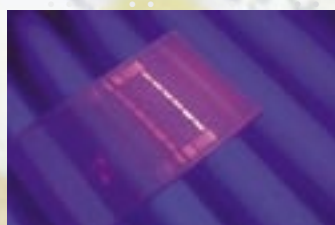




MINING MICROBIAL GENOMES FOR NOVEL ANTIBIOTICS

PROBLEM



How will humanity deal with the pressing need for new drugs to treat pathogens that are resistant to antibiotics? Widespread overuse has led to a decline in the efficacy of these drugs, and now many pathogens are resistant to all commonly used antibiotics.

Currently, 70 percent of antibiotics are derived from microbially produced natural products, or secondary metabolites — small molecules with unique, and often medically relevant, properties. Ironically, at a time of great need, many pharmaceutical companies are scaling back or eliminating metabolite screening programs. Yet evidence suggests that a multitude of useful microbial products await discovery. A better way to exploit this potential is urgently needed.

RESEARCH



The Mining Microbial Genomes for Novel Antibiotics Research Theme brings together a team of microbiologists, chemists, and engineers to search — or in essence, mine — for new metabolites. Researchers, using a novel approach based on identification of molecular signatures in genome sequences and in metabolic products, will explore:

- how to identify new, medically relevant metabolites
- how to engineer microorganisms to efficiently and cost-effectively produce these metabolites
- how to modify these metabolites to improve their effectiveness
- how to develop unique, high-output screening methods to assess the metabolite's efficacy and toxicity to pathogens

Scientists will search for these answers by unlocking the vast genetic potential of microbial genomes using sequence-based approaches. Because most microorganisms will not grow under standard laboratory conditions, this method eliminates many of the difficulties involved in traditional culture-based approaches.

By accessing microbial DNA isolated directly from the natural environment (without cultivation), the scale of the screening process can be expanded without labor-intensive growth experiments. Once promising targets are identified, researchers can conduct a more thorough investigation involving molecular biology, metabolite analysis (metabolomics), metabolic engineering, chemical and enzymatic synthesis, and analysis of host and target organism response.

BENEFITS

Success with this approach could ultimately lead to the discovery of novel classes of antibiotics, improved production methods, and better ways to examine antibiotic efficacy in human and animal hosts.

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