Molecular and enological characterization of a natural *Saccharomyces uvarum* and *Saccharomyces cerevisiae* hybrid

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Abstract

Saccharomyces cerevisiae plays a main role in the winemaking process, although other species, like *S. uvarum* or *S. paradoxus,* have been associated with must fermentations. It has been reported in recent years, that yeast hybrids of different *Saccharomyces* species might be responsible for wine productions. Although *S. cerevisiae* x *S. kudriavzevii* hybrids have been well studied, very little attention has been paid to *S. cerevisiae* x *S. uvarum* hybrids. In this work we characterized the genomic composition of S6U, a widely used commercial *S. cerevisiae* x *S. uvarum* yeast hybrid isolated in wine fermentations containing one copy of the genome of each parental species, which suggests a relatively recent hybridization event. We also studied its performance under diverse enological conditions. The results show enhanced performance under low temperature enological conditions, increased glycerol production, lower acetic acid production and increased production of interesting aroma compounds. We also examined the transcriptomic response of the S6U hybrid strain compared with the reference species under enological conditions. The results show that although the hybrid strain transcriptome is more similar to *S. uvarum* than to *S. cerevisiae*, it presents specifically regulated genes involved in stress response, lipids and amino acid metabolism. The enological performance and aroma profile of this *S. cerevisiae* x *S. uvarum* hybrid makes it a good candidate for participating in winemaking, especially at low temperatures.

Keywords: Wine, *Saccharomyces*, Hybrids, Fermentation, Transcriptomics.

1. Introduction

Yeasts contribute positively to wine flavor through alcoholic fermentation (Henschke, 1997) by several mechanisms: (i) utilization of grape juice constituents; (ii) production of ethanol and other solvents that help extract flavor components from grape solids; (iii) production of enzymes that transform neutral grape compounds into flavor active compounds; (iv) generation of many hundreds of flavor-active secondary metabolites (e.g. acids, alcohols, esters, polyols, aldehydes, ketones, volatile sulfur compounds); and (v) autolytic degradation of dead yeast cells, although this process can also negatively contribute to wine quality (Cole and Noble, 1997, Fleet, 2003 and Lambrechts and Pretorius, 2000). Thus the conversion of grape sugars into alcohol and other end-products by specific yeast populations may yield wines with different organoleptic qualities. In particular, the characterization of *Saccharomyces cerevisiae* has revealed that, as well as producing ethanol, this yeast generates many important secondary metabolites for determining wine quality (Fleet and Heard, 1993 and Lambrechts and Pretorius, 2000). Ethanol and carbon dioxide, the major volatile products of yeast metabolism, make a relatively small contribution to wine flavor respect to other volatile compounds. Conversely, the higher alcohols and esters formed during alcoholic fermentation strongly influence the sensory properties of the resulting wine (Nykänen, 1986 and Romano et al., 2003).

During natural wine fermentations, *S. cerevisiae* is the predominant yeast (Pretorius, 2000), but two other species belonging to this genus (*S. bayanus* and *S. paradoxus)* have also been described as playing a main role during wine fermentation (González et al., 2006 and Pretorius, 2000). The *S. bayanus* is a taxon that includes genetically diverse lineages of pure and hybrid strains. It has been subdivided by some authors into two well-differentiated groups of strains: the molecularly and physiologically heterogeneous group of strains belonging to *S. bayanus var. bayanus*; the homogenous group of strains pertaining to *S. bayanus var. uvarum* (Pérez-Través et al. 2014 and Vaughan-Martini and Martini, 2011). Libkind et al. (2011) recently discovered the species *S. eubayanus* and proposed the use of *S. eubayanus* and *S. uvarum* as descriptors of the *S. bayanus* species. *S. uvarum* strains are typically found in wine environments. It has been described that the interspecific hybrid strains between *Saccharomyces* species are related to wine fermentations. The *S. cerevisiae* x *S. kudriavzevii* natural (González et al., 2006 and Lopandic et al. 2007) and commercial (Bradbury et al., 2006 and González et al., 2006) yeast hybrids have been associated with wine fermentations. These hybrids have been characterized from a molecular and enological point of view. *S. cerevisiae* x *S. uvarum* hybrids have been described (Masneuf et al., 1998, Lejeune et al., 2007, Albertin et al., 2013), however, they have not been well studied from a genomic and enological point of view.

The fermentative power of *S. cerevisiae* has been used for food and alcoholic beverage production throughout human history, and industrial strains of this species are well-adapted to stress conditions, such as temperature, osmotic pressure and ethanol toxicity, conditions that are present during different fermentative processes. The *S. uvarum* fermentation profile in grape must differs from that of *S. cerevisiae* since it produces lower levels of ethanol and acetic acid, but more glycerol and succinic acid (Bertolini et al., 1995, Giudici et al., 1995 and Kishimoto et al., 1993). *S. uvarum* also generates high levels of volatile fermentative compounds, such as phenylethanol and phenylacetate (Masneuf-Pomerede et al, 2010). Commercial *S. uvarum* strains are used to produce several types of wines and cider, usually at low temperatures (Almeida et al., 2014). The *S. cerevisiae* x *S. uvarum* hybrid strains are well-adapted to the stress conditions (low pH, high sugar and ethanol content) that are common to wine fermentations (Belloch et al., 2008), and in accordance with new winemaking trends, their aroma production profile in synthetic media reveals interesting properties (Gamero et al., 2011).

Given the interesting properties of these *S. cerevisiae* x *S. uvarum* hybrids, in the present work, we set out to compare genomic composition and wine fermentation performance of one of the most used commercial strain (S6U) in four distinct natural grape musts at four different temperatures, as well as wine composition and aroma. We also analyzed the global gene expression of *S. cerevisiae* x *S. uvarum* hybrid strain S6U in comparison to a representative *S. cerevisiae* strain (commercial wine strain T73) and a strain of *S. uvarum* (CECT 12930) under enological conditions (Macabeo juice fermentation at 18ºC).

2. Materials and methods

2.1. Yeast strains and media.

Hybrid strain S6U (*S. cerevisiae* x *S. uvarum*) is a commercial active dry yeast from Lallemand (Montreal, Canada). It was first classified as *S. uvarum* and selected for its ability to ferment at very low temperatures in musts (Ciolfi et al., 1994). Originally isolated as an allotetrapoid (Naumov et al., 2000), we used a diploid industrial strain isolated from an LSA supplied by Lallemand. The *S. cerevisiae* strain T73, widely used as a wine yeast model (Gómez-Pastor et al., 2012 and Pérez-Torrado et al., 2009) and *S. uvarum* strain CECT 12930 (Pérez-Través et al., 2014) were used as reference species to represent parental strains. Yeast precultures were carried out in YPD (glucose 2%, yeast extract 1% and peptone 2%).

2.2. Fermentations, enological determinations and volatile compounds analysis.

All the fermentations were carried out in triplicate by using 450 ml of must in sterile 500 ml vessels. The Tempranillo and Bobal varieties were employed for microvinifications as red grape varieties, as were Macabeo and Parellada as white grape varieties. Assimilable nitrogen was 310.8, 274.4, 292.6 and 182 mg/l for the Tempranillo, Macabeo, Parellada and Bobal respectively. The initial sugar concentration for Tempranillo and Macabeo was 280 g/l whereas in Bobal and Parellada was 230 g/l. The initial pH was 3.3 ± 0.05 in Bobal and Parellada and 3.9 ± 0.05 in Tempranillo and Macabeo. The employed musts were supplemented with 0.2 g/l of diammonium phosphate (Panreac, Barcelona, Spain) and 0.1 mg/l of thiamine (Sigma, Steinheim, Germany). They were treated by adding 1 mg/l of dimethyl di-carbonate (Fluka, Buchs, Switzerland) to be sterilized and SO_2-free up to 20 ppm, and were allowed to settle overnight. Musts were inoculated with a final concentration of 10^6 cell/ml of pure yeast culture. The vinification process was conducted at four different temperatures, 14, 18, 22 and 32°C, until alcoholic fermentation was completed. Samples were collected daily to assess fermentation by measuring reducing sugars and to enumerate yeast populations. Prior to sampling, flasks were stirred for homogeneity.

Total yeast cells were determined by counting under a light microscope (phase-contrast) using a Thoma chamber. Throughout the fermentation process, reducing sugars and concentrations of glycerol, acetic acid (volatile acidity) and malic acid in musts and wines were measured enzymatically in an Echo-Enosys analyzer (Tecnova, San Sebastián de los Reyes, Spain) following the supplier's instructions. The ethanol concentration in wines was quantified in an Alliance Infrascan (Alliance Instruments, Eragny-Sur-Oise, France). All measurements were taken in duplicate.

Higher alcohols and esters were analyzed by headspace solid-phase-microextraction sampling (SPME) using poly(dimethylsiloxane) (PDMS) fibers

(Supelco, Sigma-Aldrich, Barcelona, Spain) following a previously described protocol (Rojas et al., 2001) and by gas chromatography-mass spectrometry (GC–MS). Gas chromatography was carried out in a Trace GC (ThermoFinnigan, San Jose, CA) gas chromatograph coupled to a Trace DSQ (ThermoFinnigan, San Jose, CA) mass spectrometer. A SolGel-WAX 0.25 (SGE, Austin, TX) 30 m × 0.25 mm ID capillary column coated with a 0.25 µm layer of cross-linked polyethylene glycol was used. The carrier gas was helium (1 ml/min) and the oven temperature program was as follows: 10 min at 40 °C, 2.5 °C/min to 150 °C, 20 °C/min to 250 °C and 4 min at 250 °C. The detector temperature was 250 °C and the injector temperature was 220 °C, splitless. The ionization voltage applied was 70 eV and the mass spectra were obtained within the 30-200 m/z scan range. A 20-µl volume of internal standard (2-heptanona at 0.05%) was added to each sample. Volatile compound concentrations were quantified by using the calibration graphs of the corresponding standard volatile compound (Fluka, Buchs, Switzerland), and are given as the average of three independent fermentations. The standard solution consisted of: ethyl acetate, isobutyl acetate, isobutanol, isoamyl acetate, isoamyl alcohol, ethyl caproate, hexyl acetate, 1-hexanol, ethyl caprylate, diethyl succinate, benzyl acetate, phenylethyl acetate, benzyl alcohol and 2-phenylethanol. For more details on calibration, see González et al. (2007).

The Statgraphics Plus v.4.0 package (Manugistics, Rockville, MD) was used to perform multiple range tests to compare sample means. The analyzed compounds data were first studied by Cochran's test and Bartlett's test to verify that there was no statistically significant difference among the standard deviations at the 95.0% confidence level. After this preliminary study, one-way ANOVAs under each particular temperature and must condition were carried out using Tukey's test to determine the difference between means (statistical level of significance was set at $p \leq 0.05$).

2.3 Nuclear gene region characterization of *Saccharomyces* interspecific hybrid S6U by PCR amplification and restriction analysis of nuclear gene regions

The characterization of *Saccharomyces* interspecific hybrid S6U was performed by PCR amplification and a subsequent RFLP analysis of 35 protein-encoding genes randomly selected in the center and ends of each chromosome. The oligonucleotide primers designed for the symmetrical amplification of the protein-coding gene regions are described in González et al. (2008). Yeast DNA was isolated and PCR was performed according to standard procedures (Garre et al., 2009). PCR amplifications were carried out in Techgene or Touchgene thermocyclers (Techne, Cambridge, UK) as follows: initial denaturing at 95 °C for 5 min and then 40 PCR cycles of the following program: denaturing at 95 °C for 1 min, annealing at 56 °C (for most genes), and extension at 72 °C for 2 min with a final extension at 72 °C for 10 min. With genes *ATF1, DAL1, DAL5, EGT2, KIN82, MNT2, MRC1, RRI2*, and *UBP7*, annealing was performed at 50 °C. PCR products were run on 1.4% agarose (Pronadisa, Madrid, Spain) gels in 0.5× TBE (Tris-borate-EDTA) buffer. After electrophoresis, gels were stained with a 0.5 µg/ml ethidium bromide dilution (AppliChem, Darmstadt, Germany) and visualized under UV light. A 100-bp DNA ladder marker (Roche Molecular Biochemicals, Mannheim, Germany) served as a size standard.

Simple digestions with endonucleases were performed with 15 µl of amplified DNA to a final volume of 20 µl. Restriction endonucleases *Acc*I, *Cfo*I, *Eco*RI, *Hae*III, *Hinf*I, *Msp*I, *Pst*I, *Rsa*I, and *Scr*FI (Roche Molecular Biochemicals) were used according to the supplier's instructions. Restriction fragments were separated on 3% agarose (Pronadisa) gel in 0.5× TBE buffer. A combination of 50-bp and 100-bp DNA ladder markers (Roche Molecular Biochemicals) served as size standards. Restriction endonucleases were selected to yield species-specific patterns to differentiate the gene copies in the hybrids from each parent species.

2.4. Cell extracts preparation and RNA extraction

Ten milliliters of each must fermentation culture were taken when 50% of sugars were consumed. Cells were harvested by centrifugation and resuspended in 0.5 ml of LETS buffer (200 mM LiCl, 20 mM EDTA, 20 mM Tris-HCl pH 8.0, 0.4% sodium dodecyl sulfate) and transferred to a screw-cap microcentrifuge tube containing 0.5 ml of phenol and 0.5 ml of glass beads (acid-washed beads, 0.4 mm diameter). The suspension was mixed vigorously 3 times for 1 min each time in a Mini Bead-Beater homogenizer (BioSpec). After centrifugation at 17900 x *g* for 10 min (at 4 °C), the upper phase was extracted successively with phenol-chloroform-isoamyl alcohol (25:24:1) and chloroform-isoamyl alcohol (24:1). These steps were repeated until the interface between the aqueous and organic layers became clear after centrifugation. Total nucleic acids were precipitated with two volumes of ice-cold 100% ethanol and a 0.1 volume of 3.0 M potassium acetate, left at -20°C for 3 h, and then centrifuged at 21100 x *g* for 15 min at 4 °C. The pellet was washed with 70% ethanol, dried and resuspended in 50 µl of sterile diethyl pyrocarbonate-treated water. Total RNA was purified with an RNeasy mini column (QIAGEN) according to the manufacturer's instructions. The total RNA concentration was quantified by A_{260}, and the A_{260} to A_{280} ratio was used to estimate RNA purity. Nucleic acids contamination was also checked on a 1% agarose gel.

2.5. Synthesis of [^{33}P] dCTP-labeled cDNA

Ten micrograms of purified RNA, 1µl of oligo(dT)$_{15}$ (Roche Molecular Biochemical, Mannheim, Germany) and 1µl of RNA inhibitor (RNA Guard, Amersham Biosciences, Roosendaal, The Netherlands) were mixed with water to obtain a final volume of 10 µl, which was heated for 10 minutes at 70 ºC and then chilled on ice. The following components were added: first strand buffer (Invitrogen, Carlsbad, Canada), 0.1 M dithiothreitol (Invitrogen, Carlsbad, Canada), 0.8 mM dATP, dGTP and dTTP, 200 U of SuperScript II reverse transcriptase, RNase H (Invitrogen, Carlsbad, Canada), 50 µCi $[^{33}P]$ dCTP (Hartmann Analytic, Braunchweig; Germany) and water to give a final volume of 30 µl. The mixture was incubated at 43 ºC for 1 h. cDNA was then purified with MicroSpin S300 HR columns (Amersham Biosciences, Roosendaal, The Netherlands) according to the manufacturer's instructions, and was quantified by a liquid scintillation counter.

2.6. Macroarrays hybridization

The *S. cerevisiae* macrochip membranes, made by the DNA chips service of the Universitat de Valencia (Spain) (http://scsie.uv.es/chipsdna and Alberola et al., 2004), were washed for 30 min in 0.5% SDS at 80 ºC. Membranes were prehybridized for 3 h with 5 mL of saline sodium citrate (SSC)-based hybridization solution (5X SSC, 5X Denhart's, 0.5% SDS, 50% deionized formamide and 100 µg herring sperm DNA/mL) at 42 ºC in a roller oven. This temperature permits the heterologous hybridization of closely related species or hybrids using *S. cerevisiae* chips, calculated by taking into account *S. kudriavzevii* homology (Belloch et al., 2009). The purified cDNA probe was denatured for 5 min at 100 ºC, cooled on ice and 3 x10^6 dpm/ml were added to the prehybridization mixture. After overnight hybridization at 35 ºC, filters were rinsed with 2x SSC - 0.1% SDS at 65 ºC for 20 min. Filters were then transferred to a plastic container and washed with 0.2x SSC - 0.1% SDS at room temperature for 15 min.

Filters were exposed to a high-resolution BAS-MP 2040S imaging plate (Fuji, Kyoto, Japan) for 48 h and scanned in a phosphor-imager (FLA-3000; Fuji).

To reduce quantification and reproducibility problems, all the used filters were taken from the same batch. Filters were stripped by pouring boiling stripping buffer (5.0 mM sodium phosphate, pH 7.5, 0.1% SDS) 2 or 3 times over the membrane. The first time, the stripping buffer was left at 65 ºC for 20 min, while filters were left at room temperature after the second and third washes. To ensure radioactivity had been eliminated, filters were checked with a Geiger counter. Membranes were not dried at any time to avoid permanent radioactivity fixation.

Hybridization experiments were performed in triplicate. Replicates were made with RNA samples from three different bottles of parallel experiments performed at the same time to avoid cell growth and handling differences. In particular, some authors have noticed that cell density, even at different densities in the mid-log phase, had a significant effect on the expression level of a small number of genes (Wodicka et al., 1997).

2.7. Data analysis and spot validation

Spot intensities were quantified as artefact-removed-density (ARM), background and background-corrected ARM density (sARM) with the Arrays Vision Software (Imaging Research, Canada). Triplicate macroarrays data were downloaded to Microsoft Excel files. To normalize the signal intensity of each replicate hybridization set, spot intensities were normalized against total spot intensity. To determine fold changes between pairs of yeast strains under the same hybridization conditions, average spots were normalized against highly conserved genes in the genus *Saccharomyces* as histones H2A and H2B (*HTA1-2* and *HTB1-2*) and translation elongation factor EF-1α

(*TEF1-2*) (Kurtzman and Robnett, 2003). These genes were chosen because previous studies carried out in our laboratory have shown that all the strains used in this study (*Saccharomyces* species strains and hybrids) have the same number of copies from these genes and more than 98% nucleotide homology. Raw data are presented in Supplementary Table S1. Log (base 2) average values were used to calculate fold change. The SAM (Significance Analysis for Microarrays) analysis, implemented in the MeV 4.8 software (Saeed et al., 2003), was used to select significant genes with a False Discovery Rate of 1% to select significant data with Bonferroni's correction for false-positives. GO (Gene Ontology) terms were investigated by using the FunSpec online software. The functional groups with Bonferroni-corrected *p*-values below 0.05 were considered significant.

3. Results

3.1. Chromosomal composition in wine *S. cerevisiae* × *S. uvarum* hybrids.

To understand the chromosomal and genetic structure of the *S. cerevisiae* × *S. uvarum* hybrid, we used a method based on PCR amplification and a restriction analysis of 35 gene regions (González et al., 2008). As shown in Figure 1, 32 protein-coding genes were located near the ends of the 16 *S. cerevisiae* chromosomes, and three were in the central positions of large chromosomes II, IV, and X. The genome of the *S. uvarum* type strain was syntenic with that of *S. cerevisiae*; therefore, these genes were expected to occupy similar positions in the hybrid chromosomes from the *S. uvarum* parent. *Saccharomyces* general PCR primers were designed to amplify the genes of interest in the conserved nucleotide sequences that flanked variable regions, where the presence of variable restriction sites allowed species differentiation. The restriction endonucleases that yielded single or combined species-specific restriction patterns were selected for each gene region (González et al., 2008).

Figure 1 summarizes the conformation of the S6U *S. cerevisiae* × *S. uvarum* hybrid genotype for each gene region according to the composite restriction patterns exhibited. The hybrid strain displayed a mixture of restriction patterns for all the gene regions due to the presence of two different alleles of each region, one exhibiting the typical restriction pattern of *S. cerevisiae* and the other displaying the same restriction pattern of *S. uvarum,* or a similar pattern. Thus we conclude that S6U is a 'perfect' hybrid that contains one copy of each species for all the genes.

3.2. Fermentation dynamics of the studied strains

Here we enologically characterized *S. cerevisiae* × *S. uvarum* hybrid strain S6U and two reference strains (*S. cerevisiae* T73 and *S. uvarum* CECT12930) as being representative of parental species in four distinct natural musts, two red (Bobal and Tempranillo) and two white (Macabeo and Parellada), at four different temperatures (14, 18, 22 and 32 ºC). Reducing sugars (glucose and fructose) were measured throughout fermentations to monitor the progress of the different studied strains (Figure 2). As a general pattern, and as expected, we observed that the fermentation rate increased with temperature in all the grape varieties. However, the behavior of the strains varied from one natural must to another. In the fermentations performed with Tempranillo must, all the yeasts behaved similarly at all the temperatures assayed, except 32 ºC where the *S. uvarum* strain was delayed by 1 day. A similar pattern was observed with Macabeo musts with the strains fermented at the same rate, except 32 ºC where the S6U hybrid showed a 1-day delayed fermentation start. Greater variability was observed when the Bobal must was used, although the strains displayed similar fermentation performance at the lowest temperature. At 18 and 22 ºC, the *S. uvarum* strain fermentation pattern was faster than the *S. cerevisiae* strain, and the hybrid strain was similar to *S. uvarum* at 22 ºC and intermediate at 18 ºC. At 32 ºC, parental strains were faster than the hybrid, as observed for the Macabeo must. During the fermentations performed with Parellada, we observed the highest variability among strains, probably because this grape juice could have low levels of some components; e.g., amino acids or vitamins. At 14 ºC, 22 ºC, and especially at 18 ºC, *S. uvarum* strain fermentation was faster than the *S. cerevisiae* strain. Once again, the hybrid strain showed variable behavior, which was slowest at 14 ºC and similar to the *S. uvarum* strain at 18 and 22 ºC. Unlike the other musts, all the strains completed fermentation with a similar pattern at 32 ºC. In summary, *S. uvarum* was best suited to low and intermediate temperature conditions, like 14, 18 and 22 °C, if compared to the reference *S. cerevisiae* strain. Hybrid strain S6U showed variable fermentation performance and the best behavior at 18 ºC.

3.3. Enological determinations

The main characteristics that influence enological properties of wine, such as alcohol production, sugar fermentation assimilation and the yield of some compounds, were studied at the end of all the fermentations. The main statistically significant differences were found in glycerol and acetic acid production (Table 1). At all the tested temperatures, reference strain *S. uvarum* (CECT 12930) produced more glycerol than commercial strain *S. cerevisiae* (T73), except at 32 °C where all the strains produced the same amount of glycerol. Commercial strain T73 usually produced the lowest amount of glycerol (with the exception mentioned at 32 °C) and the hybrid yeast generated an intermediate or similar quantity to the *S. uvarum* strain. Regarding acetic acid, it is interesting to note that the hybrid and the *S. uvarum* strain produced significantly less quantity than T73, except for the fermentation performed in Bobal must and the fermentations carried out at 32 °C, whose results were reversed. This scenario indicates that the hybrid and *S. uvarum* strain are not well-adapted at higher temperatures as they behave worse than at lower and intermediate temperatures when they produce more glycerol than *S. cerevisiae*.

3.4. Production of volatile compounds after must microvinifications

The concentrations of the major volatile compounds produced during the fermentations described above are shown in Table 2. One interesting result was that the hybrid strain was generally the major or intermediate producer of isobutanol and isoamyl alcohol, except for the fermentations at 32 °C. The S6U hybrid produced more quantity of 1-Hexanal in Tempranillo must at 18, 22 and 32 ºC, and in Macabeo at 14 and 32 ºC. Likewise, this hybrid produced a larger quantity of ethyl caprylate during the Parellada and Macabeo fermentations performed at 14 ºC and for Parellada at 18 and 22 ºC. S6U was also the best producer of diethyl succinate at 18 °C with all the assayed musts, and at 18 °C with musts Tempranillo and Bobal. Finally, T73 was a good producer of ethyl caprylate, especially at 22 and 32 ºC. It is also possible that evaporation could affect absolute values of some compounds at high temperatures respect to low temperatures.

To gain an overview of the aroma production ability of the different strains, we compared the sum of total aroma compounds or esters or higher alcohols produced during alcoholic fermentation by all the strains under each temperature and must (Table 3). A one-way ANOVA for each temperature condition and must was done with all the strains, and Tukey's test was used to determine the difference between means (statistical level of significance was set at $p \leq 0.05$). Ethyl acetate was excluded from the total sum of esters because of its distinctive contribution to wine aroma (Cabrera et al., 1998 and Lema et al., 1996). As seen in Table 3, hybrid strain S6U produced the highest levels of the total aroma compounds in musts Tempranillo and Parellada at 18 ºC. Interestingly, S6U generated the highest levels of esters in Tempranillo at 14 ºC and in Tempranillo and Parellada at 18 ºC. The reference strain of *S. cerevisiae* (T73) produced the lowest levels of aromatic compounds, mainly higher alcohols, at the low and intermediate temperatures, whereas it was the highest producer at 32 ºC. The aroma analysis confirmed that the *S. cerevisiae* strain is better adapted to ferment at high temperatures as it produces more amounts of some compounds than *S. uvarum* and the hybrid strain.

3.5. Global gene expression analysis of hybrid S6U and the *Saccharomyces* reference species.

We monitored the global gene expression in hybrid wine strain S6U compared with its reference species *S. cerevisiae* (T73) and *S. uvarum* (CECT 12930). For the transcriptome analysis, we selected Macabeo juice alcoholic fermentation at 18 ºC since all the strains presented similar fermentation performances and biases as different physiological situations can be avoided. Cells were harvested at the end of the logarithmic phase, immediately before entry in the stationary phase, when 50% of sugar was consumed. Transcriptomic values were normalized and significant data were selected for further analyses. The expression comparison made between the cells of hybrid S6U and both reference species (T73 and CECT 12930) under oenological conditions identified a relatively small number of genes (Figure 3). The comparison made between S6U and the reference strains revealed that the hybrid strain increased the expression of 196 genes if compared to *S. cerevisiae* (T73), and also the expression of 42 genes if compared to *S. uvarum* (CECT 12930), of which 22 were common in both reference strains. These 22 genes were similarly expressed between the reference strains. A smaller number of genes were down-regulated in hybrid strain S6U when compared with the reference species, 36 for *S. uvarum* (CECT 12930) and 46 for *S. cerevisiae* (T73), of which 26 were common. A few genes were up- (14) or down- (39) regulated between the parental *S. cerevisiae* (T73) and the *S. uvarum* (CECT 12930) strain. These changes were not common for the S6U differentially regulated genes, except for four up-regulated genes for the *S. uvarum* (CECT 12930) strain.

The GO terms analysis is an interesting tool for finding significantly over-represented functional groups in a gene set. This functional analysis was done with the up- and down-regulated genes in S6U vs. each reference species (Table 4). The down-regulated genes in hybrid S6U, compared to the *S. uvarum* CECT 12930 strain, performed functions relating to response to stress and to the genes related to the structural ribosome constituent. Interestingly, the comparison of S6U with the *S. cerevisiae* T73 strain also revealed the down-regulation of the functional groups related to response to stress. When we analyzed the 26 commonly regulated genes in the S6U hybrid, compared to both parents, the GO response to stress was also significant (3.21E-05). The genes up-regulated in the S6U hybrid, compared to both reference species, did not show any significantly overrepresented functional group. When we compared *S. cerevisiae* T73 with the *S. uvarum* CECT12930 strain, we observed that T73 had up-regulated ion transport genes, whereas *S. uvarum* had overexpressed the genes related to electron transport and membrane-associated energy conservation, aerobic respiration and the mitochondrial inner membrane.

The observation made of the regulation of several specific genes can help us to understand the phenotypic differences observed between hybrid and reference species when focusing on groups of genes. Among the S6U hybrid up-regulated genes, if compared to both parents, some genes were related to signal transduction (*STE18, CLA4, MSG5, RLM1, CRZ1*), amino acid metabolism (*ARG4, SHM1*) and glycolysis (*ERR1, ERR2*). Of the 26 genes commonly down-regulated in the S6U hybrid, if compared to both parents, it is worth highlighting the presence of several genes related to vitamins (*THI74, SPE2*), inositol (*OPI10*) and sterol metabolism (*ARE2, ERG25, ERG28*), the last two groups related to cold adaptation. Some other genes (*DAN2*, *PAU1, PAU2, PAU4, PAU6, PAU17, PAU18, PAU23, PAU20, PAU21*) belonged to the *PAU*, *DAN/TIR* families, which are also linked to cold shock adaptation (Table 4).

4. Discussion

Since the discovery of the participation of *Saccharomyces* hybrids in enological fermentations, several studies have focused on their characterization, mainly for hybrid strains *S. cerevisiae* x *S. kudriavzevii* (Combina et al. 2012, Gonzalez et al., 2006, Gonzalez et al., 2007 and Gonzalez et al., 2008). In this work, we describe the genomic composition of a widely used commercial *S. cerevisiae* x *S. uvarum* hybrid, its performance under enological conditions, the composition of the produced wine and its transcriptional regulation.

Regarding hybrids *S. cerevisiae* x *S. kudriavzevii*, it has been shown that certain chromosomes from the *S. kudriavzevii* parent are also completely absent in hybrids *S.* cerevisiae × *S. kudriavzevii* (Gonzalez et al., 2008 and Peris et al., 2012). In these yeast hybrids, a trend of maintaining the *S. cerevisiae* genome and of reducing the non *S. cerevisiae* (*S. kudriavzevii*-like) fraction was maintained. However, lager *S. pastorianus* strains exhibited the opposite trend, that of preserving the non *S. cerevisiae* (*S. eubayanus*-like) genome and reducing the *S. cerevisiae* fraction. In contrast, both types of natural hybrids contain the non *S. cerevisiae* mitochondrial genomes (de Barros

Lopes et al., 2002 and Petersen et al., 2002). In the *S. cerevisiae* x *S. uvarum* S6U hybrid, we observed that it equally maintained the genomes from both parents in accordance with a similar ploidy to a diploid, as previously observed (González, 2006). These data suggest that this commercial hybrid strain may be of relatively recent generation and it could present similar characteristics of hybrids newly formed by artificial methods. In fact it has been shown that new artificially generated *Saccharomyces* hybrids tend to maintain one copy of the genome of each parental (Pérez-Través, 2012 and Solieri et al., 2008).

In the present study we have seen that the *S. cerevisiae* x *S. uvarum* S6U hybrid display in glycerol produced an intermediate behavior if compared to their parental reference stains (*S. cerevisiae*, strain T73 and *S. uvarum*, strain CECT 12930), as well as a smaller quantity of acetic acid. In aromatic compound production, they are better producers of higher alcohols and esters. From both assays, we conclude that the hybrid strains between *S. cerevisiae* and *S. uvarum* are better-adapted to lower and intermediate temperatures and they produce larger amounts of aromatic compounds than their reference strains. As other authors have pointed out (Gangl et al., 2009), these data suggest that hybrid phenotypes are not just an intermediate or average from parents, but new specific abilities can arise after the hybrization event as can been seen also in artificial hybrids between strains of *S. cerevisiae* (Pérez-Través, personal comunication). This fact is even more intriguing when it happens in a hybrid with an equal genomic contribution of parental species, such as the S6U hybrid.

The global gene expression analysis indicates that, under oenological conditions, the S6U hybrid has a new transcriptional profile, which differs significantly from the expression patterns of the reference species. We also observed a down-regulation of the genes involved in cold adaptation and stress response. We propose that the interaction between both parental genomes which occurred after hybrid formation leads to the appearance of this new transcriptional pattern to adapt to fermentative conditions. In fact several genes related to signal transduction and regulation showed a differential regulation compared to both parents. It is interesting to observe that during natural Macabeo must fermentations, the S6U hybrid was the best producer of isobutanol, isoamyl alcohol, isoamyl acetate and phenylethyl acetate. This can correlate with the higher expression in the S6U hybrid compared to both reference parental strains of the genes related to amino acid biosynthesis, which are the precursors of aroma compounds via the Ehrlich pathway (Hazelwood et al. 2008). On the contrary, when we observed the total aroma profile variation and the fermentation kinetics in the S6U hybrid under all the conditions, we concluded that it was similar to the *S. uvarum* parental strain than to the *S. cerevisiae* strain. This situation was also reflected in the transcriptomic profile since the S6U hybrid strain showed 3-fold more differentially regulated genes compared to *S. cerevisiae* than *S. uvarum*. After taking into account the equal genomic composition, an open question arises to explain which molecular mechanism influenced strain adaptation to the enological conditions to favor *S. uvarum's* influence on strain physiology if compared with *S. cerevisiae*. Possibly, the environmental conditions where the S6U hybrid strain had adapted, e.g., low temperatures, benefitted the imposition of some *S. uvarum* alleles. Thus the molecular mechanism involved in the adaptative equilibrium among the parental genomes in the S6U hybrid merits further research.

In summary, *S. cerevisiae* x *S. uvarum* hybrid strain S6U seems better-adapted to low and intermediate temperature fermentative conditions, and has an aromatic compound profile that differs from its reference strains. Both genome composition and S6U structure seem to be constituted by one genomic copy of each parental species, which suggests that *S. cerevisiae* x *S. uvarum* hybrid strains tend to be a genetic mixture of *S. cerevisiae* and *S. uvarum*. However, S6U hybrid behavior under enological conditions is not seen as being intermediate between both parentals and tends to come closer to *S. uvarum* in fermentation kinetics and wine composition. Our results support the idea that the construction of laboratory hybrids using selected reference *Saccharomyces* strains of interesting species is a promising method to genetically improve wine yeasts.

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Tables

Table 1. Comparison of the mean glycerol and acetic acid production at the end of the fermentations by hybrid *S. cerevisiae* × *S. uvarum* (S6U) with the reference strains of *S. cerevisiae* (T73) and *S. uvarum* (CECT 12930) under each must and temperature condition assayed

		Glycerol (g/l)			Acetic acid (g/l)		
Temperature (ºC)	Must	T73	CECT 12930	S6U	T73	CECT 12930	S6U
14	Bobal	0.59 a	0.83 c	0.70 b	0.58 ab	0.45 a	0.47 a
	Tempranillo	0.63 a	1.12 e	0.81 c	0.59 b	0.45 a	0.43 a
	Parellada	0.54 a	0.70 bc	0.60 abc	0.52 b	0.39 a	0.42 ab
	Macabeo	0.63 a	1.00 d	0.86 c	0.67 c	0.43 a	0.44 a
18	Bobal	0.69 a	0.85 a	0.80 a	0.35 a	0.45 a	0.37 a
	Tempranillo	0.76 a	1.12 d	1.10 d	0.43 c	0.38 abc	0.35 ab
	Parellada	0.56 ab	0.73 c	0.61 b	0.63 d	0.44 ab	0.48 ab
	Macabeo	0.66 a	1.06 c	0.94 bc	0.52 a	0.40 a	0.41 a
22	Bobal	0.62 a	0.77 a	0.74 a	0.41 a	0.48 a	0.43 a
	Tempranillo	0.73 a	0.09 d	0.11 d	0.44 b	0.40 a	0.39 a
	Parellada	0.59 ab	0.72 c	0.64 bc	0.48 ab	0.52 b	0.45 a
	Macabeo	0.71 a	1.00 c	0.88 b	0.54 a	0.46 a	0.47 a
32	Bobal	0.68 a	0.77 a	0.71 a	0.55 a	1.04 a	0.66 a
	Tempranillo	0.90 abc	0.98 bc	1.02 c	0.62 a	0.83 a	0.91 a
	Parellada	0.61 d	0.62 d	0.62 d	0.63 ab	0.60 a	0.83 b
	Macabeo	0.83 b	0.81 b	0.75 b	0.63 a	0.84 c	0.76 bc

The results are the mean value of three replicates. Standard errors were always lower than 20% of the mean values. The means with the same letters do not differ significantly in Tukey's test ($p < 0.05$) within the same row of each compound.

Table 2. Mean major volatile compounds production in the musts fermented by hybrid *S. cerevisiae* × *S. uvarum* (S6U) with the reference strains of *S. cerevisiae* (T73) and *S. uvarum* (CECT 12930) at different temperatures.

Tmp (ºC)	Must	Strain	Ethylacetate (mg/l)	Isobutil acetate (mg/l)	Isobutanol (mg/l)	Isoamil acetate (mg/l)	Isoamil alcohol (mg/l)	Ethylcaproate (mg/l)	Hexylacetate (mg/l)	1-Hexanol (mg/l)	Ethylcaprilate (mg/l)	Di-ethyl succinate (mg/l)	Phenylethyl acetate (mg/l)	2-Phenyl ethanol (mg/l)
14	B	T73	26.95	n.d.	9.01	1.62	94.76	0.43	n.d.	0.72	1.01	0.22	n.d.	13.63
		CECT 12930	26.11	n.d.	23.2	1.24	143.38	0.14	n.d.	0.8	0.86	0.42	1.4	100.67
		S6U	32.8	n.d.	10.2	3.38	144.8	0.51	0.03	0.7	1.3	0.31	0.75	38.73
	T	T73	36.73	n.d.	12.07	4.28	111.77	1.48	0.12	0.66	3.06	0.15	n.d.	8.98
		CECT 12930	56.23	0.16	40.48	5.75	220.23	0.79	0.07	0.8	1.41	0.82	4.57	128.35
		S6U	63.03	0.22	16.54	8.86	145.71	1.49	0.18	0.47	1.27	0.52	1.21	22.89
	P	T73	16.6	n.d.	9.64	2.41	80.06	0.8	0.18	1.78	1.3	0.21	0.29	15.64
		CECT 12930	14.91	n.d.	23	1.1	123.16	0.23	n.d.	1.64	0.84	0.41	0.98	51.72
		S6U	27	n.d.	12.65	3.91	106.69	1.1	0.58	1.64	1.73	0.3	0.96	23.43
	M	T73	43.53	n.d.	12.42	3.77	124.98	0.89	0.26	1.19	1.1	0.18	0.02$^{n.c.}$	13.27
		CECT 12930	39.53	n.d.	25.75	2.65	187.1	0.24	n.d.	1.09	0.02	0.62	2.52	134.05
		S6U	44.66	n.d.	21.69	5.58	208.06	1.35	0.18	1.33	2.07	0.62	1.27	63.69
18	B	T73	25.13	n.d.	12.5	2.96	151.1	0.36	0.01	0.65	1.2	0.38	0.15	27.64
		CECT 12930	30.02	n.d.	29.88	3.91	171.89	0.52	0.01	0.58	1.93	0.49	3.29	123.4
		S6U	39.56	n.d.	25.78	7.02	184.49	0.6	0.04	0.5	1.54	0.38	1.96	59.92
	T	T73	56.65	n.d.	17.4	11.17	161.57	1.34	0.2	0.59	3.01	0.34	0.32	12.32
		CECT 12930	56.54	n.d.	17	5.57	176.74	0.57	0.08	0.85	1.56	0.93	3.01	94.37
		S6U	63.45	0.14	39.22	8.43	255.36	1.18	0.06	1.13	1.87	1.04	0.89	44.99
	P	T73	26.55	n.d.	9.56	2.82	103.54	1.25	0.35	1.58	1.95	0.21	0.42	16.29
		CECT 12930	24.18	n.d.	21.87	1.63	117.87	0.48	0.12	1.92	1.44	0.34	0.84	51.9
		S6U	44.08	n.d.	8.36	6.87	135.4	1.76	0.76	1.63	3.04	0.51	1.3	37.04
	M	T73	59.89	n.d.	25.9	5.59	243.52	1.25	0.3	1.23	2.62	0.44	1.53	57.67
		CECT 12930	38.48	n.d.	29.16	4.03	178.38	0.49	0.03	0.77	1.39	0.48	3.41	121.5
		S6U	56.96	0.07$^{n.c.}$	36.14	7.02	274.02	1.03	0.31	1.16	2.33	0.5	2.03	83
22	B	T73	40.36	0.10$^{n.c.}$	16.49	5.01	166.28	0.66	0.06	0.66	2.56	0.37	0.34	20.01
		CECT 12930	30.97	0.13	43.18	2.4	105.2	0.13	n.d.	0.6	1.21	0.24	1.59	59.56
		S6U	39.44	0.24	46.61	5.41	159.41	0.65	0.06	0.62	2.11	0.38	1.17	43.88
	T	T73	36.15	n.d.	17.11	6.94	141.18	1.03	0.12	0.69	2.7	0.48	0.21	17.69
		CECT 12930	30.94	n.d.	46.51	1.9	180.71	n.d.	n.d.	1.38	1.24	0.61	0.42	44.54
		S6U	29.34	n.d.	46.61	1.2	212.05	0.17	n.d.	1.79	1.27	0.7	n.d.	36.41
	P	T73	34.53	n.d.	19.83	4.02	143.32	0.91	0.52	2.03	2.53	0.54	0.59	26.84
		CECT 12930	36.27	n.d.	24.34	4.36	122.91	0.35	0.52	1.81	1.08	0.38	2.75	68.35
		S6U	45.29	0.15	29.01	6.23	138.07	1.29	0.71	1.74	3.03	0.53	1.17	43.69
	M	T73	54.27	0.03$^{n.c.}$	25.35	9.19	218.32	1.13	0.32	0.96	2.98	0.34	0.59	34.57
		CECT 12930	53.66	n.d.	33.73	5.06	189.71	0.44	0.17	1.12	1.1	0.65	4.99	197.18
		S6U	52.75	0.03$^{n.c.}$	44.8	6.62	217.78	0.97	0.25	0.95	2.67	0.64	1.76	69.01
32	B	T73	39.22	0.07$^{n.c.}$	36.4	4.17	139.42	0.04	n.d.	0.48	1.37	0.41	0.28	16.79
		CECT 12930	20.25	n.d.	13.91	0.64	57.23	n.d.	n.d.	0.71	0.04	n.d.	0.02$^{n.c.}$	19.48
		S6U	32.66	n.d.	27.93	2.58	130.3	0.1	n.d.	0.67	1.14	0.31	0.22	18.31
	T	T73	64.61	n.d.	24.02	7.18	181.71	0.25	0.01	0.51	2.16	0.55	0.49	18.88
		CECT 12930	19.11	n.d.	15.46	0.46	57.05	n.d.	n.d.	0.66	0.07	n.d.	n.d.	12.13
		S6U	45.19	n.d.	22.25	0.99	91.43	n.d.	n.d.	0.89	0.93	0.22	n.d.	16.24
	P	T73	39.29	0.08$^{n.c.}$	20.07	3.62	129.88	0.21	0.32	1.81	1.37	0.34	0.79	22.73
		CECT 12930	17.02	n.d.	10.51	0.79	64.37	n.d.	0.08	1.71	n.d.	n.d.	0.07	13.5
		S6U	25.7	n.d.	10.6	1.17	62.42	n.d.	0.18	1.68	0.17	0.12$^{n.c.}$	0.11	12.32
	M	T73	56.6	0.09$^{n.c.}$	20.62	7.07	197.37	0.22	0.09	0.84	1.59	0.48	0.66	28.39
		CECT 12930	17.31	n.d.	7.22	0.39	43.92	n.d.	n.d.	0.87	n.d.	n.d.	n.d.	10.88
		S6U	33.52	n.d.	18.43	1.33	98.19	n.d.	n.d.	0.91	0.45	0.22	0.03$^{n.c.}$	14.01

The results are the mean value of three replicates. Standard errors were always lower than 20% of the mean values. n.d.: not detected; n.c.: Under quantification limit. Tmp, Temperature; T, Tempranillo grape variety; M, Macabeo grape variety; B, Bobal grape variety; P, Parellada grape variety.

Table 3. Comparison of the mean production of total esters and total higher alcohols by hybrid *S. cerevisiae* × *S. uvarum* (S6U) with the reference strains of *S. cerevisiae* (T73) and *S. uvarum* (CECT 12930) under each must and temperature condition assayed

		Total aroma (mg/l)			Esters (mg/l)			Higher alcohols (mg/l)		
Tmp (°C)	Must	T73	CECT 12930	S6U	T73	CECT 12930	S6U	T73	CECT 12930	S6U
14	B	148.35 a	298.22 c	233.49 bc	3.28 a	4.06 a	6.28 a	118.12 a	268.04 c	194.42 b
	T	179.26 a	459.58 c	262.39 b	9.04 ab	13.49 c	13.76 c	133.49 a	389.86 c	185.60 ab
	P	128.92 a	217.82 a	179.99 a	5.19 a	3.56 a	8.58 a	107.12 a	199.52 a	144.41 a
	M	201.60 a	393.62 c	350.49 c	6.21 ab	6.10 ab	11.07 b	151.85 a	347.99 e	294.76 de
18	B	222.07 a	365.93 a	321.78 a	5.05 a	10.16 ab	11.53 b	191.89 a	325.75 a	270.68 a
	T	264.91 a	357.23 a	417.77 a	16.38 a	11.73 a	13.64 a	191.88 a	288.96 a	340.69 a
	P	164.53 a	222.59 ab	240.75 b	7.00 b	4.85 ab	14.14 d	130.97 a	193.56 b	182.42 ab
	M	399.94 bc	378.13 abc	464.50 c	11.73 a	9.83 a	13.22 a	328.32 cd	329.81 cd	394.32 d
22	B	252.86 a	245.21 a	299.98 a	9.07 a	5.70 a	10.02 a	203.43 a	208.54 a	250.52 a
	T	224.28 a	308.37 ab	329.54 ab	11.46 b	4.28 a	3.34 a	176.67 a	273.15 abc	296.86 abc
	P	235.67 a	263.12 a	216.33 a	9.12 a	9.44 a	13.12 a	192.02 a	217.40 a	170.72 a
	M	348.02 b	487.82 c	398.20 bc	14.55 a	12.41 a	12.91 a	279.21 b	421.74 c	332.54 bc
32	B	238.64 a	112.28 a	214.26 a	6.34 ab	0.70 a	4.38 ab	193.08 a	91.32 a	177.22 a
	T	300.36 b	104.94 a	178.13 ab	10.63 c	0.52 a	2.13 ab	225.11 b	85.30 a	130.81 ab
	P	220.43 b	108.06 a	114.34 a	6.64 d	0.95 a	1.62 ab	174.50 b	90.08 a	87.01 a
	M	313.99 d	80.59 a	167.06 b	10.17 d	0.39 a	2.00 ab	247.22 de	62.88 a	131.55 bc

The results are the mean value of three replicates. Standard errors were always lower than 20% of the mean values. The means with the same letters do not differ significantly in Tukey's test ($p < 0.05$) within the same row of each group of compounds. Tmp, Temperature; T, Tempranillo grape variety; M, Macabeo grape variety; B, Bobal grape variety; P, Parellada grape variety.

Table 4. Functional analysis of the transcriptomic comparison between hybrid *S. cerevisiae* × *S. uvarum* (S6U) with the reference strains of *S. cerevisiae* (T73) and *S. uvarum* (CECT 12930) during the Macabeo must fermentation at 18 ºC

Comparison		Category	*p*-value	Genes	No. genes in category	Total no. genes in category
S6U vs T73	Up-	-	-	-	-	-
	Down-	response to stress [GO:0006950]	6,22E-05	PAU2 PAU5 PAU1 PAU17 PAU18 PAU23 PAU6 ZEO1 PAU20 PAU21	10	152
S6U vs CECT 12930	Up-	-	-	-	-	-
	Down-	structural constituent of ribosome [GO:0003735]	2,10E-02	MRPL37 RPS18A RPL29 RPL34B RPL13B RPS7B RPS30B RPL20B	8	218
		response to stress [GO:0006950]	6,35E-06	PAU2 PAU1 PAU17 PAU18 PAU23 PAU4 PAU6 ZEO1 PAU20 PAU21	10	152
T73 vs CECT 12930	Up-	ion transport [20.01.01]	8,70E-05	POR1 FIT3	2	7
	Down-	electron transport and membrane-associated energy conservation [02.11]	9,19E-04	ATP1 COX9 STF1 COX20 QCR7 QCR10	6	58
		aerobic respiration [02.13.03]	7,99E-05	COX9 DLD1 COX20 QCR7 QCR10	5	77
		mitochondrial inner membrane [755.05]	2,00E-03	ATP1 SHM1 COX9 STF1 DLD1 COX20 QCR7 QCR10	8	150

Figure legends

Figure 1. Genotype of the *S. cerevisiae* × *S. uvarum* hybrid S6U. Green and purple bars represent the chromosomes of the *S. cerevisiae* and *S. uvarum* origin respectively. The presence or absence of *S. cerevisiae* (C) and *S. uvarum* (U) alleles from each parent species was determined by the restriction analysis done with the 35 gene regions amplified by PCR with general primers. Gene 1 chromosome location is represented with a light green vertical bar, gene 2 with a yellow bar and gene3 with a cyan bar.

Figure 2. Evolution of sugar content (glucose + fructose) during the fermentations of musts Tempranillo, Parellada, Bobal and Macabeo at 14, 18, 22 and 32 °C with yeasts *S. cerevisiae* T73 (♦, purple), *S. uvarum* CECT12930 (●, yellow) and *S. cerevisiae* × *S. uvarum* hybrid S6U (x, light blue).

Figure 3. Differentially expressed genes in *S. cerevisiae* T73, *S. uvarum* CECT12930, and *S. cerevisiae* × *S. uvarum* hybrid S6U. Venn diagrams showing the number of up- or down-regulated genes after 50% sugar consumption at 18 ºC Macabeo must fermentation.

Figure 1

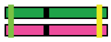
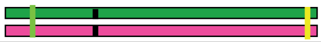
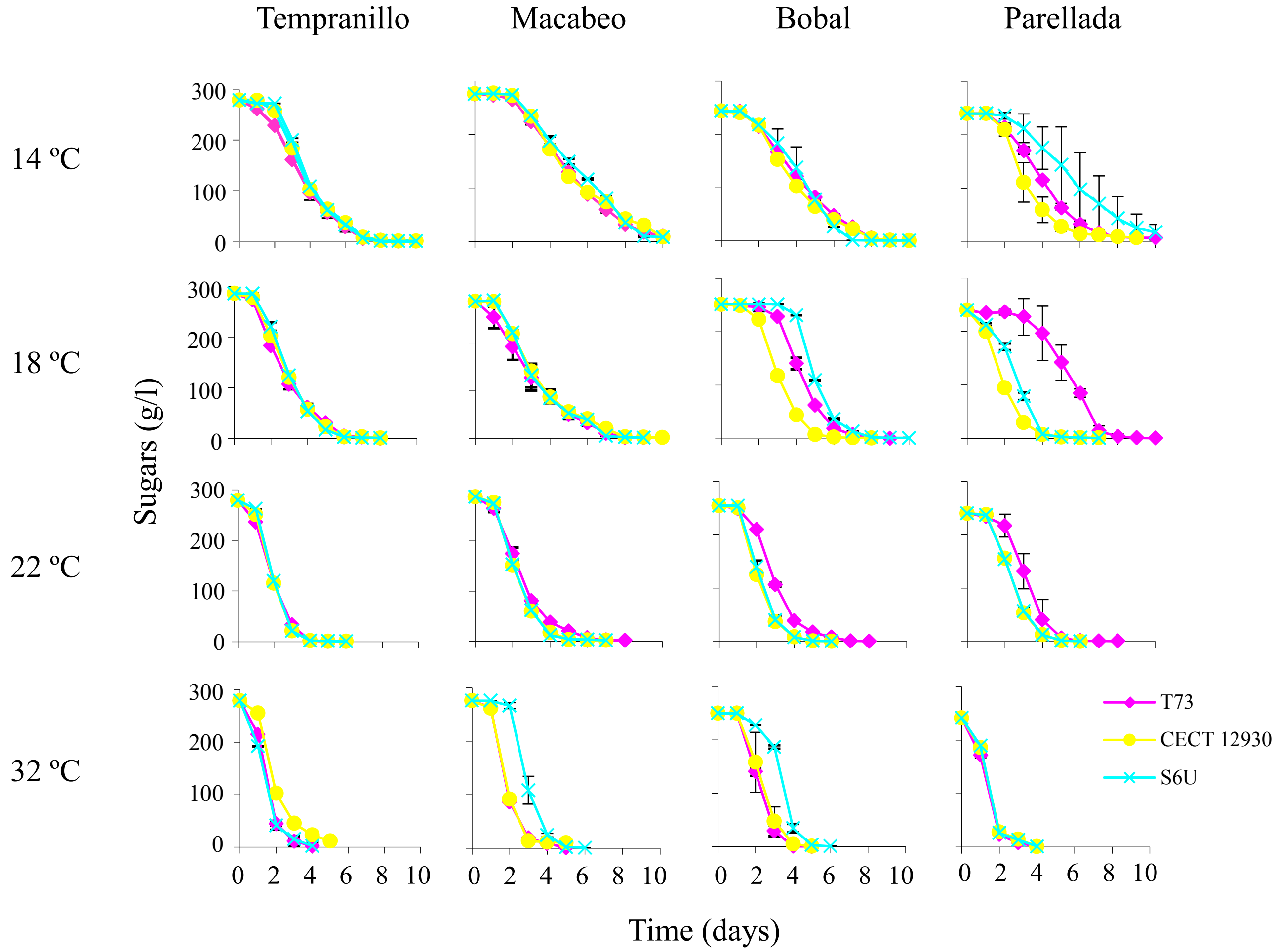
Chr	Gene marker chromosomal location	Gene 1	Alleles	Gene 2	Alleles	Gene 3	Alleles
I		*CYC3*	U C	*BUD14*	U C		
II		*PKC*	U C	*OPY1*	U C	*APM3*	U C
III		*MRC1*	U C	*KIN82*	U C		
IV		*UGA3*	U C	*RPN4*	U C	*EUG1*	U C
V		*NPR2*	U C	*MET6*	U C		
VI		*EPL1*	U C	*GSY1*	U C		
VII		*MNT2*	U C	*KEL2*	U C		
VIII		*CBP2*	U C	*MNL1*	U C		
IX		*UBP7*	U C	*DAL1*	U C		
X		*PEX2*	U C	*CYR1*	U C	*DAL5*	U C
XI		*CBT1*	U C	*BAS1*	U C		
XII		*PPR1*	U C	*MAG2*	U C		
XIII		*ORC*	U C	*CAT8*	U C		
XIV		*EGT2*	U C	*BRE5*	U C		
XV		*RRI2*	U C	*ATF1*	U C		
XVI		*GAL4*	U C	*JIP5*	U C		

Figure 2



Tempranillo
Macabeo
Bobal
Parellada
14 ºC
18 ºC
22 ºC
32 ºC
Sugars (g/l)
300
200
100
0
0 2 4 6 8 10
T73
CECT 12930
S6U
Time (days)

Figure 3

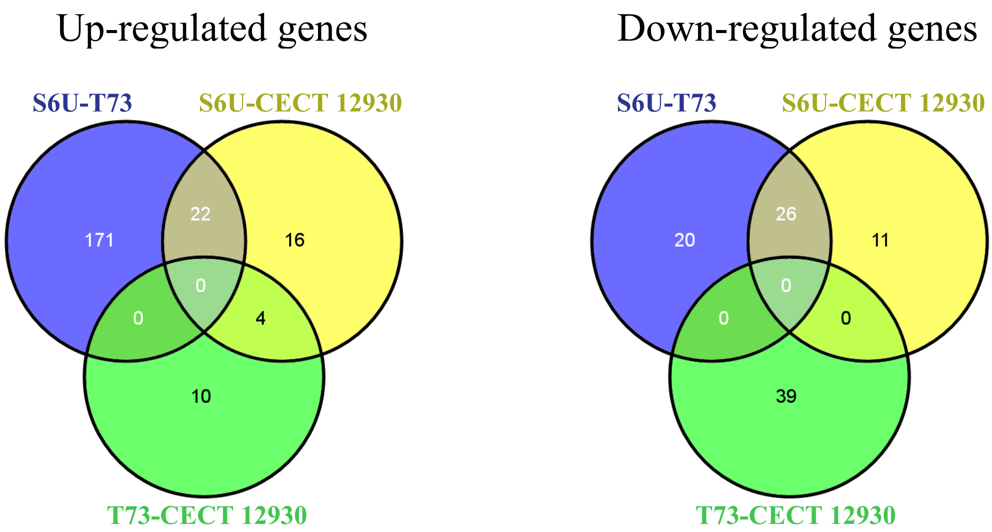

Up-regulated genes
S6U-T73
S6U-CECT 12930
171
22
16
0
0
4
10
T73-CECT 12930
Down-regulated genes
S6U-T73
S6U-CECT 12930
20
26
11
0
0
0
39
T73-CECT 12930

Table S1. Transcriptomic row data representing gene expression for each strain analyzed									
	T73			CECT 12930			S6U		
ORF name	1	2	3	1	2	3	1	2	3
YAL004W	194,824906	150,179	362,293868	100,88086	71,517854	197,982303	20,8376936	20,1469722	68,5868349
YAL005C	536,718464	373,972	528,349492	585,329826	378,011233	533,79963	547,399441	389,411323	702,003763
YAL037C-B	619,13504	605,162	793,601529	793,373904	762,902505	953,552808	737,619785	718,329948	1345,89072
YAL037W									1,42300761
YAL038W	1342,082	914,915	928,888448	1423,14325	1014,90789	1229,47454	1236,68327	1049,49988	1323,25851
YAL061W	187,862556	199,737	207,207635	261,839644	221,485302	355,728551	147,184858	138,448804	214,527724
YAR068W	84,9697899	100,851	76,7840589	443,08853	538,77666	431,409859	481,723772	668,427413	506,915816
YBL003C	82,2134926	78,1	95,283571	82,4940935	81,6689379	128,593103	77,8280757	71,407047	120,673177
YBL027W	106,278269	134,289	99,3206831	103,714265	137,641132	65,1105658	257,926901	295,351595	184,303469
YBL030C	490,52818	566,63	409,790391	478,482481	559,681588	336,765983	400,640514	416,521596	290,501407
YBL045C	103,907008	100,039	177,913382	87,3847222	84,7256121	176,772177	88,8940494	96,2232359	184,825771
YBL064C	285,220423	316,745	408,586311	249,11564	307,439132	356,534645	216,9079	239,120628	353,793268
YBL075C	67,8650166	95,882	41,850612	42,5739824	60,9645097	26,0625306	30,8604452	34,7242037	20,6975657
YBL078C	114,2936	126,324	267,920494	111,280364	123,340083	368,39021	68,2065634	59,3377747	188,004887
YBR009C	67,0738137	74,127	67,7945992	86,9149626	86,4027477	100,04717	91,3426379	88,1635465	72,0857282
YBR010W	329,951559	401,426	343,319105	491,784235	481,901587	390,469792	458,816095	422,908562	304,385058
YBR011C	163,459699	165,093	166,369659	206,825133	223,405812	218,433857	323,592282	305,090762	329,794005
YBR031W	148,42567	119,64	99,8261618	142,816347	129,90361	101,629437	148,044951	134,689117	160,599999
YBR039W	131,081423	158,142	116,315515	145,370327	171,022436	119,331823	159,08006	173,136987	134,860616
YBR054W	200,932664	314,172	753,263994	150,366247	209,886585	656,44031	108,618561	147,834515	461,438198
YBR067C	586,964542	668,219	523,993307	504,649977	590,915402	436,170742	506,713777	565,846478	495,092061
YBR072W	93,5133724	115,445	91,3169908	164,762756	223,534434	168,260669	688,954603	1091,01404	602,61441
YBR078W	113,331009	103,427	103,844801	121,384243	124,019764	140,321946	141,645699	126,51461	154,710773
YBR084C-A	100,331334	117,687	99,0133655	89,0221311	105,138748	85,0904313	272,482628	196,627154	249,804456
YBR111C	242,644551	234,347	265,705456	143,368449	156,128715	163,197062	122,363579	157,204467	139,985043
YBR113W	212,592928	210,231	373,120516	169,980057	180,435832	362,03298	61,1035992	41,0706463	150,633616
YBR118W	1443,08245	1352,904	1411,84226	1601,17942	1478,45304	1849,36254	2147,41003	2003,33261	3553,47385
YBR126C	415,792377	411,785	500,287868	426,997916	399,333553	654,284273	245,132512	268,68483	395,918557
YBR127C	101,026278	120,962	135,63622	157,596224	169,356649	162,735934	148,74249	156,21389	180,351558
YBR145W	182,315918	239,273	497,651318	118,345655	129,854431	274,327143	58,1261979	66,3821233	146,092783
YBR173C	106,976734	108,207	197,410417	178,086109	175,210231	343,985628	111,653576	89,1090967	167,40059

YBR174C	271,28633	267,512	485,063052	499,474522	423,739029	889,306417	227,319545	154,043628	340,839635
YBR178W	121,306428	111,422	197,368433	169,117481	162,201711	351,967366	93,1060331	69,2412869	173,225861
YBR188C	100,621286	88,655	188,894528	159,869428	109,994876	316,178907	88,5895191	53,4528507	145,405263
YBR194W	234,009405	222,292	460,628783	405,081204	260,867725	833,080485	198,726617	110,228635	376,198976
YBR196C	191,917177	159,658	239,420565	193,8622	145,638421	213,035844	180,38278	167,031434	314,985666
YBR206W	103,75675	100,299	254,652099	170,132594	137,509988	401,545663	97,2604029	57,8271458	173,865415
YBR241C	115,924135	125,782	145,977541	75,0886314	88,5994171	109,540774	53,9306753	72,6362622	80,343969
YBR276C	112,556241	94,365	107,964201	107,338703	110,247076	92,882086	235,282602	171,574578	180,748615
YBR286W	248,779308	232,972	290,845044	216,171728	203,162911	348,806351	172,148115	183,603327	301,504401
YBR300C	117,223633	160,346	138,615353	153,681561	168,990958	162,079442	82,9083823	87,7132845	85,5749876
YBR301W	124,919666	140,751	141,347625	140,734826	157,247225	157,066876	247,972052	191,140712	210,898255
YCL009C	231,975051	217,725	148,667829	240,572226	258,671055	183,771818	213,329669	190,253696	121,238117
YCL017C	86,7470617	114,262	170,878663	86,3561108	109,969655	164,571646	58,3772297	76,6728608	86,7821457
YCL040W	503,822502	361,982	368,697157	386,716036	303,705299	375,676736	267,198615	213,51423	269,718568
YCL043C	175,524956	209,641	111,709109	184,627645	220,524417	118,726373	182,792273	218,185698	141,120251
YCL065W	116,333824	149,561	159,899196	190,213464	190,961434	245,82521	98,0464204	87,2967922	102,627096
YCL066W	121,761898	146,688	205,83898	200,403736	180,555627	316,585474	101,287199	91,0339666	133,658788
YCR005C	52,5187327	55,451	56,4994177	54,7337349	60,5143312	97,8471318	41,5190067	38,3510639	52,0516997
YCR012W	3392,75075	3512,584	2404,14561	3500,70743	3616,25492	2403,89533	5140,40407	5837,33586	6896,03345
YCR013C	2365,99245	2416,446	1266,84041	1882,2738	2418,56951	880,083857	3730,01094	3985,25526	3776,03863
YCR021C	6,19697334	10,672	32,2985763	8,35713007	6,81824979	25,2124359	3,58851956	9,12455897	22,1925232
YCR073W-A	52,6842514	53,743	64,0144247	61,627591	67,8041966	47,7425855	41,2473986	42,3268772	35,3859889
YCR104W	70,3477971	73,264	98,8555084	57,8924628	50,6507563	80,2116269	170,415584	156,155356	209,917606
YDL022W	437,077378	512,723	538,143351	509,082995	541,332716	489,603506	590,803244	527,803844	587,60621
YDL055C	430,31811	522,112	417,859577	309,71327	426,041623	243,49317	258,070936	375,565767	216,166581
YDL062W	91,9262711	105,93	168,504089	132,302103	143,619553	296,11632	78,8301451	65,5378821	174,544941
YDL065C	120,823959	141,43	75,6975316	122,036237	146,408894	54,4307011	186,642112	188,171234	130,964667
YDL066W	129,28889	141,929	103,965713	132,573429	144,918387	101,886402	127,334831	126,755501	120,233484
YDL078C	90,7852485	87,614	76,3675848	115,408308	106,219429	96,5728698	128,470646	100,181039	115,007795
YDL086W	75,3004455	89,408	103,201617	84,3582829	92,6661557	103,794275	101,85305	123,623929	160,389479
YDL099W	137,526087	109,65	100,230881	157,814905	122,992046	89,4359464	241,348517	157,510645	218,937982
YDL107W	101,182406	105,698	48,7190765	108,577896	117,525593	42,8620211	167,236534	167,310597	124,824948
YDL108W	130,472173	142,625	63,1126239	128,728961	160,533402	58,2622874	232,187915	198,873962	144,008903

YDL110C	337,129906	300,334	469,860067	346,934963	295,005631	706,886303	389,743266	281,157087	588,949273
YDL121C	78,0708295	91,486	149,682145	127,150946	124,154692	281,865354	58,7949301	43,1531079	167,038176
YDL123W	163,148617	151,599	240,339159	184,186233	150,500853	360,086386	90,2726665	69,7770987	199,133127
YDL126C	135,641991	115,255	137,659814	235,615453	138,325857	260,292661	181,181143	124,384871	229,986277
YDL134C	142,509257	151,433	119,931115	154,793865	174,149726	128,045734	186,232643	174,503532	208,910308
YDL137W	121,12917	129,178	98,8051285	139,667068	149,029261	152,503117	110,390187	117,734502	126,554409
YDL144C	176,716456	166,738	62,8859142	208,593481	204,055702	61,2208986	291,834707	238,382199	143,395997
YDL168W	238,471367	321,253	303,812839	191,447258	291,930042	202,315498	168,380581	205,125849	178,555477
YDL171C	113,611569	119,304	114,330545	109,621357	116,054001	132,595413	102,112312	105,329784	155,787356
YDL174C	147,625076	135,425	133,636136	102,519618	101,450311	107,361856	115,583664	100,075227	123,705729
YDL185W	107,335945	133,288	119,69097	108,486104	145,294167	171,036237	94,6595493	127,383616	154,023253
YDL188C	117,595757	98,475	100,145235	126,822925	111,902775	99,9714886	150,04909	98,8325041	140,283501
YDL204W	205,134022	203,544	287,224406	160,240646	161,374492	301,672736	87,472222	99,3210383	196,801419
YDL223C	144,383961	147,479	233,285968	91,1616968	101,654594	144,260894	70,126339	76,3194052	129,10463
YDL243C	170,270617	155,415	116,236586	172,72707	164,081868	114,50582	191,448753	142,987445	179,42154
YDR012W	362,802913	353,475	155,138292	404,847674	363,078421	147,735194	490,83499	457,920934	308,856607
YDR032C	89,0878014	118,515	76,3575088	170,163641	207,944639	181,819944	113,388165	142,06891	107,255868
YDR033W	128,888593	133,695	276,800797	119,841326	118,38812	220,866219	62,1818012	95,3699895	115,793913
YDR044W	155,575843	149,835	56,2357628	173,535651	164,840993	59,393987	216,763866	200,911397	115,514108
YDR050C	331,845046	394,166	205,618987	413,212903	501,007062	243,369968	557,862527	652,920391	456,470995
YDR051C	166,890984	211,368	96,9981681	183,98915	205,451634	93,2780928	280,058849	293,100286	223,54277
YDR053W	75,8521745	80,394	121,934557	114,405344	114,632849	225,414138	51,9285942	47,2392354	135,241684
YDR063W	73,336525	83,432	139,497002	103,502334	119,086716	225,266295	61,5027808	49,2519064	124,705032
YDR074W	288,535492	371,031	364,424939	256,010846	306,749363	350,395659	200,619643	256,437704	291,631286
YDR077W	1632,10951	1937,613	1810,64983	1185,91469	1502,52183	858,486524	965,003117	1205,03838	727,97232
YDR099W	205,526101	260,17	424,85903	242,190736	230,729724	455,318113	163,466943	192,980032	281,619602
YDR100W	103,269585	119,557	170,86187	164,164758	163,711133	309,165186	93,8797048	65,6099241	159,560724
YDR126W	192,445428	226,745	147,871826	188,28583	273,390758	97,8735323	255,809592	334,294754	206,277478
YDR133C	547,506527	595,422	715,359811	940,338444	1041,54787	1486,69067	581,144694	397,011745	812,723882
YDR134C	1307,93702	1121,793	1659,71658	2524,23935	1746,59172	3732,84502	1632,30109	946,04319	2258,49961
YDR154C	305,623831	297,416	305,925438	302,716822	329,761429	292,539938	499,079943	408,353844	592,099076
YDR155C	83,2089526	90,546	66,9952375	83,6468942	89,6586606	87,2851892	94,587532	88,6520808	99,3547111
YDR156W	116,831554	150,019	217,747117	180,663037	199,391247	404,771799	94,5525522	80,8670512	215,702904

YDR157W	104,177003	128,428	182,296436	149,622461	160,279941	282,981213	91,4167128	60,9339534	147,369226
YDR158W	138,758673	160,977	68,6460201	167,1642	191,443138	61,7295473	205,306941	196,129615	110,994594
YDR171W	143,071551	168,134	137,893241	143,148418	201,019204	120,523364	273,661654	329,83716	238,455037
YDR173C	88,7297645	108,53	58,0309678	117,70176	133,14313	62,4687601	181,284025	174,595836	123,367298
YDR178W	78,129524	68,773	73,4573039	96,8204093	85,0295142	110,352148	84,005103	58,8109682	77,1808416
YDR193W	86,451241	116,719	189,499087	132,889302	142,101304	331,771017	72,5934462	71,6591937	180,777927
YDR204W	89,2732762	113,362	73,7914908	98,5037143	137,596997	76,6352451	132,254642	141,485821	106,539034
YDR214W	111,964599	123,024	50,3564243	107,682924	161,311442	48,9974872	190,983727	194,963436	118,509353
YDR224C	79,5076727	78,406	124,126084	99,9939859	86,485974	182,18955	89,0751215	70,6708687	153,071916
YDR225W	140,105127	134,177	163,785169	182,647366	140,035779	269,261776	139,016038	96,4438643	186,435315
YDR228C	80,4620465	120,022	159,595237	73,4255747	91,1706047	124,668236	9,70176017	13,2939849	19,8634808
YDR233C	62,0988614	53,181	66,6408987	65,2169318	77,8228751	95,7298152	171,477325	166,189445	211,777642
YDR265W	249,395601	247,719	94,7109191	229,055018	278,249407	86,1112489	411,463686	367,352988	211,972173
YDR273W	130,478042	158,718	73,7108829	112,793583	142,223621	54,3602999	202,018836	210,153024	129,04867
YDR279W	203,389619	229,342	89,3471354	202,286824	252,210931	83,9851322	334,162366	350,229525	220,90461
YDR293C	101,295099	147,087	201,291351	66,4588249	105,02778	131,477793	53,3216147	102,684495	104,223316
YDR304C	155,868142	197,431	189,695569	169,372609	190,777328	231,183517	154,672601	120,269477	141,927688
YDR308C	99,0623576	108,554	150,120451	151,764726	150,717746	285,566698	80,6614423	57,7370934	149,96475
YDR322W	151,67148	227,823	101,124285	157,104866	220,88002	98,7095468	242,77446	304,798092	221,632103
YDR342C	109,282257	135,082	180,768245	103,633272	127,027259	179,114777	79,000929	99,7285254	136,147719
YDR344C	49,6931758	66,235	95,4901288	78,8386084	97,1452426	173,590041	39,9510871	35,9826859	78,1321781
YDR345C	482,491719	609,378	853,387398	531,302081	717,995623	1040,03542	460,038331	576,886902	826,543577
YDR372C	113,097405	146,463	85,1739974	100,106026	152,61934	70,0421711	201,979741	217,778211	161,951057
YDR382W	128,779421	158,794	56,1030956	149,05281	189,127934	63,852144	180,249033	213,998261	122,016241
YDR385W	370,228951	372,67	355,113048	383,364275	435,197774	328,013352	427,354819	448,843652	432,029374
YDR392W	123,979379	151,527	68,8609745	128,052669	165,883843	66,3214667	202,79045	224,764025	154,324376
YDR411C	169,362025	200,221	94,8301516	165,908808	231,21395	81,895976	279,536209	298,16123	152,954664
YDR423C	107,112906	126,465	111,050811	101,175134	119,922762	121,410419	123,713389	140,909486	140,120948
YDR424C	112,643109	108,846	171,066749	153,283345	161,800712	273,635451	100,828346	71,9180944	158,276286
YDR433W	155,794187	140,446	312,938325	226,609029	171,452438	429,600548	140,662148	84,4376286	238,540311
YDR435C	142,434128	159,876	74,1710196	156,48392	176,217773	75,2782616	244,490529	239,658691	137,581386
YDR437W	67,8274521	78,282	145,574501	105,421868	118,86604	270,661	66,1242343	50,4045771	156,528172
YDR442W	105,394328	125,328	191,747712	160,177201	170,931643	338,566494	87,8714036	69,3831194	186,139522

YDR445C	123,45465	118,43	167,189173	187,189724	157,276229	349,096756	110,456031	68,5929097	177,105822
YDR453C	124,224722	155,146	100,234239	101,472109	125,782648	89,8671539	248,675764	236,740994	186,890998
YDR475C	200,453716	216,483	294,966123	325,068197	311,142702	611,784818	166,999906	126,181417	337,671178
YDR492W	171,46916	113,937	97,8764583	144,98831	134,120408	95,4974912	139,575715	130,951942	100,234098
YDR502C	174,587016	230,873	137,948659	181,725395	240,363796	131,803399	198,428259	282,012584	171,328517
YDR513W	70,1153666	68,091	91,8090348	100,519091	111,777936	166,824485	126,929476	118,198272	199,170434
YDR533C	376,019758	458,264	666,064724	239,006361	329,388172	448,922162	233,488342	298,557461	444,143592
YEL009C	274,248059	360,539	252,369888	282,858683	350,033333	274,467946	265,394067	339,639364	260,23185
YEL027W	98,7677109	96,528	131,899708	102,604661	103,179148	175,906242	106,291373	101,259416	230,751077
YEL033W	147,791769	123,995	171,726726	178,901438	155,032902	276,974229	252,367165	172,112641	293,414043
YEL034C-A	533,563043	526,531	420,889091	544,157023	517,255102	526,87039	1206,99156	1082,01555	1286,83857
YEL034W	314,268368	355,346	250,949173	314,363619	382,693342	248,583178	555,518878	683,776844	493,812953
YEL039C	314,76962	256,161	224,741531	245,145632	256,913216	197,535256	272,906501	270,846087	168,65305
YEL049W	87,9362138	103,102	102,909414	64,332758	79,4861396	54,3779002	265,799422	246,768328	242,004562
YEL060C	738,544459	797,358	938,72429	739,90771	896,224698	805,900335	601,646992	657,848508	575,937014
YEL077C	362,787653	493,631	376,383456	202,942867	319,785625	185,431526	249,809522	341,692558	243,542156
YER011W	725,727911	734,31	252,818269	627,751272	709,072758	80,621714	648,563182	785,630606	197,723443
YER043C	138,973495	120,557	129,293386	102,277989	110,098278	103,049782	98,1986856	111,361044	108,103277
YER044C	146,351404	175,008	152,199463	138,359031	146,445463	102,020164	287,307905	252,338069	310,234313
YER053C	92,6118237	111,153	158,290397	84,5945125	95,4340599	100,589259	118,97465	113,493034	139,987707
YER067W	148,420974	200,353	216,588378	132,488387	166,810681	208,839931	131,598255	156,740697	171,29654
YER088C	122,112892	123,695	152,214577	99,3635902	112,021309	98,609225	64,3176287	75,5314467	61,2452882
YER138C	177,351531	183,834	356,495137	78,5821305	93,4921134	179,586465	51,2845537	69,648774	110,085894
YER150W	439,617679	355,967	506,884281	394,845036	352,289269	454,693302	390,150678	229,057273	333,775229
YER177W	455,857294	336,799	321,518028	520,119644	395,975499	353,190587	393,374996	266,597866	233,706349
YER178W	269,885878	133,362	193,212089	247,387789	122,906298	179,758948	207,023011	122,228116	132,227786
YFL014W	1727,55511	1360,988	1867,2013	2266,56679	1778,65023	2816,3831	2287,13801	1468,65101	2685,64972
YFL020C	95,5758998	81,27	91,6814057	73,7346981	87,9600879	99,3941986	243,449365	182,031912	238,209875
YFL039C	166,480122	57,095	90,2136702	298,356698	74,1130007	125,106483	253,628497	65,4906046	113,163747
YFR017C	160,861877	181,167	201,157004	140,33931	130,662735	113,37412	180,002117	129,826287	163,600573
YFR031C-A	279,003493	168,868	26,328554	285,316821	159,798237	24,29194	228,095275	168,882011	24,6148339
YFR033C	94,3574004	98,018	109,253927	79,6350398	76,3361511	71,8655626	67,8135546	65,4253166	46,780709
YFR053C	528,765349	522,517	624,61883	576,497537	597,350306	718,729547	345,499948	398,283735	540,678936

YFR054C	136,354543	165,43	190,44623	106,528773	129,356334	108,402034	128,382168	120,25822	129,813469
YGL037C	177,630917	42,943	155,003946	329,039555	58,4059322	279,91876	343,178933	58,0342663	208,505257
YGL055W	1418,51408	1189,296	1234,95327	1363,28266	871,82931	843,570266	1631,3875	1262,4693	764,744009
YGL156W	105,354416	120,603	145,90533	80,1830926	124,477509	122,704042	72,5955039	88,3526565	84,15198
YGL187C	120,35675	164,327	128,576311	80,2897334	130,965376	55,7824045	125,904773	159,975829	82,8995201
YGL245W	97,3038681	117,21	141,764099	111,010387	119,708391	131,020185	175,388894	173,886673	177,321671
YGL253W	252,122551	273,836	338,595146	294,604021	319,965948	353,908679	127,550883	122,401467	179,887881
YGL256W	162,9291	160,734	119,262741	130,929271	149,930879	72,3548511	107,423074	112,333609	62,6149996
YGL261C	82,9683049	86,524	64,6844778	81,0105713	64,5571107	43,085545	253,363062	200,593962	150,156616
YGR019W	183,073078	155,275	82,2956238	206,062449	198,342092	112,726429	168,804454	180,34343	118,146939
YGR032W	118,639347	79,267	128,322732	99,3284933	74,9049113	120,528644	83,5565381	53,5541596	90,0492007
YGR034W	289,857294	175,705	296,63034	300,0697	182,426958	441,528274	164,608932	75,0789334	275,399939
YGR069W	242,332296	70,937	67,373087	292,17423	71,4775019	131,944201	94,661607	7,21319688	62,3058819
YGR087C	71,2763453	78,111	169,278261	71,3953496	70,913833	160,534136	23,8891698	18,757914	51,2042907
YGR088W	165,478792	107,323	324,913635	99,9980356	70,9819272	207,477667	74,3218616	55,3394483	155,904607
YGR175C	327,744643	310,759	98,0359948	376,178844	283,596065	143,98105	468,791521	474,051569	376,883832
YGR192C	204,30995	180,6	191,737636	238,516353	174,183773	179,480863	249,998825	260,84802	228,184866
YGR209C	108,128322	52,843	86,9053878	90,1425346	45,790846	65,1387263	98,4456021	36,5837857	78,8170338
YGR244C	129,413323	126,022	93,7100377	159,598101	151,354553	232,123374	100,933286	119,305916	104,300595
YGR254W	4001,22686	2622,915	1972,62635	3666,00069	2209,51519	2321,5083	3730,79284	3264,57944	3532,73098
YGR256W	307,664055	318,93	258,306323	519,798372	540,964503	583,700013	303,828676	263,497812	231,369312
YGR282C	202,936497	230,921	172,858595	205,371308	208,17162	151,242935	230,56444	228,233294	128,065355
YHL034C	109,553426	105,666	145,88014	114,233909	107,383336	134,869372	81,1532177	90,8718723	93,7479545
YHL034W-A	246,769606	254,959	308,142155	260,510008	222,017446	306,727544	183,537138	181,153901	224,123699
YHL050C	571,88121	568,068	570,472156	332,840827	248,724254	309,886798	301,065269	321,349722	309,416216
YHR007C	164,118252	112,317	49,3672983	175,121764	124,546864	36,4255898	252,021482	174,192851	88,3757011
YHR008C	343,72835	196,311	293,132293	561,156109	314,872752	525,219481	534,950735	282,793789	581,991459
YHR037W	194,162831	222,709	397,000605	198,287118	221,544569	355,249823	179,49388	203,788571	309,093775
YHR085W	103,249629	123,786	63,2822363	105,86328	155,600354	61,2560992	175,63581	209,281767	130,154565
YHR087W	209,54668	177,928	159,91431	148,229381	132,162069	86,3206925	136,13123	125,722149	77,1648527
YHR092C	70,6905735	68,776	126,920491	89,3663515	79,0359611	191,199146	63,3381934	60,494948	98,5659278
YHR094C	693,274506	684,802	824,722894	799,482128	744,441404	1201,53582	725,798658	646,540179	907,175346
YHR096C	61,8769959	58,332	100,625523	77,5103228	69,7764072	198,805997	34,1423768	34,6048843	57,7623838

YHR174W	4696,43007	3128,492	2074,79518	4462,84919	3330,13685	1726,04072	4744,38501	4033,38151	2516,46904
YHR183W	376,825048	371,28	241,724607	588,063341	561,015731	366,283453	258,000976	369,701104	211,489843
YHR190W	168,596648	185,338	124,692018	136,85661	174,208993	95,1208447	161,711778	275,229388	101,627793
YIL011W	426,416095	214,39	2,0370287	507,644019	293,037203	37,1718427	383,751426	273,254989	19,7648828
YIL018W	165,016279	101,35	74,1105637	200,23635	137,368755	71,5857178	167,471105	119,429738	102,98951
YIL033C	91,071678	74,074	126,446919	115,717431	85,5150008	137,785742	119,369716	102,166694	146,596432
YIL125W	158,4014	124,944	182,674286	121,035973	102,958472	124,103266	147,205435	104,071302	153,117218
YIL148W	147,572251	160,598	159,415549	214,477624	197,543876	202,282058	184,121507	159,268918	319,822293
YIL155C	81,7638922	76,539	60,5180572	147,608434	126,5506	102,412651	74,9453257	45,4539466	59,3106374
YIL176C	90,3286047	85,643	67,1866813	70,8958926	70,5947989	42,566336	251,027643	171,212117	234,801585
YIR016W	113,987214	123,163	184,857416	93,3701066	99,1552834	126,588429	70,9432211	67,7036422	97,5399767
YIR037W	99,38283	109,92	103,770911	97,3941099	110,598897	86,290772	131,042693	121,201519	154,828025
YIR038C	125,920996	162,816	114,674808	224,952721	321,795665	223,2581	105,550624	123,049845	81,8682393
YIR043C	312,351404	375,554	253,649538	140,205672	171,628979	71,890203	131,709368	108,078634	68,6801032
YJL001W	115,817311	138,962	104,12525	155,516053	154,122457	134,17064	273,157533	255,145452	218,311752
YJL004C	141,536101	196,373	150,264873	175,437637	228,292203	166,724163	301,513834	400,712898	318,644447
YJL011C	155,750753	176,872	112,202833	188,922975	204,310425	143,669524	335,038919	338,590253	234,964139
YJL020C	143,808755	168,997	225,759206	191,026094	209,519633	315,742419	118,073405	91,2771081	196,86271
YJL034W	164,836673	174,266	165,118558	142,131956	144,012986	131,961802	122,359464	120,195184	122,149481
YJL052W	7461,39068	9275,027	7444,93687	7998,27563	9692,19314	6620,31223	9840,4367	13376,6868	13065,832
YJL079C	994,012601	1100,983	1002,12576	801,741833	1066,4754	723,745634	705,709945	982,399593	579,646427
YJL093C	83,1690403	96,315	155,554767	125,695772	118,523047	247,384597	69,4617221	52,9935834	144,771038
YJL099W	92,8407326	75,321	186,343624	108,051442	76,1432175	323,611515	46,5437572	22,0178107	170,033421
YJL101C	59,2780001	83,78	69,7174334	45,9932379	67,6074799	46,324001	52,1775683	59,5989267	51,1003632
YJL116C	96,9822219	136,893	93,8393462	83,0029996	118,465041	68,649987	132,19497	191,266785	104,945479
YJL138C	232,338958	262,934	334,121408	281,309016	318,378344	483,179395	251,167563	316,185217	438,33964
YJL141C	114,18795	126,699	139,387845	102,805794	122,630138	135,400901	61,1180026	68,1876739	82,6943299
YJL151C	206,163524	188,508	156,006507	150,279854	174,012277	88,6984937	189,405519	159,052792	134,466225
YJL158C	215,817608	232,994	258,338231	290,802749	286,447195	364,145016	183,977472	166,416827	191,410512
YJL159W	1424,14406	1591,211	2641,90364	1299,54385	1235,5685	2728,47134	838,548955	945,505127	1831,21893
YJL166W	102,191952	95,171	123,168865	59,0317647	61,3163299	67,3070838	95,569025	76,4724943	115,127711
YJL171C	128,298126	119,4	214,934237	88,9006416	98,9888308	155,236444	84,9783655	97,5965349	149,026737
YJL172W	97,8825966	80,48	93,2851669	144,116285	106,229517	135,402661	109,357253	83,823021	110,999923

YJL196C	111,353002	139,144	57,4213706	141,533957	173,737378	76,9362103	204,586768	202,210403	136,840569
YJL223C	59,0561346	90,626	58,4524799	48,3028889	71,1572068	43,5237926	205,89131	229,548059	174,158544
YJR005W	99,7972137	101,541	177,713541	167,328885	137,378843	295,243345	104,287235	52,4127455	176,652804
YJR009C	7723,15792	7888,042	4219,38001	8719,56035	10387,1717	3991,66454	10956,7091	13942,2338	8600,28492
YJR027W	191,360752	227,581	312,790544	83,0164985	121,018574	149,276981	40,1609661	87,6164782	80,6850644
YJR030C	105,40372	104,669	156,636256	164,071616	153,056908	252,555567	100,301591	63,3023314	126,469135
YJR040W	137,997992	179,031	203,670963	238,917268	254,096132	350,145734	149,444144	101,783971	189,942203
YJR045C	309,430761	322,282	326,639988	274,226177	263,264894	258,845916	217,175393	214,88978	236,179291
YJR047C	285,861367	294,891	183,621428	342,020036	315,003897	222,877934	683,084164	591,61272	408,227307
YJR048W	93,6014143	76,421	102,153715	117,888044	108,286215	135,409701	110,931346	73,550294	93,3189204
YJR050W	158,754741	187,044	124,927125	190,456443	229,723443	160,870302	366,413774	369,775398	298,45053
YJR055W	197,882894	238,227	153,474075	247,008471	264,02654	186,848351	492,005785	462,554129	319,766332
YJR073C	200,722537	175,931	184,311633	159,785735	119,038798	125,062482	137,227951	105,437847	95,117666
YJR077C	124,149593	137,332	107,621617	126,235725	143,646034	97,3120826	105,151442	109,571252	79,885622
YJR085C	56,8797397	62,107	61,6079432	60,2291115	67,5696498	57,658597	72,282743	68,7459987	70,3935749
YJR096W	152,331207	165,507	152,364037	139,256704	155,906778	134,929213	123,522029	148,834097	138,045062
YJR104C	189,93917	243,58	274,461489	255,303507	265,063086	269,413138	223,512916	248,695449	231,028217
YJR106W	122,267845	142,842	176,323055	183,29936	182,849394	294,534053	102,223424	75,1712371	164,282764
YJR121W	112,970624	118,105	167,217722	87,1484925	85,1972277	139,292328	75,5420406	74,6421793	115,231639
YJR143C	102,731943	117,336	160,711993	152,366774	148,522337	276,685584	98,9476656	82,0084653	159,158338
YJR145C	195,77928	194,339	76,9553507	221,36473	235,406789	90,8474908	239,642736	295,880653	133,251072
YJR150C	237,184782	172,35	26,5099218	273,150319	248,662465	15,4337069	219,877071	210,983757	27,0851111
YKL029C	93,5098507	90,583	95,2533431	79,9617116	87,1921364	94,6825971	87,8035016	49,6323778	75,4327274
YKL032C	192,110869	180,501	473,264071	152,337077	171,612585	362,455387	53,4491882	50,0983989	102,770995
YKL034W	167,504929	188,216	218,509533	282,318729	292,940106	371,120017	179,730509	128,072517	203,580692
YKL035W	117,897447	83,063	107,364679	164,264649	115,433587	143,507601	112,19885	117,324763	96,2502095
YKL060C	3851,07087	4099,29	2206,07522	3877,47617	4284,3854	1865,57946	3687,60921	4575,90667	2143,2813
YKL085W	292,072428	334,505	254,044181	205,606188	265,012646	230,866712	159,86402	277,165514	118,261526
YKL096W-A	674,204639	939,523	763,697679	758,343072	1032,35893	944,817777	1035,41341	830,242563	903,362005
YKL103C	206,303217	173,906	194,857833	147,717775	97,3545693	187,499562	93,299451	114,046856	122,024235
YKL104C	174,417976	217,129	344,746536	277,194571	272,258376	543,233393	166,09043	153,012528	311,558722
YKL112W	101,795177	118,486	148,085102	124,684709	144,049555	226,955924	75,136686	78,4874166	119,873735
YKL117W	66,2450463	76,629	123,741517	84,5783139	100,399895	158,772345	84,0503711	117,975392	191,247959

YKL130C	866,215727	550,864	196,073669	908,992794	676,316912	177,761314	1188,77735	1029,15705	326,084592
YKL135C	201,405742	222,967	280,53563	315,793146	320,567447	482,248338	189,238851	130,24278	259,629604
YKL141W	176,251595	160,793	239,160269	170,591554	183,087724	256,131949	273,027902	212,910879	538,973459
YKL146W	204,731377	234,959	325,912837	347,19819	360,871664	631,997008	189,438442	160,76829	307,342996
YKL148C	166,671466	278,082	189,986093	243,124856	380,964505	270,331874	172,481452	248,287962	184,383413
YKL150W	193,840011	308,385	340,800108	112,415616	227,920207	320,758506	113,668003	234,58649	412,405726
YKL151C	99,0717488	184,548	193,900614	63,8562491	152,775705	192,800774	48,8195041	126,584401	158,617382
YKL152C	1582,23556	1498,938	540,489377	1670,62688	1708,61657	519,828508	2701,00913	2555,1084	1126,40113
YKL163W	1091,75198	2257,086	2169,90242	970,498896	1982,4222	3021,73289	755,772262	1848,82746	2342,37179
YKL164C	1013,28086	516,575	970,31251	909,864819	458,788641	954,939712	599,692237	282,937873	580,392574
YKL182W	248,56566	206,316	266,066513	191,795528	228,017304	240,772163	260,717058	277,455933	393,365671
YKL204W	87,8094335	90,966	83,4039824	95,7499515	112,346648	85,5779597	110,879905	92,2294122	113,011853
YKL212W	114,173863	121,236	104,110136	115,298967	132,231424	87,4541521	94,916754	75,0991952	68,6108182
YKL220C	166,571685	171,665	262,173823	264,817487	230,118137	475,804867	166,111007	95,4150157	253,098159
YKL222C	142,925988	139,788	189,04063	189,91244	183,621129	322,759661	118,192748	75,3648498	178,923221
YKL224C	82,2440138	70,689	86,8415733	55,3074355	52,962177	51,4456895	231,998613	151,254255	256,565074
YKR001C	180,904901	192,296	176,781513	277,858714	253,329442	303,402846	135,026279	98,7221899	171,064701
YKR004C	173,448342	144,687	53,736918	226,066375	147,220981	51,1781649	262,729427	207,762133	70,2443457
YKR020W	89,8191358	229,619	153,870397	97,2874691	270,358042	139,656655	153,16641	336,978315	324,845456
YKR024C	195,405982	168,199	255,637866	219,443846	195,919703	384,0492	186,63594	149,381165	268,924455
YKR027W	159,923937	171,45	181,428222	206,649648	215,910403	349,30796	145,193065	106,549994	204,409447
YKR029C	212,089329	220,488	212,186851	263,671436	297,991689	313,714864	217,494327	176,529711	203,769893
YKR033C	153,761007	192,391	193,074383	167,373431	216,060462	157,934571	288,091865	276,557661	323,470415
YKR039W	310,561219	184,43	175,679871	220,650642	134,371348	127,507165	109,445731	80,0858466	74,9317434
YKR040C	294,390863	121,471	175,599263	341,471984	133,107822	214,127062	469,065187	154,714518	413,823404
YKR043C	740,902807	431,207	170,697296	948,526838	447,756115	167,634099	1104,29076	683,2703	218,322411
YKR046C	250,449756	143,886	201,533175	338,38075	184,391602	241,926743	325,244565	193,047572	266,84324
YKR048C	58,7027933	50,736	46,2840463	106,611116	80,2313931	92,9243267	53,1672919	36,1447802	42,7808318
YKR049C	49,1308818	111,752	109,510865	74,5162807	159,648178	170,650791	61,6427002	128,88524	143,654484
YKR059W	201,068835	189,382	119,437391	249,096741	225,410808	130,006408	337,156228	237,119214	161,6979
YKR065C	56,2564033	185,652	176,694187	54,976714	191,00683	166,681922	79,3095746	266,667656	329,495547
YKR068C	352,352931	200,766	222,623895	382,115632	224,369219	232,204335	607,099731	318,40726	504,842595
YKR090W	90,293388	98,73	105,186587	151,408357	136,494879	147,379668	103,4292	80,4640667	116,886485

YKR094C	226,700757	147,828	137,008233	219,310207	161,433759	215,311563	302,592036	194,535687	228,032972
YKR098C	126,491507	127,265	120,587733	135,142258	131,850601	183,576454	117,069278	91,9007209	130,828761
YLL001W	142,714688	180,733	222,272914	240,479084	242,324658	383,498311	144,686887	107,180361	193,600985
YLL008W	122,571883	135,444	175,046763	187,133029	164,852342	297,594746	118,917036	88,8231803	157,908543
YLL019C	91,7947952	85,277	135,278522	104,458051	101,541103	186,80787	80,6511541	67,825213	133,445603
YLL023C	160,590708	74,246	137,584244	169,743827	76,7232794	224,743566	119,777129	66,2785631	114,485492
YLL024C	489,504547	527,787	573,672961	455,358973	596,510477	526,196298	533,166763	667,576418	660,030369
YLL025W	61,1315748	78,246	97,3457897	51,2469853	69,0172826	64,2411108	169,724218	205,839514	198,7414
YLL026W	147,540556	165,823	272,950091	129,4363	156,215724	257,487172	167,156287	178,227199	302,754196
YLL039C	185,832897	192,455	190,034794	243,699906	265,738984	257,742377	367,887042	378,996763	290,354843
YLL041C	78,7528604	62,15	84,5358516	232,15975	112,554714	294,486532	108,161766	74,5498756	90,4542515
YLL047W	153,368927	102,567	115,331426	148,094392	106,54729	97,334963	235,636516	151,26326	210,581143
YLL049W	76,7713315	92,621	133,419502	87,7532404	93,7266602	121,556502	122,495268	137,575296	286,538838
YLL052C	179,111194	73,861	79,4609128	201,28251	76,7812856	67,1786016	294,49729	111,214708	174,960651
YLL053C	354,611498	286,855	212,381654	374,01363	337,206398	176,94642	600,961799	437,760454	434,062623
YLL054C	148,285977	173,015	221,587747	222,585025	234,497605	428,046441	140,120989	117,187434	225,013744
YLR013W	337,068863	165,87	279,071253	389,353709	211,23586	250,371369	629,976544	284,594837	645,21137
YLR031W	242,282993	171,236	194,579064	276,338745	209,330483	203,862565	422,535833	328,517893	435,813402
YLR043C	85,3383919	109,297	119,093128	70,3424403	88,9575423	87,6583157	73,9000459	76,1978345	92,4608521
YLR044C	987,215769	619,709	305,814602	1064,15788	675,465734	289,000517	878,360123	665,896941	351,378952
YLR056W	150,652542	192,163	67,1262254	169,190375	238,663963	59,8762353	379,222566	406,188084	272,031621
YLR069C	245,548759	261,631	362,884992	361,664894	340,332427	625,810501	207,17116	177,819711	346,40109
YLR072W	112,921321	105,11	170,211969	145,806339	146,449246	276,308938	82,1655752	55,8144747	141,511978
YLR075W	184,455922	141,087	69,735906	229,875747	198,533764	108,794521	305,384249	254,834771	198,168466
YLR076C	125,361049	97,074	46,9255508	143,608729	130,38027	67,0994002	216,862632	137,559537	132,385009
YLR081W	48,3889824	46,8	98,0376741	128,890947	91,0306332	203,969927	26,4282943	11,071942	38,3226076
YLR104W	109,94668	72,119	87,570403	97,4008593	79,295728	78,1066305	159,757023	94,7733923	154,39899
YLR109W	971,507927	591,991	800,233208	640,419931	453,257877	426,854901	838,890523	479,630315	445,579924
YLR110C	1947,12565	1557,9	2442,62581	2680,10772	2766,31286	4270,24744	2822,83566	2049,8154	3363,90472
YLR114C	184,358489	152,194	284,445113	238,243676	193,277899	423,980771	130,865736	91,8962183	219,039244
YLR134W	678,490517	340,712	345,527425	688,749817	276,210363	278,648018	648,402686	291,717981	247,075692
YLR142W	788,841015	689,126	538,276019	562,964953	575,382352	338,696736	495,647804	487,451366	239,235826
YLR144C	123,914815	125,649	135,291957	156,859187	154,428881	220,505413	92,0833873	80,3469986	118,365453

YLR149C	203,015147	204,382	204,740697	246,56031	227,91138	296,825612	234,69206	204,16454	278,909492
YLR153C	204,15617	207,123	185,315873	213,046747	198,205903	145,788601	288,76677	269,186872	181,420146
YLR167W	341,063616	240,486	120,038592	387,328883	301,67256	168,436672	440,194477	260,370742	160,906452
YLR170C	272,374528	139,727	118,414679	285,260126	154,350699	107,127772	424,494704	205,765221	202,863858
YLR178C	420,205035	316,242	491,62084	329,989873	262,699964	405,42477	398,833908	286,290073	509,244858
YLR179C	137,611781	151,174	166,304165	122,129379	140,335898	168,514114	90,6574446	117,16492	122,242749
YLR219W	227,33818	249,266	303,387968	293,258187	309,402516	489,85695	189,224447	166,497874	271,048307
YLR233C	174,74784	153,821	222,684351	223,440852	171,690768	409,673484	141,518125	88,3031277	201,731315
YLR249W	146,690658	161,682	151,307738	152,245285	152,913154	127,195639	243,926737	215,186953	283,343732
YLR258W	113,625656	123,205	156,019941	102,743699	127,892308	177,703233	82,3980883	100,50973	124,411903
YLR259C	122,64936	79,507	97,2450298	131,978131	60,453803	79,8473006	209,712343	108,360048	111,903293
YLR266C	185,722551	194,735	232,15242	291,194215	311,625666	458,364725	157,497737	134,945766	212,827576
YLR270W	127,498706	54,483	134,489236	139,275602	57,5421443	134,543766	99,1369682	56,2219618	97,2894847
YLR277C	278,177074	244,752	295,864565	343,868027	341,033546	472,216165	250,004997	223,136328	308,161092
YLR300W	206,123612	199,571	181,094035	191,919717	187,918631	123,480215	139,285588	150,00928	89,9905749
YLR304C	346,058525	388,62	397,776456	432,500042	436,045169	504,562004	289,425214	327,295431	327,238454
YLR340W	321,984357	230,348	51,3455504	381,856455	274,143577	66,3601874	322,987337	243,07618	82,401201
YLR354C	148,482017	96,465	127,066593	222,139564	133,600874	177,655712	157,170572	97,778891	132,278417
YLR362W	175,286656	182,414	261,135996	252,063786	234,448425	414,578688	148,584052	118,403141	212,904856
YLR396C	90,6467293	96,45	161,884166	153,938039	146,509775	266,540769	89,554551	69,1850042	130,682197
YLR397C	190,23499	209,816	250,136377	274,743182	235,907407	357,312578	182,362227	133,203252	159,025098
YLR438W	225,420041	184,227	117,118235	305,612323	213,727604	121,852187	197,996155	144,417027	81,260663
YLR440C	273,847762	279,135	348,37893	423,401826	320,359382	559,24087	259,371363	186,721391	304,926015
YLR461W	71,4899936	80,3	87,7148255	49,6514227	57,7993892	40,313497	174,432092	152,922475	130,92203
YML004C	127,220494	164,536	97,0687001	215,661472	178,347609	126,213542	146,3474	148,064149	63,2199111
YML006C	135,26165	164,698	180,887477	242,595701	208,058129	340,261403	124,698997	107,531565	174,808757
YML016C	159,757245	180,021	294,190272	294,315146	211,940761	493,223888	150,071724	112,62628	247,883129
YML028W	399,236984	275,285	289,572111	401,18544	303,247554	260,655227	687,195324	492,892782	501,327713
YML070W	149,073658	93,131	100,58522	206,938523	108,859972	145,309873	112,542476	86,7001951	89,5348927
YML078W	155,048766	81,858	146,442716	165,899358	94,1970148	163,823633	138,402862	81,9791982	112,095159
YML086C	242,551814	259,861	312,704898	87,4697648	115,547077	109,487973	65,9781421	92,8395171	86,3797597
YML124C	172,90483	279,375	226,713066	259,10073	349,003092	321,58044	137,546885	206,035378	155,955238
YML126C	120,737091	106,172	59,7052609	124,484926	102,530992	59,0965418	257,398088	203,90789	128,406451

YML128C	328,668496	277,492	275,566489	400,240521	287,165968	241,398734	210,710297	204,93899	152,981312
YML131W	109,140216	112,434	70,8946445	96,6449244	96,1679644	67,9459748	78,5914591	86,7970014	51,0204189
YMR008C	151,920345	167,247	103,109254	171,91444	170,075421	73,2964673	103,709038	73,041498	48,4408845
YMR011W	65,9856163	39,421	32,7016158	80,9687249	44,2158518	51,590012	18,6833473	5,71157318	5,22302419
YMR043W	168,028484	236,306	403,929525	136,647378	141,396403	323,247189	65,2703148	57,9397113	129,768168
YMR083W	399,921363	288,736	216,895696	289,219335	162,422387	141,481806	166,339405	131,199586	87,9013652
YMR090W	359,889315	232,481	352,99709	226,541534	154,746654	214,57939	162,664464	147,571112	133,999883
YMR105C	181,913273	84,679	78,3575922	172,831011	80,0952047	78,7367214	117,332655	66,1952646	59,1054472
YMR116C	220,970992	215,347	43,1117897	233,284204	256,239839	51,2556062	231,899846	234,43115	76,799774
YMR167W	111,407001	114,048	143,87166	164,233602	126,719574	256,038667	95,103999	61,3189274	123,108812
YMR169C	418,769365	462,405	390,567087	225,214599	305,537538	192,080921	153,003857	169,658713	104,532434
YMR173W	88,8459797	99,267	69,5343863	79,226025	99,3683931	52,5404285	196,34593	188,571967	70,7320056
YMR175W	383,517403	355,248	640,045167	168,20496	196,38123	267,285262	183,323143	207,63606	288,676014
YMR186W	500,339566	404,646	473,346358	506,618107	442,57591	521,917664	591,566627	556,546317	439,850586
YMR192W	122,878269	135,093	134,885559	209,909617	177,749893	214,985957	115,735929	76,4499812	94,0943796
YMR205C	178,629899	152,316	119,010841	197,992844	160,861264	142,810629	152,353643	119,330681	97,5159934
YMR224C	156,766169	197,356	214,959427	215,305102	233,200031	309,726635	112,445767	116,635863	131,183181
YMR226C	93,3044197	90,712	175,041725	104,806321	103,312814	247,643322	92,7624077	82,4024445	223,508128
YMR237W	92,4826957	142,742	123,014367	131,141203	175,758767	156,947194	79,9186352	115,27382	75,0223469
YMR246W	355,428527	355,345	409,573757	536,308799	452,681598	640,504995	317,997566	258,398595	298,698358
YMR250W	112,96945	159,366	225,483796	72,1391355	116,810603	119,930234	39,3132195	86,3850117	65,6821939
YMR251W-A	516,17771	561,172	665,607946	276,022872	331,987101	372,848367	281,715247	266,442525	189,699705
YMR272C	122,499102	101,505	104,281427	124,237897	98,6899728	72,2703696	128,445955	122,023247	74,9770451
YMR277W	116,262216	171,011	111,536138	142,875742	174,66926	167,519697	79,675834	103,636799	60,1154095
YMR295C	199,198826	109,063	50,603286	206,125893	116,120834	43,259788	254,791062	165,572586	51,2096203
YMR297W	173,908507	93,049	84,0320522	126,768929	84,5049364	54,1561364	103,900399	73,8452156	46,0372275
YMR303C	919,826179	1872,383	1232,73487	618,561264	1456,09291	666,018396	435,548331	1373,22699	619,538607
YMR315W	160,185715	167,402	193,175143	156,917232	169,666856	210,765404	226,893615	165,964314	283,37571
YMR316C-A	6,45405558	5,133	6,42176238						
YMR322C	87,8235202	91,038	118,973896	47,3336724	52,9962241	53,6862083	37,4243084	33,571533	40,595689
YMR325W	77,3676684	100,036	53,4715837	46,0580323	77,9666295	28,4737723	144,36178	191,66977	86,6862126
YNL007C	76,6328123	89,386	130,181752	75,8702141	101,610459	130,001128	126,99532	148,097918	198,725411
YNL015W	168,566127	154,038	205,8373	80,0103074	87,5918747	83,6630466	77,7231362	79,4307155	95,0110736

YNL031C	306,051128	276,685	451,29674	352,019975	302,808725	502,515089	323,261003	251,293461	324,770842
YNL040W	115,705792	118,031	130,751045	137,389814	127,260545	157,839529	91,2541595	115,206281	143,49726
YNL052W	188,950753	181,224	182,519787	161,068125	190,312017	158,730105	170,275665	191,196995	215,582988
YNL055C	217,519751	221,951	237,937716	297,901787	291,353763	280,536531	280,501241	254,985609	281,419741
YNL112W	141,399929	136,192	134,962808	217,208438	162,535877	263,245992	115,293537	35,14745	209,347337
YNL128W	220,022488	235,711	254,238983	232,354134	234,628749	271,512855	169,168656	206,46763	196,756118
YNL134C	152,805459	146,834	221,720415	135,452731	142,374942	204,71442	143,701278	152,512737	254,662401
YNL135C	94,3667915	77,711	87,0850763	105,945623	81,4293471	103,866436	152,933897	119,814712	162,372097
YNL143C	1169,01987	1010,473	950,919593	1379,68375	1026,8723	1613,78246	571,372974	128,000475	763,019878
YNL152W	108,781006	122,607	77,5783825	224,349323	218,904027	207,410786	84,6902963	141,355245	94,1290221
YNL160W	815,119751	896,595	1487,33659	726,958276	933,540335	1396,4099	805,29342	935,842505	1290,35878
YNL166C	154,374952	197,04	224,145369	122,620737	127,162187	148,835213	40,6733178	51,4626927	50,2049876
YNL190W	226,995403	270,398	302,365256	171,501376	244,477192	224,083555	122,468518	152,906716	147,427852
YNL200C	124,945492	165,808	158,40963	142,576068	232,399294	144,510819	119,90676	153,365983	128,638289
YNL208W	269,07824	285,831	210,101122	268,459473	245,919781	183,884459	318,452304	362,672515	268,887148
YNL209W	622,419588	467,546	394,060096	635,361916	434,286068	394,491461	439,103929	348,926017	265,0365
YNL241C	451,903627	342,399	439,575009	292,631841	318,871397	392,761351	149,660196	242,974871	235,012105
YNL280C	104,357782	139,069	78,4264448	115,689084	130,376487	68,9280718	119,301814	145,511163	92,0344828
YNL305C	86,7881479	82,775	63,4955114	119,91422	113,731231	98,5898647	94,2541948	69,2773079	88,4982822
YNL309W	182,247832	130,817	137,54226	128,776206	89,3850227	140,904516	108,760538	80,4528101	169,521777
YNL317W	148,185022	188,44	86,2168621	151,609489	206,435217	76,3888408	201,148456	258,234249	284,750751
YNL333W	19,3539495	14,265	17,7102265	25,4574569	17,2164905	24,9308311	13,5433691	9,73466395	15,1547646
YNR016C	188,003423	174,086	202,485355	165,579436	165,835925	197,943583	199,85626	185,316573	283,02662
YNR036C	132,587526	142,821	138,583446	81,2818979	102,861375	94,8409999	80,9824338	93,0218732	112,838641
YNR045W	178,179124	241,882	316,434692	264,423321	262,495681	396,18285	227,05411	255,019379	245,945813
YNR076W	77,5014921	81,482	69,7879653	66,9636814	53,7881347	45,4070251	239,276476	178,146151	191,767597
YOL002C	118,957471	129,238	79,9613535	110,504181	116,611365	48,7440428	148,349481	128,919009	68,8213381
YOL040C	139,783481	141,556	85,8608438	133,531847	158,256029	68,9720726	172,401204	185,75783	144,272719
YOL043C	131,469981	133,654	93,6714131	137,777231	156,208158	77,8919068	209,199991	221,168683	177,303017
YOL064C	83,875723	90,817	56,4759071	118,473894	122,051337	71,1017094	168,02461	145,21399	105,62767
YOL086C	1382,01662	1297,867	906,541588	1428,75877	1291,11195	727,987307	1524,61669	1590,51216	1143,49321
YOL104C	133,055908	154,422	80,8917029	171,467629	164,431166	78,7244012	267,877636	243,238274	181,574705
YOL107W	99,447394	112,427	62,5618033	99,2326515	132,228902	53,3958033	151,189021	172,304002	116,023087

YOL116W	116,391344	137,631	80,8194917	138,766696	132,401659	87,389031	195,650449	229,883504	181,198967
YOL120C	162,575758	185,756	68,3336645	195,656195	209,619253	67,0219589	259,149138	256,869956	124,124104
YOL136C	102,939721	108,079	98,3433124	108,801977	125,719598	88,1581643	175,497948	173,996987	183,765177
YOR007C	178,132169	200,507	131,86948	181,310981	229,724704	109,524934	285,678256	308,798669	221,770673
YOR010C	494,25059	490,396	147,079182	433,004898	427,110954	84,1065743	350,802479	419,256938	101,888944
YOR049C	126,352988	144,857	82,4753122	144,114935	160,736424	76,9643708	193,862362	210,468207	148,29125
YOR052C	62,0753836	71,813	114,338942	100,254513	88,886926	159,902285	71,2642125	52,6288712	112,766691
YOR054C	203,904957	169,823	241,279585	377,358642	288,375271	548,430763	108,879881	61,3346866	111,202449
YOR063W	263,34965	250,057	101,428244	248,170721	260,977432	106,941209	338,316735	355,17115	201,081102
YOR065W	144,652783	159,552	210,670415	154,062228	151,508395	200,347784	161,28379	176,887669	192,327206
YOR120W	113,058666	129,008	229,480604	147,450498	128,970467	245,049037	119,345025	111,881096	150,228566
YOR122C	161,734078	139,067	124,377983	149,939683	104,131206	80,7660365	138,444015	97,4862208	50,3195743
YOR133W	203,676048	162,086	149,881986	204,732813	186,370118	136,312597	191,940529	177,33568	160,855821
YOR136W	156,048921	166,725	183,885083	156,050607	188,388986	169,853497	170,923821	217,521561	161,140955
YOR139C	92,4087405	71,813	74,5707004	152,743392	102,104772	148,229763	68,8012206	36,331639	69,8313004
YOR142W	146,045018	168,309	97,5305161	200,793852	190,798765	106,886648	225,659032	209,092657	131,169857
YOR173W	119,537374	123,001	109,957567	152,813586	171,427218	169,923898	118,285342	148,665248	131,169857
YOR176W	112,921321	130,653	90,9391413	129,283763	140,682674	93,9081837	149,221919	182,223274	134,026531
YOR185C	72,6087122	98,543	103,775949	123,708743	136,349864	143,651924	160,510118	162,465778	140,915061
YOR204W	140,222516	103,189	89,7300229	112,358921	88,0243992	84,8281867	63,646839	57,1540041	47,5508386
YOR226C	121,245386	145,51	265,310814	262,567231	207,273785	515,477713	128,182577	88,6498294	227,345452
YOR239W	92,4556961	119,921	55,3003753	120,763297	144,748152	52,6530704	187,292326	173,609762	120,603892
YOR261C	125,318789	160,878	100,387058	144,561747	178,33626	90,3300419	199,129914	222,879679	148,749597
YOR285W	255,250972	229,803	324,594562	257,58616	203,919513	393,030636	198,806865	141,118858	259,277849
YOR331C	310,342875	288,908	343,579401	339,506553	339,662834	370,630728	176,063799	233,195181	191,058758
YOR332W	231,749664	308,72	222,672595	263,995408	378,385751	270,997166	253,128491	400,805202	188,092826
YOR333C	108,574401	115,067	203,665925	224,96757	155,631879	388,750242	115,330574	65,0133269	174,808757
YOR338W	185,068694	277,733	123,328401	209,52895	296,257808	103,366587	313,36171	352,726228	191,589055
YOR339C	61,8406053	65,979	123,514807	105,906477	78,0536388	290,151577	51,6755048	32,3175534	117,947078
YOR348C	808,253659	674,934	875,232138	567,838033	543,600002	640,629957	346,275677	369,203565	402,287449
YOR352W	208,231921	236,079	112,543737	218,172255	262,921901	101,404153	411,607721	343,489103	208,803716
YOR369C	111,477434	110,979	67,3193484	141,659497	133,040989	85,9493261	126,993263	121,609006	82,2173292
YOR374W	79,7952761	86,081	60,3434068	147,882461	130,84558	63,327655	112,881986	85,2233358	32,5159904

YOR389W	109,390255	122,741	116,918394	70,543573	85,4406015	58,1109248	48,7660055	63,8403945	33,8190816
YOR391C	146,764613	156,255	141,552503	90,4341095	99,7832635	81,6460517	72,0481723	100,856432	46,4529376
YOR393W	61,2231384	55,528	44,456934	55,0428583	56,3958915	46,1198374	20,9117685	22,6684393	13,3080524
YPL003W	54,6082596	78,253	49,3740156	34,9579385	83,2805013	35,9363014	15,0680784	36,1943091	17,8408913
YPL004C	277,896514	307,231	284,828	247,2528	266,578813	221,149584	138,011911	156,121587	78,2467649
YPL087W	115,256191	171,003	201,806906	122,986555	149,082223	158,795226	122,01378	134,337912	131,169857
YPL097W	130,093006	115,475	169,70649	110,249053	105,736464	139,612654	72,0378841	87,2967922	116,580032
YPL111W	463,58737	338,966	319,215665	279,431328	220,726178	198,117826	176,699609	187,477831	125,373899
YPL152W	139,025147	185,138	64,9363775	180,769677	192,301882	67,0043586	268,889993	270,229228	138,479426
YPL154C	649,172576	655,118	485,541661	651,021917	652,040059	411,030467	435,486602	566,458835	287,532811
YPL171C	62,8419348	56,736	37,2895485	89,093675	82,6827853	79,8279403	95,9414574	76,4589864	68,1471416
YPL209C	198,325451	204,46	84,5375309	214,758399	233,234078	82,2303818	325,160202	315,813751	166,944908
YPL215W	142,969422	181,967	69,7678133	153,936689	192,619655	45,7203105	210,549801	206,690509	81,2233557
YPL220W	105,993013	161,006	60,5566818	177,523207	194,752013	62,3719585	180,39101	189,927256	86,6755534
YPL223C	74,1418145	88,284	95,5002047	276,460234	274,330206	411,864721	61,2517491	95,0683139	90,2650501
YPL227C	147,655597	160,801	56,541401	148,383267	178,820486	46,4806437	220,463498	205,346477	100,40731
YPL236C	120,009278	125,696	78,4449174	119,586198	135,545343	72,0767663	209,241144	205,774226	142,988282
YPL240C	78,4253447	101,032	118,08385	80,3801756	90,0937071	90,1452387	124,441793	180,714896	112,665428
YPL264C	259,098989	312,604	138,954578	290,385635	325,123455	125,374008	511,292021	442,918205	243,997839
YPL274W	121,974372	112,069	158,020025	77,5305711	75,2996056	107,173533	59,9039966	64,5157874	67,7687388
YPL276W	107,575419	93,025	157,784918	143,498038	122,307321	277,187193	78,7828194	55,4475112	124,705032
YPL280W	143,394371	132,784	124,288979	95,6487103	84,6020337	85,5462792	78,5544217	84,1111887	49,2616455
YPL281C	66,0889187	59,476	49,1892892	60,374899	54,0453796	44,8983763	21,368564	19,6381761	19,3651616
YPR004C	96,2485397	166,226	81,7448032	148,12409	166,636663	66,5590709	197,193677	211,393496	122,956918
YPR035W	187,363652	167,502	116,977171	334,156964	307,089834	191,222026	363,697692	365,626234	159,61402
YPR041W	135,8709	117,216	65,0623274	142,234547	128,305918	71,2319517	195,183365	179,715314	133,456262
YPR064W	119,666502	94,45	166,690412	213,760835	130,003229	282,036077	106,754342	44,2922707	129,957369
YPR074C	155,24011	125,557	81,3300084	232,078757	223,386897	132,757335	125,215464	140,751894	76,4373601
YPR080W	1506,13804	999,709	676,076896	1636,24264	907,936905	747,271961	2085,98338	1531,67868	1090,39957
YPR086W	133,601768	138,047	71,8485046	128,367192	146,154171	46,1937587	165,685076	146,573782	75,1422633
YPR110C	149,047832	211,043	61,2099417	146,238302	248,543931	41,6388	209,804936	324,546582	88,1065554
YPR127W	186,550145	248,225	162,47697	264,278883	294,028353	140,710913	220,288599	283,863161	109,315764
YPR128C	133,797808	181,582	66,3923576	140,746975	172,598691	55,5993614	187,613317	249,55545	95,6879349

YPR149W	331,765222	303,787	300,205636	333,171549	365,020368	275,180758	283,597985	360,993038	168,4372
YPR154W	88,8201541	111,698	95,6597412	103,881651	123,265684	95,8653376	75,6552106	96,3245448	57,9702388
YPR156C	97,2228696	115,482	84,3276145	83,5321541	105,044173	90,9671729	54,3545486	78,867888	43,7614812
YPR165W	84,200891	106,083	91,5520972	132,404694	116,758902	61,0589758	102,564992	122,496022	44,9633097
YPR184W	237,390213	380,374	381,901738	197,135668	353,745729	266,433407	79,9659609	233,161411	176,404977
YPR191W	142,913075	122,034	108,907985	143,525036	121,651599	92,7712041	96,0834344	116,426491	59,9368673