IDENTIFICATION OF GENETIC VARIANTS RESPONSIBLE FOR HIGH LIPID CONTENT OF AN INDUSTRIAL YEAST STRAIN

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Strains of industrial microorganisms that have been developed using classical strain improvement techniques can nowadays be characterized on the level of the whole genome sequence, thanks to the accessibility of next-generation sequencing technologies. However, hundreds or even thousands of genetic variants relative to reference wild-type, laboratory or environmental strains are typically present in such industrial strains, making it extremely difficult to decipher which of the mutations are responsible for the biotechnologically important characteristics. Recently, a method named Extreme QTL mapping (X-QTL), which enables mapping of complex traits, has been described for the baker's yeast Saccharomyces cerevisiae (Ehrenreich et al. (2010) Nature 464:1039). We expanded this method and made it more costeffective, with the aim of making it useful in real life applications and accessible for the characterization of any strain of baker's yeast. A haploid industrial yeast strain with a high neutral lipid content, which differs in $\sim 5 \times 10^4$ genetic variants from the reference laboratory strain, was crossed to the reference haploid strain and through sporulation $\sim 2 \times 10^8$ genetically distinct segregants were obtained. The population of segregants with the highest neutral lipid content was selected using a lipid-binding fluorescent dye and fluorescence-activated cell sorting, and genotyped by whole-genome tiling DNA microarrays and whole-genome sequencing. QTLs were identified at a single allele resolution and the identified alleles, specific for segregants with high neutral lipid content, were introduced into the reference strain. Two of the identified alleles, when both present in the same strain, explain 50% of the phenotypic difference between the parental strains. This modified X-OTL method represents a new approach for an educated and targeted design of strains of industrial microorganisms.