The Molecular Treasure Hunt for Novel Bioactives

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Abstract

In silico genome mining has become an indispensable tool to complement the classical chemistry-centered approach to identify and characterize novel secondary / specialized metabolites. Bioinformatics platforms, such as the open-source genome mining pipeline antiSMASH (https://antismash.secondarymetabolites.org)[1], which we develop in collaboration with M. Medema's group (U. Wageningen, Netherlands) give us convenient access to assess the genetic potential of microbial producers of natural products. Extensions, like BGCFlow[2] allow to perform comprehensive studies on hundreds to (ten)thousands of genomes. One such dataset are genomes of our proprietary "NBC collection", which contains actinomycetes primarily isolated in Denmark and adjacent countries. We have sequenced more than 1000 species with hybrid illumina/ONP technology that allowed us to assemble high quality genomes[3] and perform large-scale pangenomics analyses.[4]

To make practical use of such datasets, efficient engineering approaches for the specialized metabolite producers, in our case filamentous actinomycetes, are required. We have therefore developed an extensive CRISPR-based toolkit for streptomycetes.[e.g., 5]

These tools, in combination with BGC cloning and expression methods, allowed us to identify and characterize many BGCs encoding the biosynthesis of natural products with antibiotic or plant-protective properties.

References

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