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| Title | Transcriptional response to lactic acid stress in the hybrid yeast <i>Zygosaccharomyces parabailii</i> |
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| Publication date | 2017-12-21 |
| Original citation | Ortiz-Merino, R. A., Kuanyshev, N., Byrne, K. P., Varela, J. A., Morrissey, J. P., Porro, D., Wolfe, K. H. and Branduardi, P. (2017) 'Transcriptional response to lactic acid stress in the hybrid yeast <i>Zygosaccharomyces parabailii</i> ', <i>Applied and Environmental Microbiology</i> . [In Press] DOI: 10.1128/aem.02294-17 |
| Type of publication | Article (peer-reviewed) |
| Link to publisher's version | http://aem.asm.org/content/early/2017/12/18/AEM.02294-17.abstract http://dx.doi.org/10.1128/aem.02294-17 Access to the full text of the published version may require a subscription. |
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| Item downloaded from | http://hdl.handle.net/10468/5487 |

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Supplemental Material

Transcriptional response to lactic acid stress in the hybrid yeast *Zygosaccharomyces parabailii*

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Table S1. Control-specific genes.

| ID | NCBI_ID | Description |
|-----------|----------------|---|
| A00140_N | BZL39_A00140 | related to L-lactate dehydrogenase |
| A01200_B | BZL39_A01200 | uncharacterized protein ZBAI_04890 |
| A02950_B | BZL39_A02950 | uncharacterized protein ZBAI_04711 |
| A04460_B | BZL39_A04460 | related to PCH2- ATPase |
| A05220_N | BZL39_A05220 | uncharacterized protein ZBAI_04496 |
| A09510_B | BZL39_A09510 | related to IRC11-Strong similarity to YDR391c |
| A09995_N | BZL39_A09995 | ---NA--- |
| A10080_N | BZL39_A10080 | ZYBA0S13-00232g1_1 |
| B03300_A | BZL39_B03300 | ZYBA0S04-07030g1_1 |
| B09380_A | BZL39_B09380 | A Chain Crystal Structure Of Yth Domain Of Zygosaccharomyces rouxii Mrb1 In Complex With N6-methyladenosine RNA |
| B09470_A | BZL39_B09470 | related to IRC11-Strong similarity to YDR391c |
| B09730_A | BZL39_B09730 | ZYBA0S13-00980g1_1 |
| B10130_N | BZL39_B10130 | CIC11C00000000719 |
| C03800_A | BZL39_C03800 | BN860_11408g1_1 |
| D01770_B | BZL39_D01770 | uncharacterized protein ZBAI_02445 |
| E02670_A | BZL39_E02670 | BN860_10704g1_1 |
| E07220_N | BZL39_E07220 | Y element ATP-dependent helicase |
| G06420_N | BZL39_G06420 | related to ketopantoate reductase |
| H01670_B | BZL39_H01670 | uncharacterized protein ZBAI_06090 |
| H04800_B | BZL39_H04800 | uncharacterized protein ZBAI_05789 |
| H06370_A | BZL39_H06370 | related to ornithine aminotransferase |
| I04800_A | BZL39_I04800 | related to Peroxisomal membrane PAS20 |
| J00180_N | BZL39_J00180 | related to ornithine aminotransferase |
| J03940_A | BZL39_J03940 | cell wall CWP1 |
| K04960_A | BZL39_K04960 | probable OPT1-High-affinity glutathione transporter |
| K05090_N | BZL39_K05090 | related to permease of the major facilitator superfamily |
| M00100_N | BZL39_M00100 | Y element ATP-dependent helicase |
| M00110_N | BZL39_M00110 | Y element ATP-dependent helicase 1 copy 6 |
| M00290_N | BZL39_M00290 | related to ornithine aminotransferase |
| N00210_N | BZL39_N00210 | related to MFS multidrug transporter |
| N05030_A | BZL39_N05030 | related to Peroxisomal membrane PAS20 |

Table S2. Lactic acid-specific genes.

| ID | NCBI_ID | Description |
|------------|----------------|--|
| A00170_N | BZL39_A00170 | threonine dehydratase |
| A00180_A | BZL39_A00180 | probable Allantoate permease |
| A00210_B | BZL39_A00210 | probable Constitutive acid phosphatase |
| A00290_A | BZL39_A00290 | related to thermophilic desulfurizing enzyme |
| A05200_N | BZL39_A05200 | uncharacterized protein ZBAI_04498 |
| A07530_B | BZL39_A07530 | uncharacterized protein ZBAI_04271 |
| A09010_N | BZL39_A09010 | uncharacterized protein ZBAI_08640 |
| A10020_N | BZL39_A10020 | Fit2p |
| A10040_B | BZL39_A10040 | related to Siderophore iron transporter 3 |
| B00200_A | BZL39_B00200 | related to ketopantoate reductase |
| B10000_A | BZL39_B10000 | related to Siderophore iron transporter 3 |
| C00430_A | BZL39_C00430 | BN860_18976g1_1 |
| C05100_A | BZL39_C05100 | BN860_08460g1_1 |
| E00130_A | BZL39_E00130 | BN860_16600g1_1 |
| E01370_A | BZL39_E01370 | related to Similarity to YIL123w and Sun4p |
| E02440_A | BZL39_E02440 | BN860_11232g1_1 |
| E06720_A | BZL39_E06720 | BN860_01398g1_1 |
| F06250_N | BZL39_F06250 | probable Vacuolar sorting targeting 10 |
| G00240_N | BZL39_G00240 | Fit2p |
| G01010_A | BZL39_G01010 | Gor1p |
| J00140_N | BZL39_J00140 | 1-aminocyclopropane-1-carboxylate deaminase |
| J05500_A | BZL39_J05500 | ZYBA0S03-00892g1_1 |
| K00230_N | BZL39_K00230 | uncharacterized protein ZBAI_09841 |
| K05040_N | BZL39_K05040 | ZYBA0S13-00144g1_1 |
| K05170_A | BZL39_K05170 | related to ketopantoate reductase |
| L05300_N | BZL39_L05300 | related to Soluble epoxide hydrolase |
| M00150_N | BZL39_M00150 | uncharacterized protein ZBAI_01365 |
| M00180_N | BZL39_M00180 | uncharacterized protein ZBAI_01367 |
| M00220_N | BZL39_M00220 | related to MFS multidrug transporter |
| N00200_N | BZL39_N00200 | Hxt3p |
| N00290_A | BZL39_N00290 | probable Fluconazole resistance 1 |
| O04150_N | BZL39_O04150 | uncharacterized protein ZBAI_08167 |
| O04170_A | BZL39_O04170 | related to Arsenical-resistance 3 |
| P00180_N | BZL39_P00180 | Fit2p |
| P02220_N | BZL39_P02220 | Fdh1p |
| ZPARMT0022 | BZL39_MT0022 | NA |

Supplemental file 2: **Data Set S1.** Full annotation table for the *Z. parabailii* genome. The table includes the *Z. parabailii* gene codes, their corresponding *Z. bailii* homeolog (if any), the *S. cerevisiae* homolog(s) (if any), and the gene category as reported in Ortiz-Merino *et al.* 2017 (1). It also includes the PFAM (2) category and a logical column TM indicating if the gene has more than 2 transmembrane domains and has hits in TransportDB (3) as described in the method section. The names and systematic IDs for the corresponding *S. cerevisiae* homologs assigned by YGAP (4) are also included with a link to their description in the Saccharomyces Genome Database (<http://www.yeastgenome.org>).

Supplemental file 3: **Data Set S2.** *Z. parabailii* functional annotation obtained using Blast2GO (5). The table includes a brief description of the best blast (6) hit including the number of hits and e-Value found by Blast2GO as described in the software documentation. In addition, it shows the assigned Gene Ontology terms and Enzyme Classification codes with a brief description.

Supplemental file 4: **Data Set S3.** Averaged Reads Per Kilobase of transcript per Million mapped reads (RPKM) values for homeolog gene pairs. Columns are labels as C or LA corresponding to control or lactic acid and 18 or 42 corresponding to the timepoint. Columns with the suffix _A correspond to the A gene similar to _B and B genes.

Supplemental file 5: **Data Set S4.** Duplicated genes differentially expressed during lactic acid exposure. In separate sheets, the *Z. parabailii* duplicated genes found as up- or downregulated in the different time points. Each sheet includes the corresponding statistical values obtained for each gene from the Limma-Voom analysis (7, 8) and the functional metadata described in the methods section.

Supplemental file 6: **Data Set S5.** Differentially expressed genes during lactic acid exposure. In separate sheets, the *Z. parabailii* genes found as up- or downregulated in the different time points. Each sheet includes the corresponding statistical values obtained for each gene from the Limma-Voom (7, 8) analysis and the functional metadata described in the methods section. Enriched GO terms amongst the differentially expressed genes. In separate sheets, the terms found as enriched with an adjusted P value ≤ 0.05 using goseq (9) for the upregulated and downregulated gene sets. The value was \log_{10} transformed to facilitate visual interpretation and it is shown when obtained at each individual time point or both.

Supplemental file 7: **Data Set S6.** Enriched GO terms among differentially expressed genes. In separate sheets, the terms found as enriched with an adjusted P value ≤ 0.05 using goseq (9) for the upregulated and downregulated gene sets. The value was \log_{10} transformed to facilitate visual interpretation and it is shown when obtained at each individual time point or both.

Supplemental file 8: **Data Set S7.** List of differentially expressed genes controlled by Haa1 and Aft1/2. *Z. parabailii* genes whose *S. cerevisiae* homolog is under control of either Haa1 or Aft1/2 according to YEASTRACT (10). The \log_2 -fold change values are shown in the case they were found as differentially expressed at 18 h or 42 h. The *S. cerevisiae* standard or systematic names are shown including the corresponding paralog if there is any.

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