UQ STRATEGIC FUNDING

PROGRESS REPORT

Recipients of Strategic Funding are required to provide a short report to the VC and/or DVC(R) on an annual basis unless they are excluded as per the advice below.

Notes:

- Payment of any subsequent year's allocation will be subject to VC / DVC(R) approval of the progress report.
- Annual Progress and Final Progress Reports are required for strategic funding allocations of $100,000 per annum or higher (i.e. after combining both VC & DVC(R) contributions).
- A Final Progress Report is required where total strategic funding allocations of $50,000 or higher are awarded across the duration of the commitment (i.e. after combining both VC & DVC(R) contributions).
- Reports are not required where the funding commitment forms part of a UQ Internal Scheme listed at http://www.uq.edu.au/research/research-management/grants-uq-internal.

1. ADMINISTRATIVE SUMMARY

Is this a Progress or a Final Report?	Progress
Report Year:	2020
UniFi Project Number:	024246
Commitment IDs:	VCSF20001A DVCR19300A
Project Title:	Queensland Cystic Fibrosis Research Program (QCFRP)
Lead CI / Funding Recipient Name:	Prof Peter Sly
Administering Unit:	CHRC
Faculty/Institute/Central Area:	Medicine
Years of Funding (YYYY - YYYY):	2020 - 2024
Are you intending to submit a variation request? (Yes/No)	No

Note: Dot points are acceptable for the below items

2. SUMMARY OF OBJECTIVES

100 word summary of strategic objectives (as outlined in the original proposal)

UQ's Child Health Research Centre (CHRC) hosts two internationally recognised research leaders in Cystic Fibrosis (CF), Professors Peter Sly and Claire Wainwright. They work in close collaboration with Professor Scott Bell. Their work has resulted in > 300 publications in this field and improved clinical treatment for children with CF around the world.

In recognition of their work, they were recently invited by the American Cystic Fibrosis Foundation (CFF) to apply for special 'out of round' funding. This was successful with more than $7.5 million USD awarded, across three awards, one fronted by each of them.

This funding request is to leverage funds ($2.5 million AUD) committed by the Qld Children's Hospital Foundation (CHF) in support of this program. This will enable expansion of the project and ensure timely completion. Most importantly, it will enable the team to deliver better outcomes for patients with CF.

3. STATEMENT ON PROGRESS/OUTCOMES

How have you progressed towards your stated objectives to date?

All three components of the program have commenced and are progressing satisfactorily.

1. Early Life Origins of CF Lung Disease (ELO):

(1) ***The scope of work accomplished during the year***:

Clinical research database: the project required a new clinical research database to be constructed in RedCap. This includes detailed demographic and environmental data; CF complications and treatment, symptomatology and acute pulmonary exacerbations. This task has been completed and the database is live and in use.

(2) ***The progress of training or work in clinic***:

Recruitment and collection of data has been severely impacted by the Covid-19 pandemic. CF clinics were closed and many assessments done remotely by telehealth. Despite this we have managed to recruit 154 children from the QCH CF clinic.

Training: Our lung function post-doctoral scientist has received training and certification in the Multiple Breath Washout / Lung Clearance Index and Oscillometry / Intra-breath Oscillometry techniques.

(3) ***Research progress***:

To overcome the slow data collection, we have taken advantage of the longitudinal data available from the CF FAB study (ACTRN12613000778785), a follow-up of the Australasian Cystic Fibrosis Bronchoalveolar Lavage (ACFBAL) study. This was a randomised clinical trial conducted in Australia and New Zealand between 1999 and 2009 to determine the safety and utility of bronchoalveolar lavage (BAL)-directed treatment of an acute exacerbation during the first 5-years of life, thereby reducing *P. aeruginosa* infection and preventing bronchiectasis in young children with CF (ACTRN0126050006656635). These data have been used to develop the statistical methods to be used with the Early Life Origins of CF Lung Disease (ELO) data to examine trajectories in lung function and the factors associated with loss of lung function. Children from the QCH clinic participated in ACFBAL and CF FAB and these have been recruited into ELO.

Results: Lung function data were available for 110 children who participated in ACFBAL and CF-FAB studies. Lung function was available for 99 children on the first visit (CF-FAB1) and for 97 on the second visit (CF-FAB2), with 86 providing lung function on both visits. Participants were in early childhood at the end of ACFBAL [mean 5.1-years (SD 0.2)], in late childhood to early adolescence at the beginning of CF-FAB [mean 12.8-years (SD 1.5)] and in mid to late adolescence at the end of CF-FAB [mean 14.6-years (SD 1.6)]. Mean lung function shows a progressive fall from the end of ACFBAL to the end of CF-FAB for FEV_1/FVC%, FEV_1 and FEF_{25-75} (all $p<0.001$), but not for FVC ($p=0.83$)

Factors present at 5-years of age predicting spirometry in adolescence

ACFBAL spirometry and presence of NE activity and *Aspergillus* in BAL were the variables with the strongest associations. The best multivariable model to predict FEV_1/FVC% (Table 3) contained two ACFBAL variables: spirometry 5-years (FEF_{25-75} $p<0.001$) and *Aspergillus* in BAL ($p=0.01$) (Table 4). Using this model to predict the other spirometry outcomes in adolescence, expressed as Z-scores, yielded similar results, although the levels of statistical significance varied.

2. FORMaT Trial:

- Focus on establishing the conduct and regulatory processes of the trial across the international sites including development of the FORMaT Trial Master File documentation.
- EudraCT number granted to the Brisbane FORMaT Trial Management Team (TMT) will be used in submission of regulatory applications for the trial in all European sites.
- Drafted the first version of the Clinical Trials Application (CTA) for Denmark - currently awaiting the local Danish sponsor/legal representative and pharmacy team. The CTA will provide further guidance for the process of obtaining the required information for each FORMaT investigational medicinal product (IMP) from the recommended local site pharmacy references to complete the required fields within the CTA.
- Drafted the FORMaT Pharmacovigilance and Safety Plan for European sites which includes the gold standard definitions of all safety events. Specific reporting templates are included in the plan where available and the relevant stakeholder, committees and other governing body's contact and report submission details have been included to ensure notification and reporting processes are documented for all parties.
- Established the FORMaT Drug Safety Monitoring Board (DSMB) charter which acknowledges the inclusion of two additional DSMB members. The Brisbane TMT are collaborating with the FORMaT Trial Database Management Team at the Murdoch Children's Research Institute (MCRI) to develop the FORMaT Safety Database (SD). The FORMaT Safety Database will import all adverse events possibly- to definitely- related to the FORMaT IMPs which are reported during the trial in real time. The FORMaT Safety Database will allow the FORMaT Pharmacovigilance Team to categorise the adverse events (AEs) based on the Common Terminology and Categorisation of Adverse Events (CTCAE). The FORMaT Safety Database will also generate deidentified serious adverse event (SAE) reports for all events that require expedited and batched reporting to FORMaT Site Principle Investigators (PIs), relevant governing bodies in accordance with the reporting procedures outlined in the FORMaT Pharmacovigilance and Safety Plan.
- The FORMaT Trial Monitoring Plan has been drafted, a risk assessment has undertaken and identified risks have been addressed where possible. The plan will be used provide a clear procedure to local European FORMaT Trial Project Managers undertaking trial monitoring with the oversight and extensive support of the Brisbane FORMaT Trial Management Team.
- Developed a database in REDCap, including complex statistical modelling and design of randomization programming.
- Trial website is being drafted and will have two portal functions. One providing lay information to potential participants as well as participants who are enrolled in the study, the other having an Investigator-only portal
- Opened two Australian sites both located in Brisbane, Queensland - The Prince Charles Hospital (adults) and Queensland Children's Hospital (pediatrics) - and recruited one participant to the Interventional Program (although these sites are not funded by CFF).
- The FORMaT Trial had anticipated that more Australian sites would be open at this time however, the current COVID-19 pandemic has impacted on these plans.

3. NTM infection in cystic fibrosis: acquisition and transmission

To date the NTM program has concentrated in obtaining the necessary permissions and agreements involving: UQ, QUT, Metro North Hospital and Health Service (TPCH), and The South Australian Health and Medical Research Institute. Covid-19 has caused significant delays in establishing the program. In Q2/3 2020 we have made significant progress with studies 1 & 2 and have undertaken preliminary work to allow study 3 to commence in 2021.

- Study 1: We have obtained 45 historical NTM samples stored at the Queensland Mycobacterial Reference Laboratory and full genome sequencing is underway.
- Study 2: Agreements have been reached to obtained water samples for NTM culture, which will commence in Q1 2021.
- Study 3: To commence in 2021.
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4. EXPECTATIONS FOR COMING YEAR (not applicable for Final Reports)

How do you expect to use your funding allocation for the coming year?

The funding allocation for 2021 will follow the initial proposal. This covers mainly gaps in staff funding and allows additional positions not covered by CFF or CHF funds.

CERTIFICATIONS

Note: Approvals by email are acceptable.

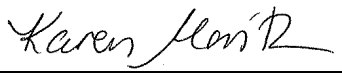
Annual Report:

Lead CI or Funding Recipient:

Name	Signature	Date
Professor Peter Sly		26/11/2020

Head of School/Centre/Institute:

I have read and endorse the annual report.

Name	Signature	Date
Professor Karen Moritz		09/12/2020

SUBMISSION OF THE REPORT

Please email the completed form to strategicfunding@uq.edu.au

Submission requirements:

- Send a separate email for each annual report submitted
- Attach a single PDF document containing all approvals
- Use descriptive subject lines to help categorise emails
  e.g. {Project number} Annual Report