PROJECT SNAPSHOT

2C: Development Of Antimicrobial Therapeutics From The Natural Products Of Microbiomes

Pillar: Optimization
Theme: Innovation and Commercialization
Keywords: Natural Products; Microbial Ecology; Antibiotic Potentiators; Counter-Resistance

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CO-INVESTIGATOR(S): Kathy McCoy, PhD; Darren Derksen, PhD

AIM

The proposed program seeks to elucidate microbial chemical interactions that drive the AMR of bacterial communities. This research is predicated on an ecological principle that we term “counter-resistance,” which posits that many Archaea, bacteria and other microbial eukaryotes have evolved the means to produce metabolites that block AMR because of competitive interactions for resources and space.

WHY IS THIS IMPORTANT?

Microbiologists have acquired most of the information known about the genetic and biochemical mechanisms of AMR by studying model organisms in monocultures. However, bacteria are rarely found in any environment alone and we know very little about the scope and impact of polymicrobial interactions on the AMR of even the best-studied model organisms.

OUTCOMES

We have identified that many bacteria produce low molecular weight molecules (called N-acylamides) that block AMR, including carbapenem-resistance of Pseudomonas aeruginosa and Acenitobacter baumanii. These carbapenem-resistant bacteria top the World Health Organization (WHO) global priority list of antibiotic-resistant pathogens to guide research, discovery, and development of new antibiotics.

RESEARCH QUESTIONS

1. Can we identify additional microbe-microbe interactions and bioactive, natural small metabolites that prevent AMR?
2. How do microbial metabolites, such as the N-acylamides, block AMR?
3. Can we develop models to measure the AMR and fitness of organisms in polymicrobial communities?

OUR APPROACH

Our team has led the development of technology platforms for prospecting chemical microbe-microbe interactions. Our platforms include the Alberta Microbiota Repository (a living library containing hundreds of species of bacteria and fungi native to Canada) and robotics enclosed in air-tight chambers to handle these organisms. We also work with experts in natural product chemistry and processes for identifying bioactive molecules from complex mixtures. We will use synthetic chemistry to execute structure-activity relationship studies of identified biomolecules. Our expertise in biochemistry and molecular genetics will be used to elucidate mode-of-action. Using gnotobiotic animal models, we will investigate the impact of natural antibiotic adjuvants and the microorganisms that produce them on antibiotic therapy outcomes.

ALIGNMENT WITH THE AMR - ONE HEALTH CONSORTIUM

LEVERAGED SOURCES OF SUPPORT

Alberta Children's Hospital Research Institute • Canada Foundation for Innovation • Canadian Institutes of Health Research • Natural Sciences and Engineering Research Council of Canada • University of Calgary, Office of the Vice President (Research)

KNOWLEDGE & TECHNOLOGY EXCHANGE AND EXPLOITATION

- We will develop molecules that can rescue existing antibiotic drugs from AMR.
- We are developing polymicrobial biofilm susceptibility testing models with a corporate partner.

HIGHLY QUALIFIED PERSONNEL

- 1 Postdoctoral Fellow
- 1PhD
- 1MSc

AFFILIATIONS:

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