Comparative Transcriptome Analysis Shows Conserved Metabolic Regulation during Production of Secondary Metabolites in Filamentous Fungi

Filamentous fungi possess great potential as sources of medicinal bioactive compounds, such as antibiotics, but efficient production is hampered by a limited understanding of how their metabolism is regulated. We investigated the metabolism of six secondary metabolite-producing fungi of the Penicillium genus during nutrient depletion in the stationary phase of batch fermentations and assessed conserved metabolic responses across species using genome-wide transcriptional profiling. A coexpression analysis revealed that expression of biosynthetic genes correlates with expression of genes associated with pathways responsible for the generation of precursor metabolites for secondary metabolism. Our results highlight the main metabolic routes for the supply of precursors for secondary metabolism and suggest that the regulation of fungal metabolism is tailored to meet the demands for secondary metabolite production. These findings can aid in identifying fungal species that are optimized for the production of specific secondary metabolites and in designing metabolic engineering strategies to develop high-yielding fungal cell factories for production of secondary metabolites.

IMPORTANCE Secondary metabolites are a major source of pharmaceuticals, especially antibiotics. However, the development of efficient processes of production of secondary metabolites has proved troublesome due to a limited understanding of the metabolic regulations governing secondary metabolism. By analyzing the conservation in gene expression across secondary metabolite-producing fungal species, we identified a metabolic signature that links primary and secondary metabolism and that demonstrates that fungal metabolism is tailored for the efficient production of secondary metabolites. The insight that we provide can be used to develop high-yielding fungal cell factories that are optimized for the production of specific secondary metabolites of pharmaceutical interest.

General information
Publication status: Published
Organisations: Biosynthetic Pathway Engineering, Department of Biotechnology and Biomedicine, Fungal Physiology and Biotechnology, Department of Systems Biology, Bacterial Synthetic Biology, Novo Nordisk Foundation Center for Biosustainability, Chalmers University of Technology
Corresponding author: Nielsen, J.
Contributors: Nielsen, J., Prigent, S., Grijseels, S., Workman, M., Ji, B., Nielsen, J.
Number of pages: 14
Publication date: 2019
Peer-reviewed: Yes

Publication information
Journal: mSystems
Volume: 4
Issue number: 2
Article number: 00012-19
ISSN (Print): 2379-5077
Ratings:
Web of Science (2019): Indexed yes
Original language: English
Keywords: Cell factories, Comparative transcriptomics, Filamentous fungi, Secondary metabolism
Electronic versions:
mSystems_2019_Nielsen_e00012_19.full.pdf
DOIs: 10.1128/mSystems.00012-19
Source: FindIt
Source-ID: 2446793863
Research output: Contribution to journal › Journal article – Annual report year: 2019 › Research › peer-review