

Interim Report for Conquer CF Innovation Grant 2021

Designing Optimal Phage Cocktails for Kids with Cystic Fibrosis: DOCK-CF

Lay summary of the project: Phages (viruses that selectively infect and kill bacteria) that demonstrate potent killing activity against the most common and problematic bacteria that infect children with cystic fibrosis will be identified. These bacteria and phages will have their full genetic material sequenced and this data will be combined with the results of laboratory experiments on phage-bacteria interactions to predict phage combinations that can be tested in future clinical trials in children with cystic fibrosis.

Progress to date:

Unfortunately, progress on this project has been hampered by COVID-19 restrictions in Sydney which have limited our team's access to the lab for a considerable period between July-September 2021. Despite this, the following has been achieved to date.

- 57 x *Pseudomonas aeruginosa* isolates and 187 x *Staphylococcus aureus* isolates have been collected from children with cystic fibrosis at The Children's Hospital at Westmead.
- DNA has been extracted from all of the *P. aeruginosa* isolates and has been sent for sequencing.
- The process for DNA extraction of the *S. aureus* isolates has been optimised.
- The *P. aeruginosa* isolates have all been screened against a panel of 16 lytic phages and at least one lytic phage has been identified with activity against each bacterial target.
- Human Research Ethics Committee approval obtained to use left-over clinical (non-CF or CF) samples from The Children's Hospital at Westmead for *de novo* isolation of *S. aureus* phages.
- A number of *S. aureus* phages have been obtained from collaborators in WA (Prof Steven Stick). These are being revived to check for viability.

Immediate next steps:

- Perform analysis of sequencing data on *P. aeruginosa* isolates.
- Extract DNA from *S. aureus* isolates, submit for sequencing and perform analysis of sequencing data.
- Continue process of *de novo* isolation of *S. aureus* phages from clinical specimens.
- Screen any new phages and any viable phages (from WA) against *S. aureus* isolates.

We thank Conquer CF and the Australian Cystic Fibrosis Research Trust (ACFRT) for their support of our research. Due to maternity leave of the CIA for the next 12 months, a final report on research activities will be submitted by March 2023.

Dr Ameneh Khatami, on behalf of the DOCK-CF research team.