

Breeding and domestication have generated widely exploited crops, animals and microbes. However, many *Saccharomyces cerevisiae* industrial strains have complex polyploid genomes and are sterile, preventing genetic improvement strategies based on breeding. Here, we present a novel strain improvement approach based on the budding yeasts' property to promote genetic recombination when meiosis is interrupted and cells return-to-mitotic-growth (RTG). We demonstrated that two unrelated sterile industrial strains with complex triploid and tetraploid genomes were RTG-competent and developed a visual screening for easy and high-throughput identification of recombined RTG clones based on colony phenotypes. Sequencing of the evolved clones revealed unprecedented levels of RTG-induced genome-wide recombination. We generated and extensively phenotyped a RTG library and identified clones with superior biotechnological traits. Thus, we propose the RTG-framework as a fully non-GMO workflow to rapidly improve industrial yeasts that can be easily brought to the market.