Harnessing Cold-Adapted Microbiomes for Antimicrobial Discovery Through Functional Metagenomics

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Abstract

Antimicrobial Resistance (AMR) is a burgeoning global health crisis with an estimated 10 million deaths globally by 2050. The rapid emergence of multidrug-resistant pathogens, coupled with the dwindling efficacy of existing antibiotics, underscores the urgent need for novel antimicrobial agents. Conventional culture-dependent techniques capture only a small fraction of microbial diversity, leaving the vast number of distinct genetic and metabolic lineages, often referred to as "microbial dark matter", unexplored, particularly from extreme habitats. Metagenomics, as a culture-independent and high-resolution approach, enables access to untapped microbial communities directly from environmental samples. Among these, psychrophilic environments such as polar soils, glacial sediments, and deep-sea ecosystems harbor metabolically unique microorganisms shaped by extreme selection pressures, making them a promising avenue to yield novel biosynthetic gene clusters (BGCs) encoding structurally unique and functionally potent antimicrobial compounds.

In this context, our research lab leverages functional metagenomics to explore psychrophilic microbial communities from cold environments of J&K. A metagenomic fosmid library was constructed from environmental DNA isolated from a cold-active niche. Function and sequence-based screening led to the identification of a fosmid clone exhibiting significant antimicrobial activity against multiple test pathogens. We are trying to address the problem of AMR through functional metagenomics by the discovery of novel antimicrobial compounds.

Our findings reinforce the potential of cold-adapted metagenomes as valuable sources of antimicrobial scaffolds to address the AMR crisis. Systematic exploration through functional metagenomics of psychrophilic microbiomes offers a promising frontier for the identification of novel antimicrobial scaffolds, aligning directly with global AMR mitigation strategies and WHO's priority pathogen targets.

Keywords

Antimicrobial resistance (AMR), Functional metagenomics, Psychrophilic microbiomes, Biosynthetic gene clusters, Novel antibiotics.