A Tai
Progress Report
CFSA Innovation Grant 2021

Project Title: Sphingosine-1 phosphate and zinc – novel mediators of vascular dysfunction in children with CF

We continue to collect lung and blood samples from children with CF and controls. There was a delay with bronchoscopy procedures for a few months during the recent COVID surge. Samples will be tested in parallel when sufficient numbers are obtained. We have optimised all techniques, completed testing of markers of vascular dysfunction in blood from adult CF patients (as comparators for the paediatric bloods), and are undertaking mechanistic in vitro studies focusing on changes in the sphingosine signalling pathway and markers of endothelial functions in cell lines. Significant changes to date have included an activation of the ET-1/TGFb/pSmad axis in adult CF patients; data that will advise our investigations using the paediatric CF samples. In a mechanistic approach the effects of the CFTR inhibitor CFTRinh172, and CFTR correctors (Ivacaftor and Elexacaftor) are used for testing whether these changes are caused intrinsically by CFTR impairment in the patients cells.