2.53 2.53 2.38 EYCL 128CYGK3YGK3TYE7positiveregulation of glycolysis 2.254 2.71 15 YDR405WMRPL16MAC1from Pol II promoter 2.54 2.71 15 YBL038WMRPL16MAC1from Pol II promoter 2.54 2.71 15 YBL038WMRPL16MAC1from Pol II promoter 2.54 2.71 15 YBL038WMRP16MAC1from Pol II promoter 2.54 2.71 15 YBL065CMDN1SMP1from Pol II promoter 2.56 2.17 5 YLR106CMDN1SMP1from Pol II promoter 2.56 2.17 5 YLR106CMDN1SMP1from Pol II promoter 2.56 2.17 5 YLR106CMDN1SMP1from Pol II promoter 2.56 2.71 5 YLR106CMDN1SMP1positive regulation of transcription 2.55 2.17 <td>YOR273C</td> <td>TPO4</td> <td>polyamine transport</td> <td>-2.14</td> <td>-2.18</td> <td>4</td> <td>YDL079C_ex1</td> <td>MRK1</td> <td>protein amino acid phosphorylation</td> <td>-3.25</td> <td>-2.55</td> <td>0</td>	YOR273C	TPO4	polyamine transport	-2.14	-2.18	4	YDL079C_ex1	MRK1	protein amino acid phosphorylation	-3.25	-2.55	0
alt FTK1 polyarine transport 3.72 4.05 0 YDL079C_eX2 MRK1 alt FTK1 positive regulation of 5.07 5.38 0 YOL100W PKH2 YK13 TYE7 positive regulation of glycolysis 2.53 2.53 2.53 2.53 2.53 $YOL128C$ YGK3 YOL128C YGK3 PRP45 positive regulation of glycolysis 2.53 2.33 E YUR13C RSM10 RSM10 PRP45 trom Pol II promoter 3.27 3.36 E YUR13C RSM7 RSM10 MAC1 from Pol II promoter 2.54 2.71 15 RDN5-1 RDN5-1 RDN5-1 MAC1 from Pol II promoter 2.56 2.17 5 YLR106C MD11 MAC1 from Pol II promoter 2.56 2.17 5 YLR106C MD11 MAC1 from Pol II promoter 2.56 2.17 5 YLR106C MD11 <tr< td=""><td>YKL198C</td><td>PTK1</td><td>polyamine transport</td><td>-4.07</td><td>-4.45</td><td>0</td><td>YDL159W</td><td>STE7</td><td>protein amino acid phosphorylation</td><td>-2.79</td><td>-3.01</td><td>0</td></tr<>	YKL198C	PTK1	polyamine transport	-4.07	-4.45	0	YDL159W	STE7	protein amino acid phosphorylation	-2.79	-3.01	0
positive regulationof \cdot <t< td=""><td>YKL198C_alt</td><td>PTK1</td><td>polyamine transport</td><td>-3.72</td><td>-4.05</td><td>0</td><td>YDL079C_ex2</td><td>MRK1</td><td>protein amino acid phosphorylation</td><td>-3.35</td><td>-4.14</td><td>0</td></t<>	YKL198C_alt	PTK1	polyamine transport	-3.72	-4.05	0	YDL079C_ex2	MRK1	protein amino acid phosphorylation	-3.35	-4.14	0
SIP4gluconeogenesis -5.07 -5.38 0 $VOL128C$ $YGK3$ TVE7positive regulation of glycolysis -2.53 -2.59 0 $VOL128C$ $YGK3$ PRP45positive regulation of transcription -3.2 -3.38 E $VDR405W$ $RRM10$ PRP45positive regulation of transcription -3.2 -3.38 E $VDR405W$ $RRM7$ MAC1from Pol II promoter -2.54 -2.71 15 $VDR465W$ $RRM7$ MAC1from Pol II promoter -2.54 -2.71 15 $VDR462W$ $RRM7$ NMP1from Pol II promoter -2.54 -2.71 15 $VDR452W$ $RM7$ SMP1from Pol II promoter -3.58 -5.03 5 $VDR452W$ $RM7$ SMP1from Pol II promoter -3.56 -2.71 15 $VDR452W$ $RM7$ SMP1from Pol II promoter -3.56 -2.71 5 $VDR452W$ $RM5-1$ SMP1from Pol II promoter -2.55 -2.71 5 $VDR452W$ $RM5-1$ SMP1from Pol II promoter -2.56 -2.77 5 $VDR452W$ $RDN5-3$ SMP1from Pol II promoter -2.56 -2.77 5 $VDR452W$ $RDN5-3$ SUB1from Pol II promoter -2.56 -2.77 5 $VDR45W$ $RDN5-3$ SMP1from Pol II promoter -2.36 -2.77 5 $VDR45W$ $RDN5-3$ SMP1from Pol II promoter -2.36 -2.7			regulation				YOL100W	PKH2	protein amino acid phosphorylation	-2.75	-2.70	0
TVE7positive regulation of gycolysis -2.53 -2.59 0 $VDR041W$ $RSM10$ PR45trom Pol II promoter 3.22 -3.36 E $VJR13C$ $RSM7$ $MRP20$ PR45trom Pol II promoter 3.22 -3.36 E $VJR13C$ $RSM7$ $MRP16$ MAC1from Pol II promoter -3.25 -3.36 E $VJR13C$ $RSM7$ $MRP16$ MAC1from Pol II promoter -2.54 -2.71 15 $VDR465W$ $MRP16$ MAC1from Pol II promoter -3.56 -2.71 15 $VDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.71 15 $VDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.71 15 $VDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.71 15 $VDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.71 5 $VCR462W$ $MRP16$ SMP1from Pol II promoter -2.55 -2.17 5 $VCR462W$ $MRP16$ SMP1from Pol II promoter -2.56 -2.17 5 $VCR462W$ $MRP16$ SMP1from Pol II promoter -2.56 -2.17 5 $VCR462W$ $MRP16$ SMP1from Pol II promoter -2.56 -2.17 5 $VCR462W$ $MRP16$ SMP1from Pol II promoter -2.56 -2.17 5 $VCR462W$ $MP16$ SMP1from Pol II promoter -2.36 -2.78 <	YJL089W	SIP4	gluconeogenesis	-5.07	-5.38	0	YOL128C	YGK3	protein amino acid phosphorylation	-2.48	-2.55	0
PRP45positive regulation of transcription 3.2 3.36 E $YDR405W$ MRP20PRP45trom Pol II promoter 3.2 3.36 E $YJR113C$ $RSM7$ $RSM7$ MAC1from Pol II promoter 2.54 2.71 15 $YDR462W$ $MRP16$ MAC1from Pol II promoter 2.54 2.71 15 $YDR462W$ $MRP16$ MAC1from Pol II promoter 2.54 2.71 15 $YDR462W$ $MRP16$ SMP1from Pol II promoter -3.58 -5.03 5 $YDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.17 5 $YDR462W$ $MRP16$ SMP1from Pol II promoter -3.56 -2.17 5 $YDR462W$ $MRP16$ SMP1from Pol II promoter -2.55 -2.17 5 $YDR462W$ $MRP16$ SUB1from Pol II promoter -2.56 -2.17 5 $YCR469C$ $DOA4$ SUB1from Pol II promoter -2.86 -2.78 5 $YCR406C$ $HSP2$ STP2from Pol II promoter -2.96 -2.78 5 $YCL40C$ $HSP2$ MSS11from Pol II promoter -3.97 -2.92 0 $YCR09W$ $SIG1$ MSS11from Pol II promoter -2.97 -2.92 0 $YCR09W$ $SI21$ MSS11from Pol II promoter -2.97 -2.92 0 $YCR09W$ $SI21$ MSS11from Pol II promoter -2.97 -2.92 0 $YCR04W$ $ZI61$ </td <td>YOR344C</td> <td>TYE7</td> <td>positive regulation of glycolysis</td> <td>-2.53</td> <td>-2.59</td> <td>0</td> <td>VDR041W</td> <td>RSM10</td> <td>protein biosynthesis</td> <td>-5.25</td> <td>-3.75</td> <td>шi</td>	YOR344C	TYE7	positive regulation of glycolysis	-2.53	-2.59	0	VDR041W	RSM10	protein biosynthesis	-5.25	-3.75	шi
PRP45 trom Pol II promoter -3.2 -3.36 E VJR13C RSM7 MAC1 from Pol II promoter -2.71 15 YBL038W MRP-16 MAC1 from Pol II promoter -2.54 -2.71 15 YBL038W MRP-16 MAC1 from Pol II promoter -2.54 -2.71 15 YBL038W MRP-16 SMP1 from Pol II promoter -3.58 -5.03 5 RDN5-1 RDN5-3 RDN5-3 SMP1 from Pol II promoter -3.56 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -3.56 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.56 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.85 -2.17 <	ener verste style state time of a link of a subscript of the subscript of the subscript of the subscript of the		5				YDR405W	MRP20	protein biosynthesis	-3.12	-2.74	14
MAC1 positive regulation of transcription -2.54 -2.71 15 YBL038W MRPL16 MAC1 from Pol II promoter -2.54 -2.71 15 YDR462W MRP-138 SMP1 from Pol II promoter -3.58 -5.03 5 RDN5-1 RDN5-1 RDN5-3 SMP1 from Pol II promoter -3.58 -5.03 5 RDN5-3 RDN5-3 RDN5-3 SMP1 from Pol II promoter -3.58 -5.03 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YDR085C DOA4 SUB1 from Pol II promoter -2.85 -2.17 5 YDR085C DOA4 GCR2 from Pol II promoter -2.85 -2.78 5 YLR106C HSP2 STP2 from Pol II promoter -3.07 -2.92 0 YCL047C YPS2 MSS11 from Pol II promoter -3.07 -3.56 0 YCL045W RT61 MSS11 from Pol II promoter -3.07 -3.50 0 YCL045W YPS3	VAL032C	PRP45	trom Pol II promoter		-3.36	ω	YJR113C	RSM7	protein biosynthesis	-2.24	-2.29	6
MAC1 from Pol II promoter -2.54 -2.71 15 YDR462W MRPL28 NMP1 from Pol II promoter -3.58 -5.03 5 RDN5-1 RDN5-1 RDN5-3 SMP1 from Pol II promoter -3.58 -5.03 5 RDN5-3 RDN5-3 RDN5-3 SMP1 from Pol II promoter -3.56 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.65 -2.17 5 YLR106C MDN1 STP2 from Pol II promoter -3.07 -2.78 5 YLL240C HSP82 MSS11 from Pol II promoter -3.07 -2.92 0 YLR106T YPS3 MSS11 from Pol II promoter <							YBL038W	MRPL16	protein biosynthesis	-2.64	-2.38	0
positive regulation of transcription3.585.035RDN5-1RDN5-1RDN5-1SMP1from Pol II promoter -3.58 -5.03 5RDN5-3RDN5-3RDN5-3SUB1from Pol II promoter -2.55 -2.17 5 $\sqrt{1.R106C}$ $MDN1$ $ND11$ SUB1from Pol II promoter -2.55 -2.17 5 $\sqrt{1.R106C}$ $MDN1$ $ND11$ SUB1from Pol II promoter -2.85 -2.17 5 $\sqrt{1.R106C}$ $DOA4$ $ND11$ GCR2from Pol II promoter -2.85 -2.18 5 $\sqrt{1.R106C}$ $DOA4$ $ND11$ GCR2from Pol II promoter -2.85 -2.18 5 $\sqrt{1.R106C}$ $DA44$ $ND11$ STP2from Pol II promoter -3.07 -2.92 0 $\sqrt{1.R1067C}$ $RT61$ $ND16$ MSS11from Pol II promoter -3.07 -2.92 0 $\sqrt{1.R121C}$ $\sqrt{PS3}$ $ND16$ MSS11from Pol II promoter -3.07 -3.56 0 $\sqrt{1.R121C}$ $\sqrt{PS3}$ $ND1$ D1112 -2.160 -2.92 0 0 $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ D1112 -2.92 0 0 $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ D1112 -2.92 0 0 $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ D1112 -2.92 0 0 $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ $\sqrt{1.R121C}$ <	YMR021C	MAC1	from Pol II promoter		-2.71	15	YDR462W	MRPL28	protein biosynthesis	-2.60	-2.50	0
SMP1 from Pol II promoter -3.58 -5.03 5 RDN5-3 RD	and the second sec		ð				RDN5-1	RDN5-1	protein biosynthesis	-8.69	-8.91	0
positive regulation of transcription 2.55 2.17 5 YLR106C MDN1 SUB1 from Pol II promoter -2.55 -2.17 5 YDR069C DOA4 P SUB1 from Pol II promoter -2.55 -2.17 5 YDR069C DOA4 P GCR2 from Pol II promoter -2.85 -2.18 5 YPL240C HBP5 P STP2 from Pol II promoter -3.07 -2.92 0 YCL067C RT61 P MSS11 from Pol II promoter -3.07 -2.92 0 YCL045W RT61 P MSS11 from Pol II promoter -3.07 -2.95 0 YCL045W RT63 P	YBR182C	SMP1			-5.03	5	RDN5-3	RDN5-3	protein biosynthesis	-3.19	-3.95	0
SUB1 from Pol II promoter -2.55 -2.17 5 YDR069C DOA4 positive regulation of transcription -2.85 -2.17 5 YPI2069C UBP5 YPI240C UBP5 YPI240C HSP82 GCR2 from Pol II promoter -2.85 -2.78 5 YPI240C HSP82 YPI240C YPI240			oť				YLR106C	MDN1	protein complex assembly	2.24	-2.22	ω
positive regulation of transcription 2.78 5 YEL34C UBPS GCR2 from Pol II promoter -2.85 -2.78 5 YPL240C HSP82 STP2 from Pol II promoter -3.07 -2.92 0 YLR121C YPS3 MSS11 from Pol II promoter -3.97 -3.65 0 YLR121C YPS3 D111 anticipant of transcription -3.97 -3.65 0 YLR121C YPS3	YMR039C	SUB1	from Pol II promoter	-2.55	-2.17	ۍ	YDR069C	DOA4	protein deubiquitination	-2.77	-2.90	25
GCR2 from Pol II promoter -2.85 -2.78 5 YPL240C HSP82 positive regulation of transcription -3.07 -2.92 0 YOL067C RTG1 STP2 from Pol II promoter -3.07 -2.92 0 YLR121C YPS3 MSS11 from Pol II promoter -3.97 -3.65 0 YCL045W RIM8							YER144C	UBP5	protein deubiquitination	-2.29	-2.18	0
positive regulation of transcription -3.07 -2.92 0 YOL067C RTG1 STP2 from Pol II promoter -3.07 -2.92 0 YIR121C YPS3 MSS11 from Pol II promoter -3.97 -3.65 0 YGL045W RIM8	YNL199C	GCR2		-2.85	-2.78	5	YPL240C	HSP82	protein folding	-2.17	-2.75	2
STP2 from Pol II promoter -3.07 -2.92 0 YLR121C YPS3 positive regulation of transcription -3.07 -2.55 0 YGL045W RIM8 MSS11 from Pol II promoter -3.65 0 YDR409W SIZ1			đ				YOL067C	RTG1	protein localization	-2.62	-3.51	9
positive regulation of transcription YGL045W RIM8 MSS11 from Pol II promoter -3.97 -3.65 0 YDR409W SIZ1	YHR006W	STP2	- 1	-3.07	-2.92	0	YLR121C	YPS3	protein metabolism	-2.05	-2.28	0
MSS11 from Pol II promoter -3.65 0 YDR409W SIZ1							YGL045W	RIM8	protein processing	-3.38	-3.44	14
DIMI accitica at transmistion 3 20 3 20 0 0	YMR164C	MSS11	from Pol II promoter	-3.97	-3.65	0 (YDR409W	SIZ1	protein sumoylation	-3.32	-3.88	0
KLIMI PUSITIVE REGILIATION OF LATING -0.22 -0.32 V YDR313C P1B1	YPL089C	RLM1	positive regulation of transcription	-3.22	-3.32	0	YDR313C	PIB1	protein ubiquitination	-4.22	-5.04	2

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Table 11A		uo	FC	Э Ц	tivity	Table 11A	e Geu	u ctio Fun	MT FC	Э ∃ 36ш	sitiv ity
ORF	əuəĐ	functi	TW	ស្រយ	isnə2	ORF					
YLR417W	VPS36	protein-Golgi retention	-2.72	-2.15	30	YNL197C	WHI3	regulation of cell size	-2.70	-3.10	4
YNR006W	VPS27	protein-Golgi retention	-2.01	-2.32	7	YGI_134W	PCL10	regulation of glycogen catabolism	-3.80	-3.73	ω
YEL030W	ECM10	protein-mitochondrial targeting	-3.33	-4.32	30	YPL219W	PCL8	regulation of glycogen catabolism	-2.37	-2.78	æ
YBR165W	UBS1	protein-nucleus export	-2.32	-2.09	0	YBR212W	NGR1	regulation of growth	-2.26	-2.46	13
YJR074W	MOG1	protein-nucleus import	-2.27	-3.12	2	YJL106W	IME2	regulation of meiosis	-3.03	-2.63	2
YAL055W	PEX22	protein-peroxisome targeting	-2.51	-2.43	21	YFL021W	GAT1	regulation of nitrogen utilization	-3.60	-2.69	5
YOL044W	PEX15	protein-peroxisome targeting	-2.42	-2.42	20	YJL110C	GZF3	regulation of nitrogen utilization	-2.41	-2.35	2
YHR160C	PEX18	protein-peroxisome targeting	-10.05	-9.60	11	YKR034W	DAL80	regulation of nitrogen utilization	-4.14	-3.96	0
YDL065C	PEX19	protein-peroxisome targeting	-2.64	-2.59	7	YPL036W	PMA2	regulation of pH	-4.58	-5.90	0
YDR142C	PEX7	protein-peroxisome targeting	-2.49	-2.64	4			regulation of transcription from Pol II			
YDR329C	PEX3	protein-peroxisome targeting	-2.96	-2.60	4	YBR049C	REB1	promoter	-2.23	-2.24	ш
YML041C	VPS71	protein-vacuolar targeting	-2.06	-2.41	15			regulation of transcription from Pot II			
YFL016C	MDJ1	proteolysis and peptidolysis	-4.29	-5.96	0	YFL024C	EPL:	uromole.	-2.73	-2.92	ш
YJL172W	CPS1	proteolysis and peptidolysis	-3.22	-2.71	0			regulation of transcription from Pot II			
YNL142W	MEP2	pseudohyphal growth	-6.62	-7.83	4	YOR244W	ESA1	promotei	-2.75	-2.59	ω
YMR316W	DIA1	pseudohyphal growth	-3.87	-3.29	0			regulation of transcription from Pot II	1		l
YDL024C	DIA3	pseudohyphal growth	-10.02	-13.61	0	YMR043W	MCM1	promoter	82.2-	-2.30	ш
YOR032C	HMS1	pseudohyphał growth	-6.77	-6.02	0		ł	regulation of transcription from Pot II		00.11	c
YER020W	GPA2	pseudohyphal growth	-3.78	-3.44	0	YGL 162W	LINS	promoter	- 14.03	-11.30	
YKL166C	TPK3	pseudohyphal growth	-2.65	-2.68	0	0110000		regulation of transcription from Pot II	, r , c	0.1	c
YKL043W	PHD1	pseudohyphal growth	-4.41	-4.64	0	YIRU1/C	ME 1 28	promoter	-0.14	-4.32	-
YMR016C	SOK2	pseudohyphal growth	-7.85	-5.94	0			regulation of transcription from Pol II	, ,	02.0	c
YKL216W	URA1	pyrimidine base biosynthesis	-3.28	-3.13	2	AJLUDOC	ZAP1	promoter	64.7-	-2.10	5
YOL081W	IRA2	RAS protein signal transduction	-2.62	-2.01	23	VNI 27RW	CAF120		-6 46	-6 11	C
YLL016W	SDC25	RAS protein signal transduction	-2.40	-2.26	0			regulation of transcription DNA-			
		re-entry into mitotic cell cycle after	3 01	2 13	c	YOR213C	SAS5		-2.21	-2.33	0
111 12200		prieronione arrest		01.7	,			regulation of transcription, DNA-			
VDP316M			-4.82	-3.68	18	YMR037C	MSN2	dependent	-2.61	-2.95	0
		recupation of carbohvdrate		2010	2	YPL223C	GRE1	response to dessication	-164.51	-200.56	5
VGI 2370	НАРЭ	5	-2.43	-2.49	0	YMR175W	SIP18	response to dessication	-67.73	-65.22	2
		requilation of carbohydrate				YMR216C	SKY1	response to drug	-3.44	-3.56	15
YKL109W	HAP4	5	-3.83	-2.52	0	YOR028C	CIN5	response to drug	-14.89	-15.13	4
YMR036C	MIH1	regulation of CDK activity	-7.31	-6.85	0	YOR031W	CRS5	response to metal ion	-18.76	-13.25	4
YOL078W	AVO1	regulation of cell growth	-2.33	-2.05	u.i	YPL059W	GRX5	response to oxidative stress	-2.10	-2.28	5
YMR068W	AV02	regulation of cell growth	-2.83	-2.95	0	YCR083W	TRX3	response to oxidative stress	-4.83	-5.64	0
						VCR021C	HSP30	response to stress	-6.94	-8.03	0

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ວ∃ ເຄີເມ		-2.12	-9.62	-4.00	-4.81	-2.85	-3.66	-2.50	-2.32	-2.71	-2.89	-4.46	2.70		-2.21		-3.76	0	-6.23	t	16.1-	000	-3.98		87.2-	00.0	90.7-	90°C-	-2.55	-4.04	-2.22	-6.45	-2.45	-110.14	-2.76	-4.71	-2.57	-2.04
TW FC		-2.14	-6.73	-3.15	-5.31	-2.65	-3.47	-2.45	-2.12	.2.27	-3.11	-4.25	-2.58		-2.51		2.94	į	-4.81		-8.34	000	-3.68	c L	0C.2-	06.7-	-0.21	-3.74	-2.01	-3.54	-2.28	-4.94	-2.14	-91.20	-2.72	-3.70	-4.50	-2.33
n ctio Fun		relornere capping	thiamin biosynthesis	thiamin biosynthesis	thiamin biosynthesis	threonine catabolism	transcription	transcription	transcription from Pol 1 promoter	transcription from Pol II promoter	transcription from Poi II promoter	transcription from Pol II promoter	transcription from Pol III promoter	transcription initiation from Pol II	promotei	transcription initiation from Pol II	promoter	transcription initiation from Pol II	ŀ	transcription initiation from Pol II		transcription initiation from Pol II		transcription initiation from Pol II	promoter transcriptional game silancing		iranslational elongation	translational initiation	transport	transport	transport	transport	transport	transport	transport	transport	transport	trehatose cataholism
e Geu		STN1	THI4	THI21	SNZ1	ICL2	SKN7	MOT3	RRN3	MED7	ROX3	SOH1	FHL1		TFA2		ccL1		HAL1		cuP2		HAL9				HEr3	UEDI	LST8	АТОЗ	ESBP6	GAP1	MCH2	STL1	PDR15	PDR18	AGP1	NTHO
Table 11A	ORF	YDR082W	YGR144W	YPL258C	YMR096W	YPR006C	YHR206W	YMR070W	YKL125W	YOL 135C	YBL093C	YGL127C	YPR104C		YKR062W		YPR025C		YPR005C		YGL166W		YOL089C				YNLU14W	YORZ04W	YNL006W	YDR384C	YNL125C	YKR039W	YKL221W	YDR536W	YDR406W	YNR070W	YCL025C	VRP0010
ţivity	suəS	0	4	ω	0	0	0	0	0	0	ш	7	2	0	0	0		0	0	ω	ιω	0	ш		9		4	19	0	0	0	0	ш	2		ш		L
0-1	бш	-2.35	-2.99	-5.21	-2.07	-3.09	-2.47	-3.73	-3.62	-7.03	-2.03	-3.70	-5.70	-4.40	-2.22	-7.87		-2.54	-6.61	-8.06	-6.55	-4.16	-3.60		-2.15		-4.91	-4.34	-2.25	-20.49	-3.07	-5.04	3.97	-6.16		-2.43		
FC	TW	-2.29	-3.53	-4.89	-2.04	-2.75	-2.06	-4.54	-3.60	-6.31	-2.31	-4.62	-5.88	-4.57	-2.32	-8.20		-3.67	-2.10	-8.09	-5.27	-5.15	-3.62		-2.04		-5.02	-3.40	-2.15	-18.05	-2.01	-2.81	-4.36	-4.10		-2.68		
uoi	Functi	response to stress	response to xenobiotic stimulus	Rho protein signal transduction	RNA elongation from Pol II promoter	RNA elongation from Pol II promoter	RNA elongation from Pol II promoter	RNA processing	RNA splicing	siderochrome transport	signal transduction	signal transduction	signal transduction	signal transduction	signal transduction	signal transduction	small GTPase mediated signal	transduction	S-methylmethionine transport	sodium ion transport	sodium ion transport	sphingolipid biosynthesis	spliceosome assembly	spore wall assembly (sensu	omyces)	spore wall assembly (sensu	Saccharomyces)	sporulation (sensu Saccharomyces)	sterol metabolism	succinate transport	sulfate assimilation	sulfate transport	sultur amirio acid nietabolism	sulfur amino acid metabolism	telomerase-dependent telomere	maintenance	telornerase-dependent telomere	
	eneð	PSR1	RDS2	RHO5	PAF1	PSH1	ELA1	REX3	BI3	FIT1	TOR2	GPB1	MTH1	TIP41	GPB2	SYG1		BAG7	MMP1	ENA2	ENA5	SUR1	CUS1		DTR1		DON1	BDF1	UGT51	SFC1	MET1	SUL1	METa	MET32		LCD1		
Table 11A	ORF	YLL010C	YPL133C	VNL180C	YBR279W	YOL054W	YNL230C	YLR107W	Q0115	YDR534C	YKL203C	YOR371C	YDR277C	YPR040W	YAL056W	YIL047C		YOR134W	YLL061W	YDR039C	YDR038C	YPL057C	YMR240C		YBR180W	_	YDR273W	YLR399C	YLR189C	YJR095W	YKR069W	YBR294W	YNL103W	YDR253C		YDR499W		

ORF		noii	L FC	Э Ц	tivitia	
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YKL141W	SDH3	rricarboxytic acid cycle	-2.62	-2.81	111	I
YLL041C	SDH2	tricarboxylic acid cycle	-3.05	-3.47	0	L
YDR148C	KGD2	tricarboxylic acid cycle	-2.52	-2.73	0	L
YDR178W	SDH4	tricarboxylic acid cycle	-2.09	-2.36	0	I
YPR001W	CIT3	tricarboxylic acid cycle	-16.21	-16.66	0	L
RPR1	RPR1	tRNA processing	-4.78	-7.20	0	I
YDR463W	STP1	tRNA splicing	-3.46	-3.63	4	J
YDL020C	RPN4	ubiquitin-dependent protein catabolism	-4.45	4.81	15	LL
YBR021W	FUR4	uracil transport	-10.81	-14.27	0	
YBL042C	FUI1	uridine transport	-9.07	-8.95	0	-J
YBR105C	VID24	vesicle-mediated transport	-4.48	-3.70	0	J
YBL033C	RIB1	vitamin B2 biosynthesis	-2.91	-3.25	7	,
YPR192W	ΑαΥ1	water transport	-16.56	-15,19	0	I
YJL221C	FSP2	NA	-4 54	-9.17	ш	ł
VKL095W	VJU2	NA	-2.38	-2.38	u	
VKR071C	DRE2	NA	-2.25	-2.63	ίIJ	I
YOR077W	RTS2	NA	3.88	-4.57	51.0	
YGL128C	CWC23	NA	-2.03	-2.26	ω	
YDL139C	SCM3	NA	2.22	- 2.14	ü.:	L
YOR353C	sog2	NA	-2.30	2.12	ιu	I
YNL036W	NCE103	NA	-4.35	-5.97	ш	L
YLR323C	CWC24	NA	-2.71	-3.32	ιIJ	
YPL024W	NCE4	NA	-2.89	-3.13	27	L
YDR334W	SWR1	NA	-4.27	-3.80	15	L
YDR482C	CWC21	NA	-5.03	-5.25	13	I
YER033C	ZRG8	NA	-2.55	-2.32	10	
YBR059C	AKL1	NA	-2.28	-2.60	9	
YOR141C	ARP8	NA	-2.53	-2.20	5	L
YLR136C	TIS11	NA	-3.20	-3.50	5	L
YJR108W	ABM1	NA	-2.04	-2.12	4	L
YKR046C	PET10	NA	-2.91	-3.63	4	
YLR099C	ICT1	NA	-2.29	-2.31	4	l
YDR505C	PSP1	AN	-2.39	-2.87	4	I
YPL221W	BOP1	NA	-2.59	-2.21	4	l
УКL076С	PSY1	NA	-2.34	-2.03	e	

Table 11A ତି ୍	otto nu 1	TW FC	ວ _] ຸງ6ພ	sitiv ity
YDR525W-A SNA2	NA	-2.23	-3.35	2
ISR1	NA	-2.51	-2.64	2
APJ1	NA	-7.02	-10.48	0
CWC27	NA	-2.52	-2.73	0
CRP1	NA	-4.84	-4.15	0
PIN3	NA	-3.36	-5.36	0
SPG1	NA	-56.63	-50.00	0
TBS1	NA	-6.86	-6.53	0
FUN19	NA	-5.14	-4.95	0
HUA1	NA	-2.51	-2.92	0
SEF1	NA	-4.12	-4.74	0
UBP13	NA	-2.20	-2.64	0
SDS23	NA	-4.27	-4.62	0
IES1	NA	-2.45	-2.42	0
NGL3	NA	-7.28	-6.50	0
SNA4	NA	-2.26	-2.80	0
AKR2	NA	-3.18	-3.70	0
YR02	NA	-10.52	-6.04	0
SAP1	NA	-2.99	-2.70	0
CRR1	NA	-2.12	-2.08	0
YTP1	NA	-6.90	-5.40	0
SLZ1	NA	-12.56	-13.53	0
HVG1	NA	-4.79	-6.32	0
DCR1	NA	-5.04	-4.84	0
ККОВ	NA	-2.32	-2.08	0
RDN37-	NA	7 66	. E 11	c
CEN12	NA	-2.44	-2.90	0
SNO4	NA	-13.14	-14.68	0
UGX2	NA	-2.68	-2.89	0
PCS60	NA	-2.36	-2.68	0
STP4	AA	-3.63	-2.49	0
GIN1	NA	-2.64	-2.18	0
ICS2	NA	-15.06	-16.77	0
PSP2	NA	-2.17	-2.26	0
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Table 11B: I

There were 60 genes in this category. Genes which had a known function are included here. The essential genes are highlighted in red.

Sensitivity	0	0	0	0	0	0	0	0	0		0	0	ш	0	0	0	0	0	0	0	4	2	9	0	5	0	0	0	0	0]
J∃ĵ₿₩		9	9	-	1	9	0	6	2		5	4	2	 	2	2	33	2	3	2	5				2	6		2		-	
	-4.51	-5.26	-4.26	-4.01	-10.31	-2.36	-2.50	-5.09	20.7-		-25.55	-3.64	-2.17	-6.51	-4.45	-9.37	-14.53	-9.77	-3.63	-4.72	-81.45	-2.28	-2.90	-2.58	-4.65	-3.09	-3.17	-2.22	-2.85	-3.72	
MT FC	-4.70	-13.63	-6.08	-9.82	-11.27	-3.73	-3.06	-5.44	-6.85		-16.90	-3.86	-2.77	-6.43	-4.04	-8.11	-10.74	17.7-	-4.35	-7.29	-77.47	-4.10	-2.03	-5.01	-4.89	-4.97	-3.07	-2.05	-2.90	-5.15	
Function	ative stress	s	s	s	s	ç	5	sporulation (sensu Saccharomyces)	sporulation (sensu Saccharomyces)	cotranslational	ng, translocation		Pol III promoter		sm	atabolism															
	response to oxidative stress	response to stress	response to stress	response to stress	response to stress	signal transduction	signal transduction	sporulation (sens	sporulation (sens	SRP-dependent	membrane targeting, translocation	transcription	transcription from Pol III promoter	transport	trehalose catabolism	vacuolar protein catabolism	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
eneð	GPX1	ALD3	ALD3	CTT1	XBP1	GPG1	SIP2	SGA1	SGA1		SSA3	GAT2	RPC37	FUN34	ATH1	PAI3	LEE1	MOH1	MPM1	OM45	PHM7	PIG2	RMD5	RTN2	RTS3	SPI1	STB3	TCM10	TOS8	UIP4	
ОКЕ	YKL026C	YMR169C	YMR169C	YGR088W	YIL101C	YGL121C	YGL208W	YIL099W	YIL099W		YBL075C	YMR136W	YKR025W	YNR002C	YPR026W	YMR174C	YPL054W	YBL049W	YJL066C	YIL136W	YOL084W	YIL045W	YDR255C	YDL204W	YGR161C	YER150W	YDR169C	YDR350C	YGL096W	YPL186C	
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Sensitivity	0	0	9	0	0	11	0	4	0	0	6	10	4	2	0	0	0	0	0	0	0	0	4	0	0	0	5	0	w	0	0
ე_ეემ	-5.06	-15.41	-2.40	-2.89	-2.18	-2.29	-3.63	-6.01	-3.27	-2.14	-2.63	-7.15	-2.44	-6.24	-4.22	-2.76	-2.26	-10.02	-56.14	-3.49	-2.60	-2.84	-2.17	-10.28	-2.65	-12.33	-6.42	-2.31	-2.30	-2.86	-3.50
MT FC	-6.91	-19.55	-2.49	-2.48	-2.38	-2.47	-3.71	-5.32	-3.16	-2.28	-2.58	-6.15	-2.17	-5.33	-4.30	-2.61	-2.39	-9.74	-57.40	-2.92	-2.49	-2.79	-2.80	-9.74	-3.30	-9.98	-5.19	-2.92	-2.59	-3.17	-4.06
Function	aerobic respiration	aerobic respiration	autophagy	autophagy	beta-alanine biosynthesis	bud site selection	carbohydrate metabolism	carnitine metabolism	cell adhesion	cell wall organization and biogenesis	ceramide metabolism	deadenylation-dependent decapping	ethanol metabolism	fatty acid beta-oxidation	fatty acid transport	fructose 2,6-bisphosphate metabolism	gluconeogenesis	glucose metabolism	hexose transport	histone deacetylation	intracellular accumulation of glycerol	intracellular signaling cascade	mitochondrial genome maintenance	NADPH regeneration	N-terminal protein myristoylation	proline catabolism	protein amino acid phosphorylation	protein amino acid phosphorylation	protein complex assembly	protein folding	protein monoubiquitination
ənəð	ISF1	MBR1	APG1	AUT7	ALD2	BUD20	AMS1	CAT2	NA	MTL1	YPC1	EDC2	ALD4	FOX2	PXA2	PFK26	FBP26	GND2	HXT5	STB2	GPD1	GIS1	PRP12	IDP3	FAA1	PUT1	KNS1	YAK1	PN01	SSE2	UBC8
ОКЕ	YMR081C	YKL093W	YGL180W	YBL078C	YMR170C	YLR074C	YGL156W	YML042W	YLR001C	YGR023W	YBR183W	YER035W	YOR374W	YKR009C	YKL188C	YIL107C	YJL155C	YGR256W	YHR096C	YMR053C	YDL022W	YDR096W	YMR302C	YNL009W	YOR317W	YLR142W	YLL019C	YJL141C	YOR145C	YBR169C	YEL012W

Table 12: Genes involved in DNA replication and repair.

is derived from SGD). While most genes did not have an appreciable fold change (induction ≥ 2 or repression <0.5), there were 25 genes that were induced (Table 12A) and 20 genes that were repressed. Table 12C includes genes that are a part of the ESR subset of the same category. A total of 133 genes were selected from the Affymetrix annotation file (which Table 12A lists several genes that are induced in WT and mgtl (except CCE, PRI2, UNG1, SIR2). Table 12C lists 20 genes that are repressed in WT and mgtl.

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Table

Mgt1 FC	-23.61	-2.58	-44.54	-3.13	-3.34	-4.35	-2.51	-1.57	-2.88		-2.26	-7.41	-3.19	-3.40	-2.29	-2.55	-2.04	-2.14	-2.27	-3.15	-1.56		U_ 1771
WTFC	-2.05	-2.23	-36.50	-4.19	-3.80	-4.21	-2.52	-2.80	-3.32		-1.89	-4.95	-3.44	-2.97	-2.28	-2.46	-2.31	-2.30	-1.93	-3.39	-2.58		101 11
Basal mgt1	-26.49	1.14	1.12	-1.01	-1.03	-1.55	1.38	1.14	-1.09		-1.18	-1.49	-1.32	1.45	-1.09	-1.07	-1.21	1.19	1.27	1.11	-1.04	nes.	
Sensit	12	0	0	11	8	5	0	4	17		6	ш	5	e	2	0	ш	шı	ш	11	0	pair ge	
Function	DNA dealkylation	DNA dependent DNA replication	DNA metabolism	DNA recombination	DNA recombination	DNA repair	DNA repair	DNA repair	DNA replication	DNA replication and	chromosome cycle	DNA replication licensing	DSB repair via NHEJ	nucleotide-excision repair	nucleotide-excision repair	nucleotide-excision repair	NER, DNA damage recognition	NER, DNA damage recognition	Table 12C: ESR subset of the DNA repair genes.				
Gene	MGT1	PES4	ADY2	SLX8	HEX3	IXR1	NSE1	RAD28	RRM3		CBF1	TAH11	YKU80	FYV6	SIR4	LRP1	TFB3	DPB11	SSL1	RAD4	RAD16	2C: ESF	
ORF	YDL200C	YFR023W	YCR010C	YER116C	YDL013W	YKL032C	YLR007W	YDR030C	YHR031C		YJR060W	YJR046W	YMR106C	YNL133C	YDR227W	YHR081W	YDR460W	YJL090C	YLR005W	YER162C	YBR114W	Table I	A DESCRIPTION OF THE OWNER OWNER OF THE OWNER OWNER OF THE OWNER

MAG1 OGG1 NUC1 NUC1 PDR48 POL1 MSH6 MSH6	Function	Sensit	Basal mgt1	WTFC	Mgt1 FC
OGG1 NUC1 DDR48 POL1 RNR1 MSH6	se-excision repair	30	-1.15	1.37	1.44
NUC1 DDR48 POL1 MSH6 MSH6	ER, AP site formation	0	-1.09	4.85	4.95
DDR48 POL1 MSH6 MSH6	VA recombination	0	-1.44	1.45	1.59
POL1 RNR1 MSH6	VA repair	0	-1.10	1.42	1.50
RNR1 MSH6	VA repair synthesis	ш	1.44	2.75	3.26
MSH6	VA replication	5	-1.13	23.03	22.30
	smatch repair	0	1.26	1.98	2.21
YJR043C POL32 nucleotide-excision repair	cleotide-excision repair	30	-1.22	1.13	1.05

Table 13: Genes that are incrementally induced in both WT and mgt1

The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60th minute to mean expression at the 10th minute. A cut-off of FC>2 (for induction) was used to select genes that have been included in this representation. There were 39 genes induced incrementally. Only 2 (out of 24 genes with known function, 8%) were essential.

			T					·													. .
0110m/031pm	2.19	3.61	3.37		4.06	2.72	12.44	3.52		4.76	2.10	77.7			2.11	3.41	4.28		2.09	6.39	7.80
0 3 	600.34	180.67	10050.09		340.60	221.79	5847.35	141.61		6225.60	431.35	1649.19			204.88	248.12	1075.80		5949.84	488.60	2048.97
0 Շ វ ըm ըvA	420.49	98.94	7827.92		288.55	214.98	5247.58	133.90		5072.30	535.09	1773.16			303.04	133.42	1081.11		4389.40	253.88	1115.98
0 1	542.11	109.99	8394.84		301.26	234.30	3790.19	126.85		4698.10	604.96	1305.01			314.79	175.24	361.38		4208.10	236.06	913.24
0£ îgm gvA	511.48	91.68	10176.58		198.48	246.65	3375.48	135.31		3752.06	614.32	1743.23			192.07	211.63	763.52		4011.68	344.48	1438.37
0S îgm gvA	463.21	100.60	6985.08		159.57	161.68	1346.56	83.82		2807.29	590.58	864.02			118.93	85.00	369.45		3689.45	154.61	569.14
01 tgm gvA	273.83	50.03	2983.0		83.79	81.64	470.02	40.23	1308.1	7	205.33	212.22			97.00	72.86	251.08	2850.6	2	76.46	262.80
0111/091/	2.82	2.48	2.17		2.10	3.41	8.57	2.57		2.11	2.13	2.49			2.57	3.05	2.60		2.40	4.73	4.13
09 TW _{BV} A	1195.9	398.6	16622.5		234.7	414.4	7118.5	209.5		3032.7	846.6	852.9			232.1	164.5	1703.6		3727.5	469.9	1244.5
03 TW ₈ vA	644.3	384.5	14098.1		243.5	267.8	5718.7	175.2		3591.1	734.8	662.2			185.7	160.6	1776.4		4050.6	397.4	1158.6
04 TW 8vA	937.6	339.1	14634.7		205.4	246.7	5185.8	170.8		3218.4	676.0	756.4			148.6	142.2	2044.6		3871.6	432.2	1305.0
05TW _{BVA}	792.4	229.8	9717.4		136.3	173.7	3511.9	145.3		2417.8	267.4	483.8			113.0	99.96	1313.1		2533.5	280.2	976.3
0STW _{BV} A	729.3	250.2	11532.1		126.7	197.8	2239.6	117.9		2484.8	324.8	517.8			109.8	83.6	945.9		2195.4	211.4	764.1
01TW gvA	423.5	160.7	7650.0		111.9	121.4	830.7	81.5		1440.2	398.4	342.4			90.3	54.0	655.0		1552.6	99.4	301.4
<u>V</u> iiviisn92	10	e	-5		0	0	0	0		0	0	0			0	0	0		0	0	0
Functional group	aldehyde metabolism	aldehyde metabolism	aldehyde metabolism	amino acid	biosynthesis	arginine metabolism	cell cycle arrest	chitin biosynthesis		DNA replication	glucose metabolism	glutamate biosynthesis	mitochondrion	organization and	biogenesis	ornithine metabolism	phosphate transport		salinity response	thiamin biosynthesis	thiamin biosynthesis
Gene	AAD4	AAD6	NA		AN	ARG80	HUG1	SHC1		RNR3	MIG2	CIT2			NCA3	ARG3	PHO89		GCY1	SN01	SNZ1
Yname	YDL243C	YFL056C	YFL057C		YHR033W	YMR042W	YML058w-a	YER096W		YIL066C	YGL209W	YCR005C			YJL116C	YJL088W	YBR296C		YOR120W	YMR095C	YMR096W

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Table 13B: ESR sub
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0 t 1 gm/091 gm	7.7.7	3.88	4.85	3.51
0 3 	499.22	2134.98	253.60	1056.03
0č tpm pvA	575.23	1678.78	252.49	936.17
04 igm gvA	357.24	1755.88	247.98	720.33
0£ tgm pvA	625.14	1714.70	288.23	493.51
02 tgm pvA	274.66	1064.81	154.91	559.44
0f tgm gvA	64.27	549.72	52.30	301.14
0 [.1m/091m	3.79	2.47	2.55	2.36
09 TW _{BV} A	407.5	2083.2	216.4	333.2
03 TW _{8v} A	374.8	1853.3	209.3	308.1
04 TW ₈ vA	307.1	1460.6	176.3	394.6
0 ETW 	231.9	1152.4	101.7	269.8
02TW gvA	169.1	1080.3	144.1	215.4
01TW gvA	107.6	843.6	84.8	0 141.1
Sensitivity	0	5	8	0
Functional group	NA	NA	NA	NA
Gene	BOP2	RTS3	AN	AN
Yname	YLR267W	YGR161C	YBL054W	YDL222C

Table 14 Genes that are incrementally induced specifically in WT

The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60th minute to mean expression at the 10th minute. A cut-off of FC>2 (for induction) was used to select genes that have been included in this representation. There were 61 genes in this category. Genes that have a known function are indicated here. The genes that are essential are highlighted in red.

Symbol Functional group WTWTO Vability WT10 WT20 WT30 CYB2 electron transport 0.07 0 99.13 203.26 238.41 NDE2 ethanol fermentation 0.07 0 144.10 184.81 238.13 252.13 NDE2 ethanol fermentation 0.09 0 161.05 238.13 255.13 255.13 MIG1 glucose metabolism 0.09 0 161.05 238.13 255.13 255.13 MIG1 glucose metabolism 0.01 0.21 7 126.07 133.19 156.80 MIG1 glucose metabolism 0.22 615.69 791.77 74.285 MMT1 iron iron homeostasis 0.28 4.01 7 177.1.32 277.167 2488.43 MMT1 iron iron homeostasis 0.28 0 217.56 190.34 MMT1 iron iron homeostasis 0.28 4 177.52 277.67 2488.43 MMT1 iron iron		Gene		Av	MMS,	Avg	Avg	Avg	Avg	Avg	Avg	
CYB2 electron transport 0.07 0 99.13 203.26 238.41 NDE2 ethanol fermentation 0.04 0 144.10 184.81 238.17 NDE2 ethanol fermentation 0.04 0 144.10 184.81 238.17 NDE2 fatty acid metabolism 0.09 0 161.05 238.13 252.13 MIG1 glucose metabolism 0.01 0.1105 238.13 252.13 255.13 MIG1 glucostatis 0.024 0 281.74 428.32 460.85 GDH3 glutathione metabolism 0.01 0.21 7 1771.32 2721.67 248.43 MA glyoxylate cycle 0.22 261.66 791.77 72.86 460.85 MMT1 iron iron homeostasis 0.22 215.66 791.77 72.86 280.4 MMT1 iron iron homeostasis 0.22 261.56 791.77 742.85 MMT1 iron iron homeostasis 0.206 277.56	Yname	Symbol	Functional group	WT/WT0	viability	WT10	WT20	WT30	WT 40	WT 50	WT 60	WT60/WT10
NDE2 ethanol fermentation 0.04 0 144.10 184.81 238.17 CRC1 fatty acid metabolism 0.09 0 161.05 238.13 252.13 MIG1 glucose metabolism 0.09 0 161.05 238.13 252.13 MIG1 glucose metabolism 0.04 0 281.74 428.32 460.85 GDH3 glutamate biosynthesis 0.04 0 281.74 428.32 460.85 GT22 glutathione metabolism 0.01 0 281.74 428.32 460.85 MMT gluovalite cycle 0.22 0.156.71 7 742.85 MMT1 iron ion homeostasis 0.28 0 271.52 280.04 MMT1 iron ion homeostasis 0.28 0 271.52 280.04 MMT1 iron ion homeostasis 0.28 0 271.52 210.68 MMT1 iron ion homeostasis 0.28 4.33 277.96 210.68 SU2 ASE1	YML054C	CYB2	electron transport	0.07	0	99.13	203.26	238.41	238.78	256.01	220.98	2.23
CRC1 faty acid metabolism 0.09 0 161.05 238.13 252.13 MIG1 glucose metabolism 0.21 7 126.07 133.19 156.80 MIG1 glucose metabolism 0.21 7 126.07 133.19 156.80 GDH3 glutamate biosynthesis 0.04 0 281.74 428.32 460.85 MM1 gluxovytate cycle 0.22 615.69 791.77 742.85 MM11 iron ion homeostasis 0.98 0 206.71 257.03 254.06 MM11 iron ion homeostasis 0.99 0 206.71 257.03 254.06 MM11 iron ion homeostasis 0.99 0 206.71 257.03 254.06 MM11 iron ion homeostasis 0.99 0 206.71 257.03 254.06 MM11 iron ion homeostasis 0.99 0 206.71 250.08 379.03 MM11 iron ion homeostasis 0.206 0 217.52 32	YDL085W	NDE2	ethanol fermentation	0.04	0	144.10	184.81	238.17	265.54	269.26	325.05	2.26
MIG1 glucametabolism 0.21 7 126.07 133.19 156.80 GDH3 glucamate biosynthesis 0.04 0 281.74 428.32 460.85 GT72 glucathione metabolism 4.01 7 1771.32 2721.67 2488.43 NA glyoxylate cycle 0.22 2 615.69 791.77 742.85 NA glyoxylate cycle 0.22 2 615.69 791.77 742.85 MMT1 iron ion homeostasis 0.22 2 615.69 791.77 742.85 MMT1 iron ion homeostasis 0.28 4 175.28 328.19 288.04 MMT1 iron ion homeostasis 0.90 0 206.71 257.03 254.06 MMT1 iron ion homeostasis 0.28 4.33 0 271.56 1197.71 1083.34 MMT1 iron sulfur cluster assembly 0.90 0 1022.65 1197.71 1083.34 MAE1 pyruvate metabolism 1.	YOR100C	CRC1	fatty acid metabolism	0.09	0	161.05	238.13	252.13	339.38	311.16	394.92	2.45
GDH3 glutamate biosynthesis 0.04 0 281.74 428.32 460.85 GTT2 glutathione metabolism 4.01 7 1771.32 2721.67 2488.43 NA glyoxylate cycle 0.22 2 615.69 791.77 742.85 NMT1 iron ion homeostasis 0.98 0 206.71 257.03 254.06 MMT1 iron ion homeostasis 0.90 0 271.52 328.19 298.04 NMT1 iron ion homeostasis 0.90 0 271.52 328.06 310.93 NMT1 iron ion homeostasis 0.90 0 271.56 1197.71 1083.34 MMT iron ion homeostasis 0.92 4.24 0 271.56 210.68 ASE1 mitotic anaphase B 0.20 0.20 4 175.89 310.93 ASE1 metabolism 1.76 3.33 2 4 351.76 283.04 MAE1 pyruvate metabolism 1.76 4	YGL035C	MIG1	glucose metabolism	0.21	7	126.07	133.19	156.80	218.41	251.11	298.64	2.37
GTT2 glutathione metabolism 4.01 7 1771.32 2721.67 2488.43 NA glyoxylate cycle 0.22 2 615.69 791.77 742.85 HMX1 iron ion homeostasis 0.98 0 206.71 257.03 254.06 MMT1 iron ion homeostasis 0.98 0 271.52 328.19 298.04 MMT1 iron ion homeostasis 0.90 0 271.52 328.19 298.04 MMT1 iron ion homeostasis 0.90 0 271.52 310.92 281.06 MMT1 iron sulfur cluster assembly 0.90 0 271.52 310.58 310.58 ASE1 metabolism 4.33 0 259.66 377.95 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1083.34 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 182.08 MAE1 pyruvate metabolism 1.23 3.33.06 317.95 310.93 <td>YAL062W</td> <td>GDH3</td> <td>glutamate biosynthesis</td> <td>0.04</td> <td>0</td> <td>281.74</td> <td>428.32</td> <td>460.85</td> <td>472.53</td> <td>535.90</td> <td>573.41</td> <td>2.04</td>	YAL062W	GDH3	glutamate biosynthesis	0.04	0	281.74	428.32	460.85	472.53	535.90	573.41	2.04
NA glyoxylate cycle 0.22 2 615.69 791.77 742.85 HMX1 iron ion homeostasis 0.98 0 206.71 257.03 254.06 MMT1 iron ion homeostasis 0.98 0 207.152 328.19 298.04 MMT1 iron ion homeostasis 0.90 0 271.56 3197.71 1083.34 MMT1 iron ion homeostasis 0.90 0 271.56 3197.71 1083.34 ASE1 mitotic anaphase B 0.92 0.90 0 271.56 310.93 ASE1 mitotic anaphase B 0.202 0.2 21.565 310.33 ASE1 mitotic anaphase B 0.22 21.56 310.33 310.33 ASE1 metabolism 1.76 4 377.95 310.93 310.33 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 182.06 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 182.03	YLL060C	GTT2	glutathione metabolism	4.01	7	1771.32	2721.67	2488.43	2979.29	2854.34	4535.04	2.56
HMX1 iron ion homeostasis 0.98 0 267.03 254.06 MMT1 iron ion homeostasis 4.24 0 271.52 328.19 298.04 MMT1 iron-sulfur cluster assembly 0.90 0 1022.65 1197.71 1083.34 ASE1 mitotic anaphase B 0.20 0 1022.65 1197.71 1083.34 ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 ASE1 mitotic anaphase B 0.28 6 4 377.35 310.33 ASE1 mitotic anaphase B 0.28 0.28 6 126.68 106.33 ASE1 metabolism 0.28 4 375.96 377.35 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 MAI1 response to toxin 3.32 2 1860.31 2924.27	YFL030W	NA	glyoxylate cycle	0.22	2	615.69	791.77	742.85	1090.96	1076.14	1343.21	2.18
MMT1 iron ion homeostasis 4.24 0 271.52 328.19 298.04 ISU2 iron-sulfur cluster assembly 0.90 0 1022.65 1197.71 1083.34 ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 ASE1 megative regulation of fatty acid 4.33 0 259.66 377.95 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 RIO1 S phase of mitotic cell cycle 1.03 3.32 2 1860.31 2924.27 2831.04 NOG1 S phase of mitotic cell cycle 1.03 7.35 333.06 355.78 NOG2 NA NG	YLR205C	HMX1	iron ion homeostasis	0.98	0	206.71	257.03	254.06	372.90	324.28	455.81	2.21
ISU2 iron-suffur cluster assembly 0.90 0 1022.65 1197.71 108.334 ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 FRM2 negative regulation of fatty acid 4.33 0 259.66 377.95 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 ME1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 RIO1 S phase of motion 3.32 2 1860.31 2924.27 2831.04 RIO1 S phase of motion acid metabolism 1.23 0 86.10 105.89 102.16 NOG1 S phase of motion acid metabolism 1.23 3 1935.66 126.31 NOG1 NA NA 1.23 3 3 3 102.16 NOG2 NA 1.25 -5 2 <td>YMR177W</td> <td>MMT1</td> <td>iron ion homeostasis</td> <td>4.24</td> <td>0</td> <td>271.52</td> <td>328.19</td> <td>298.04</td> <td>300.36</td> <td>341.23</td> <td>581.03</td> <td>2.14</td>	YMR177W	MMT1	iron ion homeostasis	4.24	0	271.52	328.19	298.04	300.36	341.23	581.03	2.14
ASE1 mitotic anaphase B 0.28 4 175.89 217.26 210.68 10.68 10.68 10.68 10.68 10.68 10.68 10.68 10.68 10.68 10.68 10.68 217.26 210.68 217.35 217.35 210.33 217.35 310.33 10.33 10.31 295.06 317.35 310.33 10.33 10.33 217.35 310.33 310.33 217.35 310.33 210.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 20.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 2924.27 2831.04 10.31 293.104 10.31 293.104 10.31 293.104 10.31 293.104 10.31 293.104 10.31 293.104 10.31 200.31 <td>YOR226C</td> <td>ISU2</td> <td></td> <td>06.0</td> <td>0</td> <td>1022.65</td> <td>1197.71</td> <td>1083.34</td> <td>1132.19</td> <td>1165.73</td> <td>2268.71</td> <td>2.22</td>	YOR226C	ISU2		06.0	0	1022.65	1197.71	1083.34	1132.19	1165.73	2268.71	2.22
negative regulation of fatty acid negative regulation of fatty acid 1.33 0 259.66 377.95 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 FLR1 response to toxin 3.32 2 1860.31 294.27 2831.04 RIO1 S phase of mitotic cell cycle 1.03 5 79.87 135.66 126.31 NOG ⁺ NA 1.25 -5 231.33 333.06 335.78 NOG ⁺ NA 1.26 -5 231.33 333.06 335.78 NIT1 NA 1.26 -5 231.33 333.06 335.78 OYE3 NA 2.43 4 2957.80 439.72 490.99	YOR058C	ASE1		0.28	4	175.89	217.26	210.68	202.42	194.98	381.23	2.17
FRM2 metabolism 4.33 0 259.66 377.95 310.93 MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 FLR1 response to toxin 3.32 2 1860.31 294.47 2831.04 RIO1 S phase of mitotic cell cycle 1.03 5 79.87 135.66 126.31 NIO1 S phase of mitotic cell cycle 1.03 5 79.87 135.66 126.31 NOG* NA 1.23 0 86.10 105.89 102.16 NOG* NA 1.25 -5 231.35 333.06 335.78 NIT1 NA 1.25 -5 231.35 333.06 335.78 OYE3 NA 3.12 4 2957.80 439.72 4090.99 OYE3 NA 2.43 4 2957.80 4399.72 4090.99	YCL026C-		regulation of fatty									
MAE1 pyruvate metabolism 1.76 4 951.71 1629.09 1822.08 FLR1 response to toxin 3.32 2 1860.31 2924.27 2831.04 RIO1 S pnase of mitotic cell cycle 1.03 -5 79.87 135.66 126.31 NIO1 S pnase of mitotic cell cycle 1.03 -5 79.87 135.66 126.31 NOG1 S pnase of mitotic cell cycle 1.23 0 86.10 105.89 102.16 NOG1 NA 1.23 0 86.10 135.66 126.31 NOG2 NA 1.23 0 73.13 333.06 335.78 NOG3 NA 3.13 0 751.69 131.47 1385.40 OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DTA NA 0 751.69 1703.90 1703.90 1703.90	A	FRM2	metabolism	4.33	0	259.66	377.95	310.93	349.26	287.34	568.32	2.19
FLR1 response to toxin 3.32 2 1860.31 2924.27 2831.04 RIO1 S phase of mutotic cell cycle 1.03 -5 79.87 135.66 126.31 SDL1 Serine family amino acid metabolism 1.03 -5 79.87 135.66 126.31 NOG ⁺ NA 1.23 0 86.10 105.89 102.16 NOG ⁺ NA 1.25 -5 231.35 333.06 335.78 NOG ⁺ NA 3.13 0 751.69 1311.47 1385.40 OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DET10 NA 0 74 4 703.07 1703.90	YKL029C	MAE1	pyruvate metabolism	1.76	4	951.71	1629.09	1822.08	1584.07	1886.66	2290.81	2.41
RIO1 S phase of mutotic cell cycle 1.03 5 79.87 135.66 126.31 SDL1 serine family amino acid metabolism 1.23 0 86.10 105.89 102.16 NOG5 NA 1.25 -5 231.35 333.06 335.78 NIT1 NA 3.13 0 751.69 1311.47 1385.40 OYE3 NA 2.43 4 2957.80 439.72 4090.99 DET10 NA 0.34 4 2957.80 1703.97 1703.90	YBR008C	FLR1	response to toxin	3.32	2	1860.31	2924.27	2831.04	4072.04	3361.60	6093.18	3.28
SDL1 serine family amino acid metabolism 1.23 0 86.10 105.89 102.16 NOG* NA 1.25 -5 231.33 333.06 335.78 NOG* NA 1.25 -5 231.33 333.06 335.78 NIT1 NA 3.13 0 751.69 1311.47 1385.40 OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DETION NA 0 74 4 2967.80 1303.97 1703.99	YOR119C	RIO1		1.03	ιç	79.87	135.66	126.31	166.09	132.27	168.18	2.11
NOG ⁺ NA 1.25 -5 231.35 333.06 335.78 NIT1 NA 3.13 0 751.69 1311.47 1385.40 NIT1 NA 3.13 0 751.69 1311.47 1385.40 OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DET10 NA 0.34 4 2967.80 1303.97 1703.99	YIL168W	SDL1	serine family amino acid metabolism	1.23	0	86.10	105.89	102.16	138.24	120.22	219.88	2.55
NIT1 NA 3.13 0 751.69 1311.47 1385.40 OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DET40 NA 0.34 4 2967.01 1303.97 1703.96	YPL093W	NOG:	NA	1.25	÷	231.33	333.06	335.78	359.10	399.49	486.67	2.10
OYE3 NA 2.43 4 2957.80 4349.72 4090.99 DET10 NA 0.34 4 266.70 1303.97 1703.99	YIL164C	NIT1	NA	3.13	0	751.69	1311.47	1385.40	1584.14	1600.41	1617.29	2.15
DET10 NA 0.34 4 960.20 1303.97 1703.99	YPL171C	OYE3	NA	2.43	4	2957.80	4349.72	4090.99	6722.06	6444.98	7782.61	2.63
	YKR046C	PET10	NA	0.34	4	960.20	1303.97	1703.99	1782.36	1939.97	2113.00	2.20

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	Gene		Av	MMS.	Ava	Ava	Ava	Ava	Ava	Ava	
Yname	Symbol	Functional group	WT/WT0	viability	WT10	WT20	WT30		WT 50	>	WT60/WT10
YLR074C BUD20	BUD20	bud site selection	0.41	11	268.72	441.26	400.32	416.72	458.51	591.42	2.20
YKR076W	ECM4	cell wall organization and biogenesis	0.65	2	740.90	850.44	1087.85	850.44 1087.85 1278.07 1313.60	1313.60	1881.47	2.54
YNR002C FUN34	FUN34	transport	0.16	0	391.12	457.98	594.61	935.55	839.85	993.69	2.54
YFL014W HSP12	HSP12	response to dessication	0.43	4	3372.85	6607.11	7848.80	6607.11 7848.80 8372.66 8140.08	8140.08	8758.40	2.60

Table 14B ESR subset of genes that are induced specifically in WT

Table 15: Genes that are incrementally induced specifically in mgt1

cut-off of FC>2 (for induction) was used to select genes that have been included in this representation. There were 210 genes in this category. Genes that are not a part of the ESR are included in Table 15A. The genes that are incrementally induced specifically in *mgt1* but are a part of The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60th minute to mean expression at the 10th minute. A the ESR are included in table 15B

Table 15A

				Avg	Avg	Avg	Avg	Avg	Avg	
	Gene			mgt	mgt	mgt	mgt	mgt	mgt	
Yname	Symbol	Functional group	Sensit	10	20	30	40	50	60	mgt60/mgt10
		adaptation to pheromone during conjugation with cellular								
YLR452C	SST2	fusion	0	535.84	1189.53	1061.18	1368.06	898.91	1108.25	2.07
YGL032C	AGA2	agglutination during conjugation with cellular fusion	0	1156.57	1572.32	1600.66	2038.59	1719.50	2442.50	2.11
YER024W	YAT2	alcohol metabolism	0	176.02	321.47	508.51	304.97	405.29	422.34	2.40
YDR309C	GIC2	axial budding	2	447.75	473.49	703.90	839.48	710.11	1012.98	2.26
YKR063C	LAS1	bud growth	ŵ	108.40	165.29	239.29	199.82	227.87	226.67	2.09
YDR006C	SOK1	cAMP-mediated signaling	0	223.62	276.11	430.32	437.23	367.69	478.14	2.14
YIL046W	MET30	cell cycle	ιç	135.63	181.78	206.90	239.95	225.18	283.71	2.09
YGR032W	GSC2	cell wall organization and biogenesis	0	705.35	958.25	1177.00	1324.83	1623.21	1697.65	2.41
YGL178W_ex2	MPT5	cell wall organization and biogenesis	0	949.12	1710.98	1678.09	1835.80	1947.02	2006.64	2.11
		cellular morphogenesis during conjugation with cellular								
YDL223C	HBT1	fusion	0	222.27	415.99	402.08	373.65	476.12	503.29	2.26
YPL156C	PRM4	conjugation with cellular fusion	0	273.84	450.16	567.68	554.08	516.00	554.65	2.03
YIL117C	PRM5	conjugation with cellular fusion	0	1644.14	3106.99	3972.19	2667.34	2895.99	3509.93	2.13
YDR030C	RAD28	DNA repair	4	172.86	286.26	412.05	371.45	413.01	527.46	3.05
YFR028C	CDC14	exit from mitosis	ц.	186.25	307.10	282.50	358.03	339.11	381.43	2.05
YJL098W	SAP185	G1S transition of mitotic cell cycle	0	95.92	198.27	270.67	195.22	205.64	218.20	2.27
YKR099W	BAS1	histidine biosynthesis	0	61.87	123.49	228.52	154.09	148.25	152.60	2.47
YHL040C	ARN1	iron-siderochrome transport	0	173.35	442.71	559.06	394.39	356.55	362.35	2.09
YPL135W	ISU1	iron-sulfur cluster assembly	2	811.84	1207.80	1567.37	1583.01	1343.19	1657.97	2.04
YIL026C	IRR1	mitotic sister chromatid conesion	-2	77.52	158.40	178.61	180.67	173.41	188.15	2.43
YDR021W	FAL1	ImRNA splicing	-5	26.46	34.08	58.12	61.11	49.26	60.75	2.30
LSR1_0	LSR1	mRNA splicing	0	293.43	568.81	494.57	551.71	547.21	639.08	2.18
YNR053C_ex1	NOG2	mRNA splicing	0	38.26	48.71	78.62	101.24	79.94	84.24	2.20
YNR053C_ex2	NOG2	mRNA splicing	0	355.63	422.71	886.09	906.71	662.12	752.72	2.12

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				Avg	Avg	Avg	Avg	Avg	Avg	
	Gene			mgt	mgt	mgt	mgt	mgt	mgt	
Yname	Symbol	Functional group	Sensit	10	20	30	40	50	60	mgt60/mgt10
YML113W	DAT1	negative regulation of transcription from Pol II promoter	0	103.27	263.23	455.26	434.78	273.80	286.74	2.78
YPR175W	DPB2	hucleotide-excision repair	ę.	161.01	255.32	454.76	424.68	354.83	370.46	2.30
YNL279W	PRM1	plasma membrane fusion	0	123.52	215.43	210.81	310.69	257.61	352.05	2.85
YGR138C	TPO2	polyamine transport	0	212.01	269.46	386.15	577.69	545.78	623.60	2.94
YOR078W	BUD21	processing of 20S pre-rRNA	0	128.72	241.50	350.43	335.94	263.00	306.34	2.38
YHR205W	SCH9	protein amino acid phosphorylation	-5	238.67	413.50	455.03	476.89	471.06	517.77	2.17
YPL026C	SKS1	protein amino acid phosphorylation	0	65.88	128.16	185.92	200.14	113.32	135.20	2.05
YOR056C	NOB1	protein complex assembly	÷	213.54	326.29	507.79	534.51	532.25	672.08	3.15
YGR239C	PEX21	protein-peroxisome targeting	0	16.77	101.48	151.15	131.93	122.36	192.95	2.48
YHR187W	IK1	requiation of transcription from Poi II promoter	ιĢ	68.79	129.86	150.29	117.18	140.67	144.32	2.10
YHR023W	MY01	response to osmotic stress	-5	62.02	136.94	151.44	122.15	138.73	131 45	2.12
YHR178W	STB5	response to xenobiotic stimulus	18	80.82	138.28	149.74	150.48	154.32	179.96	2.23
YGL145W	TIP20	retrograde (Golgi to ER) transport	ų	66.37	111.36	*21.10	112.12	125.64	138.08	2.08
YGR159C	NSR1	ribosomal small subunit assembly and maintenance	2	718.77	1014.86	1492.63	1679.17	1411.31	1449.98	2.02
YHR085W	P14	iRNA processing	ċ	46.36	79.40	149.02	118.70	93.36	103.27	2.23
YOL144W	NOP8	rRNA processing	\$- -2	127.31	196.94	273.96	258.70	260.83	264.37	2.08
YBR257W	POP4	rRNA processing	÷	85.36	109.57	178.43	162.65	151.04	183.74	2.15
YOL010W	RCL1	rRNA processing	-j2	60.09	89.39	187.41	176.05	125.07	174.79	2.91
YGR055W	MUP1	sulfur amino acid transport	0	364.89	563.47	983.59	976.29	779.42	1075.34	2.95
YHR124W	NDT80	transcription	0	67.34	107.72	142.09	121.87	123.07	143.62	2.13
YOR337W	TEA1	transcription	0	136.41	226.25	376.04	367.70	263.19	323.40	2.37
YKL125W	RRN3	transcription from Pol I promoter	ιç	131.44	181.94	280.60	287 73	237.07	284.92	2.17
YER028C	MIG3	transcription initiation	0	144.30	312.65	355.47	308.67	379.82	407.84	2.83
YPL202C	AFT2	transcription initiation from Pol II promoter	0	225.87	437.58	518.65	471.65	448.07	543.32	2.41
YGL243W	TAD1	tRNA modification	0	242.44	443.35	639.68	475.38	528.97	598.55	2.47
YNL077W	APJ1	NA	0	72.90	81.46	90.50	97.50	131.96	158.21	2.17
YPL250C	ICY2	NA	0	489.29	1161.48	2085.00	1376.20	1456.37	2160.60	4.42
YHR156C	LIN1	NA	0	76.30	124.46	142.05	128.88	131.00	171.54	2.25

	Gene					Avg	Avg	Avg	Avg	
Yname	Symbol	Functional group	Sensit	Avg mgt 10	Avg mgt 20	mgt 30	mgt 40	mgt 50	mgt 60	mgt60/mgt10
YHR169W	DBP8	35S primary transcript processing	ą	38.86	10.14	168.25	174.38	143.42	139.09	2.02
YGR158C	MTR3	mRNA catabolism	φ	121.55	275.23	279.80	280.19	265.57	260.10	2.14
YLR129W	DIP2	processing of 20S pre-rRNA	ę	233.64	464.57	633.84	626.48	553.49	515.36	2.21
YLR222C	UTP13	processing of 20S pre-rRNA	-5	139.65	258.53	430.32	384.16	345.47	377.06	2.70
YML093W	UTP14	processing of 20S pre-rRNA	ę	127.02	219.35	356.51	298.95	267.95	276.32	2.18
YMR093W	UTP15	processing of 20S pre-rRNA	ŝ	83.62	144.76	275.57	246.58	150.70	182.60	2.18
YDR398W	UTP5	processing of 20S pre-rRNA	φ	231.09	276.21	420.64	389.90	371.88	466.21	2.02
YDR449C	UTP6	processing of 20S pre-rRNA	ę	41.81	64.58	120.76	104.82	86.62	103.70	2.48
YER082C	UTP7	processing of 20S pre-rRNA	-5	87.69	116.60	176.64	140.72	155.32	176.84	2.02
YHR196W	UTP9	processing of 20S pre-rRNA	-ç-	47,43	84.42	137.08	148.50	96.77	122.52	2.58
YOR145C	PN01	protein complex assembly	-2	274.33	352.01	624.30	600.34	632.53	647.92	2.36
		ribosomal large subunit assembly and								
YHR088W	RPF1	maintenance	ې	73.38	153.45	235.87	189.68	240.99	293.72	4.00
YNL308C	KRI	ribosome biogenesis	÷	242.25	150.99	555.31	527.63	497.87	571.39	2.36
YD1_060W	TSR1	ribosome biogenesis and assembly	÷	425.12	621.10	959.29	937.47	884.10	937.44	2.21
YHR148W	IMP3	rRNA modification	ų.	81.45	117 42	149.50	137.99	168.08	166.53	2.04
YLL011W	SOF1	rRNA modification	ų	84.65	171.27	349.76	329.96	213.21	250.61	2.96
YHR197W	IP12	NA	ŵ	208.42	302.67	431.26	404.92	445.96	438.12	2.10
YNL182C	ମସ	NA	ιċ	46.32	69.30	110.25	110.04	92.08	33.80	2.03
YGL248W	PDE1	cAMP-mediated signaling	0	857.73	1515.46	1984.02	1475.29	1777.83	1938.20	2.26
YGL156W	AMS1	carbohydrate metabolism	0	267.04	363.48	458.83	396.14	487.11	593.61	2.22
YHR096C	HXT5	hexose transport	0	128.78	224.38	273.32	255.55	278.39	296.70	2.30
		ribosomal large subunit assembly and								
YGL078C	DBP3	maintenance	0	177.58	277.67	375.11	321.56	350.27	358.39	2.02
YKR056W	TRM2	tRNA modification	0	153.85	219.86	375.37	299.41	345.23	367.08	2.39
YDR496C	PUF6	NA	0	101.08	150.90	240.93	207.74	219.70	249.32	2.47
YGL180W	APG1	autophagy	9	219.66	365.16	347.27	310.44	334.26	443.67	2.02
VKD004C	7007	ribosomal large subunit assembly and	y	48.51	R5 74	138 75	143.84	99.38	117 27	2 42
2420441	UDL	Level antimite anomable.	>	5				20100		
VHPOGRW	SSE1	ribosomal large subunit assembly and	ÿ	47.26	124.74	244.82	242.50	148.78	190.84	4.04
	- 50		,		- - -	->				

Table 15B: ESR subset of genes that are incrementally mgt1

Table 16: Genes that incrementally repressed in both WT and mgtl

minute. A cut-off of FC<0.5 (for repression) was used to select genes that have been included in this representation. There are 35 genes The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60th minute to mean expression at the 10th in this category. Genes included in Table 16B are the ones that are in this category but are a part of the ESR.

Table 16A

										·····		·····
0 է քըա/0ծքըա	0.49	0.24	0.37	0.44	0.37	0.15	0.30	0.37	0.31	0.35	0.39	0.41
01TW/09TW	0.44	0.24	0.40	0.47	0.40	0.24	0.44	0.45	0.47	0.49	0.30	0.44
0ðigm gvA	231.3	32.0	54.9	113.3	15.0	284.9	328.0	354.7	221.2	123.8	54.0	111.6
0č tgm vA	236.6	28.5	71.3	152.8	19.4	481.7	462.3	449.0	319.0	129.7	56.2	172.6
04igm vA	303.3	50.6	110.2	150.9	24.5	514.0	511.1	481.8	354.8	144.8	74.6	154.1
0£ tgm vA	346.6	6.67	9.69	136.3	31.7	915.9	768.7	873.9	418.5	123.5	93.6	118.0
0S tgm vA	416.2	84.7	126.2	150.3	40.1	####	852.4	939.4	389.5	153.7	134.8	194.0
01 tgm vA	473.4	133.2	149.2	255.0	40.7	1840.0	1094.5	949.0	717.7	357.5	136.9	271.1
0tgm gvA	185.3	66.4	88.4	188.1	7.1.7	875.7	376.5	566.5	271.4	371.9	48.6	35.9
09TW vA	206.9	30.1	35.0	109.0	17.9	421.9	473.1	267.3	297.0	253.5	28.0	59.0
02TW vA	213.4	28.1	42.8	108.1	16.8	631.9	453.6	302.5	336.2	288.9	36.4	79.7
04TW vA	253.5	30.2	42.5	104.3	17.8	626.8	506.4	360.2	386.2	220.7	35.8	88.6
0ETW vA	371.1	77.5	57.3	162.5	27.0	1280.5	930.7	558.6	726.1	376.1	73.0	112.4
02 TW vA	429.7	93.0	72.4	191.4	30.3	1266.2	1032.4	555.4	510.7	369.5	81.8	122.4
01TWVA	467.3	123.5	87.7	233.9	45.3	1740.8	1064.6	600.6	626.5	518.5	94.7	134.8
0TWvA	177.6	52.4	87.4	175.2	54.3	1310.6	423.6	645.3	242.9	381.7	39.7	34.7
Sensitivity	0	0	0	0	0	0	0	0	0	0	0	0
Function	nul	cytokinesis, completion of separation	cell cycle arrest	chromatin assembly disassembly	cell cycle	cell wall organization and biogenesis	NA	NA	protein biosynthesis	methionine metabolism	cytokinesis, completion of separation	telomerase-dependent telomere maintenance
ອບອອ	AMN1	DSE4	FAR1	HTB2	PCL9	PIR1	PRY3	PST1	RPS22B	SAM2	SCW11	тьс1
ORF	YBR158W	YNR067C	YJL157C	YBL002W	YDL179W	YKL164C	YJL078C	YDR055W	YLR367W_ex1	YDR502C	YGL028C	TLC1_0

Table 16B: ESR subset of genes that are repressed in both WT and mgt1

0110m/0010m		0.36
01TW/09TW		0.48
0ðigm gvA		261.7
0č tgm vA		334.4
0 1 30m vA		384.2
0£ 1gm vA		501.5
0S tpm vA		633.9
01 igm vA		734.2
0tgm gvA		166.6
09TW vA		398.0
08TW vA		387.8
04TW vA		410.3
06TW vA		734.0
02 TW vA		747.8
01TWvA		822.5
0TWvA		144.3
Sensitivity		0
noitonuA	and	
	organization	
	mitochondrion	biogenesis
eneට		SUN4
ОКЕ		YNL066W

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Table 17: Genes that are incrementally repressed specifically in mgt1

The net fold-change (FC) over time, was calculated from ratio of mean expression at the 60^{th} minute to mean expression at the 10^{th} minute. A cut-off of FC<0.5 (for repression) was used to select genes that have been included in this representation. There are 118 genes in this category. The genes that are in this category and are a part of ESR are included in table 17B.

					-														
0110m/0310m	0.42	0.48	0.45	0.39	0.36	0.49	0.43	0.40	0.38	0.46	0.49	0.35	0.44	0.48	0.46	0.48	0.34	0.37	0.48
0ðigm gvA	166.0	265.8	28.4	34.0	59.3	232.4	230.7	20.1	319.6	465.1	159.0	535.0	117.4	115.3	68.0	1922.5	349.8	114.7	566.3
0č jpm vA	214.4	316.5	33.6	36.6	51.2	290.9	226.7	28.0	313.5	428.5	204.8	671.7	126.2	128.4	71.9	2329.0	414.8	125.6	769.5
04jpm vA	195.5	326.1	54.4	50.7	58.0	177.0	231.9	24.3	408.6	406.3	190.2	438.9	151.0	130.5	66.3	1828.0	359.0	119.1	753.6
0£ tgm vA	192.8	270.8	46.1	46.5	54.6	405.0	257.9	21.7	374.6	419.4	176.3	467.4	153.8	102.4	75.3	1505.2	316.5	107.7	662.9
02 tgm vA	202.0	335.1	44.5	50.1	81.3	460.9	258.9	36.6	442.2	490.2	236.7	978.6	169.3	160.9	89.4	1477.4	478.7	165.6	883.7
01 tem vA	390.6	549.2	62.7	87.5	165.1	478.9	533.0	50.0	842.2	1012.1	326.1	1521.5	268.6	241.6	146.3	3974.1	1029.1	307.9	1168.7
0tpm pvA	204.7	383.8	91.3	21.6	963.4	2330.1	111.1	18.9	239.7	1309.1	175.0	563.8	109.8	73.7	26.3	2391.0	637.9	202.1	864.2
Sensitivity	0	0	0	0	0	0	0	0	0	0	0	0	4	0	5	0	0	0	
Function	adaptation to pheromone during conjugation with cellular fusion	adenylate cyclase activation	ammonium transport	ATP ADP exchange	ATP synthesis coupled proton transport	cell wall organization and biogenesis	cellular response to phosphate starvation	endocytosis	glucan metabolism	glutamate biosynthesis. using glutamate dehydrogenase (NAD(P)+)	glycerophospholipid metabolism	glycogen metabolism	intracellular copper ion transport	lipid metabolism	lipid transport	methionine metabolism	mRNA-nucleus export	mRNA-nucleus export	nuclear membrane organization and biogenesis
eneo	CNB1	RAS2	MEP3	AAC3	INH1	PIR3	PHO5	COS10	EXG1	GDH1	PLB2	GSY1	FET4	TGL1	FAT1	SAM1	YRA1	YRA1	ACC1
ОВЕ	YKL190W_ex1	YNL098C	YPR138C	YBR085W	YDL181W	YKL163W	YBR093C	YNR075W_0	YLR300W	YOR375C	YMR006C	YFR015C	YMR319C	YKL140W	YBR041W	YLR180W	YDR381W_ex1	YDR381W_ex2	YNR016C

0 է քնա/09 քնա	0.42	0.45	0.46	0.44	0.32	0.48	0.41	0.33	0.44	0.30	0.46	0.39	0.46	0.44	0.39	0.40	0.35	0.44	0.34	0.45	0.45	0.44	0.48	0.46		0.40		0.16	0.43	0.41
0 ð tgm gvA	253.2	316.1	44.7	15.6	869.4	213.4	244.3	235.3	59.F	214.9	52.9	45.2	152.8	23.6	155.0	206.0	135.8	116.7	41.9	837.6	54.2	93.1	126.7	393.9		404.4		41.1	264.5	86.6
0ĉ tgm vA	284.1	387.2	ô1.8	23.2	815.1	250 7	247.6	279.4	+ 22	219.2	55.6	47.5	195.7	30.8	226.8	292.2	186.0	119.8	56.6	905.4	58.4	100.8	163.1	409.7		278.7		31.6	284.7	63.0
041pm vA	282.0	305.7	58.4	23.2	884.3	249.9	243.8	233.3	58.3	231.8	89.2	62.9	197.9	30.7	206.0	252.2	166.5	107.6	66.4	856.0	55.8	93.8	157.2	371.8		101.4		32.0	245.1	85.1
0£	293.4	310.3	59.7	24.2	571.5	211.6	273.4	233.4	56.2	170.9	88.4	43.3	167.7	34.8	128.8	221.4	137.8	126.9	56.7	677.9	45.5	91.9	165.9	441.4		38.9		16.7	268.2	50.0
0S igm vA	364.3	389.6	55.6	27.5	736.6	290.6	317.4	265.4	64.4	192.3	105.9	76.0	178.7	32.0	221.8	274.0	165.7	128.4	76.2	1336.2	56.5	119.3	180.9	543.0		87.5		26.6	353.6	86.0
01 tgm vA	599.2	705.1	96.96	35.0	2736.6	448.7	591.0	703.0	135.9	705.2	115.0	117.1	331.3	53.2	398.9	518.6	391.6	266.9	122.5	1852.4	120.5	213.3	265.5	859.8		1001.5		256.9	619.6	208.8
0tgm gvA	460.4	118.8	71.0	23.8	201.9	441.0	544.2	906.4	144.2	76.7	197.9	57.4	69.4	10.8	57.5	84.3	61.3	1161	46.9	1641.9	327.6	91.2	61.8	127.7		878.6		381.6	477.2	600.0
Sensitivity	9			0	œ		0	2		0	18	4	0	0	0	0	0		0	0	0	4	4	7		0		0	0	0
Function	peptide transport	phosphate metabolism	protein biosynthesis	protein folding	protein folding	protein folding	protein-vacuolar targeting	pyrimidine base biosynthesis	regulation of transcription. DNA- dependent	regulation of translational fidelity	response to hydrogen peroxide	Rho protein signal transduction	sulfur metabolism	threonyl-tRNA aminoacylation	translational elongation	translational elongation	translational initiation	iransfational initiation	triacylglycerol biosynthesis	tricarboxylic acid cycle	tRNA processing	ubiquitin-dependent protein catabolism	AA	AA		NA		NA	NA	NA
əuəĐ	PTR2	PH011	MRPL19	MDJ2	SSA2	SSC1	VPS70	URA1	SPT5	RPS9B	SSK1	WSC4	OPT1	MST1	TEF4	TEF4	ANB1	TIF11	LR01	MDH1	RPR1	ASI1	ILM1	PHO36	RDN37-	-	RDN37-	-	RSN1	YRO2
ОВЕ	YKR093W	YAR071W	YNL185C	YNL328C	YLL024C	YJR045C	YJR126C	YKL216W	YML010W	YBR189W_ex2	YLR006C	YHL028W	YJL212C	YKL194C	YKL081W_ex1	YKL081W_ex2	YJR047C	YMR260C	YNR008W	YKL085W	RPR1	YMR119W	YJR118C	YOL002C		RDN37-1_2		RDN37-1_3	YMR266W	YBR054W

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17B: ESR subset of genes that are specifically repressed in mgt1

0110m/0ծքըm	0.37	0.49	0.44	0.50	0.50	0.49	0.38	0.41	0.50	0.44
0ðtgm gvA	43.3	541.9	773.5	696.1	365.3	60.4	38.9	470.5	361.9	9.77
0č tem vA	56.9	659.0	885.3	639.5	487.0	62.0	28.6	578.3	435.8	83.8
04tpm vA	48.8	670.6	730.1	744.5	460.5	65.9	22.3	530.8	458.9	77.1
0£ fpm vA	41.7	669.1	763.5	565.7	446.6	74.4	25.4	480.5	436.7	77.0
02 tgm vA	58.7	669.2	1239.9	902.1	507.4	68.8	25.1	635.1	519.4	141.8
01 tem vA	117.8	1116.1	1743.8	1398.7	734.4	122.1	101.4	1150.2	730.7	178.1
0î gm gv A	34.4	58.8	495.1	2091.3	63.9	60.1	18.7	423.4	112.2	284.8
Sensitivity		0	0	0	10	0	0	0		0
notion	GTP biosynthesis	fatty acid biosynthesis	glycogen metabolism	intracellular accumulation of glycerol	mRNA localization, intracellular	protein amino acid glycosylation	protein biosynthesis	protein biosynthesis	tryptophanyl-tRNA aminoacylation	NA
eneð	1MD1	SUR4	GSY2	GPD1	SCP160	MNN11	RPL4A	RPL9B	WRS1	RTN2
ORF	YAR073W	YLR372W	YLR258W	YDL022W	YJL080C	YJL183W	YBR031W	WL30LNY	YOL097C	YDL204W

Table 18 Genes that are incrementally repressed specifically in WT

There are 90 genes in this category. Genes that have a known function are included in Table 18A. 2 of the genes that had a known function and are also a part of the ESR are included in table 18B. The genes that are essential are included in red.

												1							-
01TW/09TW	0.35	0.38	0.47	0.46	0.41	0.49	0.49	0.39	0.39		0.44	0.42	0.45	0.50	0.45	0.49	0.43	0.49	0.50
09TW vA	25.9	46.5	1247.9	36.8	80.3	36.1	14.8	362.8	36.1		36.6	472.6	37.6	261.7	82.6	44.5	70.9	91.6	46.5
02TW vA	32.9	56.5	1771.1	33.4	68.5	41.9	14.8	519.2	40.7		45.7	1096.1	47 1	417.1	119.3	79.9	72.0	127.9	7.97
04TW vA	37.0	50.5	1867.6	42.5	91.3	44.1	19.5	720.8	53.1		38.5	719.1	34.4	397.8	128.8	58.5	94.8	119.0	64.5
0ETW vA	53.1	113.7	2417.3	46.4	96.5	56.9	19.7	703.8	48.6		53.2	1594.5	50.0	459.9	147.5	67.0	138.9	132.4	70.9
0S TW vA	56.5	89.0	2536.6	59.6	136.6	56.0	27.2	734.5	51.1		50.2	1138.6	42.4	455.8	153.9	61.3	154.4	130.8	72.4
0fTWVA	74.4	122.5	2665.5	80.7	195.4	73.0	30.0	926.2	92.7		83.3	1136.0	83.C	524.0	183.7	89.9	166.3	185.6	93.6
0TWvA	23.0	57.3	612.7	37.1	45.3	34.3	12.5	799.7	7.3		36.6	913.9	28.6	105.9	41.5	174.4	23.8	87.0	37.4
Sensitivity	0	0	0	28	0	0	0	18	0		0	2		2	0	0	0	0	9
Function	bud site selection	cell wall organization and biogenesis	cell wall organization and biogenesis	cytokinesis	endocytosis	filamentous growth	gene conversion at MAT locus	mRNA-nucleus export	phosphatidylethanolamine biosynthesis	positive regulation of transcription from Pol II	promoter	purine base biosynthesis	RNA elongation from Pol II promoter	serine family amino acid biosynthesis	telomerase-dependent telomere maintenance	thiamin biosynthesis	threonine catabolism	transport	tubulin folding
eneo	BUD9	DSE1	DSE2	HOF1	COS10	MGA1	ОН	NPL3	EPT1		MGA2	MTD1	SPT6	SER33	TLC1	RPI1	CHA1	HNM1	GIM4
ОВЕ	YGR041W	YER124C	YHR143W	YMR032W	YNR075W_1	YGR249W	YDL227C	YDR432W	YHR123W_ex1		YIR033W	YKR080W	YGR116W	YIL074C	TLC1_1	YIL119C	YCL064C	YGL077C	YEL003W

Table 18B: ESR subset of genes that are incrementally repressed specifically in WT

01TW/09TW	0.50	0.40
09TW vA	178.2	222.3
0 2TW vA	230.2	382.2
04TW vA	205.0	271.6
0ETW vA	251.2	232.5
02 TW vA	318.2	171.1
01TWVA	359.0	561.1
0TWvA	22.6	105.8
Sensitivity	0	0
noitonuन	cell wall organization and biogenesis	protein biosynthesis
ənəĐ	UTR2	RPL9A
ОКЕ	YEL040W	YGL147C RPL9A

Total RNA synthesis

RNeasy Mini Protocol for Isolation of Total RNA from Yeast Enzymatic Lysis Protocol — standard version

Use an appropriate number of yeast cells

Important notes before starting

• For RNA isolation from yeast, cells should be harvested in log-phase growth. Use only freshly harvested cells for the enzymatic lysis protocol.

• Prepare Buffer Y1

Buffer Y1 1 M sorbitol

0.1 M EDTA, pH 7.4

Just before use, add:

0.1% -mercaptoethanol

50 U lyticase/zymolase per 1 x 10⁷ cells

Depending on the yeast strain and enzyme used, the incubation time, enzyme concentration, and composition of Buffer Y1 may vary. Please adhere to the guidelines of the enzyme supplier.

Important

• β -Mercaptoethanol (β -ME) must be added to Buffer RLT before use. β -ME is toxic; dispense in a fume hood and wear appropriate protective clothing. Add 10 μ l β -ME per 1 ml Buffer RLT. Buffer RLT is stable for 1 month after addition of -ME.

• Buffer RPE is supplied as a concentrate. Before using for the first time, add 4 volumes of ethanol (96–100%), as indicated on the bottle, to obtain a working solution.

• Buffer RLT may form a precipitate upon storage. If necessary, redissolve by warming, and then place at room temperature. Buffer RLT and Buffer RW1 contain a guanidine salt and are therefore not compatible with disinfecting reagents containing bleach. Guanidine is an irritant. Take appropriate safety measures and wear gloves when handling.

• After enzymatic lysis, all steps of the RNeasy protocol should be performed at room temperature. During the procedure, work quickly.

• After harvesting the cells, all centrifugation steps should be performed at 20–25°C in a standard microcentrifuge. Ensure that the centrifuge does not cool below 20°C.

1. Harvest yeast cells in a 12 ml or 15 ml centrifuge tube by centrifuging at 1000 x g for 5 min at 4°C. (Do not use more than 5 x 107 yeast cells.) Decant supernatant, and carefully remove remaining media by aspiration. After centrifuging, heat the centrifuge to 20–25°C if the same centrifuge is to be used in the following centrifugation steps of the protocol.

Incomplete removal of the supernatant will affect digestion of the cell wall in step 2. **Note:** Freshly harvested cells must be used.

2. Resuspend cells in 2 ml freshly prepared Buffer Y1 containing lyticase or zymolase. Incubate for 10-30 min at 30°C with gentle shaking to generate spheroplasts. Spheroplasts must be handled gently.

Depending on the yeast strain used, the incubation time, amount of enzyme and composition of Buffer Y1 may vary. For best results, follow the guidelines of lyticase/zymolase supplier.

Complete spheroplasting is essential for efficient lysis. Note: Freshly harvested cells must be used for preparation of spheroplasts.

3. Centrifuge for 5 min at 300 x g to pellet spheroplasts. Carefully remove and discard the supernatant.

Note: Incomplete removal of the supernatant will inhibit lysis and dilute the lysate, affecting the conditions for binding of RNA to the RNeasy silica-gel membrane. Both effects may reduce RNA yield.

4. Add 350 μ l Buffer RLT to lyse spheroplasts, and vortex vigorously. If insoluble material is visible, centrifuge for 2 min in a microcentrifuge at maximum speed, and use only the supernatant in subsequent steps.

Note: Ensure that β -ME is added to Buffer RLT before use (see "Important notes before starting").

5. Add 1 volume (usually 350 μ l) of 70% ethanol to the homogenized lysate, and mix thoroughly by pipetting. Do not centrifuge. Continue immediately with step 6.

A precipitate may form after the addition of ethanol, but this will not affect the RNeasy procedure.

6. Apply the sample (usually 700 μ any precipitate that may have formed, to an RNeasy mini column placed in a 2 ml collection tube (supplied). Close the tube gently, and centrifuge for 15 s at 8000 x g (10,000 rpm). Discard the flowthrough.

Reuse the collection tube in step 7.

If the volume exceeds 700 μ l, load aliquots successively onto the RNeasy column, and centrifuge as above. Discard the flow-through after each centrifugation step.*

7. Add 700 μ l Buffer RW1 to the RNeasy column. Close the tube gently, and centrifuge for 15 s at \subseteq 8000 x g (\subseteq 10,000 rpm) to wash the column. Discard the flow-through and collection tube.*

8. Transfer the RNeasy column into a new 2 ml collection tube (supplied). Pipet 500 μ l Buffer RPE onto the RNeasy column. Close the tube gently, and centrifuge for 15 s at \Box 8000 x g (\Box 10,000 rpm) to wash the column. Discard the flow-through.

Reuse the collection tube in step 9.

Note: Buffer RPE is supplied as a concentrate. Ensure that ethanol is added to Buffer RPE before use

9. Add another 500 μ l Buffer RPE to the RNeasy column. Close the tube gently, and centrifuge for 2 min at \Box 8000 x g (\Box 10,000 rpm) to dry the RNeasy silica-gel membrane. Continue directly with step 10, or, to eliminate any chance of possible Buffer RPE carryover, continue first with step 9a.

It is important to dry the RNeasy silica-gel membrane since residual ethanol may interfere with downstream reactions. This centrifugation ensures that no ethanol is carried over during elution.

Note: Following the centrifugation, remove the RNeasy mini column from the collection tube carefully so the column does not contact the flow-through as this will result in carryover of ethanol.

9a. Optional: Place the RNeasy column in a new 2 ml collection tube (not supplied), and discard the old collection tube with the flow-through. Centrifuge in a microcentrifuge at full speed for 1 min.

* Flow-through contains Buffer RLT or Buffer RW1 and is therefore not compatible with bleach.

10. To elute, transfer the RNeasy column to a new 1.5 ml collection tube (supplied). Pipet 30–50 µl RNase-free water directly onto the RNeasy silica-gel membrane. Close the tube gently, and centrifuge for 1 min at \equiv 8000 x g (\equiv 10,000 rpm) to elute.

11. If the expected RNA yield is >30 μ g, repeat the elution step (step 10) as described with a second volume of RNase-free water. Elute into the same collection tube. To obtain a higher total RNA concentration, this second elution step may be performed by using the first eluate (from step 10). The yield will be 15–30% less than the yield obtained using a second volume of RNase-free water, but the final concentration will be higher.

1st Strand Synthesis

Amount of RNA

• Using a 1.5 ml centrifuge tube, mix reagents according to the following Table.

Reagent	Volume (µl)
DEPC-water	X
RNA (1.0 µg/µl)	у
T7 Primer (100 pmol/µl)	1
TOTAL	12

- Incubate @ 70°C in a water bath for 10 minutes
- Spin briefly and place on ice till ready to proceed.
- When incubation is done, to the same tube, add reagents according to the Table below.

STEP 2				
Reagent	Volume (µl)			
Tube from step 1	12			
5X 1st strand cDNA buffer	4			
0.1 M DTT	2			
10 mM dNTP mix	1			
TOTAL	19			

- Mix well with a pipette (carefully, in and out) and incubate at 42 °C, 2 minutes.
- Add variable amount of SS Reverse Transcriptase (final reaction volume =20 μ I)
- Mix well with a pipette and incubate at 42 °C, 1 hour.

2nd Strand Synthesis

Add the following components to the 1st strand tube from above:

Reagent	Volume (µl)
1 st Strand Reaction	20
DEPC-Water	91
5X 2 nd strand cDNA buffer	30
10 mM dATP, dCTP, dGTP, dTTP	3
DNA Ligase (10 U/µl)	1
DNA Polymerase (10 U/µl)	4
RNase H (2 U/µl)	1
TOTAL	150

- Transfer this total amount to a PCR tube and place in the thermocycler at 16°C for 2 hours.
- Add 2 μ l of T4 DNA Polymerase (10 U/ μ l) and incubate at 16°C for 5 minutes.
- Add 10 μ l of 0.5 M EDTA. (The total added volume is ~162 μ l).
- Proceed to cDNA cleanup or store the reaction at -20°C.

cDNA Clean-up

- Pellet the PLG light in the green tube and set aside. .
- Transfer the 2nd strand cDNA solution from previous step back to a 1.5 ml tube.
- Add to the 2nd strand cDNA tube (equal volume, assuming 150 µl recovery):

Phenol	
75 μl	
Chloroform: Isoamyl alcoh	ol (24.1)
75 μl	01 (21.1)

The total volume is now approximately 300 µl

- Vortex the 2nd strand cDNA tube and transfer the entire amount to the pelleted PLG-light tube.
- Centrifuge at 14,000 rpm for 2 minutes. Transfer the aqueous (top) layer to a new tube.
- Add the following to the aqueous layer (assuming recovery of 150 µl):

Glycogen (5 mg/ml)	1 µl	
NH4OAc (7.5 M)		75 µl
EtOH (100 %)		562 µl

- Vortex and immediately centrifuge for 20 minutes at 14,000 rpm, RT. .
- Remove supernatant and wash pellet twice with 500 µl of 80 % EtOH.
- After the last wash, centrifuge and eliminate EtOH using a micropipettor. Centrifuge again and eliminate EtOH remnants with micropipettor.
- Air dry the pellet (5 min at 37° C and 5 min RT) and resuspend in 12 µl DEPC water

Note: Complete drying is very important. The presence of ethanol will inhibit the IVT reaction

Biotin Labeling by In Vitro Transcription Reaction (IVT)

Since we started with 5-8 µg of total RNA, the Affymetrix manual recommends using 10 µl out of the $12 \,\mu l$ cDNA solution to setup a 40 μl IVT reaction (see chart in the manual). Using reagents from the ENZO kit, add the following components to a 1.5 ml centrifuge tube.

Reagent	Volume (µl)
cDNA template	10
DEPC-Water	12
10X HY reaction buffer	4
10X biotin labeled NTP	4
10X DTT	4
10X RNase inhibitor	4
20X T7 RNA polymerase	2
TOTAL	40

- Mix the reagents and centrifuge briefly
- Incubate @ 37°C for 5 hours in an oven to avoid evaporation.
- Make sure to mix with a pipette every 30-45 minutes.
- Store @ -20°C or go to the clean up step

IVT Clean-up

RNeasy RNA Cleanup Procedure

Notes:

-Buffer RLT may form a precipitate upon storage. If this happens, warm up to redissolve.

-Add 10µl of __-ME to 1 ml of Buffer RLT before use (stable for 1 month).

-Buffer RPE is provided as a concentrate. Before using for the first time, add 4 volumes of ethanol (96-100%) as indicated on the bottle to obtain a working solution.

-All centrifugations are done at room temperature.

Work in groups of two: each group will process half of the sample for RNA cleanup

- 1. Measure the volume that you now have in your IVT tube (should be $\sim 40 \mu$ l).
- 2. Split the sample in half and continue with the cleanup procedure on half of the sample. Adjust the volume of your portion (~20 μ l) to 100 μ l using RNase-free water.
- 3. Add 350 µl Buffer RLT to the sample, and mix thoroughly.

Note: Ensure that \square -ME is added to Buffer RLT before use.

- 4. Add 250µl ethanol (96-100%) to the sample, and mix well by pipetting. Do not centrifuge.
- 5. Apply sample (now 700 µl) to an RNeasy mini spin column sitting in a collection tube. Centrifuge for 15 seconds at 12,000 rpm.
- 6. Discard flow-through and collection tube.
- 7. Transfer RNeasy column into a new 2-ml collection tube. Pipet 500µl of wash Buffer RPE onto the RNeasy column, and centrifuge for 15 sec at 12,000 rpm to wash.

Ensure that ethanol is added to Buffer RPE before use.

- 8. Discard flow-through and reuse the collection tube in the following step.
- 9. Pipet 500 µl of wash Buffer RPE onto the RNeasy column. Centrifuge for 2 min at 14,000 rpm to dry the RNeasy membrane.
- 10. Following the spin, remove the RNeasy column from the collection tube carefully so that the column does not contact the flow-through as this will result in carryover of ethanol.

It is important to dry the RNeasy membrane since residual ethanol may interfere with subsequent reactions. The following spin ensures that no ethanol is carried over during elution.

- 11. Place the RNeasy spin column in a new 1.5-ml collection tube, and discard the old collection tube with the filtrate. Centrifuge at 14,000 rpm for 1 min.
- 12. Transfer the RNeasy column into a new 1.5-ml collection tube, and pipet 30 μl of RNase-free water directly onto the RNeasy membrane. Centrifuge for 1 min at 12,000 rpm to elute.

A second elution step can be performed using another 30-50 µl RNase-free water. This might improve yield.

- 13. Dilute 1 µl of the reaction into 99 µl of water and use this for a spec reading using the Biophotometer (Eppendorf).
- 14. Store the rest at -20°C or proceed with the next step.

Fragmentation

• Use the spec reading to determine what volume will give you 20 µg for fragmentation.

Apply the convention that 1 OD at 260 nm equals $40\mu g/$ mL RNA.

- 1. Check the OD at 260 nm and 280 nm to determine the sample concentration and purity.
- 2. Maintain the A260/A280 ratio close to 2.0 for pure RNA (ratios between 1.9 and 2.1 are acceptable).
- 3. In our test run, we obtained a post- IVT cleanup concentration of $1.356 \,\mu g/\mu l$ (32 μ), for a total of 43.4 μg . This means that we need 14.7 μ l of IVT cleaned up product for the Fragmentation reaction.
- Set up the reaction. The volumes shown in the Table below are from our example run done before the workshop. Your volumes might vary...

Reagent	Volume (µl)
RNA (20 µg)	14.7
DEPC-Water	17.3
5X Fragmentation Buffer	8
TOTAL	40

- Mix well, and incubate at 94°C in a water bath for 35 minutes.
- Place on ice or at -20°C.

Adjusted cRNA calculation

• Calculate the adjusted reaction yield from the Cleanup step of the IVT reaction. This is done using the following formula:

Adjusted cRNA yield= RNAm- (total RNAi)(y)

 RNA_m = amount of cRNA measured after IVT (µg) Total RNA_i = starting amount of total RNA (µg) Y = fraction of cDNA reaction used in IVT

 $RNA_m = 43.4 \mu g$

In our example:

Total RNA_t = $7.0 \ \mu g$ Y = 10/12 (fraction of cleaned up cDNA used in the IVT reaction)

Therefore, our adjusted cRNA yield: $37.6 \ \mu g$ [i.e., 43.4 - 7(10/12)]

The volume was 30 µl (see under Fragmentation)

Hence the adjusted concentration previous Fragmentation is $1.25 \,\mu g/\mu l$

Since we used 14.7 μ l of the prefragmented cRNA in the Fragmentation step, <u>the adjusted amount was 18.4 μ g [i.e., 14.7 μ l X (1.25 μ g/ μ l)].</u>

Prepare the Target Hybridization Reaction

The Affymetrix manual recommends using 15 µg of sample in the target hybridization. Use the adjusted concentration to calculate the volume of sample needed for 15 µg.

Amount of adjusted cRNA used in the Fragmentation reaction= 18.4 μg The volume of the Fragmentation reaction was 40 μl In order to get 15 μg from the Fragmentation reaction we need: 15 μg X (40 $\mu l/18.4$ $\mu g)=32.6$ μl

Note: One group of two will perform the Test3 Array Hybridization, the corresponding partner group will perform the Species Array Hybridization.

Step 1: Test3 Array Hybridization

- Set the Test3 chip at RT before setting up the reaction.
- Prepare 85 µl of 1X Hybridization buffer. Add 80 µl of this solution to the Test3 Array Chip (Mini format) to wet it.
- Put it in the oven at 45°C for at least 10 minutes at 40-50 rpm.
- Heat the Eukaryotic Hybridization Controls to 65°C for 5 minutes prior to adding it to the reaction below.
- Set up the Target hybridization reaction according to the following Table:

Reagent	Volume (µl)
Fragmented cRNA (15 µg)	32.6
Control oligonucleotide B2	5
20X Eukaryotic Hybridization Controls	15
Herring Sperm DNA (10 mg/ml)	3
Acetylated BSA (50 mg/ml)	3
2X Hyb. Buffer	150
Water	81.4
TOTAL	300

HYBRIDIZATION COCKTAIL

• After setting up the reaction, remove 100 µl from the Hybridization cocktail solution (save the rest of the solution at -20°C) and process it as follows:

Heat at 99°C for 5 minutes Heat at 45°C for 5 minutes Centrifuge at 14,000 rpm for 5 minute to clarify the cocktail

- Remove the 1X Hyb solution from the 'Test3 Chip' and then add 80 µl of the Hyb. Cocktail.
- Incubate at 45°C at 60 RPM for 16 hours.

Step 2: Species Array Hybridization

- Set the Species Array chip at RT before setting up the reaction.
- Prepare 210 µl of 1X Hybridization buffer. Add 200 µl of this solution to the Species Array Chip (Standard format) to wet it.
- Put it in the oven at 45°C for at least 10 minutes at 40-50 rpm.
- Heat the Eukaryotic Hybridization Controls to 65°C for 5 min prior to adding it to the reaction below.
- Set up the Target hybridization reaction according to the following Table:

Reagent	Volume (µl)
Fragmented cRNA (15 µg)	32.6
Control oligonucleotide B2	5
20X Eukaryotic Hybridization Controls	15
Herring Sperm DNA (10 mg/ml)	3
Acetylated BSA (50 mg/ml)	3
2X Hyb. Buffer	150
Water	81.4
TOTAL	300

HYBRIDIZATION COCKTAIL

• After setting up the reaction, remove 250 µl from the Hybridization cocktail solution (save the rest of the solution at -20°C) and process it as follows:

Heat at 99°C for 5 minutes Heat at 45°C for 5 minutes Centrifuge at 14,000 rpm for 5 minute to clarify the cocktail

- Remove the 1X Hyb solution from the 'Species Array Chip' and then add 200 µl of the Hyb Cocktail.
- Incubate at 45°C at 60 RPM for 16 hours.

Washing, Staining and Scanning Probe Arrays

- Shortly before the 16 hour incubation is done, follow the fluidics station setup according to Chapter 4, Section 3.
- For the Test3 Array, prepare the SAPE stain solution under 'Washing and Staining Procedure 1: Single Stain' (Chapter 4, Section 4). Streptavidin Phycoerythrin (SAPE) stocks should be stored in amber tubes at 4°C. Remove SAPE stocks from refrigerator and mix well before preparing stain solution. Do not freeze concentrated SAPE or diluted SAPE stain solution. Always prepare the SAPE stain solution immediately before use.

For 600 µL of SAPE Stain solution:

300 μL 2X Stain Buffer
270 μL water
24 μL of 50 mg/mL acetylated BSA (final concentration of 2 mg/mL)
6 μL of 1 mg/mL streptavidin phycoerythrin (SAPE) (final concentration of 10 μg/mL)

• For the Species Array (Human U95A), prepare the SAPE stain solution and Antibody solution under 'Washing and Staining Procedure 2: Antibody Amplification' (Chapter 4, Section 4).

For 1200 µL SAPEStain solution:

 μ L of 2X Stain Buffer μ L of water μ L of 50 mg/mL acetylated BSA (final concentration of 2 μ g/ μ L)

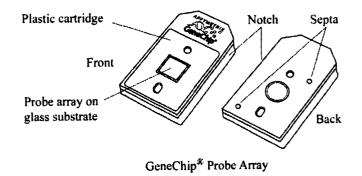
 $12 \,\mu\text{L}$ of 1 mg/mL SAPE (final concentration of $10 \,\mu\text{g/mL}$)

Mix well and divide into two aliquots of 600 μ L each to be used for stains 1 and 3 respectively.

For 660 µl of Antibody Solution:

300 µL of 2X Stain Buffer 266.4 µL of water 24 μ L of 50 mg/mL acetylated BSA (final concentration of 2 mg/mL) 6.0 μ L of 10 mg/mL normal goat IgG (final concentration of 0.1 mg/mL) 3.6 μ L of 0.5 mg/mL biotinylated antibody (final concentration of 3 μ g/mL)

• After 16 hours, remove the cocktail and save it (-20°C). Do not let the chip dry out. Immediately add 100 µl of the non-stringent wash buffer to the chip.



RNEasy Cleanup Procedure

Affymetrix recommends an additional cleanup step for the RNA sample before using in a microarray experiment. This is done using the RNeasy reagents as follows (procedure was adapted from user's instructions in the kit):

Notes: Do not exceed the RNA binding capacity (100 μ g) of the RNeasy mini spin columns.

Buffer RLT may form a precipitate upon storage. If this happens, warm up to redissolve.

Add 10 μ l of \Box -ME to 1 ml of Buffer RLT before use (stable for 1 month).

Buffer RPE is provided as a concentrate. Before using for the first time, add 4 volumes of ethanol (96-100%) as indicated on the bottle to obtain a working solution.

All centrifugations are done at room temperature.

- 1. Adjust sample to a volume of 100 μ l with RNase-free water, add 350 μ l Buffer RLT to the sample, and mix thoroughly.
- 2. Note: Ensure that \Box -ME is added to Buffer RLT before use.
- 3. Add 350 µl Buffer RLT to the sample, and mix thoroughly.
- 4. Note: Ensure that \Box -ME is added to Buffer RLT before use.
- 5. Add 250µl ethanol (96-100%) to the lysate, and mix well by pipetting. Do not centrifuge.
- 6. Apply sample (now 700 μl) to an RNeasy mini spin column sitting in a collection tube. Centrifuge for 15 seconds at 12,000 rpm.
- 7. Discard flow-through and collection tube.
- 8. Transfer RNeasy column into a new 2-ml collection tube. Pipet 500µl of wash Buffer RPE onto the RNeasy column, and centrifuge for 15 sec at 12,000 rpm to wash.
- 9. Ensure that ethanol is added to Buffer RPE before use.
- 10. Discard flow-through and reuse the collection tube in the following step.
- 11. Pipet 500 µl of wash Buffer RPE onto the RNeasy column. Centrifuge for 2 min at 14,000 rpm to dry the RNeasy membrane.
- 12. Following the spin, remove the RNeasy column from the collection tube carefully so that the column does not contact the flow-through as this will result in carryover of ethanol.
- 13. It is important to dry the RNeasy membrane since residual ethanol may interfere with subsequent reactions. The following spin ensures that no ethanol is carried over during elution.
- 14. Place the RNeasy spin column in a new 2-ml collection tube, and discard the old collection tube with the filtrate. Centrifuge at 14,000 rpm for 1 min.
- 15. Transfer the RNeasy column into a new 1.5-ml collection tube, and pipet 30 µl of RNase-free water directly onto the RNeasy membrane. Centrifuge for 1 min at 12,000 rpm to elute.
- 16. A second elution step can be performed using another $30-50 \,\mu$ l RNase-free water. This might improve yield.
- 17. Dilute 1 µl of the reaction into 99 µl of water and use this for a spec reading using the Biophotometer (Eppendorf).

18. Store the rest at -80° C or proceed with the next step.

2g. Spectrophotometric analysis

 To determine the concentration and purity of the RNA solution, transfer 2 μl of your RNA solution into an RNase-free tube containing 98 μl of DEPC-water. The lab instructors will measure the A₂₆₀/A₂₈₀. Pure RNA will give a ratio of approximately 2.0.

 $1.0 \text{ A}_{260} = 40 \ \mu g/ml \ RNA$

Dilution factor in spectrophotometric cuvette = 50

RNA solution conc. $(\mu g/ml) = (A_{260})(100)(40\mu g/ml)$

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