In January 2018, the Trustees for Australian Cystic Fibrosis Research Trust (ACFRT) signed a contract with the University of New South Wales (UNSW) for a research project called “RNA therapeutics: Novel paradigm in mutation independent CF therapy”. The Innovation Grant of $70,000 will fund the project over one year.

Cystic Fibrosis (CF) is a fatal, disease linked to more than 2000 different mutations in the CFTR gene, a chloride channel, differently. Non-coding RNA BGas interacts specifically at site of the CFTR locus to modulate the binding of several proteins, distorting access of RNA polymerase to the CFTR locus. This results in a decrease in expression of CFTR.

We set out to manipulate BGas expression in cultured mini-lungs and mini-guts (AVATARs) created from nasal and intestinal cells isolated from patients with CF.

In the last 6 months, we have:

1- created over 100 nasal and 15 intestinal organoids from individuals with CF that visit the Sydney Children’s Hospital CF clinic (Fig 1).

2- created and optimised the CF AVATAR Platform a robust predictive organoid live cell-imaging platform that allows testing out the effectiveness of different CFTR modulating therapies. AVATARs from CF individuals will swell if the exposure to a drug corrects their dysfunctional CFTR protein.

3- explored the basal level of expression of BGas in the created AVATARs and have identified those positive for presence of BGas.

Our aim for the remainder of the year is to transduce the AVATARs with our BGas removing compound (TAT cell-penetrating peptide-siBGas). The effectiveness of which will be measured by the AVATAR platform.

I would like to thank Cystic Fibrosis Research Limited (QLD) for funding my research through the ACFRT.

Fig 1. Fluorescent microscopy images of respiratory and intestinal organoids. Credit: miCF Research Center. Image subject to copyright.