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## Adaptive evolution of sugar metabolism networks in yeast

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**Purpose:** The budding yeast *Saccharomyces cerevisiae* has been used worldwide for food and beverage fermentation for thousands of years. The domesticated populations of the yeast show significantly elevated maltose or galactose utilization abilities compared with its wild lineages. The purpose of this study is to illuminate the molecular mechanisms of the improved traits of domesticated yeast lineages.

**Methods:** We sequenced *S. cerevisiae* isolates representing different wild and domesticated lineages using the Illumina and the PacBio long-read sequencing strategies and performed SNP, copy number variation, structure variation, introgression and horizontal gene transfer analyses. The phenotypic consequences of the genetic changes were confirmed by gene deletion or swap experiments.

**Results and conclusions:** We found a remarkable expansion of gene contents, copy numbers, structural complexities and translocation events in the MAL network from the wild to domesticated lineages of *S. cerevisiae*. These polygenic changes in the MAL network are collectively responsible for the significant elevation of maltose metabolism in the domesticated lineages of *S. cerevisiae*. The Milk lineage of *S. cerevisiae* has swapped all its structural GAL genes with early diverged versions through introgression and duplicated the introgressed GAL2 gene. The rewired GAL network has achieved galactose-over-glucose preference switch, abolished glucose repression, and conversed from a strictly inducible to a constitutive system through polygenic changes in the regulatory components of the network. The reverse evolution of the GAL network confers a competitive advantage to the Milk lineage of *S. cerevisiae* in spontaneously fermented milks.