

## Research Grants

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### 2017 RESEARCH GRANTS

The Margaret Pratt Foundation has donated a final amount of \$180,000 to The Alfred's Lung Transplant Service in 2017. You can read more about the future of The Foundation in our latest Newsletter.

The Margaret Pratt Foundation has also been instrumental in coordinating an additional \$60,000 per annum over the next 4 years towards a matched funding project - Defeating Lung Transplant Rejection: antibodies and strategies to control them. Further information is available via the Lungitude Foundation from 1 July 2017.

#### GRANT NO.48

\$60,000 towards the salary of lung transplant research nurse Yvonne Cristiano over the next two years whose projects including focusing on reducing late Cytomegalovirus (CMV) reactivation in lung transplant patients, and a monitoring study using QuantiFERON to measure 'net' immunosuppression post lung transplantation. In addition, a CLAD-ASSIST study - Phase 2 randomised, placebo controlled trial of bone-marrow derived mesenchymal stromal cell (MSC) infusion as treatment for new on-set chronic lung allograft dysfunction (CLAD).

#### GRANT NO.47

\$60,000 towards the salary of research assistant Tracy Phan over the next two years whose project identifies non-invasive biomarkers of acute and chronic lung allograft dysfunction following lung transplantation.

#### GRANT NO.46

\$60,000 towards the salary of research assistant Marcelle Stewart over the next two years whose project looks to define antibody mediated rejection (AMR) in allograft dysfunction following lung transplantation, and research eplet matching.

#### 2016 RESEARCH GRANTS

The Margaret Pratt Foundation donated \$90,000 to The Alfred's Lung Transplant Service in 2016.

#### GRANT NO.45

\$30,000 towards the salary of lung transplant research nurse Yvonne Cristiano whose projects including focusing on reducing late Cytomegalovirus (CMV) reactivation in lung transplant

patients, and a monitoring study using QuantiFERON to measure 'net' immunosuppression post lung transplantation. In addition, a CLAD-ASSIST study - Phase 2 randomised, placebo controlled trial of bone-marrow derived mesenchymal stromal cell (MSC) infusion as treatment for new on-set chronic lung allograft dysfunction (CLAD).

#### GRANT NO.44

\$30,000 towards the salary of research assistant Tracy Phan whose project identifies non-invasive biomarkers of acute and chronic lung allograft dysfunction following lung transplantation.

#### GRANT NO.43

\$30,000 towards the salary of research assistant Marcelle Stewart whose project looks to define antibody mediated rejection (AMR) in allograft dysfunction following lung transplantation, and research eplet matching.

#### 2015 RESEARCH GRANTS

The Margaret Pratt Foundation donated \$90,000 to The Alfred's Lung Transplant Service in 2015.

#### GRANT NO.42

\$30,000 towards the salary of lung transplant research nurse Yvonne Cristiano whose project focuses on reducing late Cytomegalovirus (CMV) reactivation in lung transplant patients.

#### GRANT NO.41

\$30,000 towards the salary of research assistant Tracy Phan whose project identifies non-invasive biomarkers of acute and chronic lung

allograft dysfunction following lung transplantation.

#### GRANT NO.40

\$30,000 towards the salary of research assistant Monika Loskot whose project looks to define the role of donor-specific antibodies in allograft dysfunction following lung transplantation.

#### 2014 RESEARCH GRANTS

The Margaret Pratt Foundation donated \$90,000 to The Alfred's Lung Transplant Service in 2014.

#### GRANT NO.39

\$35,000 supported the work of Yvonne Cristiano whose project focused on reducing late Cytomegalovirus (CMV) reactivation in lung transplant patients.

#### GRANT NO.38

\$35,000 towards the salary of research assistant Tracy Phan whose project identified non-invasive biomarkers of acute and chronic lung allograft dysfunction following lung transplantation.

#### GRANT NO.37

\$20,000 towards the salary of grade 1 year 5 scientist Kris Nielson whose project looked at novel lung function measurement techniques in the early detection of Bronchiolitis obliterans syndrome (BOS).

#### 2013 RESEARCH GRANTS

The Margaret Pratt Foundation donated \$90,000 to The Alfred's Lung Transplant Service in 2013.

#### GRANT NO.36

\$40,000 was granted to lung transplant clinical research fellow Nicholas Chin. He was focusing on the role of antibody mediated rejection in lung transplantation.

The development of new measurement techniques for the measurement of antibody against human tissue markers (HLA) may provide key information as to why some recipients thrive and others don't. Unfortunately it is unclear as to what level of antibody causes problems and also how broad can the antibody effects can be. Data will be accessed from the Red Cross as to the antibody status of patients over the last one to two years to study the broader effects (cross-reactivity) across tissue groups. Secondly researchers are grappling with high levels of antibodies directed against the transplant (donor specific antibodies). These are high at the time of transplanted lung injury but researchers don't know if they cause the lung injury or are the effect of the lung injury.

#### GRANT NO.35

\$32,000 supported the work of Yvonne Cristiano whose primary focus was to oversee the development and start-up of a large multicentre study that aims to reduce CMV infection following lung transplantation.

#### GRANT NO.34

\$4,000 topped up the salary of PhD student Aislin Meehan who completed her PhD at the end of 2013. \$5,000 part funded her laboratory costs. Aislin continued to investigate the function of Natural Killer (NK) cells during immune responses after lung transplantation.

#### GRANT NO.33

\$4,000 topped up the salary of PhD student Louise Rowntree. \$5,000 part funded her laboratory costs. Louise continued to investigate how the combination of common viruses and cross-reactive T cells influence clinical outcomes in lung transplantation.

## 2012 RESEARCH GRANTS

In 2012, The Margaret Pratt Foundation donated \$90,000 to The Alfred's Lung Transplant Service.

### GRANT NO.32

\$30,000 was granted to Dr Nicole Mifsud as part salary to support her in an ongoing project which examined blood samples taken at the time of transplant operation in order to detect patterns of inflammation which may impact on the short term function of the lungs. It is believed that these early signals also set up the lungs immunological environment in such a way as to explain long term function and dysfunction.

### GRANT NO.31

\$32,000 to support the work of Yvonne Cristiano whose primary focus was to oversee the development and start-up of a large multicentre study that aims to reduce CMV infection following lung transplantation.

### GRANT NO.30

\$4,000 to top up the salary of PhD student Aislin Meehan. \$5,000 to part fund her laboratory costs.

### GRANT NO.29

\$4,000 to top up the salary of PhD student Louise Rowntree. \$5,000 to part fund her laboratory costs.

## 2011 RESEARCH GRANTS

In 2011, The Margaret Pratt Foundation donated \$107,500 to The Alfred's Lung Transplant Service.

#### GRANT NO.28

\$45,000 to support A/Prof Bronwyn Levvey in her role of Lung Transplant Clinical Research Co-ordinator.

#### GRANT NO.27

\$7,500 to support the work of second year PhD scholar Aislin Meehan in the area of the effects of different immune suppressing drugs on sub-types of inflammatory cells (N K cells) which are linked to the development of chronic lung rejection. Aislin was awarded a NHMCR scholarship support grant as a result of the interesting results she reported in the first year of her study.

#### GRANT NO.26

\$25,000 to support final year PhD scholar Tara Bell in her work in examining the role of reduced Clara cell function as a risk factor for chronic lung rejection.

#### GRANT NO.25

\$30,000 was granted to Dr Nicole Mifsud as part salary to support her in a new project which will examine blood samples taken at the time of transplant operation in order to detect patterns of inflammation which may impact on the short term function of the lungs. It is believed that these early signals also set up the lungs immunological environment in such a way as to explain long term function and dysfunction.

#### 2010 RESEARCH GRANTS

In 2010, the MPF donated \$114,000 to the Alfred Hospital's Lung Transplant Service.

#### GRANT NO.24

\$45,000 part funded the salary of A/Prof Bronwyn Levvey to support her in her role as Clinical Research Co-ordinator. Bronwyn presented an analysis of one of the research projects co-ordinated by her at the International Society of Heart Lung Transplant's meeting in April 2010. She continued to maintain the data bases that underpin the research of Dr Tom Kotsimbos's group as well as the applied clinical research of Dr Glen Westall.

#### GRANT NO.23

\$25,000 was granted to continue to fund the research of PhD scholar Dr Tara Bull into the role of Clara cell function in relation to the development of bronchiolitis obliterans syndrome.

#### GRANT NO.22

\$12,500 was granted to first year PhD scholar Aislin Meehan to part fund her research in the area of immune system responses.

#### GRANT NO.21

\$15,000 was granted to Dr Dominic Keating to enable him to continue to analyse data collected during his Fellowship at the Alfred.

#### GRANT NO.20

\$15,000 was donated to continue to support the work of Dr Tom Kotsimbos and Dr Nicole Mifsud in the area of gene analysis as part of the Clara cell project.

#### 2009 RESEARCH GRANTS



In 2009, the MPF donated a total of \$110,000 to the Alfred Hospital for Transplant Research.

#### GRANT NO.19

The MPF assigned \$20,000 to a Lung Transplant Research Fellow in the second half of 2009. This grant allowed Dr Dominic Keating (current Irish visiting Respiratory Fellow) to extend his current appointment to ensure completion of his work.

#### GRANT NO.18

\$20,000 was assigned by the Margaret Pratt Foundation towards the salary of a Lung Transplant Research Fellow to work on two current lung rejection projects. The first project involved working with Dr Glen Westall and is a long term follow up of a study which looks at how infections might lead to chronic rejection. The second study is a collaborative project with the Toronto Lung Transplant Program which analyses long term follow up results of single lung transplantation.

#### GRANT NO.17

\$45,000 was assigned by the Margaret Pratt Foundation towards the salary of a Lung Transplant Clinical Research Co-ordinator. This person collected, collated and analysed the clinical data required for the above project as well as for other existing chronic lung rejection projects.

#### GRANT NO.16

\$25,000 was donated by the Margaret Pratt Foundation to fund a PhD Scholarship. The recipient of this scholarship worked with Associate Prof Tom Kotsimbos to expand preliminary work on how the injured lung allograft can repair itself. This project looked specifically at why transplanted lungs may not recover normally after injury or viral infection.

#### 2008 RESEARCH GRANTS

#### GRANT NO.15

The MPF has provided substantial financial support in this work looking into the factors leading to chronic lung rejection. As a result of these studies we have been able to show (part of Dr Tanya McWilliams PhD thesis) that the levels of an important chemical signal-TGF beta are increased in the wall of airways well before there is a measurable effect on lung function. Further studies presently focusing on the role of endothelin, a stimulator of TGF beta production, may develop the scientific rationale for a novel therapeutic strategy for chronic lung rejection.

\$30,000 funding for the continuation of immunohistochemistry work.

#### GRANT NO.14

\$30,000 as part salary for Dr Nicole Mifsud who is investigating the relationship between viral infections and immune response in lung transplant recipients.

It is believed that these investigations will lead to optimal immunosuppressive and anti-viral strategies that can strike the right balance in each individual lung transplant recipient.

#### 2007 RESEARCH GRANTS

#### GRANT NO.13

\$25,000 as part funding of a research assistant to support Dr Ling Zheng and Nicole Mifsud's activities. Ling has now received a Pharmaceutical award to proceed with her research freeing the MPF to fund other researchers.

\$5,000 for a dynamap which monitors blood pressure, pulse and O2 saturation during 6 minute walk tests which are a key end point in pulmonary hypertension and pulmonary fibrosis studies.

#### GRANT NO.12

\$25,000 to Nicole Mifsud who has completed her PhD and is doing a Post Doc in the Alfred Research laboratories. She

will be assisting A. Prof Tom Kotsimbos with his project looking at the relationship between viral infections and the immune response in lung transplant recipients.

The MPF has undertaken to provide funding for Nicole in 2008 so as to secure her position over the next 2 years.

## 2006 RESEARCH GRANTS

The Margaret Pratt Foundation donated \$52,000.00 to the Alfred Hospital, Melbourne supporting the following:

### GRANT NO.11

**DR LING ZHENG:** The Foundation continued to support Dr Ling Zheng who is pivotal to the research efforts of the lung transplant research unit as Laboratory Manager.

Ling's work is progressing several fronts. She has recently been a recipient of an international endothelin science research award sponsored by Actelion Pharmaceuticals. This has allowed us to study the potential role for a mediator called endothelin in chronic allograft rejection. This will compliment the continuing in-vitro work. We have discovered that endothelin is made in quite significant amounts in co-culture systems utilising lung transplant recipient cultured airways epithelial cells as well as subsequently derived recipient mononuclear cells. We are thus looking in biopsies of patients who have bronchiolitis obliterans to see whether there is over expression of both endothelin 1 and the relevant receptors to see if there is any plausibility in the role of the endothelin system in the development of BOS. We know that endothelin 1 is an intermediary in the action of TGF f1 so that the story has significant biological plausibility.

Over the next six months Ling will continue to harvest airway epithelial cells where possible from lung transplant recipients so that we can complete the initial 8 patient study looking at co-culture of airway epithelial cells and donor mononuclear cells. As always this is proving to be very difficult. We have discovered that if there is any airway colonisation with bacterial or fungus it makes it almost impossible culture airway epithelial cells. Notwithstanding this we still believe that will complete this in the next six months. In the meantime Ling will be preparing section and staining for endothelin and endothelin receptors on tissue work we already have following people through to the development of BOS to see whether endothelin is an important mediator. If it is, with the availability now of endothelin antagonists this is another potential therapeutic approach we could explore.

### GRANT NO.10

ASSOC. PROF TOM KOTSIMBOS: A. Prof Kotsimbos's project is unraveling the interrelationships between lung transplant outcome, immune response and virus activation and their implications in chronic lung rejection.

#### GRANT NO.9

CARDIAC SURGICAL RESEARCH UNIT: A project to improve preservation of donor lungs using a variety of possible antioxidants which can be given to the donor and the recipient. These include Coenzyme Q10, the antioxidant N- acetyl cystine, the antifibrinolytic aprotinin. This project has continued through 2006 so that techniques of preserving donor lungs are much better; thus ensuring that they are delivered to the recipient in the best possible state.

#### 2004 / 2005 RESEARCH GRANTS

#### GRANT NO.8

##### Chronic Lung Rejection

\$16,000 will be granted to the Department of Respiratory Medicine at the Alfred Hospital, Melbourne.

##### Lucas Law

Lucas Law is a Bachelor of Science graduate who has completed an Honours degree. He has been working with the Alfred Hospital in the last 18 months helping to study the immunological processes that lead to chronic rejection.

Lucas' PhD plans to explore the utility of in vitro modelling firstly to assess whether responses from airways cells and immune cells in the lung transplant recipient vary from normal responses.

Secondly, he will try to develop systems that will predict the best combination of anti rejection drugs for an individual lung transplant recipient. This testing is somewhat analogous to the in vitro testing that occurs with antibiotics to determine the most active antibiotic against a micro-organism. Clearly however it is much more complicated as it involves co-culture of human cells with competent human lymphocytes to assess cell - cell interactions.

#### GRANT NO.7

## Chronic Lung Rejection

\$17,350 will be granted to the Department of Respiratory Medicine at the Alfred Hospital, Melbourne.

## Specimen Freezer

This freezer will be used to store/archive research specimens and reagents for ongoing studies. Over the years the transplant unit has collected a lot of respiratory specimens kindly provided by transplant patients and control subjects. These specimens survive well in a low temperature freezer, such that studies can be performed even years after collection. The specimens actually now provide a tremendous 'library' to study new concepts and techniques.

The current studies are aimed at exploring the pathway and mechanisms of chronic lung rejection and its potential treatment/prevention with Rapamycin.

## GRANT NO.6

## Chronic Lung Rejection

\$65,000 will be granted to the Department of Respiratory Medicine at the Alfred Hospital, Melbourne.

## Dr Ling Zheng

Dr Ling Zheng is pivotal to the research efforts of the lung transplant research unit and the Margaret Pratt Foundation will be supporting her position as Laboratory Manager. Dr Zheng's investigations into airway inflammation and airway obstruction, that can lead to lung rejection, has advanced the understanding of this most difficult and devastating problem. It is hoped that Dr Zheng's research will lead to the development of early detection methods of deteriorating lung function and the implementation of useful therapeutic interventions.

## 2003 RESEARCH GRANTS

## GRANT NO.5

## Chronic Lung Rejection

\$65,000 granted to the Department of Respiratory Medicine at the Alfred Hospital.

Dr Ling Zheng is pivotal to the research efforts of the lung transplant research unit and the Margaret Pratt Foundation will

be supporting her position as Laboratory Manager. Dr Zheng's investigations into airway inflammation and airway obstruction, that can lead to lung rejection, has advanced the understanding of this most difficult and devastating problem. It is hoped that Dr Zheng's research will lead to the development of early detection methods of deteriorating lung function and the implementation of useful therapeutic interventions.

#### GRANT NO.4

##### Donor Lung Preservation

\$10,000 given to The Cardiothoracic Surgical Unit at the Alfred Hospital.

Dr Takahiro Oto is currently a Cardiothoracic Fellow with this department.

He has been involved with the lung transplant program in Japan and will be working on donor lung preservation for transplantation. It is believed that improved knowledge in this area will enhance the recovery of patients after lung transplantation.

#### 2002 RESEARCH GRANTS

#### GRANT NO.3

##### Clinical Research Fellow

\$18,000 grant to the Lung Transplant Programme. This will enable Dr Anna Reed to take up a position as Clinical Research Fellow.

Dr Reed will support the clinical research for the Lung Transplant Programme. She will assist with enrolment and monitoring of patients in the ongoing bronchoscope studies, and liaise with the laboratory providing a link between the clinical program and the scientists on the bench. It will be a key task of Dr Reed's to pull the clinical, physiological and laboratory data together in a cohesive way enabling many important papers to be written.

#### 2001 RESEARCH GRANTS

#### GRANT NO.2

##### Lung Preservation Project

\$3,000 grant to support research into lung preservation solutions.

One of the theories about chronic lung rejection is that this process may be contributed to by the ineffective preservation of the lungs at the time of harvesting and implantation. Damage incurred at this time may affect the lining of the bronchial arteries which could predispose to damage to the airways and subsequently lead Bronchiolitis Obliterans Syndrome.

#### GRANT NO.1

#### Chronic Lung Rejection

The recipient of the 2001 Research grant is Dr Tanya McWilliams.

She is researching the immunopathology of Chronic Lung Rejection.

Tanya's project is to carry on the research already underway into airway changes in Lung Transplant Recipients. This project looks further into airway remodeling and its role in the development of chronic rejection, by looking at changes in collagen in patients who remain stable and those who develop chronic rejection.