

Integrating secondary metabolome analysis into natural products discovery from myxobacteria via the MetaboScape REST-API

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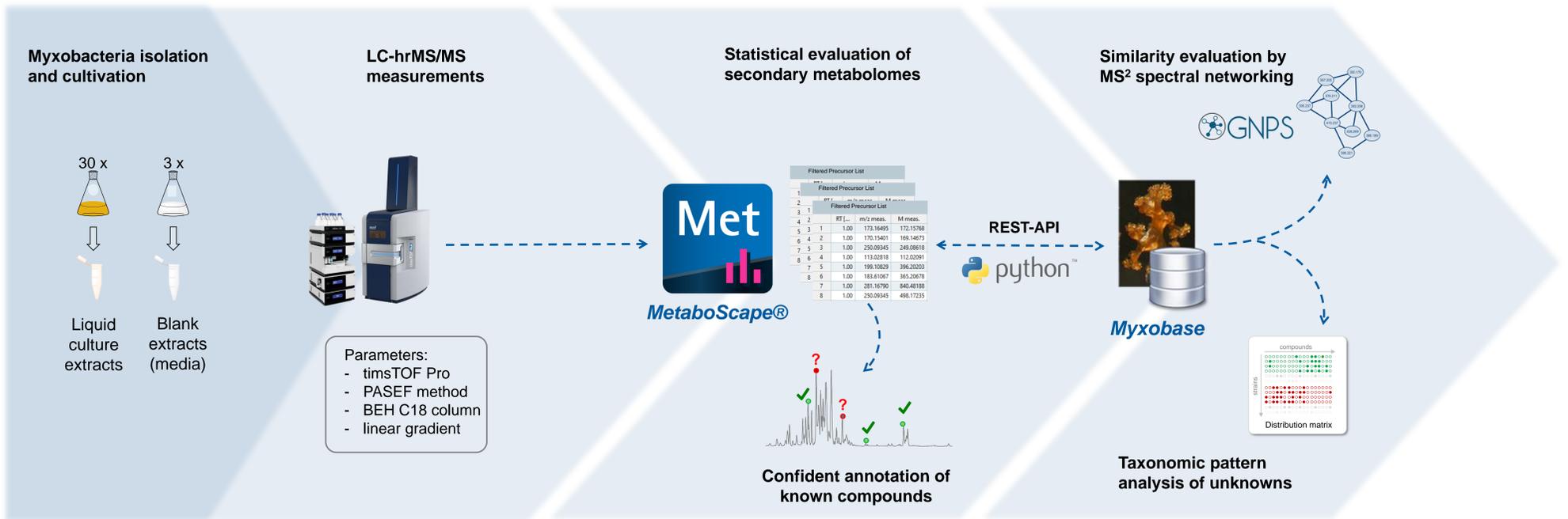
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INTRODUCTION

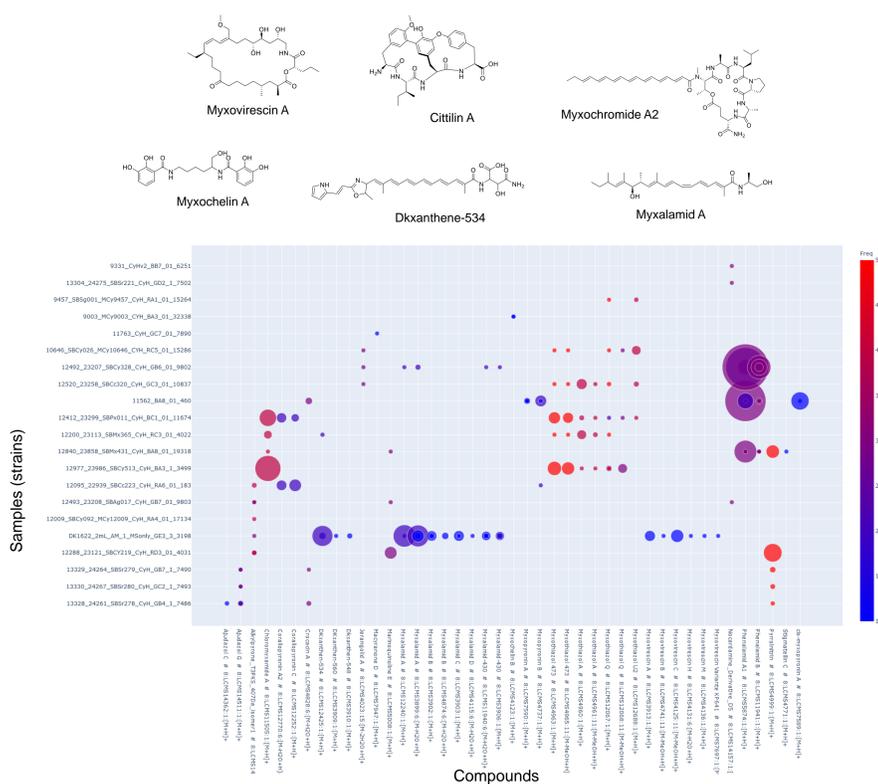
Myxobacteria contribute significantly to natural product discovery from bacterial sources [1]. The HIPS myxobacteria collection is constantly extended by newly isolated strains, which are channeled into the natural products discovery workflow. Comprehensive statistical analysis of myxobacterial secondary metabolomes has previously underpinned a correlation between phylogenetic distance and the production of distinct compound families [2]. While we continuously expand the taxonomical coverage of our strain library with strategic focus on isolation of new myxobacterial species, genera and families,

analyzing the distribution of unknowns detected by LC-MS across all taxa creates important insights. The foundation for comprehensive analysis of myxobacterial secondary metabolomes is the in-house database Myxobase that serves as both analyte dictionary and secondary metabolome data warehouse. Here we present the development of a database-supported metabolomics-based workflow aimed at exploiting the biodiversity accessible from myxobacteria for the discovery of novel natural products.

Workflow

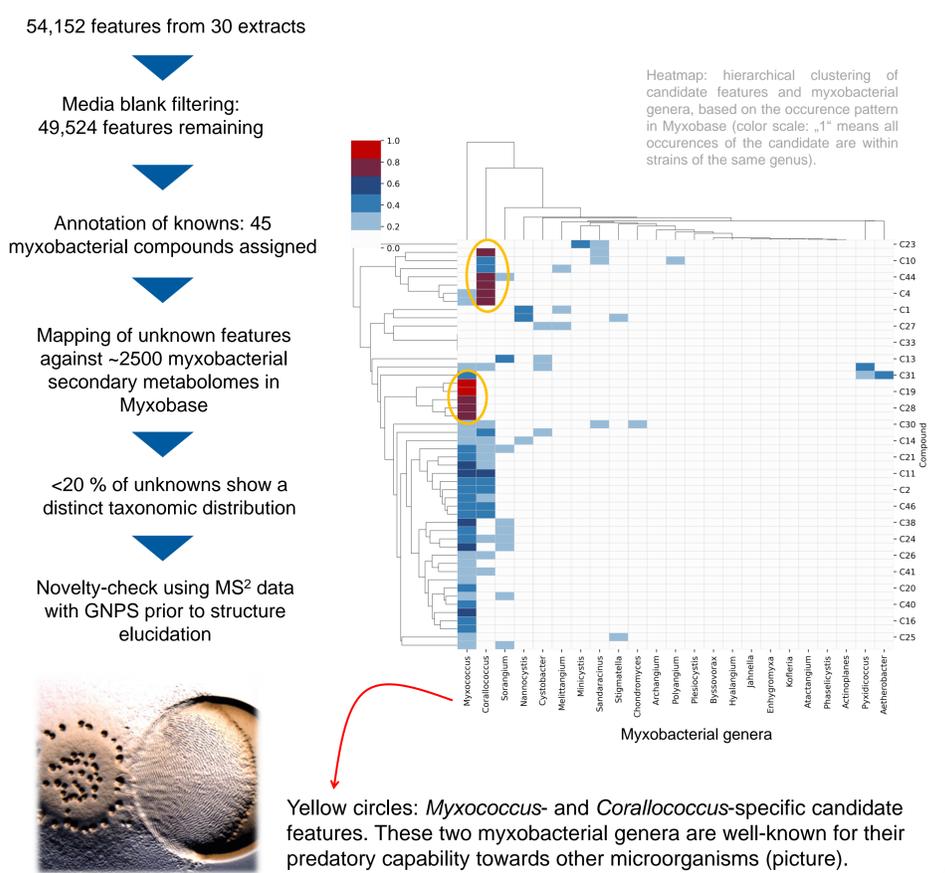


Distribution of known myxobacterial natural products in analyzed extracts



Annotation of known myxobacterial natural products in the analyzed extracts with high confidence through the combination of exact mass, retention time, isotope pattern and MS² spectra reveals distinct pattern of occurrence in relation to myxobacterial taxonomy (subset from 30 strains).

Finding new natural products with distinct taxonomic distribution pattern



Yellow circles: *Myxococcus*- and *Corallococcus*-specific candidate features. These two myxobacterial genera are well-known for their predatory capability towards other microorganisms (picture).

SUMMARY

- In this study we generated LC-MS data for 30 myxobacterial strains which were cultivated in complex media, extracts were prepared using a standardized procedure and measured using high-resolution LC-coupled TOF-MS
- Large-scale LC-MS evaluation of myxobacteria secondary metabolomes was enabled by the MetaboScape REST-API bridging a vendor processing software and a specialized research database
- In order to determine the distribution of unknowns across myxobacterial taxa we took advantage of the existing Myxobase database containing a catalog of ~2500 myxobacterial secondary metabolomes (> 16 mio. features)
- The workflow allowed us to generate a list of taxon-specific candidates for new myxobacterial natural products to be targeted with isolation and structure elucidation in the future

References

- Herrmann, J., Fayad, A.A., Müller, R., Natural products from myxobacteria: novel metabolites and bioactivities. *Nat. Prod. Rep.*, **2017**, 34 (2), 135–160.
- Hoffmann, T., Krug, D. *et al.*, Correlating chemical diversity with taxonomic distance for discovery of natural products in myxobacteria. *Nat. Commun.* **2018**, 9 (1), 803.