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HUNTER NEW ENGLAND  
NSW HEALTH

17<sup>th</sup> April 2024

CFWA Golf Classic Innovation Award 2023 – Interim report

**Project title:** Identifying molecular pathways for severe CF liver disease and predicting risk of CFTR modulators-induced liver injury using iPSC-derived hepatic organoids.

I was awarded the CFWA Golf Classic Innovation Grant 2023 (Funded by Cystic Fibrosis Western Australia) to investigate the molecular pathways for severe CF liver disease and predicting risk of CFTR modulators-induced liver injury using iPSC-derived hepatic organoids. This research aims to address liver damage in people with CF and complications from CFTR modulators treatment. It employs induced pluripotent stem cells (iPSCs) to create organoid models of the liver for research. These patient specific models will allow us to distinguish characteristics of CF patients with liver disease and assess the effects of CFTR modulator. Ultimately, this research seeks to uncover the underlying mechanisms of CF liver disease, paving the way for improved treatments and patient well-being.

My research background is in Biochemistry, and I have extensive experience with human stem cell-based 3D organoids technique (intestinal and lung organoids), primary human ALI cultures of bronchial and nasal epithelial cells, high throughput live-cell microscopy (preclinical drug assay), electrophysiological studies and ion channel pharmacology.

During the first half of the grant period, we successfully optimized and established the protocol of deriving iPSCs from Human peripheral blood mononuclear cells (PBMCs) isolated from peripheral blood. Currently, the project is focused on differentiating iPSCs towards liver organoids. Once established, we will characterize these organoids morphologically, treat them with CFTR modulators, and investigate the underlying disease mechanisms.

This research has received further support through funding from the John Hunter Hospital Charitable trust grant round 2024 (\$18,430) and The University of Newcastle, Pilot scheme 2023 (\$5,000). Additionally, we are preparing a proposal for the US CFF Spring Pilot and Feasibility Award, 2024, which will be based on the preliminary data obtained using this grant. I am incredibly grateful for the opportunity to conduct this research, which would not have been possible without the invaluable support of CF Australia.

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