Identification of a Classical Mutant in the Industrial Host Aspergillus niger by Systems Genetics: LaeA Is Required for Citric Acid Production and Regulates the Formation of Some Secondary Metabolites

The asexual filamentous fungus Aspergillus niger is an important industrial cell factory for citric acid production. In this study, we genetically characterized a UV-generated A. niger mutant that was originally isolated as a nonacidifying mutant, which is a desirable trait for industrial enzyme production. Physiological analysis showed that this mutant did not secrete large amounts of citric acid and oxalic acid, thus explaining the nonacidifying phenotype. As traditional complementation approaches to characterize the mutant genotype were unsuccessful, we used bulk segregant analysis in combination with high-throughput genome sequencing to identify the mutation responsible for the nonacidifying phenotype. Since A. niger has no sexual cycle, parasexual genetics was used to generate haploid segregants derived from diploids by loss of whole chromosomes. We found that the nonacidifying phenotype was caused by a point mutation in the laeA gene. LaeA encodes a putative methyltransferase-domain protein, which we show here to be required for citric acid production in an A. niger lab strain (N402) and in other citric acid production strains. The unexpected link between LaeA and citric acid production could provide new insights into the transcriptional control mechanisms related to citric acid production in A. niger. Interestingly, the secondary metabolite profile of a ΔlaeA strain differed from the wild-type strain, showing both decreased and increased metabolite levels, indicating that LaeA is also involved in regulating the production of secondary metabolites. Finally, we show that our systems genetics approach is a powerful tool to identify trait mutations.
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