|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **gene** | **Ds** | **Dn** | **Ps** | **Pn** | **NI** | ***p*** | **adjusted *p*** |
| YBR136W/MEC1 | 293 | 38 | 770 | 363 | 3.63 | 5.71 x 10 -15 | 1.69 x 10 -12 |
| YLR422W/DCK1 | 122 | 26 | 335 | 280 | 3.92 | 1.13 x 10 -10 | 8.70 x 10 -9 |
| YOR326W/MYO2 | 35 | 0 | 1486 | 1273 | inf | 5.15 x 10 -10 | 2.77 x 10 -3 |
| YAL026C/DRS2 | 32 | 1 | 1399 | 1595 | 36.48 | 5.81 x 10 -10 | 2.97 x 10 -8 |
| YMR207C/HFA1 | 77 | 16 | 2215 | 2103 | 4.57 | 6.16 x 10 -10 | 3.08 x 10 -8 |
| YOR371C/GPB1 | 79 | 18 | 347 | 323 | 4.09 | 1.42 x 10 -8 | 4.02 x 10 -7 |
| YML099C/ARG81 | 96 | 16 | 351 | 247 | 4.22 | 1.61 x 10 -8 | 4.43 x 10 -7 |
| YJL062W/LAS21 | 74 | 10 | 170 | 131 | 5.70 | 2.19 x 10 -8 | 5.77 x 10 -7 |
| YPL268W/PLC1 | 112 | 16 | 245 | 146 | 4.17 | 4.57 x 10 -8 | 1.05 x 10 -6 |
| YCR042C/TAF2 | 155 | 45 | 661 | 470 | 2.45 | 1.70 x 10 -7 | 2.90 x 10 -6 |
| YPL254W/HFI1 | 76 | 10 | 150 | 106 | 5.37 | 1.66 x 10 -7 | 2.90 x 10 -6 |
| YPR049C/ATG11 | 131 | 45 | 448 | 395 | 2.57 | 1.67 x 10 -7 | 2.90 x 10 -6 |
| YNL049C/SFB2 | 32 | 1 | 773 | 587 | 24.30 | 3.22 x 10 -7 | 4.88 x 10 -6 |
| YKL114C/APN1 | 44 | 3 | 120 | 87 | 10.63 | 9.80 x 10 -7 | 1.19 x 10 -5 |
| YIL068C/SEC6 | 80 | 5 | 271 | 111 | 6.55 | 1.36 x 10 -6 | 1.52 x 10 -5 |
| YGR198W/YPP1 | 79 | 25 | 295 | 282 | 3.02 | 1.97 x 10 -6 | 2.10 x 10 -5 |
| YDR375C/BCS1 | 67 | 4 | 107 | 54 | 8.45 | 2.20 x 10 -6 | 2.28 x 10 -5 |
| YKL017C/HCS1 | 78 | 13 | 219 | 143 | 3.92 | 3.56 x 10 -6 | 3.28 x 10 -5 |
| YDR235W/PRP42 | 61 | 7 | 177 | 109 | 5.37 | 5.34 x 10 -6 | 4.57 x 10 -5 |
| YDR180W/SCC2 | 173 | 72 | 523 | 431 | 1.98 | 6.47 x 10 -6 | 5.35 x 10 -5 |
| YMR167W/MLH1 | 94 | 26 | 286 | 209 | 2.64 | 2.47 x 10 -5 | 1.54 x 10 -4 |
| YKL197C/PEX1 | 132 | 58 | 415 | 351 | 1.92 | 1.55 x 10 -4 | 6.57 x 10 -4 |
| YMR078C/CTF18 | 73 | 26 | 295 | 260 | 2.47 | 1.63 x 10 -4 | 6.82 x 10 -4 |
| YGL095C/VPS45 | 67 | 14 | 202 | 122 | 2.89 | 3.72 x 10 -4 | 1.30 x 10 -3 |
| YMR094W/CTF13 | 54 | 21 | 152 | 158 | 2.67 | 4.44 x 10 -4 | 1.50 x 10 -3 |
| YNL132W/KRE33 | 75 | 4 | 187 | 52 | 5.21 | 5.13 x 10 -4 | 1.69 x 10 -3 |
| YDR103W/STE5 | 93 | 56 | 344 | 373 | 1.80 | 1.57 x 10 -3 | 4.16 x 10 -3 |
| YOR092W/ECM3 | 16 | 1 | 648 | 498 | 12.30 | 1.92 x 10 -3 | 4.86 x 10 -3 |
| YNR045W/PET494 | 61 | 20 | 177 | 136 | 2.34 | 2.15 x 10 -3 | 5.32 x 10 -3 |
| YJR107W/LIH1 | 19 | 1 | 102 | 61 | 11.36 | 2.40 x 10 -3 | 5.79 x 10 -3 |
| YLR397C/AFG2 | 102 | 27 | 288 | 155 | 2.03 | 2.56 x 10 -3 | 6.10 x 10 -3 |
| YGL082W/MIY1 | 41 | 8 | 132 | 84 | 3.26 | 2.60 x 10 -3 | 6.17 x 10 -3 |
| YOR091W/TMA46 | 40 | 6 | 103 | 46 | 2.98 | 0.0212 | 0.0351 |
| YDR456W/NHX1 | 87 | 13 | 187 | 59 | 2.11 | 0.0278 | 0.0443 |
| YDR508C/GNP1 | 3 | 0 | 959 | 797 | inf | 0.2562 | 0.3009 |
| YIL152W/VPR1 | 19 | 11 | 70 | 59 | 1.46 | 0.4184 | 0.4669 |

**Supplementary Table 10. Whole-gene tests for evidence of non-neutral protein evolution at thermotolerance loci.** Each row reports results from the McDonald-Kreitman test on sequences from strains of European populations of *S. cerevisiae* and *S. paradoxus* of the indicated top hit from barcoded RH-seq mapping of thermotolerance. Ds, number of sites of synonymous nucleotide divergence between species; number of sites of Dn, nonsynonymous nucleotide divergence between species; Ps, number of sites of synonymous nucleotide polymorphisms within species; Pn, number of sites of nonsynonymous nucleotide polymorphisms within species. NI, neutrality index. The sixth column reports the *p*-value from a Fisher’s exact test on Ds, Dn, Ps, and ­Pn, and the seventh column reports the adjusted *p*-value after applying the Benjamini-Hochberg correction for multiple hypothesis testing. All loci exhibited NI > 1, corresponding to a dearth of divergent amino acid changes relative to synonymous changes and polymorphisms.