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Secondary Metabolite in Bacteria and Fungi

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Introduction

Antibiotics, pigments, growth hormones, anticancer medicines, and other microbial secondary metabolites are not required for microbe growth and development, but they have shown considerable promise for human and animal health. Bacteria, particularly actinobacteria, and fungi, among the microorganisms that produce the aforementioned substances, produce a varied array of bioactive small molecules with substantial potential for use in medicine. These bioactive compounds are mostly created by the activation of cryptic gene clusters that are inactive under normal conditions; consequently, increasing the expression of these clusters would aid in the exploitation of microorganism chemical diversity.

Refocusing and revitalising efforts to mine the fungal secondary metabolome has been one of the most intriguing developments in microbial research. The size of biosynthetic gene clusters (BGCs) in a single filamentous fungal genome, along with the number of sequenced genomes in the past, shows that filamentous fungi's secondary metabolite richness is mostly unexplored. Access to the chemical repertoire of fungal-derived secondary metabolites has substantially increased because to mining techniques and scalable expression platforms [1,2].

Description

Fungi have a long and close relationship with humans, especially on a chemical level. The aflatoxin poisoning episode Turkey X illness in the 1960s1 and the discovery of the first broad-spectrum antibiotic, penicillin, dubbed the "wonder drug" of World War II2, revealed that fungi were a source of both hazardous and useful substances. Secondary metabolites (also known as natural products) are bioactive molecules produced by specific fungal taxa, most notably filamentous fungi of the Pezizomycotina Ascomycete class and several Basidiomycete classes (for example, Agaricomycetes and Exobasidiomycetes), as well as unexpected taxa like Kluyveromyces lactis, where the pulcherrimin gene cluster was recently discovered. Secondary metabolites are derived from central metabolic pathways and primary metabolite pools, with acyl-CoAs serving as the critical initial building blocks for polyketide (for example, aflatoxin) and terpene (for example, carotene) secondary metabolites, and amino acids for non-ribosomal peptide secondary metabolites. In contrast to genes required for primary metabolite synthesis, which are distributed across the fungal genome, genes encoding the enzymatic activity required to create any secondary metabolite, such as aflatoxin BGC4, are grouped in a continuous form as a biosynthetic gene cluster (BGC) [3].

The polymerization of primary metabolites by specialised enzymes is the first step in the creation of secondary metabolites (often referred to as backbone or core enzymes). Additional enzymes 'decorate' the metabolites produced by the backbone enzymes, changing the bioactivities of the metabolites dramatically. The chemical class of the generated secondary metabolite is determined by the backbone enzyme. Polyketide synthases (PKSs) make polyketides from acyl-CoAs, NRPSs make non-ribosomal peptides from amino acids, and terpene synthases and terpene cyclases (TSs and TCs, respectively) make terpenes from activated isoprene units. Some secondary metabolites, such as fumagillin (PKS–TC hybrid) and echinocandin (PKS–NRPS hybrid), are hybrids made up of two synthases and/or synthetases [4].

Lipopeptides are a term used to describe compounds created from ribosomally derived peptides attached to fatty acids or isoprenoids, although this term can also apply to molecules formed from ribosomally derived peptides attached to fatty acids or isoprenoids (such as canonical fungal mating pheromones). It's possible that the two enzymes are distinct. The 'typical' classes of secondary metabolites are defined by these backbone enzymes, and the reader is directed to reviews focused on the fascinating chemistry involved in the production of these metabolites. The ribosomally derived peptide ustiloxin, fatty-acid-derived oxylipins, and the recently discovered isocyanide xanthocillin, which requires an isocyanide synthase, are examples of fungal secondary metabolites that are not produced by the synthases or synthetases listed above [5].

Fungal secondary metabolite biosynthesis genes are often organised in BGCs, a chromosomal layout that has aided the development of algorithms to anticipate BGCs that encode conserved synthases and/or synthetases in fungal genomes. Note that algorithms are only predictive and may underestimate or overestimate the inclusion of genes in a BGC. Only gene deletion can confirm a true link with a cluster. BGCs might have as little as two genes (such as the valactamide BGC) or as many as 20 genes (for example, the aflatoxin BGC). Genes encoding synthases or synthetases, as well as tailoring enzymes that adorn initial synthase or synthetase products of the secondary metabolite, are found in the smaller clusters (two to four genes).

Conclusion

Not only do BGCs contain synthases and/or synthetases, as well as many tailoring genes, but they also frequently contain a gene that encodes a cluster-specific transcription factor, as well as a number of genes that are unrelated to chemical structure production and/or are hypothetical in nature. Although numerous genes in the sterigmatocystin BGC are co-regulated during sterigmatocystin synthesis, there is no phenotype associated with gene loss (for example, stcC, stcM and stcR). Cpur 054 and Cpur 054 in the ergochrome BGC23 and AFLA 022990, AFLA 023060, and AFLA 023090 in the aspergillic acid BGC are two examples of uncharacterized genes that encode putative, fungal, and even species-specific proteins. Some of the proteins expressed by these previously missed discordant genes, on the other hand, are now recognised to provide protection from or localization and/or destination of pathogens.

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