IMPACT REPORT

The Numbers

36yrs first Australian lung transplant

5 average lung transplants per month

5th largest lung transplant program in the world

1752 lung transplants at The Alfred

75yrs oldest lung recipient

Our vision of Transplant for Life continues to drive momentum

First of all, our thoughts and thanks are with all of the health workers who continue to amaze us with their resilience and support during challenging times. We are forever grateful for your ongoing care and duty.

Over the past 12 months the Lungitude Foundation has been proud to donate the second of three years committed funding towards key research projects with your support.

This life-changing medical research is dedicated to unravelling the mystery around Chronic Lung Allograft Dysfunction (CLAD) and will help improve lung transplant survival rates and outcomes with a focus on prevention, diagnosing and treating this chronic rejection. We welcome applications for further research initiatives that align with our Lungitude Model Rules.

Our national reach continues to expand through the use of technology to bring initiatives such as the Annual Lung Transplant Research Presentation to a wider audience. We were blown away by your support of our research with our inaugural Giving Day on 1 June which well surpassed our initial goal. In order to expediate the outcomes further, funding from corporate, philanthropic, State and Federal Governments and other support channels is imperative.

We recognise that many of the lung transplant community have contracted COVID-19 and our thoughts are with those patients who may have had a difficult journey. The advocacy from lung transplant specialists on behalf of our higher-risk community enabled access to additional preventative and responsive treatments which was welcomed. Lungitude Foundation will continue to monitor the impact of COVID-19, and where we may be able to add value in alignment with what we do.

The establishment of the Lungitude Online Peer Support Network, in collaboration with Lung Foundation Australia, recognises that there is a need for further support for patients and primary caregivers beyond just the physical. In addition to monthly meetings, invited health experts shared their insights with members and we thank them for their input and time.

Our much-anticipated Lungitude Long Lunch, on hold for the last few years due to COVID, is locked in for Saturday 29 April 2023 at an iconic Melbourne location so please save the date! In the meantime, we have embraced events like the Lungitude Virtual Challenge which has garnered great support to date. Thank you to everyone who donated to Lungitude this year, your generosity during adverse times is certainly appreciated.

We encourage everyone to stay safe and up to date with the latest health precautions as COVID looks set to remain for the foreseeable future. Please check out our website for helpful information specific to lung transplantation. We thank you for your ongoing support.

Gordon Jenkins
Lungitude Foundation Chair

The Alfred's Lung Transplantation Service

Key research projects that require funding

The Alfred's Lung Transplant Service continues to be the Australia's premier lung transplant program, and despite the ongoing impact of COVID-19 on both patients and staff, their clinical and research lab teams have worked hard in very trying circumstances to ensure research project milestones are being met.

Thanks to the generous commitment of significant funding over 3 years by the Lungitude Foundation, The Alfred lung transplant research team have been able to setup a Translational Lung Transplant Research Hub at Monash University (Alfred Campus) which has now become a reality with the employment of a fantastic new senior post-doctorial fellow, Dr Sanda Stankovic, in July 2021 and the more recent employment of an excellent laboratory research assistant Ellen Reilly. Sanda and Ellen have continued the great collaboration that The Alfred researchers already had with their other Monash laboratory partners, as well as their clinical lung transplant research team at The Alfred.

The overarching aim of the 3 key projects we are funding is to better understand the mechanisms underlying or leading to development of chronic lung allograft rejection (CLAD) and how CLAD can be detected earlier, prevented, arrested or possibly reversed after lung transplantation.

"We wish to express our ongoing gratitude to the Lungitude Foundation for its support of our researchers, clinical team and these key research projects. The funding provided by Lungitude enables The Alfred's Lung Transplant Service to continue to be a world leader in Lung Transplant research, and most importantly improve our patient's quality of life and survival rates even further."

Professor Greg Snell
MBBS FRACP MD OAM Head,
Lung Transplant Service (Medical)
& Consultant Respiratory Physician

HOW YOUR FUNDING IS MAKING AN IMPACT TO OUR GOAL OF TRANSPLANT FOR LIFE

The Lungitude Foundation partners with leading medical and health organisations in the field of lung transplantation. The research we fund is translational 'bench to bedside' health and medical research – which means research undertaken in the lab ('the bench') or in the clinics by the research teams, is translated into treatments or therapies that benefit people at the 'bedside' as soon as possible.

$135,000
donated last financial year, plus funding for equipment

On 1 June 2022 we held our inaugural Giving Day where your donations were doubled with thanks to our amazing 'matchers' who committed to match dollar for dollar. We were blown away by all the support! Thanks to our 'matchers' and 387 wonderful donors we well and truly surpassed our initial goal raising $144,258!

A big thank you to Jade and David Galbally (pictured on the front cover) for being the 'faces' of our campaign, and the passionate community ambassadors who helped us spread the word and raise funds. Our fundraising committee did a brilliant job running the campaign and pictured is the Lungitude Giving Day HQ on the day.

Check out our Thank You video if you participated or donated during our Giving Day.

PROJECT 1

HARNESSING NON-CONVENTIONAL T CELLS FOR ANTIVIRAL CELLULAR THERAPIES

To help reduce the incidence of rejection for lung transplant recipients, the use of immunosuppressive medications are required; however, these same medications make it difficult for the recipient's body to control infections.

One infection that is particularly problematic is a common and often harmless virus, called cytomegalovirus or CMV. About half of all Australians are infected with CMV, but it doesn't cause major symptoms in healthy people.

However for lung transplant recipients, CMV infection can lead to very harmful complications, including inflammation, pneumonia, rejection (acute and chronic-CLAD) and in severe cases it can result in death. Recipients who experience CMV infection have a higher rate of rejection, and a death rate 6 times higher than those without CMV.

AIM 1

Elucidate the characteristics of CMV gδT cells in healthy individuals and lung transplant recipients

To address this aim, researchers performed a gene expression on over 700 genes from a sorted population of CMV (NKG2C+) gδT cells from healthy donor blood and compared to non-CMV gδT cells from the same individuals. This allows them to identify key features of CMV-specific gδT cells in a healthy state (Figure 1). This data will then be compared to gδT cells from LTx patients as they continue this work.

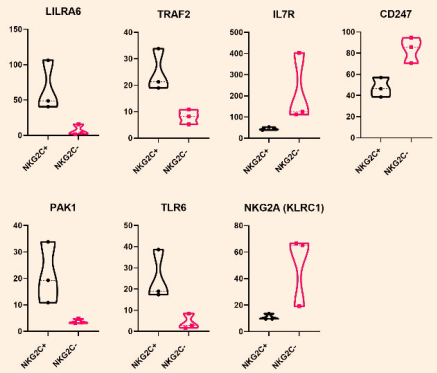
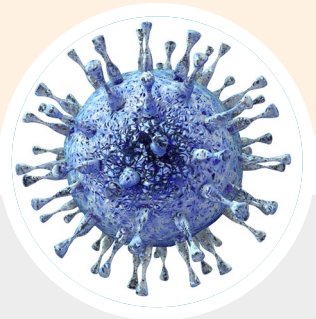


Figure 1: *Gene expression analysis of sorted CMV (NKG2C+) γδT cells and non-CMV γδT cells for a select panel of genes out of over 700 analysed. Cells were isolated from the blood of healthy donors. Y axis=normalised gene copy number.*



AIM 2

Determine the ability of CMV gδT cells to kill cells infected with CMV

To undertake this aim, the research team are in the process of setting up a CMV infection experimental system in their laboratory in the next several months.

This work has been presented at the Respiratory Department Meeting, Departments of Immunology and Pathology, Monash University, and at the Transplant Research Group meetings@ Alfred Hospital.

PUBLICATIONS

The clinical utility and thresholds of virtual and Halifaster flow crossmatches in lung transplantation. Hiho SJ, Levvey B, Carroll R, Nicolson I, Mihaljcic M, Diviney MB, Snell GI, Sullivan LC, Westall GP. HLA. 2022 Mar 27.

Determining clinical thresholds for donor HLA eplet compatibility to predict best outcomes following lung transplantation. (Accepted Manuscript Transplantation Direct 2022) Hiho. Steven J, Walton. Duncan. C, Paraskeva. Miranda, Levvey. Bronwyn. J, Diviney. Mary. B, Snell. Gregory. I, Sullivan. Lucy. C, Westall. Glen. P.

Major technological advances will enhance Australian donor- recipient matching and improve transplant outcomes (under review IMJ) Steven Hiho, Bronwyn Levvey, Rhonda Holdsworth, Lucy Sullivan, Glen Westall, Greg Snell

Comparison of HLA immunological risk stratification methods in lung transplantation (Manuscript in progress) Target journal AJT Late 2022 Impact of reporting HLA alleles from Real-Time PCR on deceased donor DSA assessments and conformance with high resolution alleles. (Manuscript in progress) Target Journal Human Immunology Aug 2022 Steven Hiho, Sue Bowman, Fiona Hudson, Lucy Sullivan, Robert Carroll, Mary Diviney

AWARDS AND GRANTS

2022 TSANZ President Prize Finalist

2022 TSANZ Early Career Researcher Award (Clinical science)

2019 Transplant Research Advisory Committee (TRAC) Grant ($53,500)

PRESENTATIONS AND CONFERENCES

2022 TTS (Oral) Comparison of HLA compatibility algorithms to predict long-term survival and CLAD following lung transplantation

2022 TSANZ (President Prize Oral) The clinical utility and thresholds of virtual and Halifaster flow crossmatches in lung transplantation

2022 TSANZ (Oral) Role of non-HLA in Lung transplantation

2020 TSANZ (Poster) Use of HLA epitopes in a virtual crossmatch to better assess lung transplant compatibility

2020 ISHLT (Virtual Oral) HLA Epitope Mismatch Load (epMM) Allows Classification of Immunological Risk and Correlates with Patient Survival Following Lung Transplantation (LTx)

2020 ISHLT (Virtual Oral) Can Avoiding So-Called HLA High Risk Epitope Mismatches (REM) Improve Lung Transplant (LTx) Outcomes?

PROJECT 2

HARNESSING DONOR IMMUNE CELLS TO PREVENT LUNG TRANSPLANTATION REJECTION

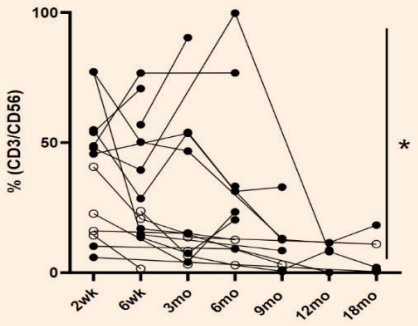


Figure 1: *The proportion of donor derived cells in the BAL of patients who subsequently developed CLAD (open circles ○) and those that did not (black circles ●).*
X axis = time post LTx ;
Y axis = proportion of donor cells of total pool of BAL cells.
Each dot represents a clinical sample at indicated times.
Lines represent individual patients.
Statistical significance (*) between groups was tested using Mann Whitney test.

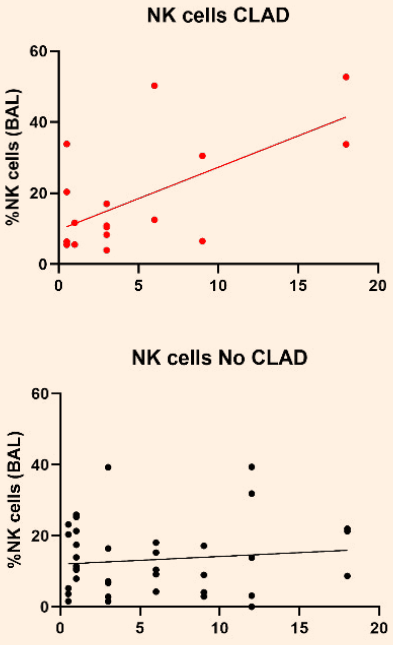


Figure 2: *Higher proportion of NK cells in the BAL is associated with CLAD development.*
LTx patients were stratified into two groups based on CLAD development within 3 years post transplant. The proportion of NK cells was correlated with CLAD.
We noted that whereas in CLAD patients the proportion of NK cells (y axis) increased between 9 and 18 months post LTx, the proportion of NK cells in the 'no CLAD' group remained steady over this time period.
X axis = time post LTx; Y axis = proportion of donor cells of total pool of tissue resident cells from BAL. ● Each dot represents a clinical sample at indicated time.

AIM 1

Assess the link between the persistence of donor-derived lymphocytes (resident immune cells) and allograft outcomes.

Up to 50% of lung transplants develop chronic rejection (CLAD) within the first five years.

The donor-derived immune cells (lymphocytes) that are transferred within the allograft appear to be associated with protection from allograft damage. The details of which cell subsets persist and the mechanism of protection they offer is not well understood.

The research teams' comprehensive study used clinical samples from lung transplant (LTx) recipients such as blood and bronchoalveolar lavage (lung fluid =BAL) to characterize donor-derived lymphocytes and to correlate their proportion with long-term allograft health.

They found that donor-derived lymphocytes are present in a higher proportion in the BAL than in blood post-LTx in all individuals, indicating that the migration out of the donor lung is minimal after transplant. This also suggests that any effects of donor-derived lymphocytes on allograft health are locally mediated.

96%
Alfred post one year survival

5 yrs
youngest lung recipient

Furthermore, donor-derived cells persist for longer in the lung suggesting the lung environment is more conducive to their survival. These cells largely consist of T cells and NK cells. When assessing the correlation between the proportion of donor-derived lymphocytes in the lung and CLAD, the researchers observed that LTx recipients with a higher proportion of donor-derived lymphocytes had a lower incidence of subsequent CLAD development, indicating that donor-derived lymphocytes are associated with protection from CLAD (Figure 1).

Further work by the research team will include more patients, especially more CLAD patients, to provide a strong basis for possible diagnostic utility. The researchers highlighted that, interestingly, donor-derived lymphocytes failed to undergo substantial expansion in the lung post-LTx, in contrast to recipient-derived cells, which could explain their loss over time in the recipient (data not shown).

When the researchers explored total cell subset composition between CLAD and CLAD-free "no CLAD" groups (including both donor- and recipient-derived immune cells), they noted that NK cells were significantly increased in the CLAD group between 9 and 18 months post-LTx (Figure 2). This data points to the role of NK cells in the development of lung allograft damage. The team will continue to explore the role of NK cells in CLAD in more detail.

AIM 2

Assessing the contribution of acute lung injury to lung 'resident' immune cells.

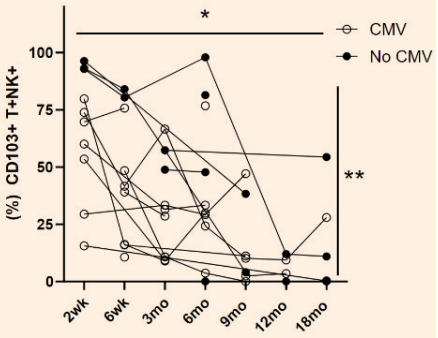


Figure 3: *Tissue-resident donor-derived cells are associated with protection from CMV. LTx patients in whom there was CMV replication detected in the BAL (CMV open circles ○) and those that did not have CMV replication (no CMV black circles ●) were compared for the proportion of donor-derived tissue resident cells. X axis=time post-LTx; Y axis- proportion of donor cells of the total pool of tissue-resident cells in BAL. Each dot represents a clinical sample at indicated times. Lines represent individual patients. Statistical significance (**) between groups and over time (*) using mixed model (two-way ANOVA) analysis is shown.*

The researchers shared that cells termed 'tissue-resident', are located directly within the lung epithelium (lung lining), along the lung airways. These cells have been shown to play a key role in the local anti-viral immunity as a first-line defence against pathogens and have been identified to express marker CD103 on the cell surface.

As cytomegalovirus (CMV) is a pathogen that has been associated with worse lung transplant outcomes, the researchers aimed to explore if donor-derived cells in this location are associated with protection from CMV reactivation in the lung.

Using BAL samples, they discovered that the proportion of tissue-resident donor-derived cells was higher in the LTx recipients without CMV reactivation.

This indicated to the researchers that either these cells are more capable of expanding after LTx, or that it was their high proportion in the first place that offered strong anti-viral (anti-CMV) protection.

The researchers also noted a higher proportion of HLA-matching between donor and recipient in LTx individuals who did not have CMV reactivation in the lung. This offered a hypothesis that it is the recognition of the 'similar' HLA in the recipient that may allow donor-derived cells to protect from CMV reactivation. (Figure 3.)

Future work will focus on this observation and the role HLA matching may have in the protection from virus reactivation.

LUNGITUDE FOUNDATION
Mental Health Initiatives

Did you know that we have a range of mental health resources on our website for both patients and caregivers? These include our popular video series where you can hear direct from other patients and caregivers, and our 'Coping with Stress' booklets.

We also invite patients or their primary caregivers to join our Lungitude Online Peer to Peer Support Network, which enables the sharing of ideas and tips for managing the practical and emotional challenges of the lung transplant journey. Since launching in collaboration with Lung Foundation Australia, we have welcomed a number of expert speakers in the areas of physiotherapy, nutrition and dietetics, social support services and dermatology, with more planned.

We are currently looking for patients, caregivers and supporters who would like to be part of a Mental Health Champions focus group, where we will be exploring what additional initiatives and advocacy are key in the transplantation mental health space.

To learn more please contact Wendy Jenkins wendy@lungitude.com.au.

GO TO SITE

PROJECT 3

REASSESSING DONOR-RECIPIENT MATCHING TO IMPROVE LUNG TRANSPLANTATION OUTCOMES

AIM 1

To improve donor-recipient matching by understanding the impact a donor's HLA-C has on a recipient's immune cells, and to determine the likelihood of the recipient developing CLAD after lung transplantation.

AIM 2

To understand the extent to which donor HLA-C impacts on the function of recipient immune cells.

AIM 3

To determine whether mismatched HLA-C can lead to the formation of antibodies and contribute to the development of CLAD.

There are many factors that are now known to lead to the development of CLAD, however the team are still are lacking obvious biomarkers and investigations that make early diagnosis of CLAD possible.

This research project focuses on improving donor-recipient matching to minimise the impact of CLAD. A major barrier to improving life expectancy rates is the difficulty in matching human leukocyte antigens (HLA), which are proteins, between donors and recipients in the early stages of matching.

Currently two proteins HLA-A and HLA-B are matched as closely as possible between donors and recipients while a third protein HLA-C has been largely ignored in the matching process.

The research team have been exploring some exciting preliminary data which shows that when the mismatching of donor and recipient HLA-C occurs the development of CLAD is highly likely.

The research looks specifically at HLA-C matching in the hope of reducing the incidence of CLAD, thereby improving the survival rates and outcomes for lung transplant recipients.

DEFINING STRUCTURAL DETERMINANTS OF OUTCOMES FOLLOWING LUNG TRANSPLANTATION

"I would like to extend my sincere thanks to the Lungitude Foundation which has supported me and allowed to me pursue this study. I have been working with the RedCross Lifeblood in transplantation for over 10 years and this support for this PhD has allowed me dedicated time to answer some of these important questions about lung transplant compatibility, and improve the process of the pre-transplant compatibility assessment for those awaiting a lung transplant."

– Steven Hiho, PhD Candidate

The overall aim of Steven's PhD was to identify immunological factors, which can be used to match donor and recipients to provide better outcomes. So far, the research has shown that the use of HLA compatibility, specifically B-cell epitopes, provide a way of evaluating the risk of antibody formation and rejection post- transplant, and that limiting epitope mismatching between recipient and donor increases long term survival following a lung transplant.

The research investigated all 'epitope' algorithm's available, and determined which algorithms and epitope mismatch levels; best predicts long-term survival and reduces risk of rejection. The goal is to incorporate this into the pre- transplant assessment through RedCross Lifeblood once the current manuscript is published, "Comparison of HLA immunological risk stratification methods in lung transplantation" (Late 2022).

The second aim of Steven's PhD was to determine which method most accurately defines the pre-transplant antibodies, which are of concern in a recipient-donor pair. This work investigated both the flow cytometry and virtual assessment methods to evaluate whether the use of a virtual assessment can provide the pre-transplant antibody assessment. The research demonstrated that a virtual assessment is a faster and more accurate way to define these dangerous antibodies. This significant work has provided, not only the lung transplant teams, but other Australian based transplant units the ability to move forward with the use of a virtual assessment of transplant risk.

Future directions of this PhD will include investigating the role of non-HLA antibodies in lung transplantation. From the work with the flow and virtual crossmatching, the research identified that non-HLA antibodies interact with cells on these assays and the wish is to determine any clinical impact this has on recipients, and whether these non-HLA antibodies need to be incorporated into the pre-transplant assessment.

Spotlight on... **DR LOUISE FULLER** PHD BAPP SC (PHYSIO) APAM

Senior Clinical Physiotherapist, Transplant Services, The Alfred & Adjunct Associate Professor Physiotherapy School, Swinburne University.

We are fortunate to have Dr Louise Fuller managing the lung and heart transplant rehabilitation program, and patients will attest to the benefits of her care and support. Louise has over 20 years' experience at The Alfred in lung and heart transplantation, including presenting at national and international events, where and strongly believes the clinical research underpinning the rehab program are key to the remarkable patient outcomes being achieved.

Lung transplant recipients are eager to make the most of their second chance at life and Louise and the team aim to help patients resume their "peer age normal" active lifestyles. The complexity of poor pre transplant health, time spent in the operation and in ICU on strong medications, immunosuppressant side effects, particularly impacting muscle and bone health, and ongoing chronic health considerations all need to be managed carefully.

Louise's passions include educating patients around these topics, clinical research into rehabilitation models, physical activity outcome measures and the usage of ultrasound in physiotherapy ... as well as a much loved first grandson!

Louise was quick to thank the Lungitude Foundation and our wonderful supporters for many years of funding physiotherapy research, as well as enabling the purchase of much needed gym and research equipment.

In recognition of her dedication, Louise was awarded a prestigious Churchill Fellowship in 2019 – one of only 115 in Australia that year – and now travel restrictions have eased, will depart in early 2023 to spend time internationally investigating four of the best post-lung transplant rehabilitation models in Belgium, UK, USA and Canada, to help her develop further guidelines for Australia.

Dr Fuller, along with the senior dietician at The Alfred's Lung Transplant Service, were also awarded the inaugural Jeffrey Gittus Lung Transplant Fellowship in December 2019 for their project 'Body Composition and Muscle Morphology after Lung Transplant'. While on hold during pandemic times, a key piece of equipment has recently been purchased in preparation for the project commencing shortly. You can hear directly about the aims of this project in an interview with Louise. We want to acknowledge the generosity of The Gittus Family for funding this important research fellowship in memory of Jeff.

JEFF GITTUS FELLOWSHIP

Jeff had two lung transplants, and alongside his wife Liz were instrumental in enabling the Lungitude Foundation to flourish from day one. Future Fellowships of $20,000 will be awarded every two years.

Congratulations to Lungitude co-founder, Board Secretary and Fundraising Committee Chair Wendy Jenkins OAM for being awarded a Medal of the Order of Australia (OAM) in the 2022 Queen's Birthday Honours List "for service to community health, particularly lung transplant research."

VIEW PRESS RELEASE

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

THE LUNGITUDE FOUNDATION EXTENDS OUR THANKS TO OUR KEY SUPPORTERS:

Gillespie Family Foundation

The Gittus Family

Mr Tony Pratt

Lung Foundation Australia

MONASH University

Apt. WEALTH PARTNERS

hta. delivering actionable insight

astellas

81

HALLOW BRANDS

theAlfred FOUNDATION

WE RELY ON YOUR KINDNESS AND GENEROSITY TO FUND THESE WORLD-CLASS RESEARCH PROJECTS AND CONTINUE TO BE THRILLED BY YOUR ONGOING SUPPORT FOR THIS WORTHY CAUSE.

Save the dates

29 APRIL 2023 — **Lungitude's Long Lunch** — INNER CITY

Stunning location, entertainment, fabulous food & wine

1 JUNE 2023 — **Lungitude Giving Day** — FUNDRAISER

Double your impact with your donation matched on the day

OCT EACH YEAR — **Annual Research** — PRESENTATION

World-class researchers showcasing their latest project outcomes

OCT EACH YEAR — **Lungitude Challenge** — VIRTUAL EVENT

Choose your challenge and join us from where you live

Our team

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YOU CAN MAKE A VITAL DIFFERENCE

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

Find out more on how you can support us
www.lungitude.com.au/get-involved/

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/our-community/**

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Lungitude FOUNDATION

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