OVERCOMING BIOFILM MEDIATED RESPIRATORY INFECTIONS THROUGH EXPLOITATION OF PATHOGEN AND HOST-DIRECTED NOVEL PEPTIDES.

Dhammika Leshan Wannigama1*, Cameron Hurst2, Peter Monk3, Anthony Kicic4, Stephen Stick4, and Tanittha Chatsuwan5

1Department of Microbiology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thailand, and School of Medicine, Faculty of Health and Medical Sciences, The University of Western Australia, Nedlands, Western Australia, Australia. 2QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia., Australia, 3Department of Infection, Immunity & Cardiovascular Disease University of Sheffield Medical School, United Kingdom, 4Division of Pediatrics, School of Medicine, Faculty of Health and Medical Sciences, The University of Western Australia, Nedlands, Western Australia, Australia and Telethon Kids Institute, Centre for Health Research, The University of Western Australia, Nedlands, Western Australia, Australia., Australia, and 5Department of Microbiology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand., Thailand

Background and Aims: The recurrent and chronic P. aeruginosa, biofilm colonization on the respiratory tract is the most prevalent cause of morbidity and mortality in patients with ventilator-associated pneumonia, cystic fibrosis (CF), chronic asthma and lung cancer. This situation has generated an urgent need for development of innovative, efficient and targeted treatments. Interest in host defence peptides (HDPs) has grown due to their potential therapeutic applications and their possible use against biofilm. This study, short, synthetic cationic peptides were tested for their anti-biofilm effectiveness as well as their ability to inhibit and disperse the ability of P. aeruginosa biofilms.

Methods: The clinical isolates of P. aeruginosa from patients with chronic lung infections were used as a model to investigate inhibit and disperse of bacterial biofilms by synthetic short sequence defence peptides (HDPs).

Results: The number of different novel anti-biofilm peptide candidates was tested against P. aeruginosa, and was found to exhibit an anti-microbial, anti-attachment as well as anti-biofilm activity at concentrations in the low μg/ml range compare with current conventional antibiotics. Confocal laser scanning microscopy and CFU count revealed that peptide treatment inhibited biofilm formation resulting in bio-volume reduction followed by induced disruption of mature biofilms and other chronic virulent factors. Further, peptides significantly reduce the extracellular matrix substance of mature biofilms.

Conclusion: These findings highlight the potential of novel peptides as a new group of antimicrobial weapons for disrupt biofilms and suggesting its potential use as a model for designing new treatment for chronic lung infections.
Distribution of the Presto Blue stained viable cells (color bar chart) and CFU (color bar line) PEP-FOLD_Q17752281929970 of peptides on mature biofilm of P. aeruginosa seven clinical isolates (Minimal Biofilm Eradication Concentrations (MBEC))

- 4 μg/ml
- 9-18 μg/ml

Bioluminescence imaging with Alexa Fluor 647 dye

High density matrix

0 HR. | 8 HR. | 16 HR. | 24 HR.

Very low density matrix

Sequential staining with LVC/DLD-4 DAPI, BacLight Bacterial Viability kit

Green = Live cells
Red = Dead cells

0 HR. | 8 HR. | 16 HR. | 24 HR.

Time-lapse effect of PEP-FOLD_Q17752281929970 peptide on mature biofilm MBEC ≤ 8μM/ml (Minimal Biofilm Eradication Concentrations (MBEC)) analyzed with high resolution confocal laser scan microscopy.