

**Supplementary Figure S3.** Variations of the ratio *R*, of the rates of transitions having occurred at third codon positions in the lineage of Saccharomyces cerevisiae since its divergence from Saccharomyces paradoxus. The sequences of S. cerevisiae strain S288C were downloaded from the Saccharomyces Genome Database web pages (http://www.yeastgenome.org), those of S. paradoxus and Saccharomyces mikatae from the Broad Institute web pages (http://www.broad.mit.edu/annotation/fungi/ comp yeasts/downloads.html). A total number of 3,967 sets of orthologous open reading frames were analyzed. The substitutions having occurred in the S. cerevisiae lineage since its divergence from S. paradoxus were estimated using S. mikatae as an outgroup to infer the ancestral sequences. Analysis of substitution patterns were performed exactly as described for the Candida species in Materials and Methods. Replication timing data were taken from Raghuraman MK et al. 2001. Replication dynamics of the yeast genome. Science 294:115-121. The times are given in minutes after the beginning of S phase. As for the Candida species, 1 kb genome fragments were ranked by their replication times and pooled into bins of 100 kb to compute their average transition rates in the S. cerevisiae lineage.