

BIOPHARMA

Novel therapeutic compositions for degrading bacterial and fungal biofilms

BACKGROUND

Approximately 65-80% of all bacterial infections in humans are biofilm-related. Microbial biofilms, communities of adherent bacteria or fungi embedded in a matrix of exopolymeric substances, represent a significant medical challenge as they are highly resistant to antimicrobial agents, disinfectants and immune defenses. In fact, biofilm embedded microorganisms can tolerate antibiotic doses up to 1,000 times greater than doses that kill free-floating bacteria. Exopolysaccharides are a major component of the biofilm matrix, where they contribute to biofilm adhesion, architecture, and resistance. Biofilms can form on biotic surfaces, such as lung epithelial cells or other organs, and abiotic surfaces including, medical devices and implants, and they are responsible for biofouling in industrial and commercial settings.

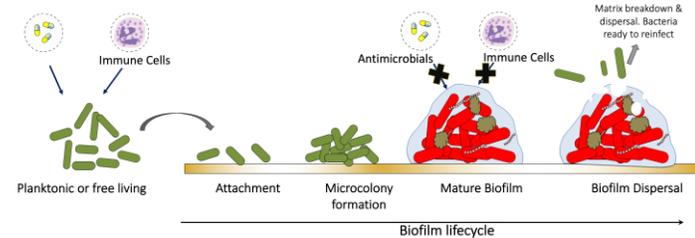


Fig 1: Biofilm formation and dispersal.

DESCRIPTION OF THE INVENTION

Our scientists have identified novel therapeutic enzymes for degrading and inhibiting production of bacterial and fungal biofilms. These compositions target and degrade the exopolysaccharides produced by a number of pathogenic species including, but not limited to; *Pseudomonas spp*, *Escherichia coli*, coagulase negative *Staphylococcus spp*, *Acinetobacter baumannii*, and *Aspergillus fumigatus*. Dispersing the biofilm and releasing the microbes into their free-floating state increases the efficacy of existing anti-infectives and immune defenses.

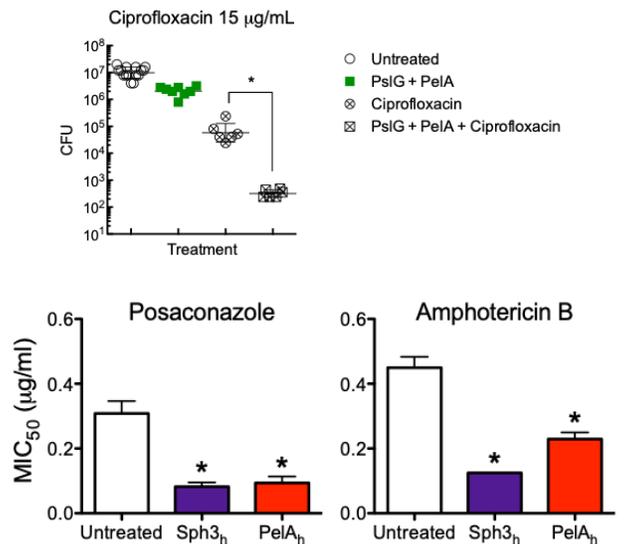


Fig 2: Antimicrobial potentiation using the enzymes PsIG, PeIA and Sph3

KEYWORDS

Anti-microbial, enzyme, biofilm degradation, therapeutic

The specificity of these novel enzymes allows for the selective dispersal of the pathogenic organism while eliminating off-target effects, including the disruption of host cells and the host microbiota.

In vitro data show that the hydrolases successfully potentiate the effect of antibiotics (Fig 2). We have also shown in an *in vivo* mouse burn wound model that these enzymes can increase the effectiveness of tobramycin treatment during wound infection (Fig 3).

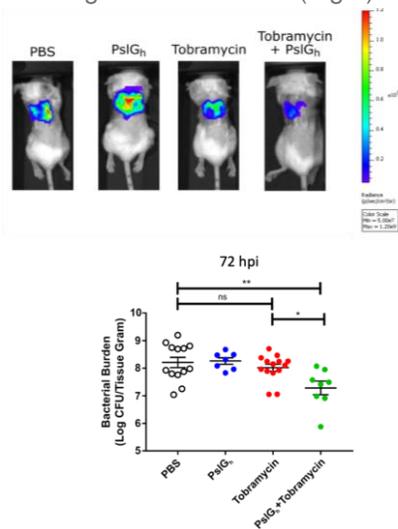


Fig 3: Effect of PslG on tobramycin treatment of burn wound infections

These enzymes can also be easily coated onto the surfaces of medical devices such as catheters to prevent biofilm formation (Fig 4). *In vitro* and *in vivo* proof of concept studies to prove the efficacy of a combination of these enzymes on multispecies biofilms are currently underway.

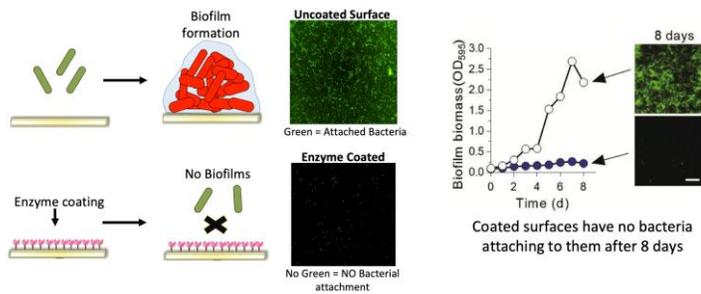


Fig 4: Efficacy of enzyme coating on abiotic surfaces

COMMERCIAL APPLICATIONS & ADVANTAGES

- Diverse applications:
 - Anti-infectives for lung diseases and wounds
 - Coatings for medical devices and implants
 - Disinfecting products
- Low (nanomolar) quantities of enzyme can prevent biofilm formation, protect lung epithelial cells from fungal damage prior to biofilm formation, or disperse existing biofilms in less than 1 hour. This high level of specificity for the biofilm matrix will lessen the likelihood of resistance.
- Enzymes synergize with standard antimicrobials and make them more effective.
- Enzymes are easy to produce, stable and non-toxic. High (milligram) quantities of enzymes are non-toxic to human lung fibroblast cells and preliminary toxicity studies in mice are promising.
- Enzyme coatings are active and stable for up to 8 days on surfaces.

DEVELOPMENT STAGE

Extensive *in vitro* data available; animal studies testing efficacy, toxicity and PK in bacterial and fungal models of pulmonary infection; porcine models of burn wound infection; and rat models of catheter infection are in progress.

The current findings point to a promising avenue for the development of these enzymes as novel therapeutics for the treatment of a wide variety of chronic infections, including pulmonary diseases (cystic fibrosis, invasive aspergillosis, and whooping cough), wound infections which affect 1-2% of the world's population and medical device associated infections.

PATENT STATUS

PCT national phase application (US 2017/0216410 A1) covering bacterial and fungal applications. First US patent allowed January 2021.

IP&C is seeking partners to advance this technology.

LEAD INVENTORS:

Dr. Lynne Howell, PhD, Senior Scientist, Molecular Medicine, The Hospital for Sick Children
 Dr. Don Sheppard, MD, McGill University

LICENSING CONTACT:

Ed Kenney, Senior Manager, Tel: 416.970.1713, ed.kenney@sickkids.ca
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