# GENOME-GUIDED METHODS FOR DISCOVERING NEW NATURAL PRODUCT FROM FUNGI

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For decades, fungi have been an important source of medically relevant natural products (NPs). Recent advances in DNA sequencing have revealed that the biosynthetic potential of fungal genomes is much deeper than previously realized. Difficulties in culturing and genetically engineering many fungi, combined with the fact that many NP biosynthetic gene clusters (BGCs) are not expressed under standard laboratory conditions has lead to much of this biosynthetic potential remaining untapped. Here we describe the realization of a pipeline based in *S. cerevisiae* encompassing bioinformatic tools for BGC curation, genetic parts for BGC refactoring, and improved DNA assembly for BGC building.

With this pipeline, we have successfully detected novel NPs from several previously unstudied fungal BGCs, and have structurally characterized a subset of the BGC-associated compounds. We also developed activity-guided methods to discover natural products of new function, and validated the biological activity using higher-order model systems. Our pipeline demonstrates how high-throughput synthetic biology tools can facilitate the rapid discovery of complex chemical scaffolds of potential pharmaceutical relevance and their production in model fungal hosts.