

New avenues towards drug discovery in fungi.

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Abstract

With a largely unexplored biodiversity, fungi are an untapped source of novel compounds, many of which exhibit biological activity. Some of the already known molecules, such as penicillin, lovastatin, or cyclosporines, have become successful pharmaceutical drugs. Two major hurdles need to be overcome in order to access this hidden treasure. Only about 8% of all fungi have been identified to date, and few of those have been successfully cultured in the laboratory, revealing merely a fraction of their biosynthetic potential. The present work discusses recent scientific advances that could facilitate the discovery of these valuable molecules encoded in biosynthetic gene clusters. Molecular biology methods largely rely on the verified techniques of regulatory manipulation of gene clusters (e.g., promoter exchange, transcription factor overexpression). The advent of novel methodologies, such as CRISPR-Cas9, or synthetic biology provides additional means to discover and manipulate secondary metabolites. Furthermore, microbial co-cultivation approaches inspired by ecological interactions have proved fruitful in activating silent biosynthetic pathways. The use and integration of omics methods and large datasets represent yet another avenue toward the discovery of novel fungal chemistries that may serve as drug leads and drug candidates.

Beteiligte Forschungseinheiten

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