

ExMODE: A comprehensive resource for extremophile genomic and functional exploration

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Background



Glacier



Salt mine



Hot spring



Acid mine drainage



Deep sea

- **Extreme environments are defined by one or more harsh physicochemical parameters**—such as extreme temperature, pressure, salinity, or pH. Typical habitats include hot springs, polar glaciers and permafrost, salt lakes, acid mine drainage, and the deep sea.
- Extreme environments host unique extremophiles distinguished by **high novelty and diversity**.
- **The genetic diversity of extremophiles represents a rich resource for bioprospecting**, e.g., Taq DNA polymerase and deep-sea PETases.



Background

Current challenges

01 Data fragmentation and lack of standardization



Fragmentation impedes integration

Metagenomic data are scattered across global repositories without unified indexing or retrieval, making cross-repository integration laborious and hindering large-scale mining.



Inconsistent metadata standards

Inconsistent sample annotations and environmental metadata, coupled with missing or ambiguous information, hinder cross-environment and cross-study comparisons and data mining.



02 Database breadth-depth imbalance

MGnify offers broad coverage but limited depth in extreme environments, whereas databases such as 4GDB focus on specific habitats (e.g., glaciers).

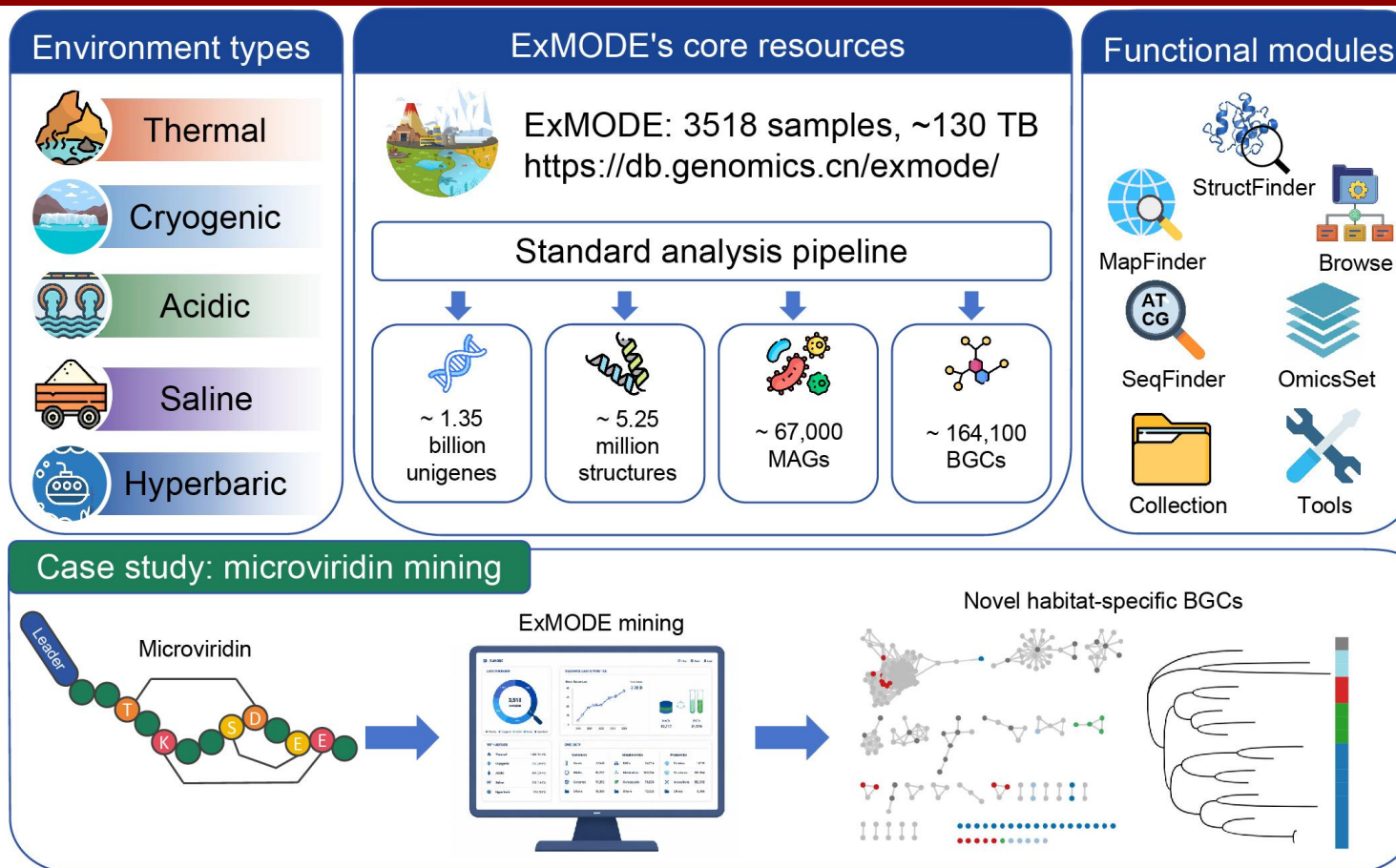


03 Sequence-centric resources limits dark-matter exploration

Existing resources focus on nucleic acid sequences but lack complementary protein structural information, hindering the annotation of microbial “dark matter” and the discovery of novel functional enzymes and biomolecules.



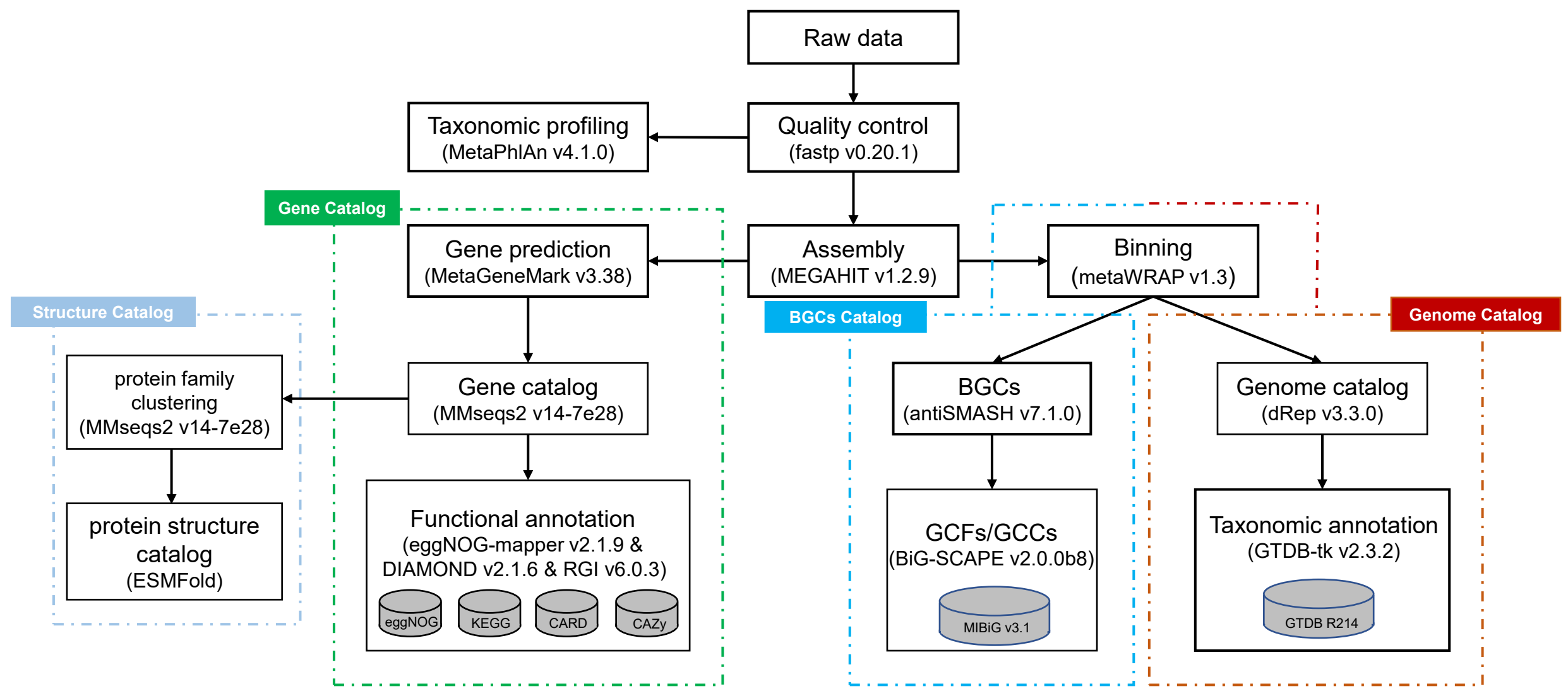
Highlights



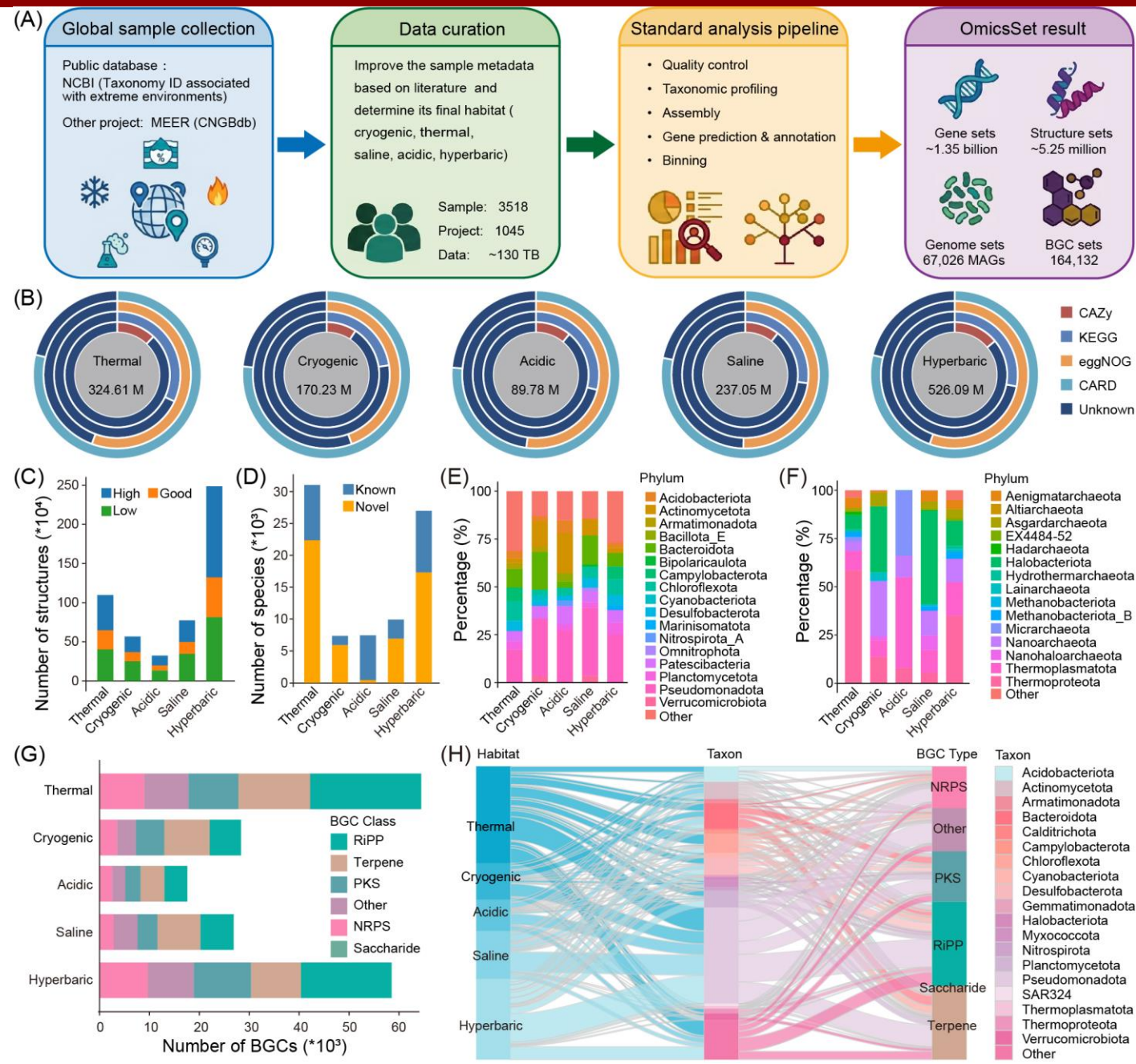
- ExMODE integrates 3,518 samples into a unified resource containing 1.35 billion genes, 5.25 million protein structures, 67,026 MAGs, and 164,132 BGCs.
- ExMODE enables integrated sequence-, structure-, and genome-based exploration across five extreme environments to uncover microbial dark matter.
- Cross-habitat mining of microviridins demonstrates ExMODE's potential for discovering novel BGCs and valuable natural products.



Analysis workflow



ExMODE's Extremophile Resource Display



- **Large-scale resource integration:** 3,518 samples yielding 1.35 billion genes, 5.25 million protein structures, 67,026 MAGs, and 164,132 BGCs.
- **Rich functional dark matter:** Most genes lack database annotations, harboring substantial potential for novel functions.
- **Structure-enabled functional mining:** 5.25 million representative protein structures support structure-guided exploration of uncharacterized proteins.
- **Broad microbial diversity:** Many MAGs remain unclassified at the species level, revealing potentially novel microbial resources.
- **Diverse biosynthetic potential:** 164,132 BGCs span five extreme environments, exhibiting distinct biosynthetic profiles.

Fig 1. Comprehensive analysis of ExMODE's extremophile resources



ExMODE's platform interface and functional modules

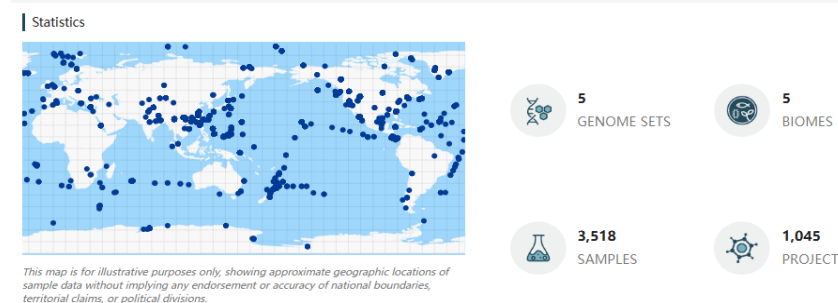
ExMODE | MapFinder | SeqFinder | StructFinder | Browse | OmicsSet | Collection | Tools | Help

Extremophile Multi-Omics Databases

Explore extreme environments and protect the code of life on earth

Keywords (Biome/Project/Sample/Genome)

Examples:



Biomes

Acidic environment	Cryogenic environment	Hyperbaric environment	Saline environment	Thermal environment
150 Samples 3,668.811 GB	406 Samples 5,347.794 GB	2,177 Samples 105,028.129 GB	502 Samples 4,927.105 GB	769 Samples 16,437.151 GB

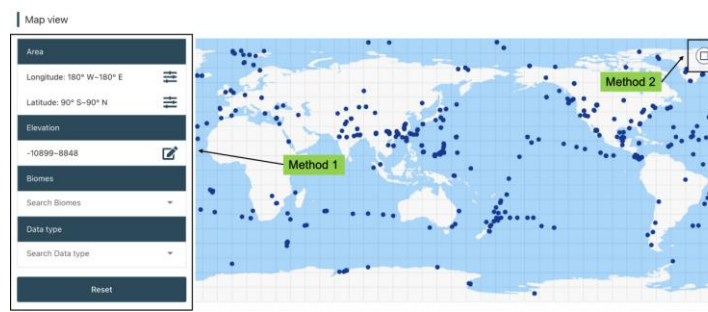
Collections

MEER

The Mariana Trench Environment and Ecology Research Project (MEER). The goal of this project is to collaboratively address significant scientific challenges, including the formation and evolution of deep-sea geological systems, the origins of life and adaptability to environmental conditions, biodiversity, and the impacts of climate change. This initiative is set to further deepen research and bolster international cooperation in the domain of deep-sea science.

Hadal adaptation | Hadal currents

Home Page



MapFinder

SeqFinder

Gene/Protein search | Genome search | RGC search

Module Switching | Enter the query sequence | Select one or more databases | Input additional parameters | Input Job name

Search based on task status or keywords

Summary of input information | Detailed search results | Gene search results page | protein search results page

SeqFinder

StructFinder

Upload a protein structure (PDB/mmCIF) file or use the example | Input genebank file | Summary of input information | Detailed search results | Structure search results page

Mode: 3D/AA | TM-align | Submit | Input information section | Task status section | Detailed structure information page

StructFinder

Browse

Thermophilic (Genome set ID: ES000001) | Metadata of the sample | Taxonomic assignment and abundance | MAGs information | Sample details page

Redirect to home page | Redirect to sample page | Redirect to project page | Redirect to sample page | Redirect to sample page | Redirect to sample page

Browse

OmicsSet

Project | Summary of the biome | Summary section | Project section

Functional annotation overview | Overview of MAGs | Overview of Biomes | Detailed information of MAGs | Detailed information of Biomes | Species phylogenetic tree | Related analysis result files | Gene catalog analysis section | Genome usage analysis section | Biome usage analysis section

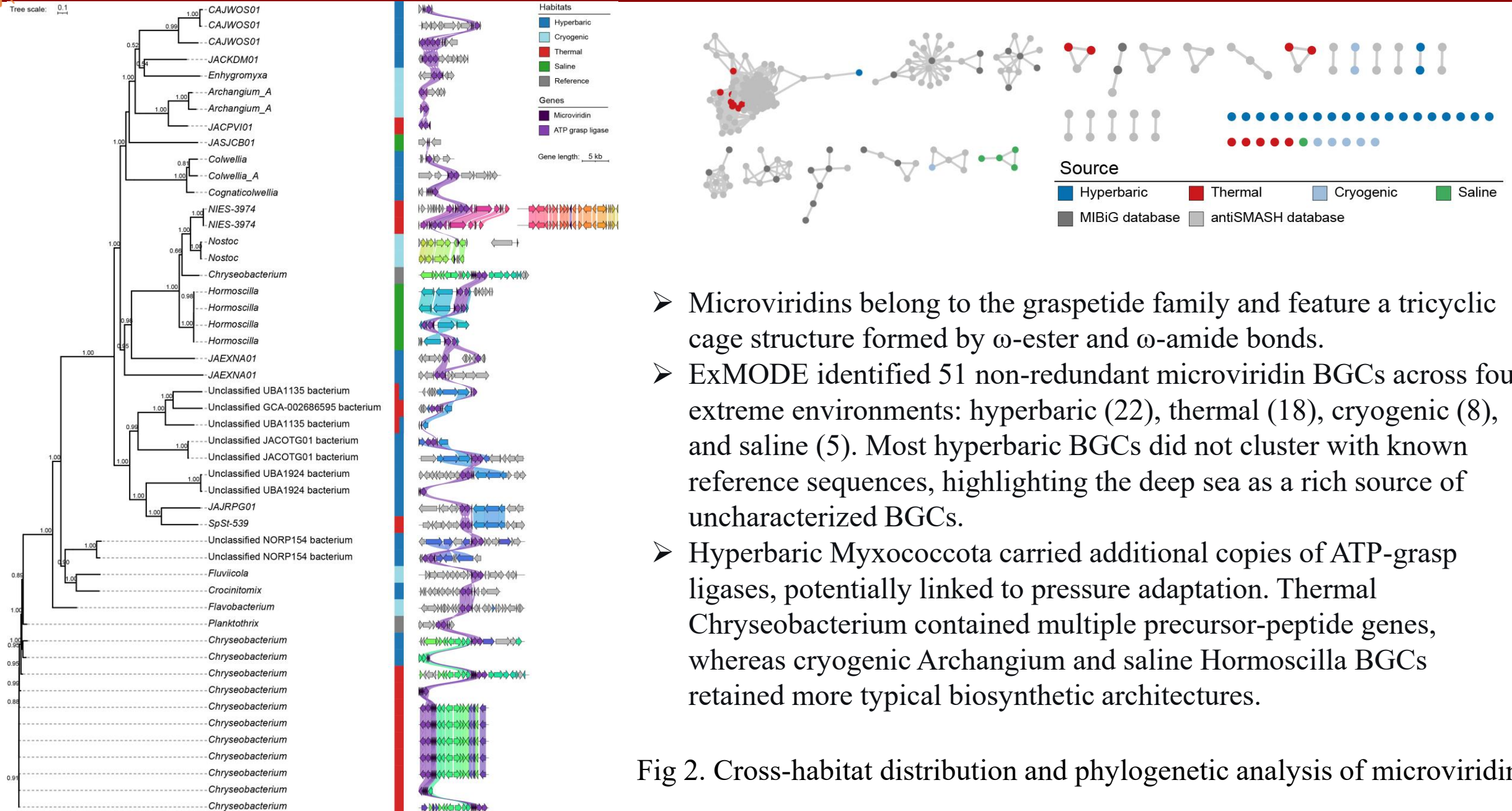
OmicsSet

Collections & Tools

The genetic repertoire of the deep sea: from sequence to structure and function | MEER: Extraordinary flourishing ecosystem in the deepest ocean | Microbial ecosystems and ecological driving forces in the deepest ocean sediments | The amphipod genome reveals population dynamics and adaptations to hadal environment

Collections & Tools

Case study: Cross-habitat mining of microviridin BGCs



- Microviridins belong to the graspetide family and feature a tricyclic cage structure formed by ω -ester and ω -amide bonds.
- ExMODE identified 51 non-redundant microviridin BGCs across four extreme environments: hyperbaric (22), thermal (18), cryogenic (8), and saline (5). Most hyperbaric BGCs did not cluster with known reference sequences, highlighting the deep sea as a rich source of uncharacterized BGCs.
- Hyperbaric Myxococcota carried additional copies of ATP-grasp ligases, potentially linked to pressure adaptation. Thermal Chryseobacterium contained multiple precursor-peptide genes, whereas cryogenic Archangium and saline Hormoscilla BGCs retained more typical biosynthetic architectures.

Fig 2. Cross-habitat distribution and phylogenetic analysis of microviridin



Summary

- ❑ ExMODE integrates microbiome data from five extreme environments, providing multidimensional resources spanning genes, protein structures, MAGs, and BGCs.
- ❑ The database enables interactive searches of gene/protein sequences, protein structures, genomes, and BGCs, supporting cross-environment comparisons and functional mining.
- ❑ A cross-environment mining of microviridin BGCs demonstrates ExMODE's potential for natural product discovery.
- ❑ Website: <https://db.genomics.cn/exmode/>

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