Actinobacteria bioprospecting from ore-forming environments

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Introduction. The phylum Actinobacteria has long been recognized as a prolific source of natural products, including antibiotics and drugs. However, discovering new bacterial natural products (NP) has grown increasingly challenging over time. Bacteria produce NP through specialized or secondary metabolism that is environment specific. The genetic heritage of Actinobacteria has provided them with a remarkable capacity to produce specialized metabolites, enabling them to colonize diverse ecosystems. A potential solution to discovering new natural products is to explore unique and harsh environments, such as mine soils, characterized by their acidity, salinity, and limited capacity to sustain life. These environments may harbor unexplored natural product chemistry and unusual bacterial diversity. Of particular interest are fluorine-related soils, known for their extreme abiotic conditions and the limited ability of living organisms to synthesize and metabolize fluorine-containing molecules.

Methodology. Soil samples were procured from fluoride and topaz mines and subsequently subjected to isolation and sequencing of diverse actinobacterial strains. An integral analysis comprising evolutionary genomic, metagenomic, and metabolomic mining was undertaken to ascertain the biotechnological potential of various strains and metabolites. Bioactivity assays were conducted against ESKAPE pathogen strains and human cancer cell lines to identify promising strains and their metabolites. Furthermore, NMR analyses were carried out to determine the chemical structure of promising molecules.

Results. Here we present for the first time biodiversity data and the potential for NP biosynthesis from ore-forming environments. This comprehensive bioprospection led to the identification of novel molecules with promising antibiotic and anticancer properties.

Conclusions. This study provides novel data on bacterial biodiversity in ore-forming places, revealing a vast diversity of actinobacteria with significant biosynthetic capacity for secondary metabolites. These findings underscore the potential of these harsh environments as a valuable resource for discovering novel chemistry with biotechnological applications, particularly in the pharmaceutical industry. Our study has led to identifying promising new molecules with antibiotic and anticancer properties, highlighting the potential of bioprospecting in these unique environments to discover new natural products.

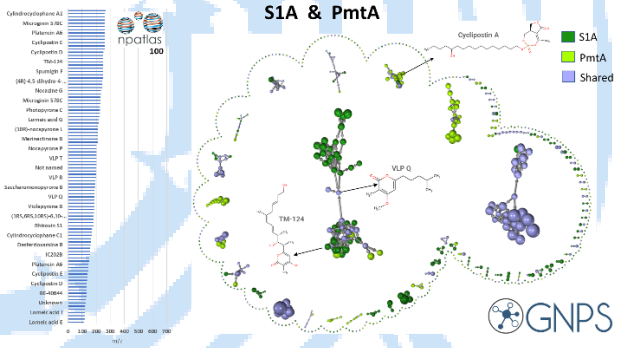

Figure 1. Evolutionary genomic, metagenomic, and metabolomic mining of two strains isolated from ore-forming places.

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References.

1. Demain AL. (2014). Importance of microbial natural products and the need to revitalize their discovery. *J Ind Microbiol Biotechnol* 41:185–201.
2. Van Bergeijk DA, Terlouw BR, Medema MH, van Wezel GP. (2020). Ecology and genomics of Actinobacteria: new concepts for natural product discovery. *Nat Rev Microbiol*.
3. Kenderes SM, Appold MS. (2017). Fluorine concentrations of ore fluids in the Illinois-Kentucky district: Evidence from SEM-EDS analysis of fluid inclusion decrepitates. *Geochim Cosmochim* Acta 210.