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ANALYSIS OF THE TRANSCRIPTION AND OVEREXPRESSION OF THE MEVALONATE-ISOPRENOID BIOSYNTHESIS PATHWAY GENES IN *MUCOR CIRCINELLOIDES*

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Zygomycetes have a great practical significance in industrial-biotechnological and agricultural fields and also as opportunistic pathogens. *Mucor circinelloides* is a carotenoid producing filamentous fungus, which has been used as a model organism in various genetic, biochemical and molecular studies. Terpenes are synthesised by a side-route of the general mevalonate-isoprenoid biosynthetic pathway in fungi. Terpene-type metabolites (such as sterols, carotenoids, hormones/pheromones, functional groups of different proteins, e.g. farnesylated or geranylgeranylated proteins) are involved in the formation of the structure of the cell membrane, morphogenesis, electron transport, signal transduction, apoptotic processes, protection against free radicals, cell differentiation, adaptation to environmental changes, etc. Today, ergosterol and its synthesis is a major target of antifungal therapy.

Our aim is to reveal the function, regulation of the mevalonate-isoprenoid pathway genes in *M. circinelloides*. In this study, effects of cultivation time, light, salt stress, media, temperature, oxygen tension, and statin treatment on the transcription of six terpenoid pathway genes, encoding the the 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) synthase (*hmgS*), mevalonate kinase (*mvk*), diphospho-mevalonate decarboxylase (*dmd*), isopentenyl-pyrophosphate isomerase (*ipi*), farnesyl-pyrophosphate synthase (*isoA*) and geranylgeranyl-pyrophosphate synthase (*carG*), were analysed.

The nucleotide sequences of the genes and their regulatory regions, as well as the amino acid sequences of the encoded proteins were analysed. Autonomously replicating vectors, carrying one of the mevalonate-isoprenoid genes under the control of own and *Mucor* glyceraldehyde-3-phosphate dehydrogenase (*gpd1*) promoter and terminal sequences were constructed. The promoter of *gpd1* is very effective and can be induced by glucose. PEG/$CaCl_2$-mediated protoplast transformation with plasmids harbouring one of the isoprenoid genes (*ipi*, *isoA* and *carG*, respectively) was used to elevate the copy number of the examined genes in *M. circinelloides*. Viability and germination of spores, morphology, growth intensity and terpene production (e.g. carotenoid and ergosterol) of the resulting transformants were analysed. Investigation of the copy number of the introduced DNA, transcription of the overexpressed genes and effect of the elevated copy numbers on the transcription of the other terpenoid gene are in progress.

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