# IMPACT REPORT

## The Numbers

**1623** lung transplants at The Alfred

**5yrs** youngest lung recipient

**74%** Alfred post five year survival

**33yrs** first Australian lung transplant

**5th** largest lung transplant program in the world

**7** average lung transplants per month

*Australian statistics available as at 2020*

## Our vision of Transplant for Life remains strong, even in the face of extraordinary recent challenges.

Since the establishment of The Lungitude Foundation, best practice governance and operational management have been key metrics. This has proved fruitful during the impacts of COVID-19, enabling us to maintain our support towards global best practice research, which is now positively impacting the whole lung (and organ) transplant cycle.

During the last 12 months, we welcomed new board and fundraising committee members, providing further knowledge and expertise in the areas of respiratory research and medicine, marketing and communications, as well as risk management.

Lungitude is proud to provide and support excellence in the areas of Research, Advocacy, Support and Education. We have launched several new initiatives and resources that have been warmly received.

It would be remiss not to mention that due to COVID-19 we were unable to host one of our major fundraising events, the much anticipated Lungitude Long Lunch. An event that provides us with the opportunity to meet in person and thank you for your continued support, as well as having plenty of fun and to fundraise. It will be back in 2021. In the meantime, we have embraced virtual events with our Lung Transplantation Research Presentation and the Melbourne Marathon.

We encourage everyone to continue safe distancing and infection control practices. Please check out our website for helpful information specific to lung transplant patients and caregivers. We thank you for your ongoing support.

**Gordon Jenkins**
**Chair, Lungitude Foundation**

**WE ARE CONTINUOUSLY STRIVING FOR EXCELLENCE FOR LUNG TRANSPLANT PATIENTS AND THEIR CAREGIVERS IN AUSTRALIA**

# Lungitude Patient & Caregiver
## RESOURCES

**As promised, we have been busy creating new educational resources for you with more to come. We are proud to announce the launch of our new video series and booklets, available within our Patient & Caregiver Resources sections of our Lungitude website.**


**Patient & Caregiver Video Series**
Our first video features four lung transplant patients sharing their journeys and mental health tips. If you are interested in participating in future videos please **contact us.**

**Patient & Caregiver 'How to Cope with Stress' Booklets**
We were keen to provide more support for patients and caregivers who may be dealing with stress.

Our new booklets are a great resource that you can read online or download for printing. We encourage you to share them widely with anyone who may benefit.

**PATIENT BOOKLET** **CAREGIVER BOOKLET**

## THE LONG-TERM EFFECTS OF COVID-19 ON LUNGS

The impact of COVID-19 on lungs is something we will continue to review, as it is uncertain whether it will result in long-term lung damage or post COVID-19 patients requiring lung transplants in the future.

The pandemic research being undertaken globally is fascinating and the race is on to find not only a vaccine, but to better understand how the virus spreads and ways to treat it.

## NEW MACHINE FUNDED

While restrictions are in place the lung transplant researchers have traded the laboratory for home working but are still able to progress with their work. We were pleased to hear that one of their machines, a QuantStudio 5 real-time PCR machine that we funded for lung transplant antibody applications and other research projects, was loaned to undertake important COVID-19 research.

# Centre for Transplant Excellence
## POST TRANSPLANT CARE & SUPPORT

**Lungitude's long-term vision for the establishment of The Centre for Transplant Excellence.**

The establishment of the Organ and Tissue Authority (OTA) and Donatelife Register in 2009 has greatly increased organ donations to enable more transplants. These two initiatives have been a remarkable success – however this success is causing unprecedented strain on the health system, which is beyond capacity.

Annual growth in the number of transplants is not matched by growth in vital health support services needed to keep post transplant patients healthy and alive to enjoy a productive life.

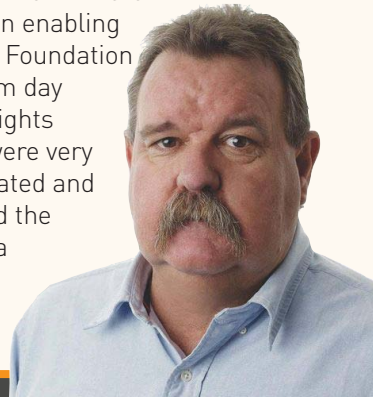
**Over the next 12 months, we will continue our advocacy for The Centre of Transplant Excellence (CTE). We believe that the Centre will rapidly leverage Victoria's status as the world leader in transplant care and establish a national and globally significant centre of knowledge, education, research and innovation.**

**THE ALFRED'S PATIENT OUTCOMES FOLLOWING LUNG TRANSPLANTATION REMAIN THE WORLD'S BEST WITH 96% AT ONE YEAR AND 74% AT FIVE YEAR SURVIVAL RATES**

# Jeff Gittus
## FELLOWSHIP

**The inaugural Jeff Gittus Fellowship, funded by the Gittus Family in memory of Jeff, was awarded to Dr Louise Fuller (Physiotherapist) and Ms Christie Emsley (Dietician) for their project – Body Composition and Muscle Morphology after Lung Transplant.**

Jeff had two lung transplants, and alongside his wife Liz were instrumental in enabling the Lungitude Foundation to flourish from day one. Jeff's insights and support were very much appreciated and respected, and the Fellowship is a wonderful tribute.



# The Alfred's Lung Transplantation Service

## KEY RESEARCH PROJECTS THAT REQUIRE FUNDING

**The Lungitude Foundation is a major benefactor of The Alfred's Lung Transplantion program which remains the premier lung transplant service in Australia, and 5th largest program internationally. Lung transplant activity continues to grow each year, along with ongoing significant improvements in patient survival.**

The Alfred's clinical research focus remains on how to better identify, prevent and/or treat several of these key factors: a) AMR 'antibody mediated rejection' and b) the link between virus(es) (particularly CMV), infection and development of chronic rejection.


## 1 DEFEATING LUNG TRANSPLANT REJECTION ANTIBODIES AND STRATEGIES TO CONTROL THEM

**The major cause of reduced long-term survival after lung transplantation is chronic graft rejection—also known as Chronic Lung Allograft Dysfunction (CLAD). Disappointingly, CLAD occurs in ~50% of all lung transplant recipients by 5 years, with long-term results far inferior to other solid-organ transplants.**

The introduction of modern medicines called immunosuppressors has improved one form of rejection called cellular rejection, however another form called 'Antibody Mediated Rejection' is now believed to be the main cause of organ loss following lung transplantation.

Our immune system is designed to recognise 'foreign' invaders such as bacteria and viruses and produce antibodies to fight them off. However, the transplanted lung is also seen as 'foreign' to the recipient's immune system, and antibodies known as donor specific antibodies (DSA) can be produced which attack the transplanted donor lung.

### PROJECT:

***Defeating Transplant Rejection: Antibodies and Strategies to Control Them,*** aims to identify and understand the production of DSAs and identify the mechanisms that lead to damage of the transplanted lung. Ultimately, researchers anticipate this will lead to new therapies to prevent rejection.

DSAs are routinely measured prior to transplant, and when present they influence whether a lung donor is compatible or not. Researchers also look for the presence of these antibodies after transplantation that may develop in response to the donor lung(s). Their aim is to select the 'best matched' donor organ to a particular recipient in order to prevent new antibodies being formed. PhD student, Mr Steven Hiho, who is based at the Australian Red Cross Blood Service has made further inroads to this project.

### RECENT PROGRESS:

In an exciting development during this project, researchers discovered that antibodies that are produced by the donor's immune cells can also contribute to the immune response in recipients. This area of research has the potential to cause a paradigm shift in the way we think about antibodies that can cause damage to a transplanted lung.

Researchers now have new data showing the donor's immune cells can persist in the blood of recipients for quite a long time following transplantation. However, they have found that the number and type of the donor's immune cells is extremely variable between different recipients. Work is underway to determine the correlation between these findings and the later development of donor-specific antibodies.

In new research, work is being done to establish the link between viral infection and antibody-mediated rejection. In particular, researchers are investigating possible links between infection with a virus called cytomegalovirus (CMV) and antibody-mediated rejection.

In Australia, 50% of individuals are infected with cytomegalovirus (CMV), even so, the virus persists without symptoms in healthy people. However uncontrolled CMV infections can occur in states of immunosuppression, such as following lung transplantation, with approximately 50% of recipients experiencing active viral infections.

Researchers have previously observed that CMV replication was associated with the development of CLAD, however the link between the two is not well understood. Therefore, their new work is aimed at finding novel therapeutics and diagnostics to prevent CMV infections, thereby also limiting antibody-mediated rejection.

The researchers are generating fantastic data on this project, which has resulted in a recent patent application. Moreover, they have received seed funding from the University of Melbourne to continue work in this area (University of Melbourne School of Biomedical Sciences Translational Research Award).

The research team are very pleased with the considerable progress they have made into this project and anticipate further progression as they continue in the coming year.

## 2 ASSESSING NEW TOOLS FOR IMPROVING DONOR-RECIPIENT MATCHING

Lungitude has committed to 3 years of funding a PhD candidate, Steven Hiho, as he continues to work on projects to improve donor-recipient matching.

**PROJECT:**
The last few years has seen the creation of several new computer programs to assess 'compatibility' between a lung transplant recipient and a potential donor. These programs use the differences between donor and recipient proteins to give a 'score' of compatibility between any particular pair.

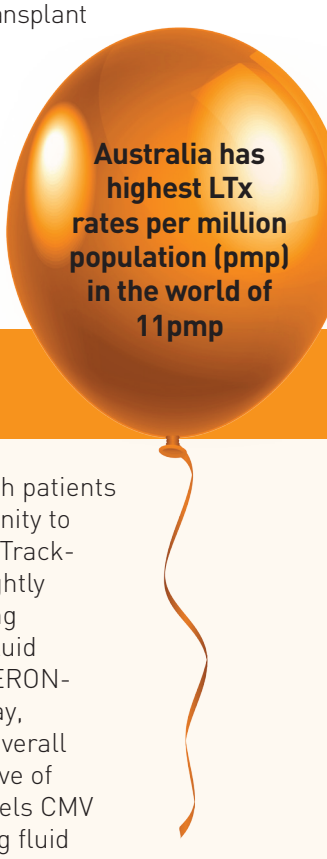
Developing better tools for donor-recipient matching may be a key to preventing the development of CLAD, with the added aims of improving and prolonging life post lung transplantation.

**RECENT PROGRESS:**
In the first year of his PhD project, Steven has concentrated on looking at blood samples from a group of 310 Alfred lung transplant patients to assess the effectiveness of these different computer programs in their ability to provide a recipient and donor compatibility score, and try and correlate this compatibility/matching score with the patient outcomes. Put simply, Steven has been trying to work out what level of HLA compatibility is required to give the best post transplant outcomes.

It also appears that not all HLA 'mismatches' are equal in their ability to cause rejection. Thus, Steven has looked to see if individual high Risk Epitope Mismatches (REM) that have been shown by other international groups to contribute to development of chronic rejection (CLAD) and reduce survival after lung transplantation, were present in the 310 Alfred patients samples. Whilst there were 27% of HLA high REM in the Alfred patient group, surprisingly these REM did not predictably correlate with CLAD or reduced survival post lung transplant in our patients.

In the same 310 patients, Steven also used the computer program HLA Matchmaker to evaluate HLA epitope mismatch load (epMM) to see if he could use this data to predict the immunological risk of developing CLAD and post-transplant survival. This study did show that there was a cut-off level for a specific HLA Class II epMM (⇱31) that predicted better patient survival than if the epMM was higher, thus identifying a group of lung transplant recipients with a lower immunological risk of developing CLAD.

Expanding on the results of early project work, this year Steven had been working with the VITS/Red Cross tissue typing team to try and work on the best way to use HLA epitopes and epMM scoring clinically, plus better HLA screening of donors, to be able to select more compatible recipients for each potential donor. He is also extending his PhD research to look at other (non-HLA) immunological markers which could also potentially be used in the pre-transplant compatibility assessment of lung donors.




## 3 INVESTIGATING THE LINK BETWEEN VIRAL INFECTION AND REJECTION FOLLOWING LUNG TRANSPLANTATION

This project will continue to extend on previously funded CMV research work, further evaluating the link between viruses and rejection.

**PROJECT:**
Rejection of the transplanted lung is linked to infection, with the most important being Cytomegalovirus (CMV). Monitoring whether the immune system of a particular lung transplant patient can control the amount of CMV in their blood, will provide information regarding duration of antiviral medication treatment.

A commercially available test called the QuantiFERON-CMV assay is currently available and is being used by The Alfred (via previous research funded by Lungitude) to test if a patient's immune system is able to control CMV. A new test called T-Track CMV measures the function of several other important immune cells and claims to be a better predictor of a patient's ability to fight CMV. In this second project, researchers aim to compare the utility/benefit of QuantiFERON-CMV with the new T-Track CMV assay.

**RECENT PROGRESS:**
T-Track-CMV assays were performed on cryopreserved blood cells from 34 Alfred lung transplant recipients. We compared the results of the T-Track-CMV assay to previously performed QuantiFERON-CMV monitor assay results from the same recipients. The amount of CMV virus load in both the blood and the lung fluid collected post-transplant was compared in both assay results.

QuantiFERON-CMV and T-Track-CMV assays were both equally predictive of high level CMV in the blood. Both were able to show which patients have better immunity to CMV. However, T-Track-CMV was only slightly better at predicting CMV in the lung fluid than the QuantiFERON-CMV Monitor assay, and both assays overall were less predictive of detecting high levels CMV virus levels in lung fluid compared to blood.

Thus, the overall study conclusions are that both commercially available immune monitoring assays appear to predict high level CMV in the blood, however both the T-Track CMV and the QuantiFERON Monitor CVM assays are less beneficial in trying to predict CMV virus levels in the actual transplanted lung.

# 4 MEASUREMENT OF BIOMARKERS II

This project extends the previous Biomarker I study — Identifying of biomarkers of immune function and infection in the blood and lung aiming to predict episodes of acute rejection and the onset of chronic lung allograft dysfunction (CLAD) following lung transplantion. Identifying immune and physiological markers early could assist in preventing long-term damage to the transplanted lungs, plus inform more targeted use of immunosuppression and other treatment therapies and patient-specific regimes.

**RECENT PROGRESS:**

The Measurement of Biomarkers II project aimed to initially follow 100 post lung transplant patients for 3 years. Patients enrolled into the study consented to have samples of blood, lung fluid (BAL) and tissue biopsies collected at specific time points.

Enrolment of 100 lung transplant patients was achieved and Alfred Ethics approved an amendment to increase study enrolment to 150.

As at Feb 2020, a total of 105 patients had been enrolled and more than 50 patients had reached the 12 month time point to date, however the impact and uncertainty due to COVID-19 resulted in the cessation of new patient enrolment into research projects from 20 March 2020 onwards until further notice.

Due to the high risk posed by undertaking bronchoscopies during COVID-19 all clinical and research bronchoscopies were also ceased, unless absolutely necessary for clinical diagnostic reasons so no research specimens could be collected.

Additionally, due to COVID-19, many research labs had shut access to research staff unless they were working specifically on COVID-19 research projects.

Thus, only the 105 patients already enrolled in the study could contribute further specimens at the relevant time points, and contribute to the overall analysis.

A significant number of specimens (blood/BAL/Biopsies) from these 105 patients have already been collected and sent to all the participating laboratories & collaborating teams for processing. At present, everyone across the different laboratories in Melbourne is collating all the results and data from specimens already analysed.

There is still a huge amount of stored specimen processing work for the relevant teams to complete once the laboratories are allowed to re-open. Hopefully, as the COVID-19 restrictions lift, bronchoscopies on patients already enrolled will be able to continue at important time points and additional research specimens and clinical data will be collected for these patients and be able to sent to the various labs again to provide a more complete cohort of data.

There have been quite a few manuscripts relating to the research supported by Lungitude Foundation accepted for publication past 12 months (listed on pg 6) along with research abstracts accepted for oral presentation at 2020 International Society of Heart and Lung Transplant (ISHLT) international scientific meeting in Montreal, which was unfortunately cancelled due to COVID-19.

## DID YOU KNOW?

**Although it has been known for decades that our gut is full of bacteria, the lung was thought to be sterile until as recently as 10 years ago. The discovery of lung microbes sparked Ben's interest in this field of research as he sought to understand how these microbes impacted respiratory diseases.**

## Spotlight on... PROFESSOR BENJAMIN MARSLAND

**New Zealand born immunologist Professor Ben Marsland began his post-doctoral research in Switzerland in 2004 at the Swiss Federal Institute of Technology in Zurich, followed by establishing his own research group at the University Hospital in Lausanne where he and his team gained international recognition.**

Ben's wife, who is a professor of intestinal immunology, and their two children returned to Melbourne in 2018. Ben now leads Monash University's Respiratory Immunology laboratory, where the main focus of research revolves around the microbiome in the gut, lung and skin and how it can influence respiratory diseases such as those found in lung transplantation.

Working closely with The Alfred's Prof Glen Westall, Prof Greg Snell and their wider research teams, a key focus for Ben is a NHMRC Project – Clinical implications of trans-kingdom microbial interactions in the transplanted lung. Funding provided by Lungitude was instrumental in this project grant coming to fruition.

The project's aim is to build a bigger picture of what is a 'healthy' lung habitat versus one at risk. It uses samples taking during bronchoscopies resulting in 'big data' that requires high performance computational clusters, as large as any used by Google or Amazon, to work non-stop 24/7 for days to derive results. Data that will give clearer indications on when to intervene in pathways leading to respiratory illness like CLAD and for diagnostic value.

Ben spoke highly of the proactive and motivational nature of his collaborators at The Alfred, and the strong focus on linking translational research to clinical practices.

## THE LUNGITUDE FOUNDATION EXTENDS OUR THANKS TO OUR KEY SUPPORTERS:

**GILLESPIE FAMILY FOUNDATION**

**THE GITTUS FAMILY**

**MR TONY PRATT**

Fred & Ginger Catering

Chez Ami Yarra Valley

Apt. Wealth Partners

theAlfred Foundation

astellas

hta. delivering actionable insight

Gordon Jenkins

Hallow Brands

Dixon Kestles

## Save the dates

**5-13 DEC 2020** — **Melbourne Marathon** VIRTUAL EVENT

Join the Lungitude Team & choose a virtual run or walk

**MID 2021** — **Lungitude's Long Lunch** INNER CITY

Spectacular entertainment, fabulous produce & amazing location

**SEP/OCT 2021** — **Annual Research** PRESENTATION

World-class researchers showcasing their latest projects

## Our team

### BOARD MEMBERS

Gordon Jenkins, Lungitude Chair
Andrew Dunbar, Board Chair
Julie Ramke-Meyer, Treasurer
Wendy Jenkins, Secretary
A/Prof Bronwyn Levvey
Mark Ferrari
Craig Wood
Katharine Terkuile
Bridget Mullahy

### FUNDRAISING COMMITTEE

Wendy Jenkins, Chair
Kerrie Coghlan
Liz Gittus
Cindy Watson
Elise Patterson

## YOU CAN MAKE A VITAL DIFFERENCE

- Sponsor the Lungitude Foundation
- Make a Donation
- Sponsor or Attend an Event
- Run your own fundraiser supporting the Lungitude Foundation
- Encourage staff, colleagues, suppliers or clients to support the Lungitude Foundation
- Donate Goods & Services
- Subscribe to our Online Community

Have you been receiving our latest emails? Please add the following email to your address book **Info@lungitude.com.au** or subscribe to our database **www.lungitude.com.au/community**

## PUBLICATIONS AND PUBLISHED MANUSCRIPTS


*Enrichment of cytomegalovirus-induced NKG2C+ Natural Killer cells in the lung allograft.*
H1. Harpur, C. M., S. Stankovic, A. Kanagarajah, J. M. L Widjaja, B.J . Levvey, Y. Cristiano, G. I Snell, A. G. Brooks, G. P Westall and L. C. Sullivan (2019). Transplantation. 103:1689-1699.

*Consequences of donor-derived passengers (pathogens, cells, biological molecules and proteins) on clinical outcomes*
Snell, G.I., S. Hiho, B. J. Levvey, L.C. Sullivan and G.P. Westall (2019). J Heart Lung Transplant. 2019. 38: 902-906

*Transfer of donor anti-HLA antibody expression to multiple transplant recipients- a potential variant of the Passenger Lymphocyte Syndrome?*
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Sullivan, L.C., E. M. Shaw, S. Stankovic, G. I. Snell, A. G. Brooks and G. P. Westall (2019). Invited Review. Clin Transl Immunology 8(9):e1078

*T Cells in Transplantation: Friend and Foe*
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*Comparison of immune monitoring modalities for assessing cytomegalovirus immunity following lung transplantation.*
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*Antibody Mediated Rejection: Are We There Yet?*
Book Chapter · August 2019 Essentials in Lung Transplantation, pp.79-86DOI: 10.1007/978-3-319-90933-2_7 GP Westall and L C Sullivan.

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*Enrichment of Cytomegalovirus-induced NKG2C+ Natural Killer Cells in the Lung Allograft.*
Transplantation. 2019 Aug;103(8):1689-1699 Harpur CM, Stankovic S, Kanagarajah A, Widjaja JML, Levvey BJ, Cristiano Y, Snell GI, Brooks AG, Westall GP, Sullivan LC.

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Am J Transplant. 2020 Apr;20(4):954-966. Halloran K, Parkes MD, Timofte IL, Snell GI, Westall GP, Hachem R, Kreisel D, Levine D, Juvet S, Keshavjee S, Jaksch P, Klepetko W, Hirji A, Weinkauf J, Halloran PF.

*Cytomegalovirus replication is associated with enrichment of distinct T cells substes following lung transplantation: A novel therapeutic approach?*
LC Sullivan et al Accepted by J Heart Lung Transplant May 2020


Lungitude Foundation

## Contact us


**LUNGITUDE FOUNDATION**
PO Box 25132, Melbourne VIC, 3004

03 9525 2448
info@lungitude.com.au
lungitude.com.au