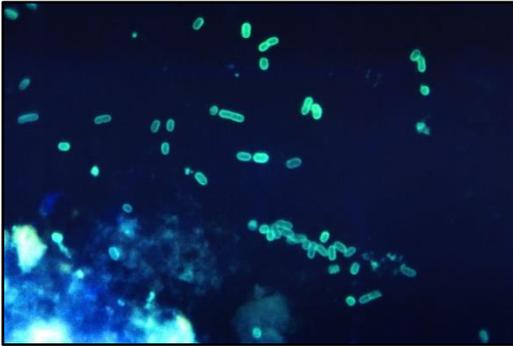


Antibiotic Resistance Platform (ARP): for Adjuvant Discovery and Antibiotic Dereplication



The ARP platform for adjuvant discovery and antibiotic dereplication consists of a cell-based library of *Escherichia coli* expressing individual resistance genes. Image is purely illustrative.

Source: CDC/ Charles Farmer, PHIL, public domain

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Stage of Research

The minimal ARP kit is available for academic use.

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Abstract

Solving the antibiotic resistance crisis requires the discovery of new antimicrobial drugs and the preservation of existing ones. With no new antibiotics on the horizon, blocking resistance with antibiotic adjuvants have emerged as a viable strategy. Antibiotics are co-formulated with an inhibitor of resistance, blocking the resistance element and freeing the antibiotic to target the bacterium. A major difficulty in identifying new antibiotics is the frequent rediscovery of known compounds, necessitating laborious "dereplication" to identify novel chemical entities.

The antibiotic resistance platform (ARP) developed by researchers at McMaster can be used for both the identification of antibiotic adjuvants and for antibiotic dereplication. The ARP is a cell-based library of *Escherichia coli* expressing mechanistically distinct individual resistance elements in an identical genetic background.

The strength of the ARP lies within the mechanistic diversity and rigorously curated substrate specificity of the resistance strains. Using either a low copy plasmid or integration of the gene into the bacterial chromosome, the researchers are able to control resistance gene copy number. Expression is further regulated through the use of two promoter systems differing in strength. This platform is optimized for antibiotic dereplication and the identification of potentiators of existing antibiotics.

Applications

- Adjuvant and antibiotic discovery & development
- Novel natural products discovery
- Dereplicate known antibiotic scaffolds
- Antimicrobial resistance (AMR) research

Advantages

- Mechanistic diversity and rigorously curated substrate specificity of resistance strains
- Simple, low-cost and effective method that does not rely on time-consuming and technologically intricate methods