Multi-action antibiotics to treat chronic biofilm infections

18 Month Progress Report – May 2017

In August 2015, the Trustees for the Australian Cystic Fibrosis Research Trust (ACFRT) signed a contract with the University of Wollongong (UOW) for a research project called – '*Multi-action antibiotics to treat chronic biofilm infections'*. The ACFRT has committed to fund the project to $588,687 over three years.

Biofilms often build up in the lungs of people with CF. The biofilms contain large populations of bacterial cells and are encapsulated within gum-like materials.

Biofilms protect bacteria against the action of antibiotics and against the action of cells in the patient's immune system. Antibiotic resistance can be increased up to 1000-fold in biofilms.

The Chief Investigator for the project is Associate Professor Michael Kelso from UOW. Members of his research team were the first to discover that low concentrations of nitric oxide (NO) act as a signal that triggers bacteria in biofilms to disperse.

When this happens the bacteria become more sensitive to antibiotics and to the body's immune system. When the researchers combined NO-releasing compounds with antibiotics (cephalosporins), they developed a new way of targeting delivery of NO to biofilms.

Since the start of the project, the researchers have greatly improved the chemical synthesis of the NO-donor cephalosporins. Recently, they completed the synthesis of four structurally complex, 2nd generation "all-in-one" cephalosporin NO-donor antibiotics, which are designed to both disperse biofilms and kill the released bacteria.

Preliminary experiments have shown that the new compounds are able to kill bacteria at clinically relevant concentrations and experiments with biofilms are in train. Evaluation of the compounds is continuing through collaborators at Nanyang Technological University (Singapore) and the University of Southampton (UK).