CYSTIC FIBROSIS Australia

The Australian Cystic Fibrosis Research Trust 2019-2021

Research Review

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The Australian Cystic Fibrosis Research Trust

History and Achievements

In 1989 the Australian Cystic Fibrosis Research Trust (ACFRT) was founded by a group of parents, patients and doctors to secure resources to support cystic fibrosis (CF) research in Australia.

The Trust was supported by all of the CF state and territory organisations who recognised that combining resources could lead to better research. There was recognition that this would allow the ability to build strong peer review processes and having pooled funding rather than each having a small amount and limited expertise to review proposals was a benefit. It was also agreed that all those who supported the foundation of the ACFRT wanted the best research funded rather than being parochial in regard to place.

Cystic Fibrosis Australia (CFA) has provided all of the administrative work involved with running the ACFRT. This allows the ACFRT to spend 100% of every dollar it receives on research.

Today, after funding more than 350 research projects valued at over $6.5 million, the ACFRT is recognised as Australia's largest and most prolific CF research body.

The ACFRT's remit is to secure funding from public, private and corporate entities along with the CF organisations and to allocate funds to high quality peer reviewed research.

The ACFRT is passionate about ground-breaking, innovative research concepts that consider new treatments and models of care that ultimately improve life expectancy and quality of life for people with CF.

Attracting the brightest young minds into CF medicine, allied health, mental health and research is a key priority and former ACFRT grant recipients are a testament to this.

The ACFRT is administered by CFA and supported by CF organisations from all states and territories.

Australian Cystic Fibrosis Research Trustees

A Message from the Trustees

It is a pleasure to introduce the Australian Cystic Fibrosis Research Trust (ACFRT) to the community. The ACFRT has been in operation since 1989, working hard to improve the lives of those affected by cystic fibrosis by funding innovative research and supporting young scientists to become involved in the search for answers.

The Trustees feel that while we have been supporting research and have funded hundreds of projects over the past 32 years, many of which have led to changes in treatment, we should take this opportunity to promote the work we have supported and the aims of the ACFRT.

Mitch Messer
Founding Trustee
1989 to present

Conrad Guerra
Founding Trustee
1989 to present

Laurie Daly
Trustee
2018 to present

Patrick O'Connor
Trustee
2015 to present

Paul Dalby
Trustee
2018 to present

Jo Armstrong
Secretary
2022 to present

Innovation Grant 2021

RESEARCHER: Dr Elena Schneider-Futschik

PROJECT: Safety and effectiveness of triple-caftor combinations in cystic fibrosis during pregnancy

INSTITUTION: University of Melbourne, VIC

BUDGET: $80,000 (1 year)

SUMMARY: Cystic fibrosis (CF) is a life limiting disease caused by defective or deficient cystic fibrosis trans-membrane conductance regulator activity. The recent approval of the novel CFTR modulator triple combination Trikafta targets the majority of CF patients, but potentially excludes pregnant women as the clinical efficacy of these important drugs is limited by our lack of understanding what short- and long-term effects these drugs could have on developing babies. This project will investigate the entry of the triple combination across the placenta in an animal CF model that replicates a common CF mutation. The project will also assess the potential of maternal administration of these drugs to reduce the amount of CF damage occurring before birth. This innovative approach has significant potential in improving clinical practice worldwide.

Innovation Grant 2021

(sponsored by CFSA - managed by ACFRT)

RESEARCHER: Dr Andrew Tai

PROJECT: Sphingosine-1 Phosphate and Zinc - novel mediators of vascular dysfunction in children with cystic fibrosis

INSTITUTION: Women & Children's Hospital Adelaide, SA

BUDGET: $50,000 (1 year)

SUMMARY: We continue to collect lung and blood samples from children with cystic fibrosis (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 patient's cells.

Innovation Grant 2020

RESEARCHER: Dr Abdullah Al Tarique

PROJECT: Enhancing the innate ability of cystic fibrosis macrophages to kill and clear M. abscessus (MABS)

INSTITUTION: Child Health Research Centre, QLD

BUDGET: $80,000 (1 year)

SUMMARY: Multi-drug resistant MABS bacterial infection is an emerging threat to patients with cystic fibrosis (CF). Macrophages are the professional phagocytes (bacterial killing white blood cells) in the lungs. Bacterial killing and clearance has been previously found to be defective by CF macrophages against many respiratory bacteria. However, research related to multi-drug resistant MABS is still limited. This project aims (1) to comprehensively investigate whether and why CF macrophages fails to kill and clear MABS and (2) to evaluate the efficacy of several adjuvants that potentially could enhance MABS killing by CF macrophages. This adjuvant therapy is independent of antibiotic and the class of CFTR mutations. Such adjuvant therapy could simplify the current antibiotic treatment strategy for the patients with CF.

David Millar Giles Innovation Grant 2019

RESEARCHER: Dr Shafagh Waters

PROJECT: An Australian Alliance of personalised lab grown mini-organs to save the rarest of them all

INSTITUTION: University of New South Wales, NSW

BUDGET: $95,000 (2 years)

SUMMARY: Some individuals with rare CFTR mutations have been shown to benefit from the available modulator therapies. Sadly, most will have no opportunity to access these breakthrough treatments. Currently no clinical test exists to predict patient's response to a modulator drug. We are using new technology in the field of personalised medicine. Stem cell derived mini-organs are generated from small biopsies serving as a personal cystic fibrosis (CF) model or an AVATAR. They are tested in the lab to predict an individual CF patient's responses to therapeutic agents. Should one or more therapies prove effective in the lab, these can be recommended for use as targeted therapies for the patient.

In the last 2 years we have created Avatars from children with CF that visit the Sydney Children's Hospital and have predicted outcomes of modulator therapies. In this application we propose to extend our platform to create an Australian wide alliance for people with rare CF by extending to 11 (6 paediatric and 5 adult) CF clinics. This project will provide a novel therapeutic opportunity, ultimately enabling 'managed' off-label access to the CFTR modulator therapies for individuals with rare CFTR mutations who show response to the therapy in a prospective mini-organ test.

Innovation Grant 2019

RESEARCHER: Dr Gerard Kaiko

PROJECT: Optimising patient-derived stem cell technology in cystic fibrosis to predict CFTR modulator response

INSTITUTION: University of Newcastle, NSW

BUDGET: $80,000 (1 year)

SUMMARY: CFTR modulator therapy offers great hope to improve the quality of life of cystic fibrosis (CF) patients with an array of different mutations. However, the high-cost, high variability in response, and restrictions of therapies to clinical trial targeted mutations has created a powerful need for a lab test to better predict which CFTR mutations and which individual patients will respond to a given therapy. This type of precision-medicine is already critical but will only become more vital in the future as CFTR therapy options increase. Stem cell technology has enabled patient cells to be readily grown in the laboratory. The use of 'mini-guts' grown from tiny patient biopsies enables such a precision medicine CFTR test and will be used to determine whether this can predict a patient's response to CFTR therapy in the clinic by testing the drugs on their own cells. In the future, this personalised approach could be used to increase access to CFTR modulators for the patients that currently miss out.

Innovation Grant 2019

(sponsored by CFCC VIC - managed by ACFRT)

RESEARCHER: A/Prof (Keith) Chee Y. Ooi

PROJECT: Colerectal Cancer

INSTITUTION: School of Women's and Children's Health, Medicine, University of New South Wales, NSW

BUDGET: $50,000 (1 year)

SUMMARY: Adults with cystic fibrosis (CF) now face new complications such as colorectal cancer (CRC). The cause is unknown but gut inflammation and gut bacteria imbalances are possible causes. The risk for CRC in CF is high enough that new CRC screening guidelines recommend colonoscopy for patients >40 years and for post-transplant patients >30 years old. Performing colonoscopies in adult CF patients is complex due to comorbid diseases including poor lung function and diabetes. Non-invasive screening tests are needed, similar to faecal occult blood testing (FOBT) used for general population screening. While FOBT utility in CF remains unclear, other stool tests for gut inflammation (calprotectin and M2-PK) have shown promise in detection of CRC and polyps in the general population. They are elevated in children with CF and may be potential early markers of future CRC in adults with CF. To investigate this further, we will invite patients who meet criteria for CRC screening to provide stool samples prior to their scheduled colonoscopies. Markers of gut inflammation including calprotectin and M2-PK, FOBT and imbalances in gut bacteria will be assessed and compared with the incidence of CRC and number of adenomas. Predictors for colorectal cancer and precancerous lesions will also be assessed.

Conquer CF (GI) Innovation Grant 2021

(sponsored by Conquer Cystic Fibrosis - managed by ACFRT)

RESEARCHER: Dr Josie van Dorst

PROJECT: Short chain fatty acids and gastrointestinal complications in cystic fibrosis

INSTITUTION: University of New South Wales, NSW

BUDGET: $50,000 (1 year)

SUMMARY: Cystic fibrosis (CF) is a life-shortening genetic condition, which causes thick mucus, chronic infection, and inflammation not only in the lungs but also the gut. People with CF have an imbalance between beneficial and harmful gut bacteria, which is linked to poor growth, gut symptoms, chronic gut inflammation and increased cancer risk. Short chain fatty acids (SCFA) are produced by beneficial bacteria in the gut and have many important roles locally in the gut and for wider health, including combating inflammation and cancer activity, and regulating the communication with the lungs (gut-lung axis) and the immune system. Despite this, there is limited knowledge regarding SCFA in individuals with CF. This project aims to measure SCFA levels in individuals with CF and to explore the relationship between SCFA, diet and the microbiome. SCFA may provide a useful therapeutic target to improve gastrointestinal inflammation and complications for individuals with CF.

Conquer CF (GI) Innovation Grant 2020

(sponsored by Conquer Cystic Fibrosis - managed by the ACFRT)

RESEARCHER: A/Prof (Keith) Chee Y. Ooi

PROJECT: Towards understanding gut host-microbe interactions and personalised probiotic therapy in cystic fibrosis using organoid-derived 2D intestinal models

INSTITUTION: University of New South Wales, NSW

BUDGET: $50,000 (1 year)

SUMMARY: Cystic fibrosis (CF) is a life-shortening genetic condition, which causes thick mucus, chronic infection, and inflammation in the lungs and gastrointestinal (GI) tract. People with CF have an imbalance in their GI bacterial population (microbiome) known as “dysbiosis”, and chronic GI inflammation, both of which are linked to poor growth, GI symptoms and increased cancer risk. A survey of CF patients and clinicians globally has ranked GI symptoms 2nd in priority, ahead of respiratory issues, yet no GI-specific therapies currently exist.

Stem cells obtained from gut biopsies from people with CF can be used to grow 2-dimensional and 3-dimensional organoid culture systems which replicate real life (“mini guts”). We will investigate the host-microbe interactions involved in GI dysbiosis, inflammation and malignancy, using CF patient-specific intestinal organoids. We believe this study will provide a crucial step towards personalised therapies based on host-microbe interactions with the aim of reducing GI complications in CF. Successful personalised therapies would revolutionise CF treatments and other conditions subject to host-microbe interactions.

Conquer CF (Respiratory) Innovation Grant 2021

(sponsored by Conquer Cystic Fibrosis - managed by the ACFRT)

RESEARCHER: Dr Samuel Montgomery

PROJECT: Establishing a pipeline for repurposing anti-inflammatory drugs to tackle viral-induced exacerbations in children with cystic fibrosis

INSTITUTION: Curtin University/Telethon Kids Institute, WA

BUDGET: $50,000 (1 year)

SUMMARY: This study aims to improve the lung health of young children with cystic fibrosis (CF) following a viral infection. Rhinovirus infection (the "cold" virus) is common in young children, often resulting in presentation to hospital emergency departments. This is worsened in children with chronic airway disease such as the inheritable disease cystic fibrosis (CF) where infection with rhinovirus results in deteriorating lung health, sadly often permanently, leading to chronic bacterial infection and increased hospitalisation. Rhinovirus infects the cells lining the airway (the "epithelium") provoking a large inflammatory response, which can lead to lung damage. We have previously identified a specific type of inflammation which is associated with decreasing lung health in children without bacterial infection. We propose to block this inflammation using a drug, interleukin-1 receptor antagonist, as a new anti-inflammatory treatment for the cold virus in children with CF. We will use a model of the airway in the laboratory to test the safety and effectiveness of this drug to reduce this inflammation. This study aims to provide evidence to progress to a clinical trial, as this drug is already approved for use in other diseases and could be rapidly translated into clinical use for children with CF.

Conquer CF (Respiratory) Innovation Grant 2020

(sponsored by Conquer Cystic Fibrosis - managed by the ACFRT)

RESEARCHER: Dr Ameneh Khatami

PROJECT: Designing Optimal Phage Cocktails for Kids with cystic fibrosis (DOCK-CF)

INSTITUTION: The University of Sydney, NSW

BUDGET: $50,000 (1 year)

SUMMARY: To manage chest infections, children with cystic fibrosis (CF) are exposed to broad-spectrum, toxic antibiotics several times per year. This is only moderately effective, with infections often becoming increasingly difficult to treat due to evolving antimicrobial resistance. Bacteriophages (phages) are viruses that replicate within bacteria, causing highly selective bacterial killing. They offer a safer and more precise solution than antibiotics to treat bacterial infections. We hypothesise that Pseudomonas aeruginosa and Staphylococcus aureus strains that colonise children with CF can be eradicated effectively by combinations of phages ("phage cocktails"). This would result in reduced lung damage and allow recovery of normal lung growth. In addition, reduced toxicity and microbiome effects compared to antibiotics would improve quality of life for patients and their families. This proposal aims to identify phages with 'killing' activity against the main strains of these bacteria isolated from a large cohort of children with CF. Research outcomes will feed into a translational pipeline to investigate this promising therapy in children with CF within 5 years.

Golf PhD Top-up Scholarship 2020

(sponsored by CFWA - managed by ACFRT)

RESEARCHER: Joshua Iszatt

PROJECT: Investigating an alternative therapeutic agent for the treatment of bacterial infections in kids with cystic fibrosis

INSTITUTION: Curtin University, WA

BUDGET: $37,500 (3 years)

SUMMARY: People with cystic fibrosis (CF) are typically treated with a range of antibiotics from an early age to combat bacterial infections. Over time, many of these bacteria, including Staphylococcus aureus (S. aureus), become resistant to antibiotics and persist in the airways causing permanent damage.

My project involves isolating bacteriophage, (viruses that kill specific bacteria), that can infect and kill S. aureus, in the hope of producing an effective antibacterial therapy. Bacteriophages have been shown to successfully treat life threatening infections in "last resort" circumstances. However, we still need more information to make them a more common therapy here in Western Australia.

Over the last couple of years, we have discovered numerous bacteriophages from environmental and biological sources. We are currently testing how effective they are on this bacterium and to conduct preclinical studies to prove they are safe to use in humans.

Golf PhD Top-up Scholarship 2020

(sponsored by CFWA - managed by ACFRT)

RESEARCHER: Maggie Harrigan

PROJECT: Me, myself and I: An exploratory study of self-concept in adults with Cystic Fibrosis in an evolving era of care

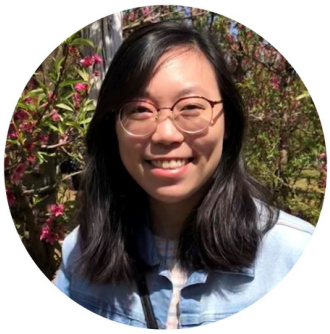
INSTITUTION: The University of Western Australia. WA

BUDGET: $37,500 (3 years)

SUMMARY: I am undertaking a PhD to explore self-concept in adults with cystic fibrosis (CF). Self-concept is commonly defined as one's self-perception, a sense of who you are as a person, and is widely associated with mental and social wellbeing beyond the CF context. There is a significant lack of self-concept research within CF despite several pertinent disease factors, including CFTR modulator drugs which have the potential to revolutionise what it means to have CF. As medical treatment advances, so too must our understanding of associated psychosocial needs. Mixed methods research will be applied to produce contemporary self-concept knowledge and psychosocial resources.

Golf Classic Scholarship 2019

(sponsored by CFWA - managed by ACFRT)



RESEARCHER: Renee Nicole Ng Yun Wen

PROJECT: Exploring the therapeutic potential of phage therapy to treat Pseudomonas aeruginosa infection in people with cystic fibrosis

INSTITUTION: University of Western Australia, WA

BUDGET: $37,500 (3 years)

SUMMARY: Multidrug resistance is a current global health crisis and alternative treatments are required. This study aims to explore a new treatment option for patients with bacterial lung infections using bacteriophages ('phages'), a virus that targets and "eats" bacteria, eradicating them.

This project will be the first to compare how effective isolated phage are against clinical-derived isolates of Pseudomonas from people with CF, and to conduct some preclinical safety studies to help justify clinical trials downstream. It also aims to identify which phage therapy can kill the bacteria as well as reduce the inflammation caused by infection. Overall, this work will test the feasibility of phage therapy in this setting and in so doing develop a screening tool for high throughput phage assessment.

Golf Classic Scholarship 2019

(sponsored by CFWA - managed by ACFRT)

RESEARCHER: Naomi Chapman

PROJECT: The MetaNeb® System in adults with cystic fibrosis: investigating its effects during periods of clinical stability and disease exacerbation

INSTITUTION: School of Allied Health, Curtin University and Physiotherapy Department, Sir Charles Gairdner Hospital, WA

BUDGET: $37,500 (3 years)

SUMMARY: Effective airway clearance techniques (ACT) are integral to the clinical management of patients with CF and are believed to help reduce exacerbations and slow disease progression. Although there are a range of ACT used to clear secretions, there is no evidence to support one over others. Therefore, the choice of technique is based largely on patient/therapist preference. A new device to facilitate airway clearance (The MetaNeb® System) offers promise, but remains largely untested in the CF population. This body of work will look at the effects of the MetaNeb®, on lung function, secretion clearance and symptoms in adults with CF who are well and those hospitalised with an exacerbation. It will also explore the responsiveness of a range of novel outcome measures to detect change following ACT.

Golf Top-up Scholarship 2021

(sponsored by CFWA - managed by ACFRT)

RESEARCHER: Andrew Vaitekenas

PROJECT: Studying how pseudomonas aeruginosa becomes resistant to phage therapy to identify how to prevent it occuring

INSTITUTION: Curtin University and Telethon Kids Institute, WA

BUDGET: $30,500 (3 years)

SUMMARY: Pseudomonas aeruginosa causes harmful lung infections in people with cystic fibrosis (CF) and becomes resistant to existing antibiotic treatments. There is a lack of antibiotics being developed and alternative treatments are needed. A therapy using viruses that specifically kill bacteria (called phages) is effective, but P.aeruginosa can become resistant to this too. My project aims to understand how P.aeruginosa becomes resistant to phages and how this affects the bacteria in other ways. I will use this knowledge to develop and test strategies that increase the effectiveness of phage therapy and prevent resistance occurring. These strategies can aid our group in making phage therapy a regularly used therapy, preventing further resistance and treating those with infections that are currently untreatable.

Golf Classic Grant 2021

(sponsored by CFWA - managed by ACFRT)

RESEARCHER: Luke Garratt

PROJECT: Neutrophils in cystic fibrosis

INSTITUTION: University of Western Australia/Telethon Kids Institute, WA

BUDGET: $28,000 (1 year)

SUMMARY: In cystic fibrosis (CF), neutrophils accumulate in areas of the lung as mucus builds up and germs infect the airways. My research has found that in CF airway inflammation, neutrophils choose to actively release their harmful products rather than trying to eat and kill the germs causing infection. In a laboratory model of CF airway inflammation, we have found that only certain germs induce this behaviour. We are now studying how the gene expression of neutrophils determines their function, with the aim to understand whether we can prevent certain functions by inducing or repressing genes within the neutrophil. This CFWA funded project is exploring the ability of new nanoparticle technologies to modify gene expression in neutrophils, as neutrophils are short-lived cells that do not respond to traditional methods. The hope is that this technology could inform a new class of anti-inflammatories for controlling neutrophil behaviour in CF airways.

CFRL Post Graduate Studentship Grant 2021

(sponsored by CFRL - managed by ACFRT)

RESEARCHER: Rebecca Keating

PROJECT: Investigation of factors influencing glucose control in cystic fibrosis

INSTITUTION: University of Queensland. QLD

BUDGET: $15,000 (3 years)

SUMMARY: People with cystic fibrosis (CF) are surviving well into their 4th decade of life with more than 50% aged over 25. Improvements in life expectancy however have come at a cost with many CF individuals developing other comorbid conditions.

Glucose abnormalities are considered to be the most common, non-pulmonary, co-morbidity in adults with CF. Based on current trends 40-50% of CF individuals will need to manage either impaired glucose tolerance (CFIGT) or diabetes (CFRD) by the time they are 30 years of age. Onset is gradual and is thought to be related to inadequate secretion of insulin due to chronic infection and subsequent destruction of insulin producing cells. This is further impacted by fluctuating levels of insulin sensitivity during periods acute infection. Gold standard management of these glucose abnormalities is insulin, a therapy fraught with compliance issues.

The aim of this project is to investigate glucose abnormalities in the adult CF population and its diagnosis and management. It will examine if alternative therapies utilised in early CFIGT could prevent or prolong progression to diabetes.

ACFRT Top-up Scholarship 2021

RESEARCHER: Emma Ledger

PROJECT: A paradoxical role for antibodies to Pseudomonas aeruginosa in cystic fibrosis pulmonary infections

INSTITUTION: University of Queensland Diamantina Institute, QLD

BUDGET: $15,000 (over 3 years)

SUMMARY: Pseudomonas aeruginosa is a highly multi-drug resistant bacteria which causes chronic lung infections in individuals with cystic fibrosis (CF). This bacterium is extremely difficult to eradicate and is a major cause of morbidity and mortality in CF. Our research investigates specific antibodies produced by patients that enhance, rather than clear these bacterial infections resulting in further disease burden.

This project aims to better understand the prevalence, impact, and mechanisms of these 'bad antibodies' in individuals with CF by characterising them for the first time within patient sputum and towards the patient's infecting strain. Additionally, we aim to investigate the impact the latest CF transmembrane conductance regulator (CFTR) modulator therapies have on Pseudomonas aeruginosa infection and these dysregulated antibody responses. This research is critical for the development of targeted therapies to neutralise these 'bad antibodies', clear persistent multi-drug resistant lung infections and improve patient outcomes further in this post-modulator era.

ACFRT Top-up Scholarship 2019

RESEARCHER: Dr Miro Astore

PROJECT: Computer modelling of the root cause of cystic fibrosis

INSTITUTION: University of Sydney, NSW

BUDGET: $15,000 (3 years)

SUMMARY: Modulator drugs such as trikafta act directly on the defective Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) protein to restore its function. But there are 2000 variations in the CFTR gene, changing the function of the protein differently. So not all patients respond to these treatments in the same way. To better patient outcomes we need to take a personalised approach.

By using supercomputers to run simulations known as molecular dynamics, I have simulated the motion of both healthy and mutant CFTR. This lets me understand what is going wrong with CFTR at the atomic level. This research was in collaboration with the Molecular and Integrative Cystic Fibrosis (miCF) Research Centre. These researchers take samples from patients with rare forms of CF to measure the response of the patient's tissues to specific drug regimens. Together we are working to understand what sort of defects can be treated by specific CFTR modulators. We have so far published work to demonstrate our approach to understand two rare mutations. This approach could drastically improve patient outcomes.

ACFRT Top-up Scholarship 2019

RESEARCHER: Dr Thomas Saunders

PROJECT: Adverse Early Risk Factors for Adult Cardiovascular Disease in Paediatric Cystic Fibrosis (CV-CF)

INSTITUTION: Royal Children's Hospital, VIC

BUDGET: $15,000 (3 years)

SUMMARY: Life with cystic fibrosis (CF) has dramatically changed over the past decades, thanks to early interventions throughout childhood. Unlike previous generations, current children with CF are living well beyond their twenties, and expectedly into their fifth or sixth decades. However, the new medical challenges they will face as older adults are largely unknown. In particular, the impact of cardiovascular disease (CVD- heart attacks and strokes), is unknown. Adult lung diseases like CF have much higher risks of CVD, and there are increasing case reports of people with CF developing CVD. Atherosclerosis (hardening of the arteries), the process that leads to CVD, is thought to be largely preventable, especially when intervention starts in childhood. Risk factors for atherosclerosis, such as inflammation, recurrent infection, and high fat diets are all found in people with CF, but likely play different roles than in people without CF. As life expectancy for people with CF improves, and there are more and more instances of CVD in CF adults, novel studies aiming to detect it will be crucial.

This study investigates if children with CF have early changes to their blood vessels, biomarkers and immune system that may lead to CVD in adulthood. We will undertake tests looking at the large arteries, smaller blood vessels, and measure specific biomarkers and immune cells in the blood. This study is expected to show that CF children do have changes that suggest they may be at higher risk of atherosclerosis and CVD in the future. This will indicate if our current nutritional goals are sufficient, and guide changes to minimise the impact of CVD in CF adults. As people with CF live longer, it is critical that their increased survival also has improved quality of life with any treatment side-effects minimised. As such, this study will have a direct impact on how we treat people with CF in the future.

Ann Maree Bosch Fellowship 2021

RESEARCHER: Stefanie Bader

PROJECT: Progressing novel treatment options to improve management of infections in people with cystic fibrosis (CF)

INSTITUTION: The Walter and Eliza Hall Institute of Medical Research (WEHI), VIC

BUDGET: $10,000 (1 year)

SUMMARY: This project aims to repurpose a range of clinical stage drugs as treatment options for chronic infections in people with cystic fibrosis (CF).

Bacterial infection is the most common cause of death in CF patients. The immune cells responsible for combating bacteria are often defective in people suffering from CF and can damage the lungs while trying to fight infections. This reaction worsens symptoms and fails to kill the pathogen, leading to chronic disease that is refractory to antibiotic therapy. We propose to use a new class of drugs that can tackle this problem in two ways: by killing infected host cells, reducing the number of bacteria, and by removing defective immune cells. Importantly, while bacteria rapidly develop resistance to antibiotics, leading to a decline in median survival, our proposed strategy promotes the death of defective host cells, as well as intracellular pathogens, and bacteria will not be able to adapt to this, completely circumventing the problem of bacterial resistance.

Ann Maree Bosch Fellowship 2020

RESEARCHER: Dr Katherine Frayman

PROJECT: The Gut-Lung Axis in early CF (GLAX-CF)

INSTITUTION: Murdoch Children's Research Institute, VIC

BUDGET: $9,500 (1 year)

SUMMARY: My research explores the development of the gastrointestinal and lower airway microbiota during the first two years of life in newly diagnosed infants with cystic fibrosis (CF), and their relationship to each other, to lower airway inflammation and to clinical manifestations of disease. It will examine the impact of continuous antibiotic prophylaxis on the microbial milieu in both niches, and its relationship to clinically relevant outcomes. Ultimately, my research aims to highlight opportunities for intervention, for example, modification of the gastrointestinal microbiota with pro-, pre- or antibiotics, in order to influence respiratory phenotype. The Ann Maree Bosch Career Fellowship will enable me to travel to the United States to establish key collaborations with the University of Washington and Seattle Children's Hospital, Washington and attend the North American Cystic Fibrosis Conference.

Ann Maree Bosch Fellowship 2019

RESEARCHER: Dr Shivanthan Shanthikumar

PROJECT: Targeting a forgotten cell to prevent cystic fibrosis lung disease

INSTITUTION: Murdoch Children's Research Institute, VIC

BUDGET: $9,000 (1 year)

SUMMARY: Inflammation is a key driver of lung disease in cystic fibrosis (CF) and yet we have no effective anti-inflammatory therapies that are used in clinical practice. Anti-inflammatory therapies would be beneficial to all people with CF as they could be given in addition to CFTR modulators (such as Trikafta) or to the 10% of people with CF for whom no modulator has been identified. One of the major barriers to effective inflammatory therapy is the relatively poor understanding of the exact mechanisms of inflammation in the lung in CF and in particular the role of the most abundant immune cell in the lung: the alveolar macrophage.

The Ann Maree Bosch Fellowship will fund research that uses a new laboratory technique (called single cell RNA sequencing) to study bronchoalveolar lavage samples collected from children with CF in the first 6 years of life. This new analysis method will offer unparalleled understanding on inflammation in early life CF lung disease, the role of alveolar macrophages, and how inflammation it is affected by modulator therapy. This will offer insights into how inflammation can be targeted by anti-inflammatory medications. Specifically, the funding will allow for collaboration with international experts in single cell RNA sequencing and inflammation in CF to ensure the work is carried out to the highest standard.

Abbie Fennessy Memorial Fellowship 2021

(sponsored by Mediplast - managed by ACFRT)

RESEARCHER: Dr Stella Li

PROJECT: The Early Childhood Project: Circle of Security-Parenting in cystic fibrosis

INSTITUTION: The Children's Hospital, Westmead, NSW

BUDGET: $5,000 (1 year)

SUMMARY: This project focuses on supporting parents of children with cystic fibrosis (CF) during the early childhood period (under 5). This is a period that often coincides with CF diagnosis and can be filled with stress, worry, and guilt. We are offering the Circle of Security parenting program which aims to help parents reflect on and meet their child's medical and emotional needs and ultimately strengthening the parent-child relationship.

Abbie Fennessy Memorial Fellowship 2020

(sponsored by Technipro-PulmoMed - managed by ACFRT)

RESEARCHERS: Jen Hauser & Jen Bishop

PROJECT: Development of educational videos of inhalation therapy and airway clearance techniques

INSTITUTIONS: Royal Hobart Hospital, TAS and Westmead Hospital, NSW

BUDGET: $,5000 (1 year)

SUMMARY: CFPhysio.com is an educational website currently providing education on evidence-based physiotherapy management in cystic fibrosis (CF) for both health professionals and individuals/carers impacted by CF. The Abbie Fennessey Memorial Fellowship has allowed the team at CFPhysio.com to further develop instructional videos on a variety of inhalation therapy and airway clearance techniques. These videos are now available on the website www.cfphysio.com. Home based and paediatric-focused videos were also on the project plan, these are currently in progress, to be uploaded to the website before the end of 2021.

Abbie Fennessy Memorial Fellowship 2019

(sponsored by Technipro-PulmoMed - managed by ACFRT)

RESEARCHER: Olivia McGuiness

PROJECT: Infection control and prevention with non-invasive ventilation use

INSTITUTION: Royal Prince Alfred Hospital, NSW

BUDGET: $4,800 (1 year)

SUMMARY: Interventions aimed at preventing infections and colonisation of new microbes in people with cystic fibrosis (CF) is essential to prevent morbidity and mortality. Non-invasive ventilation (NIV) is used in people with respiratory failure due to CF, however little is known about the capacity of these devices to act as reservoirs for pathogens. It is usual practice that NIV devices used by people in hospital or to acclimatise at home come from a pool of devices, hence there is a theoretical risk of cross contamination, despite current recommended decontamination processes. This project aims to explore the microbiology of air and surface samples taken from NIV devices used by people with CF and the efficacy of current NIV disinfection processes between patient use.

Golf Committee Contribution to Cystic Fibrosis 2021

(sponsored by CFWA - managed by ACFRT)

RESEARCHERS: Julie Depiazzi & Crystal Bourke

PROJECT: Does a diagnosis of Tracheobronchomalacia affect health outcomes in children with cystic fibrosis?

INSTITUTIONS: Perth Children's Hospital, WA

BUDGET: $5,000 (1 year)

SUMMARY: Around 41% of young children with cystic fibrosis (CF) in Western Australia have been reported to have tracheobronchomalacia (TBM) seen during bronchoscopy – a condition where parts of the windpipe or airways are floppier than would be considered normal. In the short-term this TBM finding can lead to a change of the child's daily physiotherapy and airway clearance program, however despite its prevalence, little is known about the long-term impact of TBM.

The aim of this study is to compare health outcomes of children with CF, both with and without TBM, up to the age of 4 years, and will include imaging, inflammation markers and infection comparisons. We hope our findings will provide clinicians and families with more insight into, if any, long-term impacts of this condition.

Special CF Research Seeding Grant 2021

(sponsored by CFACT - managed by ACFRT)

RESEARCHER: Shiyi Xi

PROJECT: Development of TFF3 antagonists as novel mucolytics for cystic fibrosis patients

INSTITUTION: Walter & Eliza Hall Institute of Medical Research, VIC

BUDGET: $5,000 (1 year)

SUMMARY: Mucus-based airway obstructions and the complications they cause are a significant source of morbidity and mortality in cystic fibrosis (CF) patients. The current leading mucolytic drug Pulmozyme® only works on 70% of patients, and many people would greatly benefit from more effective alternatives. This project will focus on a promising new target for novel mucolytic drugs - a mucus-thickening protein called trefoil factor-3 (TFF3). My lab has generated and identified 15 candidate antibodies that antagonize TFF3 activity and will be evaluated on patient sputum samples. We aim to benchmark the activity of these potential mucolytics against Pulmozyme® and to assess if they have additive or synergistic activities with the current drugs.

FBM Lung Health Grant 2021

(sponsored by For Benefit Medicines - managed by ACFRT)

RESEARCHER: Anna Middleton

PROJECT: Telehealth to promote mucoliliary clearance in adolescents with cystic fibrosis

INSTITUTION: Children's Hospital Westmead, NSW

BUDGET: $5,000 (1 year)

SUMMARY: Daily airway clearance techniques (ACTs) are prescribed from diagnosis in the management of cystic fibrosis (CF). ACTs promote secretion movement and removal from the airway to minimise infection, inflammation and permanent damage. ACTs also improve symptom control, reduce exacerbations, prevent progression of lung damage and lung function decline, and improve quality of life. With increasing age, airway clearance routines become more complex with breathing techniques, exercise and inhaled medication, and adherence to prescribed airway clearance routines is often compromised resulting in increased exacerbation frequency and requirement for hospitalisation. Poor adherence to treatment regimens has the potential to adversely impact long-term health status, survival and quality of life.

Adolescence is a particularly difficult time to keep up adherence to prescribed breathing techniques, medications and exercise. These aspects of CF care are especially important for optimising mucociliary clearance, however are often the most poorly adhered to. Adolescence is also a time when conflict around treatments can develop between children with CF and their parents. Despite this, research suggests that adolescents actually have better adherence to their prescribed therapies when they are supervised. Due to school and work commitments, as well as desire to reduce visits the hospital, some aspects of CF care can be provided over telehealth. This removes the need for you to travel.

COSMED Metabolic Monitoring Grant 2021

(sponsored by COSMED Asia Pacific Pty Ltd - managed by ACFRT)

RESEARCHERS: Andrea Kench & Hiran Selvadurai

PROJECT: The road map to personalised diet management in children with cystic fibrosis

INSTITUTION: The Children's Hospital Westmead, NSW

BUDGET: $5,000 (1 year)

SUMMARY: We know that people with cystic fibrosis (CF) need more energy from food to grow and fight infections than healthy people. However, there is very little information available on specific macronutrient (carbohydrate, protein and fat) requirements for children with CF. In particular, it is not known how macronutrients contribute towards fueling the body during periods of rest and during exercise. This information is needed so that we can implement personalised nutritional goals. This is particularly important in the context of new CF treatments (modulator medications) which have led to a significant improvement in lung function, weight and quality of life. Further, significant infections such as non-tuberculosis mycobacteria (NTM) is a growing problem in patients with CF but it is not clear how these infections impact on macronutrient use and energy expenditure in children with CF. Exciting new technologies now enable us to quantify nutritional macronutrient requirements for children. The purpose of this research study is to ascertain if we can determine macronutrient requirements for children with CF.

Cystic Fibrosis Australia (CFA) would like to thank all those who have donated to the Australian Cystic Fibrosis Research Trust (ACFRT) research projects over the past 32 years.

CFA's ability to raise funds for the ACFRT is dependent on the generosity of the business community and the general public. Tax-deductible donations can be made HERE.

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