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Australian Cystic Fibrosis Research Trust
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To whom it may concern,

With respect to "Establishing a pipeline for repurposing anti-inflammatory drugs to tackle viral-induced exacerbations in children with cystic fibrosis", I am pleased to provide the details of the manner in which the Project was conducted and the findings of the Project.

The start of this study was extensively delayed due to significant delays related to accessing samples from children with cystic fibrosis from a local biobank. To mitigate these delays further, we sought an alternative source of samples from a collaborator at Murdoch Children's Research Institute (Melbourne, Australia) and we obtained ethics approval in January, 2023. However sample access did not eventuate due to the length of time required for prospective sample collection. Fortunately, we were able to source a third suitable biobank located at the Marisco Lung Institute at the University of North Carolina (United States). We obtained ethics approval to access these samples and received bronchial airway cells from adults with cystic fibrosis in July, 2023.

We were then able to make significant progress. We completed the laboratory experiments for this study in mid-September 2023, and extracted nucleic acids from the samples. This allowed us to undertake transcriptomic analysis to understand what gene signalling is affected by infection with rhinovirus and treatment with interleukin-1 receptor antagonist, and determine differential gene expression with and without treatment.

In response to infection with a clinical strain of rhinovirus C, there was differential expression of over 8,000 genes compared to an uninfected control, and pathway analyses identified upregulation of classical antiviral responses and innate inflammatory pathways, with activation of neutrophils and resulting inflammation observed. When this response was compared to samples treated with the interleukin-1 receptor antagonist prior to infection, treatment was uniquely associated with pathways that downregulate immune responses and viral replication. Directly comparing differential gene expression between infected samples with and without treatment, a small number of genes related to neutrophilic inflammation are downregulated with treatment. These promising results suggest that treatment with interleukin-1 receptor antagonist may reduce neutrophilic inflammation in response to a viral infection in people with cystic fibrosis.

We are in the process of acquiring new laboratory equipment that will enable us to conduct small-scale proteomics to complement the transcriptomic analyses, to determine whether these differences in gene expression translate to a reduction in inflammatory cytokine release.

These results are currently being formulated into a manuscript for publication, once the proteomic data can be incorporated into the analysis. We will discuss these promising results with our consumer collaborators to determine the best path forward towards clinical translation for this project. We will also update Cystic Fibrosis Australia with these outcomes in due course.

Discover. Prevent. Cure.

This project would not have been possible without the generous support of Conquer CF and Cystic Fibrosis Australia, and I thank you both for supporting our work.

Yours sincerely,

Dr. Samuel Montgomery

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