ANNUAL REPORT 2017



institute for **RESPIRATORY HEALTH** The Institute for Respiratory Health is a collaborative respiratory research organisation. It aims to improve the life of everyone living with a respiratory condition by bringing together world class researchers and dedicated clinicians to investigate, diagnose, treat and prevent respiratory conditions.

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ABOUT US

The Institute for Respiratory Health is a non-government, not for profit organization which was founded in February 1998 by Professor Philip Thompson, one of Australia's leading respiratory clinicians who is well recognised for his achievements in research and clinical respiratory medicine.

The Institute is based at the QEII Medical Centre, with the Clinical Trials Unit being situated within Sir Charles Gairdner Hospital and the research units within the Harry Perkins Institute of Medical Research. The Institute is committed to strengthening partnerships and affiliations with other academic and respiratory organisations for the benefit of improving the respiratory health of the community.

The Institute for Respiratory Health is incorporated under the Associations Incorporation Act (WA), is a registered charity and has been endorsed by the Australian Taxation Office as a deductible gift recipient for donations.

OUR VISION

To improve the life of everyone living with a respiratory condition.

OUR MISSION

To bring together world-class researchers and dedicated clinicians to investigate, diagnose, treat and prevent respiratory conditions.

Our work gives hope for a better future to those with respiratory diseases.

OUR OBJECTIVES

RESEARCH EXCELLENCE

Conduct and foster innovative basic and clinical research to prevent and better understand respiratory conditions, and improve their diagnosis and management.

CLINICAL EXCELLENCE

Translate our research into improved treatments for people with respiratory conditions.

CAMPAIGNING AND EDUCATION

Campaign in Western Australia for an increased awareness of, and investment in, respiratory education and research.

COSIMO'S STORY

LIVING IDIOPATHIC PULMONARY FIBROSIS

My name is Cosimo. I'm a husband, father, and grandfather and I live with a chronic respiratory disease.

Three years ago, I went to my GP with what I thought was a persistent cold that I couldn't shake. He prescribed me different medications, but nothing seemed to work. He then sent me off for x-rays and this is when I was told I had idiopathic pulmonary fibrosis (IPF).

I remember in 2010 our family went to Sydney on holiday. We were walking around the Rocks, which is a very hilly area. Compared to everyone else, I was struggling to keep up; my breathing felt heavy, and I had constant phlegm. At the time, I thought I had a mild form of cold or flu. I was relatively fit, so thinking back, I guess I had IPF then.

After my diagnosis, I was referred to a Respiratory Specialist, Professor Fiona Lake, who suggested I take part in a clinical trial at the Institute for Respiratory Health. For the past 12 months, I have been on a trial that looks at the efficacy and safety of a new medication which shows potential in slowing the progression of IPF.

10 years ago, one of my sons tragically passed away in an accident. When we were at the hospital I was asked about organ donation. It was the last thing on my mind, but I felt if we can help why not! Now my wife and I are so happy that we were able to help someone else.

I guess sharing my story is along the same lines.

Researchers may not find a cure within my lifetime but if I can help out in a small way, then I would without a second thought!





CHAIR'S REPORT

2017 saw a number of changes take place within the Institute. In May, Emeritus Professor Geoff Laurent retired as the Director of the Institute to pursue his interests in regenerative medicine and to advance collaborations between The University of Western Australia, the Helmholtz Zentrum München and the University College London.

The Board appointed Emeritus Professor Geoff Stewart initially as interim and subsequently as Director. Emeritus Professor Geoff Stewart is a pre-eminent research scientist with an interest in allergy and asthma. He has had a long term relationship with the Institute as Chair of the Scientific Sub-Committee since its inception and has served on the Board since 2011. His past roles include being Head of School of Biomolecular, Biomedical and Chemical Sciences at UWA.

I would like to thank Profess Geoff Laurent for his significant contribution as Director of the Institute from 2015 to mid-2017. Geoff, and the then leadership team, undertook a number of changes in order to bring about cost savings and a more streamlined administrative service to the Institute. He remains a valued member on the Board of Directors.

Our Clinical Trials Unit continues to thrive as a world-class facility, and attracts patronage from several of the world's leading pharmaceutical companies. It is changing the delivery of respiratory care, addressing patient needs and ensuring patients receive the best possible care from a range of respiratory specialists. I would also like to take a moment to acknowledge patients and their families, who have voluntarily given their time to help achieve this outcome.

Our researchers continue to be highly successful in obtaining a number of NHMRC (National Health & Medical Research Council) and has been awarded peer-review funding. I'd like



PETER GUNZBURG CHAIR OF THE BOARD



to congratulate Professor Gary Lee for obtaining the Practitioner Fellowship from the NHMRC Medical Research Future Fund Next Generation Clinical Researcher Program.

The ongoing generosity of many individuals and organisations, in particular our long-term supporters, Westcare Inc, the Melbourne Cup Luncheon Committee and the newly formed partnership with Conquer Cystic Fibrosis is gratefully acknowledged.

In addition, we are truly appreciative of the people who have contributed to our Board fundraising initiative and donor appeals. This generosity, throughout 201,7 has had a tangible impact on the success and viability of the Institute.

On behalf of the Board, I would like to thank management, staff and students for their dedication and significant contribution to respiratory research and advocacy. It is because of such inspiring individuals that the Institute is able to remain at the forefront of respiratory health.

I also would like to take this opportunity to thank the members of the Board, all of whom give generously of their time and expertise to guide the Institute for Respiratory Health.

We look forward to another year of achievement in 2018, as we continue to strive towards the Institute's mission improving the life of everyone living with chronic respiratory conditions.

DIRECTOR'S REPORT

I was very pleased to take over from Professor Geoff Laurent as the Institute's Director midway through 2017. One of my first priorities was to establish a Leadership Team, and taking direction from the Institute as a whole, appointed Associate Professors Fraser Brims and Yuben Moodley as Deputy Directors. Fraser and Yuben have taken over from Professors Gary Lee and Peter Eastwood who, with Geoff, played a major role in guiding the Institute through a difficult period. Fraser and Yuben bring with them a wealth of expertise in respiratory health science that will both guide and strengthen the Institute as it strives for relevance and excellence.

The Institute was established more than a decade ago with the goal of playing a significant role in improving the diagnosis and treatment of respiratory diseases. To satisfy these aspirations, we must attract and support high caliber staff, not only clinical and scientific but also administrative staff. The Institute is very fortunate to possess such a cohort and it is only appropriate we highlight some of their successes as well as the exciting initiatives instigated in 2017.

The Institute is comprised of a number of groups and each group, together with their external collaborators, were highly productive last year, as judged by the number of manuscripts published in high quality journals, research grant success, competitive fellowship awards and the training of future researchers at both the undergraduate level (Honours) and the postgraduate (PhD) level.

For example, with regard to grant success, the Stem Cell Therapy Unit, led by Associate Professor Yuben Moodley was awarded an NHMRC Project Grant to investigate the pathological mechanisms involved in idiopathic pulmonary fibrosis; the Tissue Repair Group led by Associate Professors



E/PROF GEOFF STEWART DIRECTOR

G. J. Stewart

Cecilia Prêle was awarded grants-in-aid and collaborative seed funding grant from the University of Western Australia, Helmholtz Zentrum Munchen and University College London consortium in collaboration with the Centre for Regenerative Medicine as well as the Westcare Alan King Research Award to investigate various aspects of idiopathic pulmonary fibrosis; and the Pleural Medicine Group led by Professor Gary Lee were awarded the only WA-based Cancer Australia research project, three Sir Charles Gairdner Hospital Research Grants, and iCARE Dust Diseases Board Research Grants for research into pleural diseases and mesothelioma.

One of the implicit goals of research undertaken within the Institute is to translate research success into clinical outcomes. In this regard, the Pleural Medicine Group and its collaborators recently published an article in the prestigious Journal of the American Medical Association article showing that the use of an indwelling catheter is superior to conventional talc pleurodesis for combating malignant pleural effusions in patients with mesothelioma. They found that the procedure saved 3.6 bed days per patient (i.e. ~14,000 hospital bed days a year for Australia alone) as well as reducing the need for further invasive pleural procedures from 23% to 5%.

The Institute has been the beneficiary of funds raised by two community groups each interested in supporting research into cystic fibrosis (CF). They include the Melbourne Cup Luncheon Committee and Conquer Cystic Fibrosis (CF) Inc. The funds raised by the Melbourne Cup Committee each year for the last seven years are used to support researchers studying various clinical and scientific aspects of CF whereas the major goal of Conquer CF is to maximize the clinical care of adolescents with CF as they develop as adults. To this end, they have provided two PhD scholarships though Curtin University to help develop novel physiotherapy regimes for adult CF patients as well as providing research seed funding to Dr Anna Tai, a respiratory consultant working in the area of adult CF research.

In addition, Conquer CF has been instrumental in bringing together the Sir Charles Gairdner Hospital Adult CF Clinical Research Group and Paediatric CF Research Group located at the Telethon Kids Institute with the aim of developing high caliber research programs around this transition period. This collaborative approach has started to bear fruit as they have been invited to submit a research proposal to the Vertex Pharmaceuticals Innovative Grant Program as well as submitting a collaborative application to the CF Foundation.

Our strong relationship with The University of Western Australia continues. In this regard, the Institute has been negotiating with the University to reaffirm and enhance its affiliation agreement, originally established in 2006. Our centre, the Centre for Respiratory Health, is administratively located in the School of Biomedical Sciences headed by Professor Jeff Keelen. This agreement will have a major, positive, financial impact on the Institute's capacity to undertake its research.

No research institute can be considered 'an island entire of itself' as, of necessity, we interact with many different people and institutions. To this end, it is appropriate to acknowledge the support we receive from various sources. Academically, we acknowledge the support we receive from the Sir Charles Gairdner Hospital and the Fiona Stanley Hospital, in particular, their respiratory departments. In addition, we acknowledge our partnerships with Perth based universities including Curtin University, Murdoch University and the University of Notre Dame. From a community aspect, the Institute gratefully acknowledges the support of the Melbourne Cup Luncheon Committee and the Conquer Cystic Fibrosis Committee and their individual member-volunteers who work tirelessly to raise funds to support research in the Institute. In addition, the Institute acknowledges a donation for the acquisition of several pieces of laboratory equipment. These funds were raised from the proceeds of the annual NAVRANG event. The donation was made to honour the memory of one of NAVRANG's founding members 'Mrs Taraben (Diwaliben) Vallabhdas Davdra' who passed away from idiopathic pulmonary fibrosis 12 months ago.

Last but not least, the Institute would like to acknowledge the not-for-profit Westcare Inc. for their support and generosity over the last seven years. This partnership has resulted in a large donation, which has helped fund basic and applied research on infectious diseases associated with the respiratory system.

Our community support arm, L I F E continued to offer both fellowship and information to people living with chronic lung conditions. We are grateful to Dr Jenni Ibrahim, the Coordinator of L I F E who, despite being diagnosed with a serious illness in 2017, provided wonderful support to the community. With this in mind, the group took steps to develop a succession plan so that L I F E can continue to thrive into the future. This included devoting time at each meeting to progress the planning and succession process as well as a special workshop scheduled for early 2018.

Finally, I would like to thank our research and administrative staff, our collaborators, our community members and our donors for their continued support in helping us move towards achieving our goal - to improve the life of everyone living with a respiratory condition.

BOARD OF DIRECTORS



Chair Mr Peter Gunzburg B Com

Non-Executive Chairman of Bard1 Ltd



Deputy Chair Prof George Yeoh BSc PhD

(UWA appointed representative) Head of Liver Disease and Carcinogenesis Unit, Centre for Medical Research, University of Western Australia



Treasurer Craig McGown B Com

Director, New Holland Capital Pty Limited



Secretary Mr Johnson Kitto LLB

Managing Partner of Kitto & Kitto, Barristers & Solicitors



Ms Sue Morey OAM FRCNA

Nurse Practitioner in Respiratory Medicine, Sir Charles Gairdner Hospital Board of Directors Westcare Inc



BOARD OF DIRECTORS



Prof Geoff Laurent BSc PhD FRCP(Hon) FRCPath FMedSci

Director, Institute for Respiratory Health (Jan-May 2017) Honorary Fellow, UWA Honorary Fellow, University College London



A/Prof Cecilia Prêle BSc (Hons), PhD

(Staff representative) Head of Tissue Repair Group, Institute for Respiratory Health



Prof Gary Lee MBChB, PhD, FRACP, FRCP, FCCP

Respiratory Specialist, Sir Charles Gairdner Hospital Head of Pleural Medicine Unit, Institute for Respiratory Health



Prof Geoff Stewart BSc PhD

Director Institute for Respiratory Health (Jun - Current) Chair of Scientific Sub-Committee

SUB-COMMITTEES OF THE BOARD

Finance

Mr Peter Gunzburg (Chair) Mr Craig McGown

Scientific

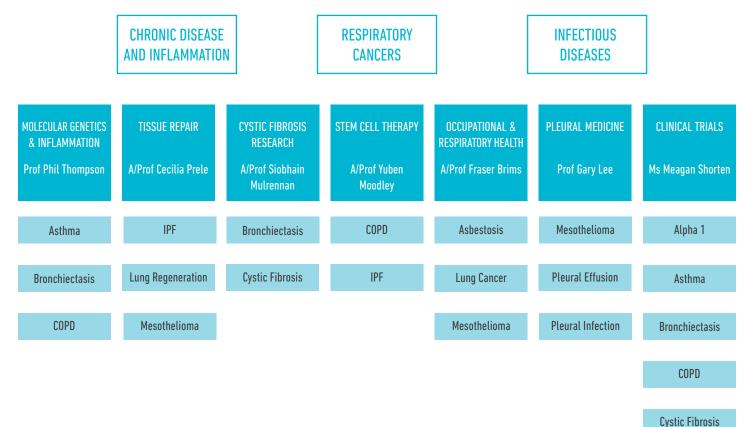
Prof Geoff Stewart (Chair) Prof Peter Eastwood Prof Robyn O'Hehir* Prof Stephen Holgate* **Conquer CF Advisory Committee**

Prof Gary Lee (Chair) Prof Scott Bell* Prof Grant Waterer*

*External to the Institute for Respiratory Health

OUR RESEARCH UNITS

The Institute advocates and practices research into a broard spectrum of respiratory conditions which are either scientifically or clinically focused. These projects are funded through a number of grants, collaborations and donations. We conduct innovative scientific and clinical research into chronic disease and inflammation, respiratory cancers and infectious diseases.





RESEARCH PROJECTS 2017

RESEARCH FOCUS 1: CHRONIC DISEASES AND INFLAMMATION

ASBESTOSIS

IT IS KNOWN THAT PEOPLE WHO HAVE BEEN EXPOSED TO ASBESTOS HAVE A GREATER CHANCE (BUT STILL A SMALL ONE) OF DEVELOPING CANCER OF THE LUNG AND MESOTHELIOMA (CANCER OF THE LINING OF THE LUNG). AT PRESENT, THE ONLY KNOWN ACTIONS THAT CAN BE TAKEN TO REDUCE THESE RISKS ARE TO STOP SMOKING AND AVOID FURTHER CONTACT WITH ASBESTOS.

THE ASBESTOS REVIEW PROGRAM (ARP)

The Occupational & Respiratory Health Group is part of the ARP; a dedicated clinic that follows up with people who have worked with, or who have had significant exposure to asbestos. The clinic specialise in dealing with asbestos related lung diseases and arrange annual health check-ups using breathing tests, blood tests and the latest CT scan technology. The careful use of a low-dose CT scan of the chest can identify lung cancer at an early stage when it is potentially curable, and the ARP offers this test. The centre also has many years of experience in dealing with other lung diseases that asbestos exposure can cause.



Asthma

IS A COMMON RESPIRATORY CONDITION WHERE THE MUSCLES AROUND THE WALLS OF THE AIRWAYS TIGHTEN DUE TO AN ASTHMATIC TRIGGER. THIS MAKES THE PASSAGEWAY NARROWER AND THE LINING OF THE AIRWAYS BECOMES INFLAMED AND START TO SWELL. SOMETIMES MUCUS ALSO BUILDS UP WHICH CAN MAKE THE AIRWAYS MORE NARROW.

CLININCAL TRIALS

The Clinical Trials Unit was involved in a number of studies trialling new medications to treat the different sub-types of asthma which included:

- The use of an auto-injector for the subcutaneous administration of mepolizumab in people with severe asthma. The study closed at the end of 2017 and is now in an evaluation phase.
- A study that compared triple therapy inhalers indacaterol, glycopyrronium and mometasone, with a double therapy inhaler of indacaterol and mometasone. The aim of the study was to determine which inhaler provides better relief of asthma symptoms and improves lung function in asthma patients. The study closed during 2017 and is now in an evaluation phase.
- A phase 2 study assessed the oral corticosteroid-sparing effect of subcutaneous lebrikizumab in patients with severe corticosteroid dependent asthma. The study closed during 2017 and is now in an evaluation phase.
- A phase 3 open label trial evaluated the safety and efficacy of mepolizumab given to patients with severe asthma. The medication was given on a monthly basis by injection and aimed at targeting the IL-5 receptor. The study closed during 2017 and is now in an evaluation phase.
- A study to assess how well benralizumab is tolerated in the long-term for severe asthma patients, and how the body accepts the medication. The study will close early 2018.

 A study to evaluate the safety, acceptability, and secondarily the effectiveness of dupilumab, in the treatment of moderate to severe uncontrolled asthma. The study will close early 2018.

RESEARCH PROJECTS

THE ROLE OF ALTERNATIVE SPLICING IN LUNG DISEASE

The Molecular Genetics and Inflammation Unit continued a research project on the molecular mechanisms underpinning pro and anti-inflammatory pathways in the lung. The particular focus was the role of alternative splicing in chronic inflammatory lung disease. New therapeutic approaches to treat severe asthma using antisense oligonucleotides continue to be explored.

EPIGENETIC MECHANISMS IN ASTHMA

Epigenetic mechanisms may play an important role in asthma as both are heritable, influenced by the environment, and modified by in utero, environmental exposures, and ageing. It regulates the expression of a large number of wellestablished asthma associated genes. The Molecular Genetics and Inflammation Unit has identified the differences in genes, regulating these processes in mild and severe asthma. This may explain why some people get asthma and what determines its severity.

PATIENT BIOBANK FOR ASTHMA, COPD AND BRONCHIECTASIS

The Molecular Genetics and Inflammation Unit continued to collect a large sample bank of DNA, serum, and RNA samples of patients with airway diseases such as asthma, COPD, and bronchiectasis. These samples are then used in genetics projects to help better understand the pre-disposition of genetic diseases and the development of future therapies.

Alpha 1 - Antitrypsin Deficiency

IS AN INHERITED GENETIC CONDITION WHERE A PERSON HAS LOW BLOOD LEVELS OF A PROTEIN KNOWN AS THE ALPHA-1 ANTITRYPSIN PROTEASE INHIBITOR. ALPHA 1 CAUSES AN INCREASED RISK OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN THE FORM OF EMPHYSEMA.

CLINICAL TRIALS

The Clinical Trials Unit continued an ongoing trial into whether a new study drug is safe and effective in slowing down the progression of lung damage in patients with alpha 1 - antitrypsin deficiency (AATD). The study drug is made from blood plasma donated from humans, and is designed to increase the concentration of AATD in the body and help prevent or reduce lung damage.

BRONCHIECTASIS

IS WHEN THE LUNG BRANCHES KNOWN AS BRONCHI DEMONSTRATE A PERMANENT ABNORMAL WIDENING AND AN INFLAMMATION THAT PREVENTS THE CLEANING OF THE MUCUS IN THE LUNGS. THE MUCUS BUILDS UP AND BACTERIA BEGINS TO GROW WHICH LEADS TO A CYCLE OF REPEATED LUNG INFECTIONS AND BLOCKED AIRWAYS.

CLINICAL TRIALS

The Clinical Trials Unit tested a new inhaled antibiotic treatment targeting bacteria in the airway to help reduce airway inflammation. The study closed during 2017 and is now in an evaluation phase.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Is a progressive chronic lung condition that causes breathlessness and reduced oxygen levels. There are two main types of COPD; Emphysema and Chronic Bronchitis.

CLINICAL TRIALS

The Clinical Trials Unit was involved in a number of studies trialling new medications to help treat COPD. These included:

- A study to compare the effect of four different inhaled COPD medications on the rate of COPD exacerbations for patients who have been diagnosed with moderate to severe COPD. This study is ongoing and will close in 2018.
- A study aimed at evaluating the efficacy and safety of benralizumab in participants with moderate to very severe COPD with a history of COPD exacerbations. The study will close early 2018.
- A phase 3 study on the safety and efficacy of subcutaneous mepolizumab on frequency of exacerbations, targeting the IL-5 Pathway. The study closed during 2017 and is now in an evaluation phase.
- A study to assess the safety and effects of fluticasone furoate, umeclidinium and vilanterol, on preventing COPD exacerbations. The study closed during 2017 and is now in an evaluation phase.

RESEARCH PROJECTS

PROTECTIVE ANTI-BACTERIAL RESPONSES

The Stem Cell Therapy Unit is currently studying the effects of mesenchymal stem cell (MSC) treatment and the role of exosomes on inflammation and immune cells of COPD patients. The aim of this ongoing study of non-typeable haemophilus influenza infection in COPD is to characterize anti-bacterial responses of T-cells and monocytes for patients living with COPD.

T-CELL CO-INHIBITORY RECEPTORS (PD-1, CTLA-4)

The Stem Cell Therapy Unit is investigating the role of Tregs and T-cell co-inhibitory receptors (e.g. PD-1, CTLA-4) in regulating anti-bacterial responses of T-cells and monocytes from patients with COPD. The goal of this project is to compare the expression of inhibitory receptors between acute exacerbations in people with stable COPD and healthy control subjects.

Cystic Fibrosis (CF)

CF IS A GENETIC CONDITION WHERE THERE IS AN ABNORMALITY OF THE MUCOUS GLANDS, THEREFORE CAUSING A THICKENING OF THE MUCUS – THIS CAUSES A BUILD-UP IN THE LUNGS AND OTHER ORGANS CREATING BLOCKAGE OF THE AIRWAYS AND IMPAIRING BREATHING. PEOPLE WITH CF NEED TO UNDERGO CONSTANT TREATMENT IN ORDER TO REMOVE THE EXCESS MUCUS FROM THEIR LUNGS. THE STRESS PLACED ON THE LUNGS RESULTS IN IRREVERSIBLE DAMAGE AND REGULAR INFECTIONS. 1 IN 25 AUSTRALIANS CARRY THE CF GENE.

CLINICAL TRIALS

The Clinical Trials Unit is the only adult CF trials unit in Western Australia conducting phase 2 to 4 studies. The Unit collaborates with the Adult CF team at Sir Charles Gairdner Hospital and offers first class care. During 2017 the Unit carried out the following trials:

- An ongoing trial that aims to evaluate the safety and effects of the combination of VX-661 and ivacaftor in patients with CF.
- A trial that aimed to evaluate whether the study drug GLPG1837 is safe, well-tolerated and effective in improving symptoms of CF. The study will also assess how the body processes the drug. The study closed during 2017 and is now in an evaluation phase.
- A study that evaluated effects of the combination of lumacaftor and ivacaftor on exercise tolerance in participants with CF. The study will close in early 2018.

RESEARCH PROJECTS

MOLECULAR MICROBIOLOGY OF COMPLEX RESPIRATORY INFECTIONS: IN CYSTIC FIBROSIS AND EMPYEMA

The CF Research Group continued a research project on the molecular microbiology of complex respiratory infections. The aim of the project is to provide comprehensive molecular microbiological characterizations of Pseudomonas aeruginosa in CF infection and Streptococcus pneumoniae strains in empyema patients, and assess the clinical utility of the information to help improve patient outcomes. The team has designed and optimised methods needed to conduct the bacterial cultivation work from the sputum samples and have started to collate a patient registry that will house all the relevant clinical and microbiological data.

MOLECULAR EPIDEMIOLOGY OF P. AERUGINOSA STRAINS IN PATIENTS WITH CF ATTENDING THE WA ADULT CF CENTRE AT SIR CHARLES GAIRDNER HOSPITAL

The CF Research Group is conducting a clinical study on the epidemiology of P. aeruginosa bacteria strains in patients with CF attending the WA Adult CF centre at Sir Charles Gairdner Hospital. P. aeruginosa is the most common bacterial pathogen affecting adults with CF. It is easily transmitted from patient to patient and infection control plays an important role in halting cross transmission. At present, systematic surveillance for cross infection is not routinely performed in most CF centres, therefore the efficacy of current infection control guidelines is unknown. This study is assessing the number of patients with bacterial pathogen using established molecular strain typing methods. This will build up local capacity for systematic molecular surveillance of P. aeruginosa strains, as well as establish a comprehensive biobank of bacterial and sputum samples from individuals for future research. Results of this study will provide important information to evaluate and update current infection control policies.

CLOSTRIDIUM DIFFICILE INFECTION IN ADULT PATIENTS WITH CF IN WA: DISEASE BURDEN AND CLINICAL IMPACT

The CF Research Group is currently conducting a number of research projects centred around clostridium difficile (C.diff) and the effects this has on CF patients, particularly patients in hospital. C.diff is a bacteria that attacks the stomach and bowel and can have serious consequences for CF patients who are in hospital and have a low immune system. CF patients who have an intense hospitalisation and antibiotic treatment requirement are of particular risk, especially for patients who have undergone a transplant. The team are investigating how many CF patients present with C.diff when in hospital, the impact of antibiotic related diarrhea and the possible use of probiotics against C.diff. The team are also establishing a comprehensive biobank of C. difficile and fecal samples from individuals for future research. The aim of the project is to reduce the health risks to CF patients when in hospital.

GASTROINTESTINAL INFECTION IN CYSTIC FIBROSIS: CLOSTRIDIUM DIFFICILE INFECTION, THE GUT MICROBIOME AND POTENTIAL ROLE OF PROBIOTICS

Patients with CF are often exposed to intensive antibiotics and as a result, can suffer from antibiotic related gastrointestinal complications. Led by Dr Anna Tai, the CF Research Unit is investigating how gastrointestinal infection affects CF patients. Clostridium difficile (C. diff) is a gut bacteria which can cause serious gastrointestinal complications. Patients with CF are at increased risk of being colonised or infected which has potentially significant clinical implications, particularly for patients post lung transplant. The study is investigating the prevalence, molecular epidemiology and clinical impact of C. diff with a view to improving strategies and procedures to prevent and eradicate C. diff in CF patients. The study will also explore the role of gut microbiome and novel strategies in personalised probiotic therapies to optimize treatment for C. diff infection.

EFFECTS OF HIGH INTENSITY INTERVAL TRAINING ON EXERCISE CAPACITY IN PEOPLE WITH CYSTIC FIBROSIS: A RANDOMISED CONTROLLED TRIAL

People living with CF not only have reduced exercise capacity but also have a high daily treatment burden involving medication, nutritional supplementation and airway clearance. For this reason it can be difficult to incorporate exercise into their daily routine. The CF Research Group, led by PhD candidate Abbey Sawyer, are undertaking a randomised controlled trial to investigate the effectiveness of a cycling-based, high intensity interval training (HIIT) program on exercise capacity in people with CF. The HIIT program comprises of 10 minutes of exercise completed three days per week for eight weeks. The aim of this randomised controlled trial is to determine what effects the program has on a person's exercise capacity, health-related quality of life, exercise self-efficacy, feelings of anxiety, depression, enjoyment and muscle oxidative capacity.



IDIOPATHIC PULMONARY FIBROSIS (IPF)

THE WORDS PULMONARY FIBROSIS LITERALLY TRANSLATES TO LUNG SCARRING; THE CONDITION ENCOMPASSES AN ABNORMAL FORMATION OF SCAR TISSUE IN THE LUNGS. THE SCAR TISSUE BUILDS UP IN THE WALLS OF THE AIR SACS KNOWN AS ALVEOLI, AND EVENTUALLY MAKES IT HARD FOR AIR TO PASS THROUGH. PULMONARY FIBROSIS CAN BE MILD, SEVERE OR OFTEN LIFE-THREATENING.

CLINICAL TRIALS

The Clinical Trials Unit continued two study trials for IPF. These included an on-going trial that aimed to evaluate the effect of the study drug CC-90001 on lung function after a period of treatment, and a phase 2 study to assess the efficacy and safety of lebrikizumab.

RESEARCH PROJECTS

The Tissue Repair Group have an extensive programme of research which investigates the cellular and molecular pathways driving IPF. Notably they have received NHMRC project grant funding for the three project listed below.

- STAT3 regulation of cell responses in IPF
- Epithelial-mesenchymal cell communication towards new therapeutic targets for fibrosis
- Fibroblast Scenecence as a driver of pulmonary fibrosis

The cause of IPF is unknown but it is widely accepted that repeated injury to the epithelium leads to dysregulated healing, initiating a cascade of processes resulting in fibroblast / myofibroblast accumulation and overproduction and deposition of collagen. The Tissue Repair Unit continues to pioneer studies in identifying the gp130-induced STAT3 signalling the pathway as pivotal in the development of lung fibrosis. What regulates STAT3-mediate fibrosis is not clear, but current studies are focusing on understanding the role of mediators known to activate the pathway, cell types that may be regulating the mediator response, as well as a possible breakdown in regulation of the naturally occurring inhibitors that normally control the STAT3 response.

Through a local, national and international collaboration, the Unit continues to investigate cross talk between epithelial cells and fibroblasts and the role this plays in the progression and development of fibrosis.

The Tissue Repair Group continue to dissect the molecular mechanisms and cell signalling pathways driving fibrosis, and together with Prof Darryl Knight at the University of Newcastle are investigating mitochondrial dysfunction in IPF

PATIENT BIOBANK FOR IPF

The Stem Cell Therapy Unit in collaboration with the Molecular Genetics and Inflammation Unit continued to manage the National biobank for IPF. Researchers collect, process and store samples from IPF patients for an Australiawide collection. This biobank aims to enrol all Australians with IPF so that the data collected can help researchers learn more about this serious disorder.

A/Prof Yuben Moodley and the Molecular Genetics and Inflammation Unit are also exploring the bio-markers for IPF. Using the samples collected in the IPF biobank, they are examining the protein and RNA signatures of the disease progression.

The Tissue Repair and Molecular Genetics and Inflammation Units continued to collaborate on the genetic analysis of IPF samples, with an aim of exploring the mechanisms in the development of IPF.

LUNG REGENERATION

THE ABILITY OF TISSUE IS HIGHLY VARIABLE ACROSS SPECIES WITH MANY AMPHIBIANS REGENERATING TAILS, LIMBS AND EVEN EYES. IN HUMANS THIS CAPACITY IS MORE LIMITED, ALTHOUGH THIS VARIES FROM ONE TISSUE TO ANOTHER. THE LUNG'S REGENERATIVE CAPACITY IS NOW RECOGNISED TO BE MUCH MORE RAPID THAN PREVIOUSLY THOUGHT EVEN IN THE ADULT HUMAN.



RESEARCH PROJECT

ASSESSING THE CAPACITY FOR ADULT LUNG REGENERATION

The Tissue Repair Group are seeking to understand what conditions are necessary to grow new lung tissue so that a patient has a better quality of life.

Researchers have developed an animal model of compensatory lung growth following surgery. This model mimics the compensatory lung growth that has been described to occur in human children, and rarely in adults.

Following the surgical removal of a complete left lung, the right lung undergoes rapid growth and reaches a similar weight and volume to that of two normal lungs by 21 days post-surgery.

The Group is monitoring the changes associated with compensatory growth using a combination of genetic, histological, functional and longitudinally using micro CT imaging.

Understanding the mechanisms of lung growth and its capacity in humans will open up transformational research programs that may allow us to cure chronic lung diseases that are currently seen as untreatable.





RESEARCH FOCUS 2: RESPIRATORY CANCER

LUNG CANCER

Lung cancer develops when cells become abnormal and grow out of control in one or both of a person's lungs. It is the world's most lethal cancer. In healthy lungs, normal lung tissue cells reproduce and develop into healthy lung tissue. With lung cancer, abnormal cells reproduce rapidly and never grow into normal lung tissue. Lumps of cancer cells form tumours which disrupt the functioning of the lung.

INTERNATIONAL LUNG SCREEN TRIAL (ILST)

The Occupational & Respiratory Health Group is part of the ILST, a large international study that plans to recruit more than 4,000 participants - with 2000 coming from Australia, 500 of which from Perth. Other centres in Australia include Brisbane, Sydney and Melbourne. The aim of the study is to understand the best way of choosing high risk people for lung cancer screening, and also the best way of following up with repeat CT scans. There are a number of sub-studies from ILST, including our own in WA examining the best way to recruit people into a lung cancer screening program.

Mesothelioma

MESOTHELIOMA IS A TYPE OF CANCER IN THE FORM OF A TUMOR THAT BEGINS FORMATION IN THE PROTECTIVE LINING/MEMBRANE OF VARIOUS INTERNAL ORGANS KNOWN AS THE MESOTHELIUM. THE MESOTHELIUM LINES PRIMARILY THE LUNGS, HEART AND ABDOMINAL CAVITY.

CLINICAL TRIALS

FGF RECEPTOR ANTAGONIST IN MESOTHELIOMA (FRAME) STUDY

Prof Gary Lee led the first phase II clinical trial (FRAME study) targeting the FGF-9 gene in mesothelioma patients. Researchers at the Institute have shown that mesothelioma may be treated by blocking a growth pathway of the FGF-9 molecule which is a key driver of the cancer. The clinical trial will enrol patients who have had previous standard chemotherapy treatment, and will explore whether this new treatment, given twice daily as a tablet, can delay tumour progression, shrink the tumour, and do so safely.

CLINICAL TRIALS

LUNGSCREEN WA PROJECT

When lung cancer is caught at an early stage, it is potentially curable. Results from previous studies have shown that there is great promise in screening for early lung cancer using low dose CT scans, yet there are many questions that need answers before it will be adopted more widely.

Over the past two years the Occupational & Respiratory Health Group ran a pilot project to better understand some of the challenges for screening for early lung cancer using lowdose CT (LDCT) scanning.

All the scans were performed in community radiology centres and tested different ways of choosing who is at risk of lung cancer, and therefore who should get a LDCT. The group also tested a different way of following up repeat CT scans using a protocol to guide decisions. The results of this study will help inform policy making within Western Australia and Australia.

NUTRITIONAL STATUS IN MESOTHELIOMA

Malnutrition and sarcopenia (loss of skeletal muscle mass and strength due to ageing) have been shown to significantly affect survival, quality of life and physical functioning in other cancers. However, there is little information on their role in mesothelioma. Dr Carolyn McIntyre and Emily Jeffery lead a study in collaboration with the Pleural Medicine Unit to identify the incidence, progression, consequences and mediators of malnutrition and sarcopenia in mesothelioma.

EXERCISE AS A THERAPEUTIC TOOL IN THE MANAGEMENT OF MESOTHELIOMA

Patients with mesothelioma often suffer with muscle loss, tiredness, poor quality of life and are often unable to do daily tasks. Exercise has been shown to be very effective in improving the health of patients with lung and other types of cancer. Until now there has been no study examining how appropriately tailored exercise could reduce functional decline, and provide a non-invasive supportive intervention for those with malignant pleural disease. Dr Carolyn McIntyre in collaboration with the Pleural Medicine Unit aims to improve outcomes for patients with mesothelioma through the application of exercise. The results of this work will be used to develop and implement clinical exercise programs to improve their functional levels, improve their fitness and therefore have a better quality of life, and better withstand any effects of chemotherapy.

EFFECTS OF EARLY PALLIATIVE CARE FOR PATIENTS WITH MESOTHELIOMA (RESPECT-MESO)

Occupational & Respiratory Health Group, led by A/Prof Fraser Brims, conducted a randomised study examining the effects of early palliative care for patients with mesothelioma. The aim of the project was to determine whether a patient's quality of life is improved with the addition of regular early palliative care, in addition to all normal care provided.

RESEARCH PROJECTS

THE ROLE OF FIBROBLAST GROWTH FACTOR 9 (FGF-9) – ON THE BODY'S NATURAL IMMUNE RESPONSE TO MESOTHELIOMA

Led by Dr Sally Lansley, the Pleural Medicine Unit continued their research into the effect fibroblast growth factor 9 (FGF9) has on the body's immune response to mesothelioma. FGF9 is a molecule that has been identified as a key driver of mesothelioma cancer as it reduces the body's natural antitumour response. While anti-FGF9 drugs can reduce tumour size, once treatment ends the tumour then returns. The Unit's research project is examining how FGF9 affects the immune system in order to improve the effectiveness of anti-FGF9 treatment. The aim of the project is to develop new and more effective treatment for people with mesothelioma.



MONOCYTE CHEMOATTRACTANT PROTEIN-1 (MCP-1)

Led by Dr Sally Lansley, the Pleural Medicine Unit continued to investigate the role of monocyte chemoattractant protein-1 (MCP-1) in the development of pleural effusions from a variety of etiologies using clinical and pre-clinical models. The study has identified the role of MCP-1 as a key mediator in tissue plasminogen activator–induced exudative pleural fluid formation and benign pleural effusion in clinical samples and pre-clinical models. MCP-1 represents a potential therapeutic target for the control of exudative pleural effusions in a variety of pleural diseases. The Unit is now determining the effect of MCP-1 blockade in pleural effusions associated with mesothelioma.

ROLES OF MALIGNANT PLEURAL FLUID IN MESOTHELIOMA

Led by PhD student Hui Min Cheah, the Pleural Disease Unit set out to challenge the conventional belief that the malignant effusion is a by-product of pleural cancers, and has a significant impact on clinical care strategies. During the study, the team aimed to determine why MPM stimulates the production of such large volumes of fluid, and that the malignant pleural fluid produced by MPM can significantly enhance tumour cell proliferation, migration, and invasion. The project also explored the formation of malignant effusion as part of a biological programme by which MPM facilitates its own growth and spread.

MIRNAS IN MESOTHELIOMA

Limited treatment options in Mesothelioma lead to a short median survival and clinical management is hampered by the lack of molecular biomarkers for diagnosis/ prognosis. There is growing evidence that short noncoding RNAs such as microRNA (miRNA), are useful biomarkers in cancer. Studies performed by the Tissue Repair Unit are trying to determine the diagnostic and prognostic potential of miRNAs in serum and pleural effusion fluids and cells from patients with mesothelioma compared with other diseases. The Unit also worked on a project seeking to determine if differentially expressed serum miRNAs are early disease markers. miRNA also have important biological roles within cells, so the Tissue Repair Unit are also looking at the biological significance of certain miRNAs in mesothelioma.

THE HEDGEHOG SIGNALLING PATHWAY IN MESOTHELIOMA

Increasing evidence is pointing to the reactivation and aberrant expression of developmental signalling pathways, such as the hedgehog (Hh) pathway, as critical to the pathogenesis of certain cancers. The Tissue Repair Unit have undertaken a study which demonstrated that Hh pathway signalling is important in the growth of mesothelioma, and are examining different antagonists to identify the best possible therapeutic approach to inhibit mesothelioma growth and to elucidate the mechanisms the Hh pathway uses to promote tumour growth.



PLEURAL EFFUSION

PLEURAL EFFUSION IS WHEN AN ABNORMAL AMOUNT OF FLUID ACCUMULATES BETWEEN THE THIN LAYERS OF TISSUE LINING THE OUTSIDE OF THE LUNG AND THE WALL OF THE CHEST CAVITY (THE PLEURA). WHEN AN EXCESSIVE AMOUNT OF FLUID IS COLLECTED, IT CAN SEVERELY IMPAIR BREATHING ON A MASSIVE SCALE AS THE LUNGS ARE LIMITED FROM EXPANDING DURING VENTILATION.

CLINICAL TRIALS

PLEURAL EFFUSION AND SYMPTOM EVALUATION STUDY (PLEASE)

Breathlessness is the most common symptom of pleural effusion and a frequent reason for pleural drainage. However, improvement in breathlessness following drainage of the effusion is variable, with some patients experiencing either no benefit or worsening of their symptoms. The mechanisms underpinning breathlessness in patients with pleural effusions are poorly understood. Led by Prof Gary Lee, the Pleural Medicine Unit continued the PLEASE study, which is a prospective study of 100 patients with symptomatic pleural effusions that require therapeutic drainage. The aim of the trial is to identify key factors that underlie breathlessness for pleural effusion patients and develop predictors of improvement following effusion drainage.



MALIGNANT PLEURAL EFFUSION (MPE)

MALIGNANT PLEURAL EFFUSION IS A CONDITION IN WHICH CANCER CAUSES AN ABNORMAL AMOUNT OF FLUID TO COLLECT IN THE PLEURA.

CLINICAL TRIALS

THE AUSTRALASIAN MALIGNANT PLEURAL EFFUSION TRIAL (AMPLE-2)

The Pleural Medicine Unit led the Australasian Malignant Pleural Effusion Trial-2 (AMPLE-2) investing the use of indwelling pleural catheters (IPCs). The trial was a multicentre open-labelled randomised study where patients were randomised into either aggressive (daily) or symptom guided drainage regimes after IPC insertion. The aim of the AMPLE-2 was to determine which regime is superior in improving clinical outcomes. The study also addressed urgent and practical questions pertinent to the care of MPE, and the results will provide useful information in guiding clinical practice. The trial was completed at the end of 2017 and involved centres in Australia, New Zealand, Malaysia and Hong Kong with results being published in 2018. An AMPLE-3 trial will commence mid-2018.

IMPROVING FLUID REMOVAL METHODS TO OPTIMISE BENEFITS IN PATIENTS WITH CANCER-RELATED FLUID COLLECTION IN THE CHEST

Key questions remain about the role indwelling pleural catheters play in managing MPE. In this research study, the Pleural Diseases Unit, led by Dr Rajesh Thomas, aim to compare standard treatments of MPE with indwelling pleural catheters, and to see if hospital care days are reduced and to assess whether drainage improves breathlessness. The project will also identify key factors that will help predict which patients respond to fluid drainage with reduced breathlessness. The results will help guide doctors in tailoring the best treatment for cancer effusion according to the patient.

RESEARCH FOCUS 3: RESPIRATORY INFECTION

PLEURAL INFECTION

Pleural infection within the pleural cavity is a common and an increasing clinical problem, especially in the elderly and in childhood. Bacteria in the pleural space can lead to pleural effusion and/or pus.

CLINICAL TRIALS

ADAPT PROJECT

The Pleural Medicine Unit, led by PhD candidate Natalia Popowicz, conducted an ADAPT pilot study recruiting patients from Australia, the United Kingdom, and New Zealand. The aim of the study was to assess the efficacy and safety of a reduced starting dose regimen of 5 mg of tPA with 5 mg of DNase administered intrapleurally for managing patients with pleural infection. The pilot data suggested this starting dose is safe and effective. The information from the study will be used for future trials.

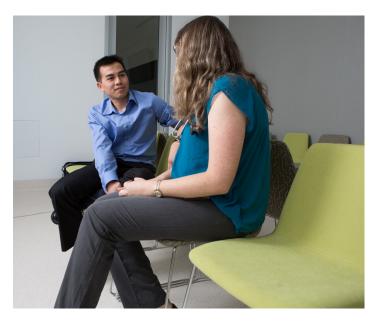
RESEARCH PROJECTS

NOVEL PHARMACOLOGICAL THERAPY FOR PLEURAL INFECTION

The Pleural Medicine Unit have developed a new tazocin assay, the most common antibiotic in respiratory infections, which will now allow research to measure antibiotics concentrations in pleural fluids during infection.

BACTERIAL GROWTH IN PLEURAL FLUID

The Pleural Medicine Unit continued to examine the effects of common bacteria in pleural infection and their biological effects on pleural mesothelium in vitro and in vivo. Led by PhD candidate, Natalia Popowicz, the team has identified key mediators governing the development of pleural infection and provided proof of concept data that antagonising these mediators can reduce bacterial invasion of the pleural cavity. These findings can potentially lead to new therapeutic approaches.





CLINICAL TRIALS

All of today's standard treatments for respiratory conditions are a result of clinical trials. The trials are completed over years of testing. The Institute's Clinical Trials Unit is the largest respiratory trials clinic in Australia, and some of today's medication has been the result of trials being conducted within the clinic.

In 2017, the Unit conducted 24 studies with 278 patients coming in for screening and 246 randomised across all studies. The trials are sponsored by a range of Australian and international pharmaceutical and biotech companies as well as some grant funding. During 2017 the Institute conducted trials for:

- Asthma
- Alpha 1-antitrypsin deficiency
- Bronchiectasis
- Chronic obstructive pulmonary disorder (COPD)
- Cystic fibrosis (CF)
- Idiopathic pulmonary fibrosis (IPF)
- Pulmonary Arterial Hypertension

The Clinical Trials Unit is made up of consultants, doctors, registered nurses and health science professionals. Patients are closely monitored, with regular health checks in the clinic. The Unit has a collaborative relationship with:

- Dr Martin Philips for asthma, COPD bronchiectasis, alpha 1-antitrypsin deficiency and IPF trials.
- A/Prof Siobhain Mulrennan for CF trials.
- A/Prof Yuben Moodley for asthma and COPD trials.
- Dr Anna Tai for CF and COPD trials
- Prof Fiona Lake for alpha 1-antitrypsin deficiency and IPF trials
- A/Prof Eli Gabbay on a study looking at people with Systemic Sclerosis-Related Pulmonary Arterial Hypertension.
- Prof Joe Hung, on a study to assess whether the pneumococcal vaccination protects against cardiovascular disease.



L I F E GROUP

Over the past year L I F E held 10 regular meetings on the first Wednesday of the month, as well as an annual Christmas party. Guest speakers included; Dr Peter Franklin, Tina Phan, Dr Anna Tai, Nola Cecins, Stephani Johnston, Arthur Harvey, Di Rosman

and Dr Bob Ziegler. The varied topics ranged from pulmonary rehabilitation, gut biome, depression, astronomy, medication reviews and indoor air pollution. LIFE also gathered for a social lunch in the community each season.

L I F E were presented with the Live it Forward together (LIFt) award from ConnectGroups, the peak body for support groups in WA. They won the award for reaching out to other respiratory support groups, to develop and host the Lung Leaders Network, enabling leaders to share ideas, information, skills and resources with each other. This included information about chronic condition self-management which can benefit group members.

The group held three 'Letter to My Lungs' workshops based on the work of Elspeth Penny: at a L I F E monthly meeting L I F E, with the Lung Leaders Network and with the sister group, Pulmonary Hypertension Australia Network. The results showed the varied ways people living with lung conditions relate to their respiratory system.

Throughout 2017, L I F E responded to many enquiries from people seeking information about living with lung conditions and sent get well and birthday cards to members through their card club. A working bee of L I F E members continued to assist the Institute's Clinical



Jenni Ibrahim and Pip Brennan, Executive Director of the Health Consumers Council

Trials Unit by sorting out medical kits and making up patient files every month or two. The quarterly Breath of L I F E magazine was posted or emailed to members and additional copies distributed to waiting areas within SCGH. It is also available online from the Institute's website.



PARTNERSHIPS

CONQUER CYSTIC FIBROSIS

Commencing in 2016, Conquer Cystic Fibrosis made the pledge of donating \$200,000 each year over five years, towards developing an adult CF research program here in WA. Coupled with the Institute's own contribution to support research, the new partnership has seen the implementation of the Conquer CF Research

Program.

Conquer Cystic Fibrosis are a dedicated group of volunteers whose goal is to increase awareness of CF and to raise funds to help support services, treatments and research in the hope of improving life expectancy, and ultimately, finding a cure for children and friends with CF. Just like the Melbourne Cup Committee, no-one at Conquer Cystic Fibrosis is paid.

The research program has established a number of scholarships, which will help create CF researchers for the future, supported seed funding for research projects and is looking at collaborative projects within the CF research community.



Sue Morey with Conquer CF Committee

WESTCARE INC.

The Institute and Westcare Inc. formed a partnership based upon a common interest in lung disease and its continuing impact on the community. Through this partnership, the Alan King Westcare Grant was established. Dr King was a pioneering West Australian respiratory physician who was instrumental in establishing Westcare Inc.

Thanks to a bequest, Westcare Inc. has contributed \$350,000 towards research into infectious diseases over the past seven years.

Westcare Inc. has supported the Institute in its aim of improving our understanding of the pathology, epidemiology



and treatment of infectious lung diseases, the ultimate goal of which is to reduce their burden on society.

MELBOURNE CUP COMMITTEE

In 2017 the Melbourne Cup Luncheon celebrated its 15th year. The event is held at the State Reception Centre at Fraser's, King Park, with over 300 guests in attendance.

The event is run by a small group of passionate volunteers. No one is paid and everything besides the discounted food Fraser's provide is either sponsored, gifted, begged for or borrowed.

For the past seven years the luncheon has raised over \$380,000 with 100% of the funds going into the Glenn Brown Memorial Grant.

Janeine Thomas and the MC Committee, (Helen De Brito, Suzanne Sheridan, Alison Harvie, Anastazja Gorecki and Sarah Cermak) set aside countless hours in planning, preparing and delivering a unique and memorable experience.



Images: Top, E/Prof with John Mitchell, Westcare CEO. Below, Sue Morey with Janeine Thomas, MCC



RESEARCH EVENTS

ALAN JAMES LUNG CLUB

Dr Anna Tai, Sir Charles Gairdner Hospital "Microevolution of antimicrobial resistance of Pseudomonas aeruginosa in cystic fibrosis"

Dr Joanne Gardner, Curtin University "Aging and mesothelioma induce increased expression of inhibitory molecules on dendritic cells"

Samuel Montgomery, Telethon Kids Institute "Elevated IL-1a in paediatric cystic fibrosis airways is associated with neutrophil influx, inflammation and structural lung disease"

A/Prof Steve Mutsaers, Institute for Respiratory Health "Splattered Hedgehogs to Treat Malignant Mesothelioma" Dr Sally Lansley Institute for Respiratory Health "(Pleural) Space: The final frontier" Dr Kim Birnie, Institute for Respiratory Health "Targeting small non-coding RNA to improve diagnostic and therapeutic strategies for malignant mesothelioma"

Rachael Zemek, National Centre of Asbestos Related Diseases "Responders versus non-responders: What immunological events determine cancer regression after immune checkpoint blockade?"

Kimberley Wang, Telethon Kids Institute "Sex dependent effects on airway responsiveness of maternal hypoxia-induced intrauterine growth restricted mice"

Thomas losifidis, Telethon Kids Institute "Identifying a novel therapeutic strategy for asthma: Targeting airway epithelial cell restitution"

MESOTHELIOMA SYMPOSIUM

A/Prof Steven Mutsaers, Institute for Respiratory Health "Gant61 as a novel Therapy for Mesothelioma"

Dr W Joost Lesterhuis, National Centre of Asbestos Related Diseases

"Novel treatments for mesothelioma - immunotherapy meets systems biology"

Dr Alistair Cook, National Centre of Asbestos Related Diseases "Exploiting the abscopal effect using immunotherapy in a mouse model of mesothelioma"

Dr Sally Lansley, Institute for Respiratory Health "Pleural (space) the final frontier"

Prof Jenette Creaney, National Centre of Asbestos Related Diseases "Neo-antigen responses in mesothelioma"

A/Prof Delia Nelson CHIRI, CURTIN "Mesothelioma and ageing adaptive immunity"

Scott Fisher, National Centre of Asbestos Related Diseases "Mesothelioma in the mouse: immunotherapy and the MexTAg Collaborative Cross"

Kim Birnie, Institute for Respiratory Health "Small non-coding RNA in malignant mesothelioma"

Prof Sam Janes, UCLH "A novel biomarker for TRAIL therapy in MM"

VISITING SPEAKERS

Dr John Blakey, Royal Liverpool Hospital "Assessment of Future Risk in Asthma: Opportunities and New Technologies"

Prof William Cookson, Imperial College London "What causes asthma? Genes, infections, and therapeutic choices"

A/Professor Loïc Guillot, Cystic Fibrosis: Phenogenomics and Physiopathology, Saint Antoine Research Centre, France "New targets in Cystic Fibrosis: Study of CF modifiers genes"

SPONSORS

GSK





COMMUNITY SUPPORT

MEMBERSHIP

The Institute for Respiratory Health continues to enjoy the strong support of its members, who comprise of individuals from the scientific / medical sector, as well as the broader community, students and the corporate sector.

Members are kept up-to-date on respiratory research, collaborations and clinical trials news via e-newsletters, social media posts, event invitations and the Breath of L I F E magazine.

Membership is open to all, reflecting the Institute's desire to be a transparent and accountable organisation, serving the needs of those who support it and aiming to be of value to as broad a group of people as possible.

Staff at the Institute recognise the contribution members make to furthering respiratory research, and would especially like to thank Turner Freeman Lawyers for their on-going support.



FUNDRAISING

The staff at the Institute for Respiratory Health would like to thank everyone who fundraised during 2017.

CONQUER CYSTIC FIBROSIS

Conquer Cystic Fibrosis ran numberous fundraising events throughout 2017, including the Conquer CF Ball. Money raised goes towards the Conquer CF Research Program where the committee has pledged \$200,000 per year over five years.

MELBOURNE CUP LUNCHEON

This year's Melbourne Cup Luncheon raised over \$45,000 for cystic fibrosis. While the emphasis of the day is fun, laughter, and entertainment, we took the time to consider the purpose of the event. Guest speaker Dr Ingrid Laing, a respiratory researcher at the Telethon Kids Institute, inspired guests as she spoke of her life with cystic fibrosis and how through her research, she strives to make a difference for children living with CF.

NAVRANG 2017 FESTIVAL

The musical band Sweet Melodies donated a microscope and centrifuge for the Institute's laboratory. The donation was made from the proceeds of the annual NAVRANG event which celebrates the Hindu religious occasion of Navratri. The event was held at the HBF Arena over four nights. The donation was also in memory of one of NAVRANG's founding members 'Mrs. Taraben (Diwaliben) Vallabhdas Davdra' who passed away from Pulmonary Fibrosis (IPF) 12 months ago. The Institute was honoured to be part of the Sweet Melodies' NAVRANG 2017 event.

FAMILY MUSIC NIGHT

Bringing in the new year, the Price family hosted a night of music and festivities with donations going towards research into pulmonary fibrosis.

BIRTHDAY CELEBRATIONS

Cassie celebrated her 18th birthday by asking friends and family to give a gift towards research for cystic fibrosis research.

HBF RUN FOR A REASON

Team Lung Busters came in strong for the 2017 HBF Run for a Reason. Together they raised over \$6,000. A sincere thank you goes out to sto all who took part.

MOVIE FUNDRAISER

Over 80 people attended a movie fundraiser night at Cygnet Cinema in May. Proceeds from the night went towards the fundraising efforts of Team Lung Busters.

CAKE STALL

Mrs Brown fundraised for COPD research and clinical trials by hosting a coffee morning and running a cake and craft stall.



DONORS

2017 saw the Board establish a Board fundraising initiative; raising funds to help future leaders in respiratory health. Members and supporters once again contributed towards the Institute's annual appeals. The appeals saw stories from Cosimo (page 4) and Peter (page 33) who shared their story of living with a chronic lung condition. A special thank you also goes to the families who have supported the Institute through the memory of a loved one.

VOLUNTEERING

The Institute is grateful to all the volunteers that have offered the gift of time during 2017. This has included helping out at an event, volunteering professional skills, assembling patient files, taking photos, producing videos and, an endless array of administrative duties.

A big thank you goes out to the following people for their support during 2017.

FUNDRAISERS

Cassie's Birthday Conquer Cystic Fibrosis Melbourne Cup Committee Sweet Melodies Staff at St John of God Subiaco Hospital, Ivy Suite The Price Family

TEAM LUNG BUSTERS

F Austin B Austin L Barrett K Birnie C Byatt K Byatt L Byatt A Cermak C Cermak S Cermak F Kelsall M Kelsall A Lucas T Miles S Mutsaers T Phan C Prêle E Stevens J Whetstone L Whetstone

DONORS

J Bond Cowaramup Lions Club P Gunzburg P Gunzburg M Hall R Lockwood C McGown D Miller M Montgomery Westcare Inc. DONORS M Agnew S Akslen P&K Barnett R Bickerton D&S Birnie B Blaikie G Bovell K Chenev S Clark J Clearv J Clinton A Costa S Costanzo G Cruickshank R Cullen W Darby D Dawson P Dav L de Sarionv V Di Tullio & Monaco C Dimasi J Dodd

C Dransfield D Dransfield R Drew M&R Flias M Fedele B Fitzgerald R Fitzgerald C Gee N Grimes B Hawson P Havne C Heath F Hills R&I Hinwood P Hodae I Hodason J Ibrahim C Jones J Keane J&H Keogh V Kitt M Kormendy G Llovd

P&M Long D&D Lonsdale J Maiorana P Martin G McLeod M&T McLoughlin **B** Miller S Mitchell S Mitchell I Mitchell S Mondello M Morris T Murnane A Murrav C Papanastasiou G Paust G Perrella M&R Philip G Potter K Punch A Purser P Reynolds W Ridley J Rinaldi W&R Robinson A Rodrigo M Ryan I Saunders C Schipp M Scott M&J Sebbes E Sharp C&A Skewes A Smith R Taylor J&H Teague P Thomson G Warner E Wells

P&S White T&A White J Whitwell G Wild J Winfield J Wright K Zongaro-Robich

IN MEMORY OF

S Gifford W Treadgold

VOLUNTEERS

F Austin K Birnie R Catterson H Cheah K Coveney L Fast S Gan A Gorecki A Harvey E Horne J Ibrahim J Kenna LIFE Busy Bee Helpers K Johnson K Morozumi V Palm A Presser S Presser V Robins E Stevens A Res C Ullrich G Underwood







PETER'S STORY

LIVING WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

My name is Peter, I'm 81 years old and was diagnosed with chronic obstructive pulmonary disease (COPD) about ten years ago.

My symptoms started with shortness of breath and low energy levels. I was having trouble doing the things I enjoyed; like running around Lake Monger and taking part in the City to Surf. It was soon after this that I was diagnosed with COPD.

Although I gave up smoking 37 years ago, the damage was already done, but not felt until many years later. If you have symptoms like mine, please go see your GP.

I first came in contact with the Institute when I saw an advert in the paper regarding a clinical trial for COPD. I am now taking part in an observational research study which aims to better understand the underlying causes of COPD in order to help support future treatments. I would really encourage anyone with a lung condition to take part in a clinical trial. The staff are so lovely, they really look after you well.

My final message is – if you want to have letters after your name like me, Peter Thomson C.O.P.D, carry on smoking. If you'd rather not, please get help and quit. It's worth it.

Thank you, Peter





GRANTS & SCHOLARSHIPS

WINNERS FOR 2017

We are grateful to Westcare Inc, the Melbourne Cup Committee and Conquer Cystic Fibrosis for helping to fund specific areas of respiratory research. The grants and scholarships are administered by independent, voluntary scientific committees which select the winners.

ALAN KING WESTCARE GRANT

Professor Steve Mutsaers, Institute for Respiratory Health Research project: The effects of infection on mesothelial gene transcription: A role for immune check point regulation in chronic disease

GLENN BROWN MEMORIAL GRANT

Professor Fergal O'Gara, Human Microbiome Programme, Curtin University and Telethon Kids Institute Research project: A Pilot Study in young CF children to determine if early intervention with Azithromycin can control bile induced pathogen establishment

CONQUER CF RESEARCH PROGRAM PHD CANDIDATE

Naomi Chapman, Curtin University

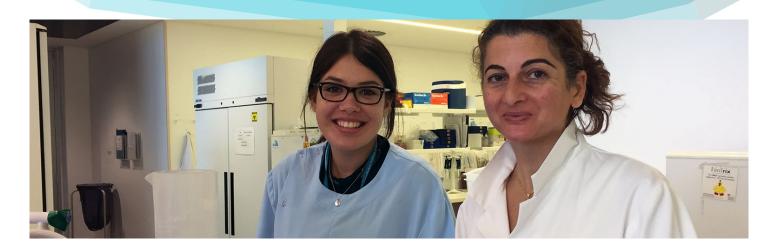
Research project: The effect of the Metaneb® System in the adults with cystic fibrosis when used in conjunction with usual airway clearance techniques (ACT) on lung clearance, lung mechanics and airflow limitation during periods of clinical stability and hospitalisation



Prof Steve Mutsaers with John Mitchell, Westcare CEO



Prof Fergal O'Gara with Janeine Thomas, Melbourne Cup Committee



EDUCATION INITIATIVES

PHD SCHOLARS

Jesse Armitage, University of Western Australia Research Unit: Stem Cells Project Title: 'The effects of MSC infusion on inflammation and immune regulation in COPD patients' Supervised by: Y Moodley, D Tan

Kimberly Birnie, University of Western Australia Research Unit: Tissue Repair Project title: 'miRNA in Malignant Mesothelioma' Supervised by: SE Mutsaers, CM Prêle, B Badrian, PJ Thompson

Hui Min Cheah, University of Western Australia Research Unit: Pleural Diseases Project Title: 'Biological Activity of Malignant Pleural Effusion in Mesothelioma' Supervised by: YCG Lee

Deirdre Fitzgerald, University of Western Australia Research Unit: Pleural Diseases Clinical Pleural Fellow, MD student Supervised by: YCG Lee **Emily Jeffery,** Edith Cowan University Research Unit: Pleural Diseases Project Title: 'Nutritional status, body composition and the effects of an exercise intervention on patients with malignant pleural mesothelioma' Supervised by: YCG Lee, R Newton

Sanjeevan Muruganadan, University of Western Australia Research Unit: Pleural Diseases Project Title: 'AMPLE-2 and PLEASE study' Supervised by: YCG Lee

Dr Natalia Popowicz, University of Western Australia. Research Unit: Pleural Disease Project Title: 'Novel Pharmacological Therapy for Pleural Infection' Supervised by: YCG Lee

Abbey Sawyer, Curtin University Research Unit: CF Research & Physiotherapy Project Title: 'Effect Of High Intensity Interval Training On Exercise Capacity In People With Cystic Fibrosis: A Randomised Controlled Trial' Supervised by: K Hill, V Cavalheri, S Jenkins

Jamie Wood, Curtin University

Research Unit: CF Research & Physiotherapy Project Title: Cystic fibrosis: Does the integration of Telehealth with usual care improve health related outcomes? Supervised by: K Hill, S Jenkins

Joe Yasa, Murdoch University Research Unit: Tissue Repair Project Title: 'The role of IGF-1 in lung regeneration' Supervised by: R Mead, GL Laurent, A Lucas, CM Prêle

MASTERS SCHOLARS

Maree Azzopardi, University of Western Australia Research Unit: Pleural Diseases Project Title: 'Improving the Care of Patients with Malignant Pleural Effusions' Supervised by: YCG Lee

Dr David Manners, University of Western Australia Research Unit: Occupational and Respiratory Health Project Title: 'Developing a patient decision aid for lung cancer screening' Supervised by: F Brims

HONOURS SCHOLARS

Natalie Vasilevski, Curtin University Research Unit: Molecular Genetics Project Title: 'Novel SETD7 splice variant affects cell response to bacteria'. Supervised by: S Baltic, PJ Thompson

Altinka Res, Murdoch University Research Unit: Tissue Repair Project Title: Therapeutic potential of combined chemotherapy and targeted inhibition of the hedgehog signalling pathway in treating malignant mesothelioma Supervisors: S Mutsaers, C Prêle, K Birnie **Tylah Miles**, University of Western Australia Research Unit: Tissue Repair Title: Jak/STAT Signalling in lung fibrosis Supervisors: C Prêle, P Henry

Daniel Ta, Notre Dame University Research Unit: Tissue Repair Research title: Investigating the role of IL-33 and IL-1a in lung fibrosis Supervisors: C Prêle, G Hoyne, S Mutsaers

Denisha Lee, University of Western Australia Research Unit: Tissue Repair Project Title: Role of Bard1 and Bard1 isoforms in lung fibrosis Supervisors: C Prêle, S Mutsaers, L Barrett

UWA WINTER SCHOOL LABORATORY RESEARCH PROGRAM

Li Bo and Tan Lichuan

Research Unit: Tissue Repair Research Title: 'PD-1 in Lung fibrosis' Supervisor: C Prêle, SE Mutsaers





RESEARCH ACTIVITIES

AWARDS

Birnie K. Awarded PhD. UWA

Birnie K. Thoracic Society of Australia and New Zealand Travel Award

Miles T. Australian Postgraduate Award Scholarship

Miles T. Lung Foundation Australia Bill van Nierop PhD Scholarship

Yasa J. Thoracic Society of Australia and New Zealand Travel Award

Yasa J. Australasian Society for Stem Cell Research Travel Award

Yasa J. Murdoch University Postgraduate Travel Award

FELLOWSHIPS

Fitzgerald D. WA Cancer Council & Palliative Care Clinical Research Fellowship

Fitzgerald D. European Respiratory Society Clinical Research Fellowship

Fysh E. NHMRC Early Career Development Fellowship.

Lansley S. iCARE Dust Diseases Board Fellowship

Lee YCG. Practitioner Fellowship, Medical Research Future Fund Next Generation Clinical Researcher Program, National Health & Medical Research Council, Australia

Tai A. Thoracic Society Australia and New Zealand Vertex Adult Cystic Fibrosis Fellowship (2017-18)

INVITED PRESENTATIONS AND CHAIRMANSHIP

INTERNATIONAL

Lee YCG. Invited speaker. Symposium (Pleural Disease -State of the Art): Pleural infection. Asian Pacific Society of Respirology Annual Congress, Sydney, Australia

Lee YCG. Invited speaker. Symposium (Interventional Pulmonology): Advances on Management of Pleural Diseases. Hong Kong Thoracic Society Autumn Respiratory Seminar, Hong Kong **Lee YCG.** Invited speaker. Workshop Thoracoscopy and Pleural Procedure: Pleurodesis for Malignant and Benign Diseases. Asian Pacific Congress of Bronchology & Interventional Pulmonology, Bali, Indonesia

Lee YCG. Invited speaker. Pleural Symposium (Malignant pleural effusion management in 2017 – Review of recent RCT's): Phenotyping malignant pleural effusions – why and what for? Postgraduate Course (Pleural effusion management): Difficult pleural effusions. European Respiratory Society annual conference, Milan, Italy

Lee YCG. Invited speaker. Bacteria, fibrinolytics and pleural space - Exciting new lessons. Practice changing clinical trials in Malignant Pleural Effusions. Advanced Trainees Course: Pleural Diseases: Approach to Pleural Effusions. New Zealand Thoracic Society annual conference, Queensland, New Zealand

Lee YCG. Invited speaker. Session (Pleural Disease): Malignant pleural effusion: AMPLE TIME or ASAP. Session (Interventional Respiratory Techniques): Pleural Interventions. Malaysian Thoracic Society annual conference, Kuala Lumpur, Malaysia

Lee YCG. Invited speaker. Plenary Session (Practice Changing Clinical Trials in Pleural Diseases: Impact on Day-to-Day Care). Practice changing clinical trials in Malignant Pleural Effusions

Lee YCG. Meet the Professor seminar. Clinical advances in Pleural Infection and in Pneumonia. American Thoracic Society International Conference, Washington DC, USA

Lee YCG. Invited speaker. Webinar: Pleural Infection. American Association of Bronchology & Interventional Pulmonology

Lucas A. Invited Presentation. Differential effects of exogenous IGF-1 administration on young adult and geriatric mice following pneumonectomy.at the July 2017 UHU network meeting, Munich, Germany

Prêle CM. Invited speaker. STAT3-mediated immune regulation in Idiopathic Pulmonary Fibrosis. University of Western Australia-Helmholtz Zentrum Munich-University College London (UHU) Collaborative Research Meeting, Munich, Germany

Prêle CM. Session Chair, Third University of Western Australia-Helmholtz Zentrum Munich-University College London (UHU) Collaborative Research Meeting, Munich, Germany. Research Meeting, Munich Germany

NATIONAL

Prêle CM. Invited speaker. The fibrotic signature and pathways. Third Biennial Australian Rare Lung Disease Short Course, Sydney NSW

Prêle CM. Invited speaker. Evaluating anti-CD20 therapy for STAT3-mediated lung fibrosis. TSANZ Annual Scientific Meeting, Canberra, ACT (Presented by D Knight on behalf of C Prêle)

Yasa J. Selected Poster Presenter. Differential effects of IGF1 administration in young and geriatric mice after pneumonectomy

LOCAL

Birnie K. Invited presentation; Small non-coding RNA in malignant mesothelioma - Perth Mesothelioma Workshop

Birnie K. Session Chair, IRH Alan James Lung Club

Lansley S. Invited Oral Presentation. Revival of an old cure. National Centre for Asbestos Related Diseases Annual Scientific Meeting

Lansley S. Invited Oral Presentation. Mouse models of mesothelioma and pleural effusion. UWA Biomedical Sciences Lecture Series

Prêle CM. Session Chair, IRH/CCTRM Mesothelioma Symposium

Prêle CM. Session Chair. Science on the Swan Conference

Prêle CM. Invited speaker. Cells in fibrosis; guilt by association. TKI Mucosal Immunity Workshop

Prêle CM. Invited speaker. Immune cell regulation in idiopathic pulmonary fibrosis. Bayliss Seminar Series

Prêle CM. Invited speaker. Jak/STAT Signalling in Idiopathic Pulmonary Fibrosis. Harry Perkins Institute for Medical Research Seminar Series and CCTRM Seminar Series

Yasa J. Selected Presentation Investigating the potential of Insulin-like Growth Factor(IGF)-1 to trigger regenerative lung growth in young and very old mice following left lung pneumonectomy Australian Society for Medical Research Research Symposium

COMMITTEES AND BOARDS

INTERNATIONAL

Laurent GJL. Editor-in-Chief, International Journal of Biochemistry and Cell Biology

Laurent GJL. Associate Editor, American Journal of Respiratory Cell and Molecular Biology

Laurent GJL. Section Editor, Fibrogenesis and Tissue Repair.

Laurent GJL. Member of Advisory Board, BARD1AG

Laurent GJL. American Thoracic Society World Lung Health Committee

Laurent GJL. Long Range Planning Committee of Cell and Molecular Biology Assembly of the European Respiratory Society

Laurent GJL. Chairman, International Colloquium on Pulmonary Fibrosis

Laurent GJL. Chairman, Academic Trust Funds Committee, University of London

Laurent GJL. American Fibrosis Association

Laurent GJL. WASOG Conference Scientific Committee

Laurent GJL. BALR president

Laurent GJL. Director of the European Respiratory Society (ERS) Lung Science Conference

Lee YCG. American Thoracic Society Working group: Evaluation and Management of Patients with Malignant Pleural Effusions Guidelines

Lee YCG. Thoracic Society of Australia & NZ WA Branch Committee

Lee YCG. Asian Pacific Society of Respirology Executive Committee

Lee YCG. Editorial Board Member. Journal of Thoracic Diseases

Lee YCG. Editorial Board Member. Respirology Case Report.

Lee YCG. Section Editor for Pleural Diseases. Current Respiratory Care Report

Lee YCG. Editorial Board member. Plevra Bülteni (Turkish)

Lee YCG. Series Editor. Translational Respiratory Medicine.

Mutsaers SE. Associate Editor Journal of Cellular and Molecular Medicine

Mutsaers SE. Editorial Board American Journal of Respiratory Cell and Molecular Biology

Mutsaers SE. Editorial Board Open Journal of Respiratory Disease

Mutsaers SE. Editorial Board World Journal of Transplantation

Mutsaers SE. International advisor International Pleural Newsletter – a publication of the International Pleural Network

Mutsaers SE. Member Virtual Respiratory Centre (VRC) Editorial Advisory Board (EAB)

Prêle CM. UWA-Helmholtz Zentrum Munich-UCL Collaborative Research Network Executive Committee

NATIONAL

Lansley S. Secretary of the WA TSANZ Executive Committee. Mutsaers SE. NHMRC Development Grants Review Panel 2017

Prêle CM. TSANZ Education and Training Sub-committee, National TSANZ

LOCAL

Armitage J. Member, Local committee, ASMR (WA branch)

Baltic S. Member of the WA TSANZ Executive Committee

Birnie K. Organising Committee for the IRH Alan James Lung Club

Lansley S. Member of the Cancer Council Western Australia Pre-doctoral Subcommittee

Mulrennan SA. Member of the Busselton Population Medical Research Institute Board and Member of the Busselton Population Medical Research Institute Research Committee

Mulrennan SA. Member of the Drug and Therapeutics Committee, Sir Charles Gairdner Hospital

Tan D. Member, Local Committee, ASMR (WA branch)

Tan D. Treasurer, TSANZ (WA branch)

Tan D. Member, Local Committee, ASI (WA branch)

Thomas R. Executive member. WA TSANZ. TSANZ.

COLLABORATIONS

ACRF Centre for Lung Cancer Early Detection Adult CF Centre, Prince Charles Hospital Adult CF Centre, Sir Charles Gairdner Hospital Australian Asthma Genetics Consortium Bispebjerg Hospital Bristol Pleural Unit, UK Burns Injury Unit, University of Western Australia Centre for Clinical Research, University of Queensland Department of Respiratory Medicine, Fiona Stanley Hospital Department of Respiratory Medicine, Sir Charles Gairdner Hospital

Harry Perkins Institute of Medical Research Institute for Biological Research, Sinisa Stankovic, Serbia National Centre for Asbestos Related Diseases Olivia Newton John Cancer Research Institute Oxford Respiratory Trials Unit, University of Portsmouth Oxford University, Pleural Unit, UK Physiotherapy Department, Curtin University Physiotherapy Department, Sir Charles Gairdner Hospital QIMR Berghofer Medical Research Institute, Queensland Respiratory Trials Unit, Oxford University Respiratory Unit, University College London Royal Australasian College of General Practitioners School of Medical and Health Sciences. Edith Cowan Universitv The Queensland University of Technology The University Hospitals Geneva (HUG) The University of Newcastle The University of Notre Dame The University of Wisconsin, USA Thoracic Research Centre, University of Queensland



PUBLICATIONS

BOOK CHAPTERS

Lee YCG. Pleural Tumors. In: Oxford Textbook of Medicine, 6th ed. Oxford, U.K.: Oxford University Press - in press

de Fonseka D, **Lee YCG** and Maskell NA. Pleural Diseases. In: Oxford Textbook of Medicine, 6th ed. Oxford, U.K.: Oxford University Press - in press

Davies HE and **Lee YCG**. Mediastinal Tumours and Cysts. In: Oxford Textbook of Medicine, 6th ed. Oxford, U.K.: Oxford University Press - in press

Rashid Ali MR, Porcel JM, Koegelenberg C, Halifax R, Maskell NA and **Lee YCG**. Pleural Diseases. In: Shah P, Hearth F, Lee YCG and Crier G, eds. Essential Clinical Pulmonology. Taylor & Francis - in press

Leong SL, Davies HE and **Lee YCG**. Malignant Pleural Mesothelioma. In: Shah P, Hearth F, Lee YCG and Crier G, eds. Essential Clinical Pulmonology. Taylor & Francis -in press

Azzopardi M and Lee YCG. Pleural Effusion Management in Malignant Pleural Mesothelioma. In: Malignant Pleural Mesothelioma: Present Status and Future Directions. Sharjah, UAE: Betham - in press

Light RW and Lee YCG. Pneumothorax, Chylothorax, Hemothorax and Fibrothorax. In: Broaddus VC, Mason RJ, Murray JF, Nadel JA, King TE, Ernst JD, Lazarus SC, Slutsky AS eds. Murray & Nadel's Textbook of Respiratory Diseases, 6th ed, in press. Philadelphia, PA, USA: Elservier - in press

McWilliams A, Brims F, Horeweg N, de Koning H, Jet J. Lung Cancer Screening (chapter 7). International Association for the Study of Lung Cancer, Thoracic Oncology Textbook, 2nd Edition, 2017

INVITED REVIEWS AND EDITORIALS

Birnie KA, **Prêle CM**, **Thompson PJ**, Badrian B, **Mutsaers SE**. Targeting microRNA to improve diagnostic and therapeutic approaches for malignant Mesothelioma. Oncotarget. 2017; 8:78193-78207

Fitzgerald DB and **Lee YCG**. Pleural Infection: To drain or not to drain? Respirology 2017 - in press

Lee YCG. Current Pulmonary Reports, 2017: Series: Pleural Diseases

Cooley J, **Lee YCG** and Gupta N. Spontaneous pneumothorax in diffuse cystic lung diseases. Curr Opin Pulm Med 2017; 23: 323-333

Porcel JM, Lui MMS, Lerner A, Davies HE, Feller-Kopman D and Lee YCG. Comparing management approaches to malignant pleural effusions. Expert Rev Respir Med 2017; 11: 273-284

Williamson JP, Twaddell S, Lee YCG, Salamonsen M, Hew M, Fielding D, Nguyen P, Steinfort D, Hopkins P, Smith N and Grainge C. Thoracic ultrasound recognition of competence – a position paper of the Thoracic Society of Australian and New Zealand. Respirology 2017; 22: 405-408

Popowicz N, Thomas R and **Lee YCG**. Reply: "Less is More Approach for Management of Intrapleural Sepsis" [Letter] Ann Am Thorac Soc 2017; in press

Popowicz N, Idell S, **Lee YCG**. Pathogenesis of pleural infection: A complex warfare. Respirology. 2018 Jan;23(1):8-9

JOURNAL ARTICLES

Bjerregaard A, Laing IA, Poulsen N, Backer V, Sverrild A, Fally M, Khoo SK, Barrett L, **Baltic S**, **Thompson PJ**, Chidlow G, Sikazwe C, Smith DW, Bochkov YA, Le Souëf P, Porsbjerg C. Characteristics associated with clinical severity and inflammatory phenotype of naturally occurring virusinduced exacerbations of asthma in adults. Respir Med. 2017 Feb;123:34-41

Halstrom S, Cherry CL, Black M, Thomson R, Goullee H, **Baltic S**, Allcock R, **Temple SEL**, Price P. A haplotype spanning P2X7R, P2X4R and CAMKK2 may mark susceptibility to pulmonary non-tuberculous mycobacterial disease. Immunogenetics. 2017 May;69(5):287-293

Halstrom S, Thomson R, Goullee H, Baltic S, Allcock R, Temple

SE, Price P. Susceptibility to non-tuberculous mycobacterial disease is influenced by rs1518111 in IL10. Hum Immunol. 2017 Apr;78(4):391-393

Ferreira MA, Jansen R, Willemsen G, Penninx B, Bain LM, Vicente CT, Revez JA, Matheson MC, Hui J, Tung JY, **Baltic S**, Le Souëf P, Montgomery GW, Martin NG, Robertson CF, James A, Thompson PJ, Boomsma DI, Hopper JL, Hinds DA, Werder RB, Phipps S; Australian Asthma Genetics Consortium Collaborators. Gene-based analysis of regulatory variants identifies 4 putative novel asthma risk genes related to nucleotide synthesis and signaling. J Allergy Clin Immunol. 2017 Apr;139(4):1148-1157

Birnie KA, Prêle CM, Thompson PJ, Badrian B, **Mutsaers SE**. Targeting microRNA to improve diagnostic and therapeutic approaches for malignant mesothelioma. Oncotarget. 2017 Aug 24;8(44):78193-78207

Brims FJH. Integrated care for resected early stage lung cancer: innovations and exploring patient needs. BMJ Open Respiratory Research, 4, e000175

Cheah HM, Lansley SM, Varano della Vergiliana JF, Tan AL, Leong SL, Creaney J and **Lee YCG**. Malignant pleural fluid from mesothelioma has potent biological activities. Respirology 2017; 22:192-199

Fitzgerald DB, Koegelenberg CFN, Yasufuku K, **Lee YCG**. Surgical and non-surgical management of malignant pleural effusions. Expert Rev Respir Med. 2018 Jan;12(1):15-26

Lansley SM, **Cheah HM** and **Lee YCG**. The role of MCP-1 in pleural effusion development in a carrageenan-induced murine model of pleurisy. Respirology 2017; 22: 758-763

Waters DW, Schuliga M, Fogarty E, Burgess JK, Grainge C, Westall G, **Laurent GJ**, **Prêle CM**, **Mutsaers SE**, Knight D. Dysregulated STAT3 Signaling Induces and Reinforces Fibroblast Senescence in Lung Fibroblasts of IPF Patients. American Journal of Respiratory and Critical Care Medicine 2017;195:A2457

Jenkins, RG, Moore BB, Chambers RC, Eickelberg O,

Königshoff M, Kolb M, Laurent GJ, Carmel B. Nanthakumar, Mitchell A. Olman, Annie Pardo, Moises Selman, Dean Sheppard, Patricia J. Sime, Andrew M. Tager, Amanda L. Tatler, Victor J. Thannickal, Eric S. White. Standards for the use of animal models for the pre-clinical assessment of potential therapies for the treatment of pulmonary fibrosis. Am J Respir Cell Mol Biol. 2017 May;56(5):667-679

Lee YCG, Levine MT. Germline Genome Protection on an Evolutionary Treadmill. Dev Cell. 2017 Oct 9;43(1):1-3

Lee YCG, Karpen GH. Pervasive epigenetic effects of Drosophila euchromatic transposable elements impact their evolution. Elife. 2017 Jul 11;6. pii: e25762

Cooley J, **Lee YCG**, Gupta N. Spontaneous pneumothorax in diffuse cystic lung diseases. Curr Opin Pulm Med. 2017 Jul;23(4):323-333

Lee YCG, Yang Q, Chi W, Turkson SA, Du WA, Kemkemer C, Zeng ZB, Long M, Zhuang X. Genetic Architecture of Natural Variation Underlying Adult Foraging Behavior That Is Essential for Survival of Drosophila melanogaster. Genome Biol Evol. 2017 May 1;9(5):1357-1369

Jeffery E, Lee YCG, McVeigh J, Straker L, Wooding T, Newton R and McIntyre C. Objectively measured physical activity and sedentary behavior in patients with malignant pleural effusion: a feasibility study. Support Care Cancer 2017 - in press

Mishra EK, Clive AO, Wills GH, Davies HE, Stanton AE, Al-Aloul M, Hart-Thomas A, Pepperell J, Evison M, Saba T, Harrison RN, Guhan A, Callister ME, Sathyamurthy R, Rehal S, Corcoran JP, Hallifax R, Psallidas I, Russell N, Shaw R, Dobson M, Wrightson JM, West A, **Lee YCG**, Nunn AJ, Miller RF, Maskell NA, Rahman NM. Randomized Controlled Trial of Urokinase versus Placebo for Nondraining Malignant Pleural Effusion. Am J Respir Crit Care Med. 2018 Feb 15;197(4):502-508

Peddle-McIntye CJ, Baker M, **Lee YCG**, Galvão DA, Cormie P, Graham V, Newton RU. The feasibility of a pragmatic distancebased intervention to increase physical activity in lung cancer survivors. Eur J Cancer Care 2017 - in press Mishra EK, Clive AO, Wills G, Davies HE, Stanton AE, Al-Aloul M, Hart-Thomas A, Pepperell J, Evison M, Saba T, Harrison RN, Guhan A, Callister M, Sathyamurthy R, Corcoran JP, Hallifax R, Psallidas I, Russell N, Shaw R, Dobson M, Wrightson JM, West A, **Lee YCG**, Nunn AJ, Miller RF, Maskell NA and Rahman NM. Randomised controlled trial of urokinase vs placebo for nondraining malignant pleural effusion. Am J Resp Crit Care Med 2017 - in press

Weber M, Yap S, Goldsbury, D, **Manners D**, Tammemagi M, Marshall H, ...Canfell, K. Identifying high risk individuals for targeted lung cancer screening: Independent validation of the PLCOm2012 risk prediction tool. International Journal of Cancer, 141(2), 242-253

Manners D, Wong P, Murray C, Teh, J, Kwok YJ, de Klerk N, ... Brims, FJH. Correlation of ultra-low dose chest CT findings with physiologic measures of asbestosis. European Radiology, 27(8), 3485-3490

Jo HE, Prasad JD, Troy LK, Mahar A, Bleasel J, Ellis SJ, Chambers DC, Holland AE, Lake FR, Keir G, Goh NS, Wilsher M, de Boer S, **Moodley Y**, Grainge C, Whitford HM, Chapman SA, Reynolds PN, Beatson D, Jones LJ, Hopkins P, Allan HM, Glaspole I and Corte TJ. Diagnosis and management of idiopathic pulmonary fibrosis: Thoracic Society of Australia and New Zealand and the Lung Foundation Australia position statement summary. Med J Aust 2017; 207(11):1

Jo HE, Troy LK, Keir G, Chambers DC, Holland A, Goh H, Wilsher M, De Boer S, **Moodley Y**, Grainge C, Whitford H, Chapman S, Reynolds PN, Glaspole I, Beatson D, Jones L, Hopkins P and Corte TJ. Treatment of idiopathic pulmonary fibrosis in Australia and New Zealand: A position statement from the Thoracic Society of Australia and New Zealand and the Lung Foundation Australia. Respirology (2017) 22, 1436-1458

Glaspole I.G, Watson A.L, Allan H, Chapman S, Cooper W.A, Corte T.J,Ellis S, Grainge C, Goh N, Hopkins P, Keir G, Macansh S, Mahar A, **Moodley Y**, Reynolds P.N, Ryerson C.J, Walters E.H, Zappala CJ and Holland A.E. Determinants and outcomes of prolonged anxiety and depression in idiopathic pulmonary fibrosis. European Respiratory Journal (2017) 50: 1700168

Glaspole IN, Chapman SA, Cooper WA, Ellis SJ, Goh NS, Hopkins PM, Macansh S, Mahar A, **Moodley Y**, Reynolds PN, Walters EH, Zappala CJ, and Corte TJ. Health-related quality of life in idiopathic pulmonary fibrosis: Data from the Australian IPF Registry. Respirology (2017)

Jo HE, Glaspole I, Grainge C, Goh N, Hopkins PMA, **Moodley** Y, Reynolds PN, Chapman, SE, Walters HE, Zappala C, Allan A, Keir GJ, Hayen A, Cooper WA, Mahar AM, Ellis S, Macansh S, and Tamera J. Corte. Baseline characteristics of idiopathic pulmonary fibrosis: analysis from the Australian Idiopathic Pulmonary Fibrosis Registry. European Respiratory Journal (2017) 49 1601592

Beers MF, **Moodley Y**. When Is an Alveolar Type 2 Cell an Alveolar Type 2 Cell? A Conundrum for Lung Stem Cell Biology and Regenerative Medicine. Am J Respir Cell Mol Biol. 2017 Jul;57(1):18-27

Hoyne GF, Elliott H, **Mutsaers SE**, **Prêle CM**. Idiopathic pulmonary fibrosis and a role for autoimmunity. Immunol Cell Biol. 2017 Aug;95(7):577-583

Popowicz N, Bintcliffe O, de Fonseka D, Blyth K, Smith N, Piccolo F, Martin G, Wong D, Edey A, Maskell NA and **Lee YCG**. Dose de-escalation of intrapleural tissue plasminogen activator therapy for pleural infection: the ADAPT project. Ann Am Thorac Soc 2017; Jun;14(6):929-936

Popowicz ND, Lansley SM, Cheah HM, Kay ID, Carson CF, Waterer GW, Paton JC, Brown JS, **Lee YCG**. Human pleural fluid is a potent growth medium for Streptococcus pneumoniae. PLoS One. 2017 Nov 30;12(11):e0188833

Popowicz N, Wood J, Tai A, Morey S, Mulrennan S. Immediate effects of lumacaftor/ivacaftor administration on lung function in patients with severe cystic fibrosis lung disease. J Cyst Fibros. 2017 May;16(3):392-394

Tan DBA, Teo TH, Setiawan A M, Ong NE, Zimmermann M, Price P, Kirkham, LAS, and **Moodley Y**. Increased CTLA-4+ T cells may contribute to impaired T helper type 1 immune responses in patients with chronic obstructive pulmonary disease. Immunology, 151: 219–226 2017

Tan DBA, Armitage J, Teo TH, Ong NE, Shin H, Moodley YP. Elevated levels of circulating exosome in COPD patients are associated with systemic inflammation. Respir Med. 2017 Nov;132:261-264

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Thomas R, Fysh E, Smith NA and **Lee YCG**. Effect of an Indwelling Pleural Catheter vs Talc Pleurodesis on Hospitalization Days in Patients With Malignant Pleural Effusion - The AMPLE Randomized Clinical Trial. JAMA. 2017;318(19):1903-1912

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Ferreira MA, Vonk JM, Baurecht H, Marenholz I, Tian C, Hoffman JD, Helmer Q, Tillander A, Ullemar V, van Dongen J, Lu Y, Rüschendorf F, Esparza-Gordillo J, Medway CW, Mountjoy E, Burrows K, Hummel O, Grosche S, Brumpton BM, Witte JS, Hottenga JJ, Willemsen G, Zheng J, Rodríguez E, Hotze M, Franke A, Revez JA, Beesley J, Matheson MC, Dharmage SC, Bain LM, Fritsche LG, Gabrielsen ME, Balliu B; 23andMe Research Team; AAGC collaborators; BIOS consortium; LifeLines Cohort Study, Nielsen JB, Zhou W, Hveem K, Langhammer A, Holmen OL, Løset M, Abecasis GR, Willer CJ, Arnold A, Homuth G, Schmidt CO, **Thompson PJ**, e.tal. Shared genetic origin of asthma, hay fever and eczema elucidates allergic disease biology. Nat Genet. 2017 Dec;49(12):1752-1757

McElvaney NG, Burdon J, Holmes M, Glanville A, Wark PA, **Thompson PJ**, Hernandez P, Chlumsky J, Teschler H, Ficker JH, Seersholm N, Altraja A, Mäkitaro R, ChorostowskaWynimko J, Sanak M, Stoicescu PI, Piitulainen E, Vit O, Wencker M, Tortorici MA, Fries M, Edelman JM, Chapman KR; RAPID Extension Trial Group. Long-term efficacy and safety of α 1 proteinase inhibitor treatment for emphysema caused by severe α 1 antitrypsin deficiency: an open-label extension trial (RAPID-OLE). Lancet Respir Med. 2017 Jan;5(1):51-60

Wood J, Jenkins S, Putrino D, **Mulrennan S**, **Morey S**, Cecins N, Hill K. High usability of a smartphone application for reporting symptoms in adults with cystic fibrosis. J Telemed Telecare. 2017 Jan 1:1357633X17723366

GRANTS

Brims FJH. Longitudinal cohort of asbestos removalists to study health effects. WA Cancer Council Collaborative Grant. **Lansley S**, Creaney J, **Lee YCG**, **Thomas R** & Feindel KW. Targeting MCP-1 as a novel therapy for mesothelioma and malignant pleural effusion. Project Grant, Cancer Council of Western Australia, Australia

Lansley SM, **Lee YCG**, Creaney J, Robinson BWS. The effect of FGF-9 on anti-tumour immunity in mesothelioma. Project Grant, Cancer Council of Western Australia, Australia

Lansley SM. Identification of the molecular networks that drive mesothelioma invasion. Cancer Council WA Research Project Grant

Lansley SM. Abscopal effect of radiotherapy in checkpoint blockade in a mouse model of thoracic cancer. Cancer Council WA Research Project Grant

Lansley SM. Exploiting immune checkpoint blockade to generate effective therapy for MM. Dust Diseases Authority NSW Project Grant

Knight D, Burgess J, Westall G, Laurent GJ, Mutsaers SE, Prêle CM. Fibroblast Scenecence as a diver of pulmonary fibrosis. NHMRC Project Grant 2016-2019

Lee YCG, Maskell N, Feller-Kopman D, Murray K, Creaney J & Newton RU. Australasian Malignant PLeural Effusion (AMPLE)

trial -3. Project Grant, iCare Dust Diseases Care Board, Australia.

Lee YCG, Creaney J, Nowak A, Millward M and Musk AW. Phase II Trial of a Novel FGF-Receptor Antagonist in Mesothelioma. Project Grant, NSW Workers' Compensation Dust Disease Board, Australia

Lee YCG. Australasian Malignant PLeural Effusion (AMPLE) Trial-3: a multicentre randomized study comparing surgical pleurodesis vs indwelling pleural catheter for management of malignant pleural effusions Project Grant, Sir Charles Gairdner Research Advisory Committee, Australia

Robinson BWS, **Lee YCG**, Creaney J, Lake R, Holt R, Nowak A, Watson M, Pearson J & Chee J. Compartmental analysis of T-cell responses in thoracic malignancies. Project Grant, National Health & Medical Research Council, Australia

Creaney J, Robinson BWS, **Lee YCG**, Muiri DO. Single cell sequencing in pleural effusions of malignant mesothelioma patients. Project Support, the Cancer Research Trust Single Cancer Cell Initiative 2017

Robinson BW, Creaney J, Lake R, Nowak A, Musk AW, Lesterhuis W, Lee YCG, Francis R, Holt R and Waddell N. National Centre for Asbestos Related Diseases. Centre of Research Excellence Grant, National Health & MRC, Australia

Brown S, Keijzers G, Smith J, **Lee YCG**. A randomised controlled trial of interventional versus conservative treatment of primary spontaneous pneumothorax. Project Grant, National Health & Medical Research Council, Australia

Lucas A, Schiller H, Lucas M and **Prêle CM**. Exploring the relationship between lung flexibility and regenerative growth, as you age. UHU Collaborative Seed Funding

Lucas M, **Lucas A**, Hansbro P, **Prêle CM**. Assessing the regenerative potential of damaged lung using a murine model Chronic Obstructive Pulmonary Disease. SCGH RAC Grant

Lucas A, Giangreco A, **Prêle CM**. Can the rejuvenation of IGF-1 levels restore the capacity for lung regeneration? UHU Seed Funding Grant **Mutsaers SE**. STAT3 regulation of cell responses. NHMRC Project Grant, 2014-2017

Mutsaers SE. The hedgehog signalling pathway in mesothelioma. Cancer Council WA, Cancer Research Career Achievement Award

McAnulty R, **Mutsaers SE**, **Prêle CM**. Pump Priming Grant. Evaluating B-cell and JAK/STAT targeted therapies for lung fibrosis. British Lung Foundation. 2015-2017

Janes S, McAnulty R, **Mutsaers SE** and **Prêle CM**. Investigating Gli as a novel therapeutic target in malignant mesothelioma. British Lung Foundation. PhD Scholarship Grant 2017-2019

Mutsaers SE, Rinkevich Y, and **Prêle CM**. Mesothelial cell involvement in serosal repair and adhesion formation. UHU Collaborative Grant In-aide

Mutsaers SE, Chakera A, **Prêle CM**, **Lansley S**. The effects of infection on mesothelial gene transcription: a role for immune check point regulation in chronic disease. Alan King Westcare Grant

Mutsaers SE, **Prêle CM** and S Janes. GANT61: A novel therapy for malignant mesothelioma. Maurice Blackburn Grant in Aid for Research on Asbestos Related Diseases

Prêle CM, Knight D, Fear M, McAnulty R, Wood F, **Laurent GJ**. Epithelial-mesenchymal cell communication; towards new therapeutic targets for fibrosis. NHMRC Project Grant 2017-2020

Janes S, **Prêle CM** and Hynds R. Investigating HGF-induced STAT6 signaling in stromal-epithelial cell crosstalk. University of Western Australia, Helmholtz Zentrum Munich, University College London Seed Funding Grant

Prêle CM, Yildrim AO, Dr. Conlon MT and Hoyne G. Investigating the role of specific B cell subsets in chronic lung disease. UHU Collaborative Seed Funding

Prêle CM, Mutsaers SE, Knight D, O'Donoghue, Hoyne G, Laurent GJ. STAT3 regulation of cell responses in IPF. NHMRC Project Grant **Sawyer A**. Effects of high intensity interval training on exercise capacity in people with cystic fibrosis: a randomised controlled trial. Conquer CF Research Program, scholarship program

Sawyer A. Top-up scholarship, Cystic Fibrosis Australia

Sawyer A. Effects of HITT on exercise capacity in people with CF. Sir Charles Gairdner Hospital Research Advisory Council Grant

Tai A. TSANZ Vertex Adult Cystic Fibrosis Fellowship (2017-19).

Tai A. SCGH, Research Advisory Committee grant

Tai A. Clostridium difficile infection in adult patients with cystic fibrosis in Western Australia (WA): disease burden and clinical impact. Conquer CF Research Program, project grant



FINANCIAL REPORT

Board members submited the financial report of Institute for Respiratory Health (Inc) for the financial year ended 31 December 2017.

Board members

The names of board members throughout the year and at the date of this report are:

Peter Gunzburg George Yeoh Cecilia Prêle Sue Morey Geoff Stewart Johnson Kitto Geoff Laurent Craig McGown

Principal activities

The principal activities of the institute during the financial year were to conduct research and conduct clinical trials in the area of respiratory health.

Significant changes

No significant change in the nature of these activities occurred during the year.

Operating result

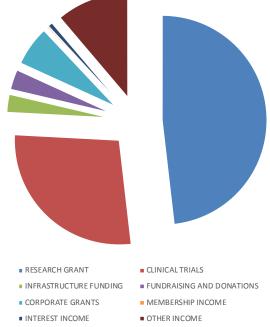
The surplus for the 2017 year amounted to \$970,320.

Signed in accordance with a resolution of the members of the board.

1 March 2018 Peter Gunzburg, Board Chair

For a comprehensive review of our financial position, please email admin@resphealth.uwa.edu.au.

INCOME BREAKDOWN FOR 2017



INCOME STATEMENT

FOR THE YEAR ENDED 31 DECEMBER 2017

	2017	2016
Revenue	2	9
Grant income	1,956,451	1,472,758
Clinical trials	1,123,850	714,242
Infrastructure funding	114,896	147,637
Fundraising income and donations	128,061	135,572
Corporate grants	250,000	250,000
Memberships income	6,6 00	5,945
Interest income	26,917	28,939
Other income	454,699	373,520
Total revenue	4,061,474	3,128,613
Expenses		
Operating expenses	(502,209)	(319,905)
Employee benefits expense	(2,238,577)	(2,148,608)
Depreciation expenses	(22,287)	(40,861)
Finance costs	(890)	(793)
Other expenses	(327,191)	(294,092)
Total expenses	(3,091,154)	(2,804,259)
Surplus for the year	970,320	324,354

BALANCE SHEET

FOR THE YEAR ENDED 31 DECEMBER 2017

	2017 \$	2016 \$
	ų	Ψ
CURRENT ASSETS Cash and cash equivalents	2,324,849	1,684,827
Trade and other receivables	1,205,663	820,170
Inventory		5,760
TOTAL CURRENT ASSETS	3,530,512	2,510,757
NON-CURRENT ASSETS		
Property, plant and equipment	94,342	116,629
TOTAL NON-CURRENT ASSETS	94,342	116,629
TOTAL ASSETS	3,624,854	2,627,386
CURRENT LIABILITIES	0(1770	270.000
Trade and other payables Employee provisions	264,770 232,009	278,009 193,625
TOTAL CURRENT LIABILITIES	496,779	471,634
NON-CURRENT LIABILITIES Employee provisions	38,601	36,598
TOTAL NON-CURRENT LIABILITIES	38,601	36,598
TOTAL LIABILITIES	535,380	508,232
NET ASSETS	3,089,474	2,119,154



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