17 January 2024

CFRL Pathways to Treat Intractable Lung Infection in CF Lung Transplant Recipients Grant 2022 – six month progress report

(funded by Cystic Fibrosis Research Limited Queensland)

Project Title: New pathways to treat intractable lung infection in lung transplant recipients with cystic fibrosis.

Our study aims to understand the prevalence and importance of, and treatment options for, cloaking antibody (cAb) exacerbated gram-negative bacterial infection in CF. *Pseudomonas aeruginosa* and *Burkholderia* spp. are opportunistic and nosocomial pathogens which are particularly problematic in chronic lung disease. We believe that these bacteria outsmart the patient's immune system by making the patient produce a specific type of antibody that instead of protecting against infection, actually cloaks and protects the bacteria from immune attack. To date we have demonstrated that cAbs exist to broader pathogens than *P. aeruginosa* and are present against several members of the *Burkholderia cepacia* complex, including *B. cenocepacia, B. multivorans, and B. anthinoferrum*. We have found that 4/9 pwCF and BCC infection have high levels of these antibodies in their serum that bind to sugars expressed on the bacterial surface and inhibit serum-mediated immune killing. Currently, we are investigating the role of cAbs in cell-mediated killing to determine if these antibodies also inhibit macrophage uptake and killing. Removal of cAbs via plasmapheresis, as previously described for individuals with life-threatening *Pseudomonas* infection, may be a useful new strategy for those with *Burkholderia* infection. We will capitalise on this knowledge to lay the foundations to develop novel, non-antibiotic-based therapies.

We thank Cystic Fibrosis Research Limited (CFRL) and Cystic Fibrosis Australia (CFA) for their ongoing support and look forward to sharing our findings.

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