Discovery of new Antimicrobial Peptides from environmental samples

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Overuse and misuse of conventional antibiotics has become one of the greatest challenges in human health; on the other hand, the rapid spread of antibiotic resistant pathogens is a major threat to our life and environment. It is clear that the broad-spectrum activity of traditional antibiotics has played a key role in the selection for resistance. Antimicrobial peptides (AMPs) provide us with a compelling alternative to antibiotics.

In response to interspecific competition, many microorganisms produce natural products to fight other microbes. Interestingly, our results show that many microorganisms only produce AMPs under stimulation on an as-need basis. We have optimised and developed a high throughput method for screening many microbial isolates and also a method for inducing AMP biosynthesis.

Our team specialise in the following:

- Collection and screening of microbial communities from varying environmental samples through the identification and development of a wide range of compatible cultivation media
- Biodiscovery of isolates producing new antimicrobial compounds
- High-throughput screening - to rapidly identify AMP producing strains
- Development of successfully demonstrated methodologies to induce beneficial isolates for antimicrobial compound production
- AMP induction using secondary metabolite biosynthesis
- Identification of new bioactive natural peptides to inhibit plant / food pathogens with a focus on control of plant pathogens Pseudomonas and Clavibacter and food pathogens Listeria and E. coli
- Peptide profiling and structure elucidation of new antimicrobial peptides or compounds (Gel electrophoresis, in situ activity assay, HPLC, MALDI)
- Early stage trials against human pathogens for use as food preservatives and biopesticides (Collaboration of research teams with industry)
Overall Aim:

Screening of various environmental microbiomes (soil, seawater, plant and insect microbiomes) to discover new antimicrobial peptides (AMPs) and bacteriocins. We anticipate that these discoveries will then lead to the development of new treatments against superbugs causing human disease and losses in the agriculture and food industries.

The focus of this team is to explore AMPs, especially bacteriocins in the environment.

After initial high throughput screening and stimulation of microbial isolates, we rapidly test the potential candidates for AMP production by directly incubating peptide profiles of each organism with pathogens. This enables immediate identification of the AMPs involved and allows us to verify whether known or new AMPs have been produced. After that the activity spectrum and structure for each new AMP is thoroughly investigated to elucidate the mode of action. We have recently identified >20 microbial isolates from soil and food spoilage which produce potentially new antimicrobial peptides against plant and food pathogens.

The discovery of new AMPs from microorganisms has recently been flagged as one of the most promising approaches to develop new antibiotics. Our initial studies have demonstrated that environmental samples from various soils, seawater, wastewater, food spoilage and even insectile sources are among the most promising sources for finding new antimicrobial peptides. We are well equipped and have the collective expertise to rapidly identify and develop new AMPs from environmental microbiomes.

We wish to collaborate with interested parties to take the next steps towards the development of new antibiotics.

High throughput screening against pathogen (example):

- Screening and identification of antimicrobial peptides or compounds

Testing antimicrobial peptide (AMP) activity. (A and B) *Clavibacter* michiganensis. Identification of antimicrobial peptides with and without proteinase K from different isolates (C) Inhibition assay using electrophoresis gel with *Listeria monocytogenes* (D) confirmation of AMP using half of the gel for sequencing.

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