# ANNUAL REPORT 2018

*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 founded 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.

# CHAIR AND DIRECTOR'S REPORT

## BOARD ACTIVITIES

The Institute's Board comprises a willing and conscientious group of individuals who volunteer their time and expertise to provide strategy and guidance to the Institute. As with all Boards, ours undergo changes with members leaving and replaced. The Board welcomed Anthony Fortina who will act as the University of Western Australia's representative on the Board. Anthony is the Deputy Director of the UWA's Office of Research Enterprise and brings a wealth of experience in the tertiary education and research sectors that are already benefitting the Institute.

On a very sad note, we would like to pay homage to Geoff Laurent, who sadly passed away mid 2018. The Institute is extremely grateful for Geoff's significant contribution as Director, Board Member and strong supporter of the Institute. I would also like to acknowledge Geoff's achievements in being an integral part of respiratory research both locally and internationally, and for his ability to bring together people to make a difference.

Finally, we would like to thank all our Board members for taking time away from other work and family to help the Institute, its staff and members to achieve its objectives of helping people with respiratory disease.

## RESEARCH SUCCESS

As with 2017, our researchers continued to be successful in obtaining a number of national and local grants in 2018. Highlights of this success include:

- Associate Professor Yuben Moodley being awarded an NHMRC Research Grant for investigating circulatory biomarkers for idiopathic pulmonary fibrosis
- Dr Sally Lansley being awarded a Dust Diseases Authority Grant for investigating bacteria as novel anti-mesothelioma agents
- Dr Ed Fysh being awarded a Dust Diseases Authority Grant for a novel minimal-invasive biopsy approach for pleural malignancies
- Associate Professor Fraser Brims being awarded two research grants on comparing primary care versus hospital-based follow up after curative surgery for patients with non-small cell lung cancer and, a research study investigating cancer-related weight loss in patients with Mesothelioma
- Professor Gary Lee being awarded a research grant for steroid therapy and outcome of parapneumonic pleural effusion
- Professor Steve Mutsaers being awarded a research grant for novel diagnostic and functional targets for malignant mesothelioma

We would also like to congratulate Professor Gary Lee and Dr Sally Lansley in being awarded highly competitive Fellowships from the NHMRC and Dust Diseases Authority respectively.

## CLINICAL TRIALS UNIT

In 2018, our Clinical Trials Unit continued to enhance its national and international reputation as judged by its involvement in numerous pharmaceutical trials. Under the management of Meagan Shorten and Felicite Kelsall (acting), the Unit enrolled over 145 patients and conducted 15 studies of new treatments. This a commendable effort which not only results in a steady income stream enabling the Institute to support its research effort but also brings novel treatments to patients with often severe respiratory illnesses. We would also like to thank the patients, who have given their time to help further medical research, as well as the many respiratory physicians in the Sir Charles Gairdner Hospital and general practice who oversee these trials.

## DONATIONS

The Institute attracts philanthropic support from individual donors as well as organisations fighting for individual respiratory diseases. We are indebted to the generosity of the Conquer CF Committee who have pledged $1 million towards adult CF research. The Institute and Conquer CF have come together to establish the Conquer CF Research Program, with the aim of maximizing clinical care for adults with cystic fibrosis (CF). Their support has facilitated the establishment of two PhD scholarships to develop novel physiotherapy treatments for adult CF patients, and a research program in support of Dr Anna Tai to continue her work on the molecular epidemiology of bacterial infections, including Pseudomonas aeruginosa and Clostridium difficile.

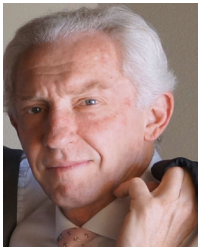
## FINANCIAL STABILITY OF THE INSTITUTE

In 2018, the Institute emerged with a small financial surplus which on current figures will increase in the coming years. A number of factors have contributed to this, including the affiliations we have established with The University of Western Australia and the National Asbestos Related Diseases (NCARD). Both are invaluable to the Institute and our affiliation with NCARD reflects joint research activity which has been ongoing for some time. We now have a combined voice for patients experiencing the full spectrum of respiratory disease.

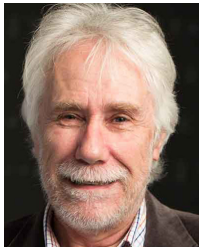
## COMMUNITY

We would like to acknowledge the Institute's community support arm, L I F E. It has continued to offer both fellowship and information to people living with chronic lung conditions. Specifically, we gratefully acknowledge the work and leadership of Dr Jenni Ibrahim, the Coordinator of L I F E who despite dealing with a serious illness provides wonderful support to people dealing with chronic respiratory disease.

Finally, we would like to acknowledge and thank the people who have contributed their time, helped fundraise or made a financial donation. Your contribution has made a tangible impact on the success and viability of the Institute.

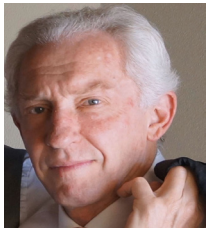


Mr Craig McGown
Chair of the Board



Emeritus Professor
Geoff Stewart
Director

# BOARD OF DIRECTORS



**Chair**
**Craig McGown**
**B Com**

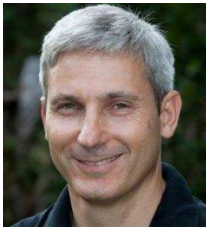
Director, New Holland Capital Pty Limited

**Ms Sue Morey**
**OAM FRCNA**

Nurse Practitioner in Respiratory Medicine, Sir Charles Gairdner Hospital

**Treasurer**
**Mr Peter Gunzburg**
**B Com**

Non-Executive Chairman of Bard1 Ltd

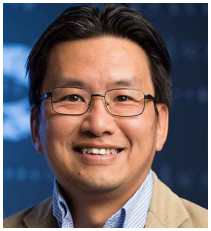


**Mr Anthony Fortina**
**BA. LLB**

(UWA appointed representative)
Deputy Director, Research Development and Innovation Office, University of Western Australia

**Secretary**
**Mr Johnson Kitto**
**LLB**

Managing Partner of Kitto & Kitto, Barristers & Solicitors



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

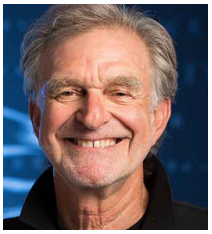
Respiratory Specialist, Sir Charles Gairdner Hospital
Head of Pleural Medicine Unit, Institute for Respiratory Health

**A/Prof Cecilia Prêle**
**BSc (Hons), PhD**

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

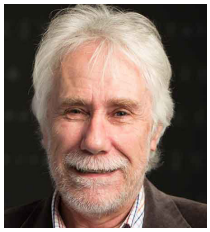
**Prof George Yeoh**
**BSc PhD**

(Retired April 2018)
Head of Liver Disease and Carcinogenesis Unit, Centre for Medical Research, University of Western Australia



**Prof Geoff Laurent BSc PhD**
**FRCP(Hon) FRCPath FMedSci**

(Up to August 2018)
Honorary Fellow, UWA
Honorary Fellow, University College London



**Prof Geoff Stewart BSc PhD**

Director Institute for Respiratory Health
Chair of Scientific Sub-Committee

## SUB-COMMITTEES OF THE BOARD

**Finance**

Mr Peter Gunzburg (Chair)
Mr Craig McGown

**Scientific**

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

*External to the Institute for Respiratory Health

# OUR RESEARCH UNITS

The Institute advocates and practices research into a broad 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.

## CHRONIC DISEASE AND INFLAMMATION

### MOLECULAR GENETICS & INFLAMMATION
Prof Phil Thompson

- Asthma
- Bronchiectasis
- COPD

### TISSUE REPAIR
A/Prof Cecilia Prele

- IPF
- Lung Regeneration
- Mesothelioma

### CYSTIC FIBROSIS RESEARCH
A/Prof Siobhain Mulrennan

- Bronchiectasis
- Cystic Fibrosis

## RESPIRATORY CANCERS

### STEM CELL THERAPY
A/Prof Yuben Moodley

- COPD
- IPF

### OCCUPATIONAL & RESPIRATORY HEALTH
A/Prof Fraser Brims

- Asbestosis
- Lung Cancer
- Mesothelioma

### PLEURAL MEDICINE
Prof Gary Lee

- Mesothelioma
- Pleural Effusion
- Pleural Infection

## INFECTIOUS DISEASES

### CLINICAL TRIALS
Ms Meagan Shorten

- Alpha 1
- Asthma
- Bronchiectasis
- COPD
- Cystic Fibrosis
- IPF

# RESEARCH PROJECTS 2018

## CHRONIC DISEASES AND INFLAMMATION

### ALPHA 1 - ANTITRYPSIN DEFICIENCY

#### 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.

### ASBESTOSIS

#### RESEARCH PROJECTS

#### 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

## CLINICAL 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:

- A study to evaluate the effectiveness and safety of Tezepelumab in patients with asthma.
- A large observational study to describe patient characteristics, treatment patterns and burden of disease over time. This study included participants with asthma and mixed disease.
- 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 closed during 2018 and is now in an evaluation phase.
- A study to evaluate the safety, acceptability, and secondarily the effectiveness of dupilumab, in the treatment of moderate to severe uncontrolled asthma. The study closed during 2018 and is now in an evaluation phase.

## 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 well-established 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.

# BRONCHIECTASIS

## CLINICAL TRIALS

The Clinical Trials Unit was involved in a number of studies trialling new medications to help treat bronchiectasis. The unit hasn't done trials in Bronchiectasis for a number of years so this was very exciting for these patients.

- A study that aims to evaluate the effect of INS1007 (study drug) compared with no study drug on time to first pulmonary exacerbation (chest flare up) over the 24-week treatment period.
- A study that aims to evaluate the effect of inhaled colistimethate sodium (study drug) compared with no study drug on the frequency of exacerbations (chest flare ups) and the number of exacerbation-free days over the 12 month treatment period.

# CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

## 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. The study closed in early 2018 and is now in an evaluation phase.
- A large observational study to describe patient characteristics, treatment patterns and burden of disease over time. This study included participants with COPD, Asthma and mixed disease.

### 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

### CLINICAL TRIALS

The Clinical Trials Unit is the only adult cystic fibrosis (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 2018 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 study to evaluate the efficacy of VX-659 in triple combination (TC) with tezacaftor (TEZ) and ivacaftor (IVA) in subjects with CF who are heterozygous for F508del and a minimal function mutation (F/MF subjects).
- A study to evaluate the efficacy of VX-659 in triple combination (TC) with tezacaftor (TEZ) and ivacaftor (IVA) in subjects with CF who are homozygous for the F508del mutation (F/F).
- An ongoing trial evaluating the long-term safety and efficacy of VX-659 combination therapy in subjects with CF who are homozygous or heterozygous for the F508del mutation.

### 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)

## CLINICAL TRIALS

The Clinical Trials Unit continued its work in IPF with an ongoing trial that aimed to evaluate the effect of the study drug CC-90001 on lung function after a period of treatment.

## 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 projects 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 Australia-wide 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.

# PULMONARY ARTERIAL HYPERTENSION (PAH)

## CLINICAL TRIALS

The Clinical Trials Unit in collaboration with Prof Eli Gabbay continued a study trial to determine whether there are any health benefits to be gained from Apixaban, an anticoagulant medication, in patients with Systemic Sclerosis related Pulmonary Arterial Hypertension ( SSc - PAH) who are already prescribed advanced Pulmonary Arterial Hypertension (PAH) therapy. This study is funded via an NHMRC grant and is ongoing.

# RESPIRATORY CANCER

## LUNG CANCER
### 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 low-dose 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 scan. 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.

#### 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
### 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.

#### 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 anti-tumour 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

### 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)

### 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.

# RESPIRATORY INFECTION

## PLEURAL INFECTION 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.

# RESEARCH ACTIVITIES

## RESEARCH GRANT PROGRAM

### GLENN BROWN MEMORIAL GRANT

**Chapman N.** Curtin University
Research project: Metaneb® System in adults with cystic fibrosis, its effects during periods of clinical stability and disease exacerbation.

## EXTERNAL GRANTS AWARDED

**Brims F.** A phase II feasibility study comparing primary care vs. hospital-based follow up after curative surgery for patients with non-small cell lung cancer. SCGH-RAC.

**Brims F.** A study to beat Cancer-related weight loss in patient with Mesothelioma. Cancer Council of WA.

**Forrest N.** Harnessing the anti-tumour effects of bacteria as a novel therapy for mesothelioma. SCGH-RAC.

**Fysh E.** AIR Study A novel minimal-invasive biopsy approach for pleural malignancies 2018. Dust Diseases Authority.

**Lansley S.** Using bacteria as novel anti-mesothelioma agents. Dust Diseases Authority.

**Lee YCG.** Steroid Therapy and Outcome of Parapneumonic Pleural Effusion (STOPPE) trial: a pilot multi-centre placebo-controlled randomized study. SCGH-RAC.

**Moodley Y.** Circulatory biomarkers for Idiopathic Pulmonary Fibrosis: improving patient outcomes. NHMRC Research Grant.

**Mutsaers S**. Novel diagnostic and functional targets for malignant mesothelioma. Cancer Council of WA.

**Thomas R**. A proof-of-principle study of pleural instillation of air to enhance CT detection of pleural malignancy. SCGH-RAC.

## FELLOWSHIPS

**Fysh E.** NHMRC Fellowship

**Lansley S.** Dust Diseases Authority Fellowship.

**Lee YCG.** NHMRC Fellowship

## ALAN JAMES LUNG CLUB

**A/Prof Cecilia Prêle.** Institute for Respiratory Health
"B cells in idiopathic pulmonary fibrosis"

**Sam Montgomery.** Telethon Kids Institute
"Differentiation between apoptotic and necrotic cell death in airway epithelial cells in response to viral infection and anaerobia using flow cytometry"

**Dr Jonathan Chee.** NCARD
"T cell specificity and phenotype in mouse models of mesothelioma"

**Dr Robert O'Donoghue.** Olivia Newton-John Cancer Research Institute
"Haematopoietic Cell Kinase signalling in lung inflammation and cancer"

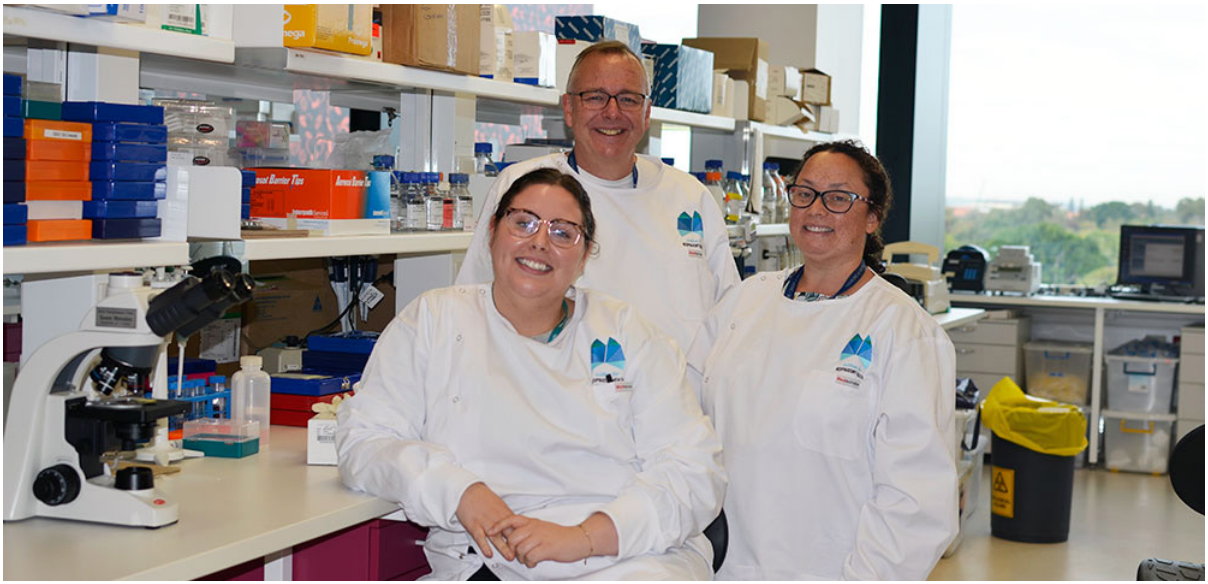
**Shaokang Ma.** NCARD
"Identifying and exploiting neo-antigens in murine mesothelioma as a model for human immunotherapy"

**Ian Dick.** NCARD
"Identifying potential neo-antigens using MHC elution"

## VISITING SPEAKERS

**Professor Harm Tiddens.** Department of Pediatric Respiratory Medicine, Erasmus University Rotterdam
"State of the art chest imaging: The time had come to standardize"

**Professor Ian Pavord.** Medical Sciences Division, University of Oxford
"New biological options in airways disease"



# 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 one of 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 2018, the Unit conducted 20 studies with 180 patients coming in for screening and 142 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 2018 we conducted trials for:

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

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:

- A/Prof Siobhain Mulrennan for cystic fibrosis trials and bronchiectasis trials.
- A/Prof Yuben Moodley for asthma and IPF 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.

# L I F E GROUP

People living with chronic lung conditions often seek further information about how to live well with their condition and often would like to meet others like them. It is often reassuring to meet others who still get out and about, have a laugh and generally enjoy life. This is what L I F E offers people with a lung condition, their family and carers.

Over the past year we have held 10 regular meetings on the first Wednesday of the month, as well as our annual Christmas party, in the Perkins Building. Our informative and inspiring guest speakers have included: Kate Baumwohl (protecting your voice when you cough), Dr Ed Harris (respiratory physician Q & A), Phil Bianchi (WA's Canning Stock Route), A/Prof Cecilia Prele and A/Prof Steve Mutsaers (consumer involvement in Institute research planning), and Di Ingelse (sharing and recording your life story). An innovation to our meeting structure has been the focussed discussions on topics chosen by members. Recently we have discussed eating well, managing the good days and the bad, and sleep. We've also gathered for a social lunch in the community each autumn, winter and spring, and sent get well, condolences and birthday wishes to members through our card club.

Our quarterly Breath of L I F E magazine is posted (60%) or emailed (40%) to members and additional copies distributed to waiting areas, and is downloadable from the Institute's website. We thank the Department of Respiratory Medicine, Sir Charles Gairdner Hospital for supporting the printing of hard copies for members who do not use email and for waiting areas.

We've continued to respond to many phone and email enquiries from people seeking information about living with lung conditions. Throughout 2018 a working bee of L I F E members continued to assist the Institute's Clinical Trials Unit sorting out medical kits and making up patient files every month or two.

We continue to work on succession planning so that more of our regular members are involved in the running of L I F E and we can continue to thrive into the future. In August we celebrated 26 years since we began in Perth as the first respiratory support group in Australia. There are now over 100.

# COMMUNITY ACTIVITES

## 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.

## FUNDRAISING

The staff at the Institute for Respiratory Health would like to thank everyone who fundraised during 2018.

### CONQUER CYSTIC FIBROSIS

Conquer Cystic Fibrosis ran numberous fundraising events throughout 2018, 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.

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.

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.

# FUNDRAISING CONT.

## MELBOURNE CUP LUNCHEON

This year's Melbourne Cup Luncheon raised an incredible $33,307 with over 230 guests enjoying fine food and wine and the spirit of the day, whilst raising funds for a good cause. The event is held annually at the State Reception Centre at Fraser's, King Park and is supported by generous guests, volunteers and local business by donating prizes. The funds raised from the day go into the Glenn Brown Memorial Grant, allowing researchers to further their investigations into researching cystic fibrosis and bronchiectasis. Dr Anna Tai, a respiratory consultant and past winner of the Glenn Brown Memorial Grant, spoke of her research and passion to one day cure CF and 14 year-old, Sarah Kerr, inspired guests as she spoke about life after her life-changing lung transplant. We are grateful to Famous Sharron for once again hosting the event.

## HBF RUN FOR A REASON

Team Lung Busters came in strong for the 2018 HBF Run for a Reason. Together they raised over $4,000. A sincere thank you goes out to all who took part.

## CRAFT STALL

Mrs Brown fundraised for COPD research by running a craft stall at Bassendean Shopping Centre and raised the amazing amount of $1,196.

## MOVIE FUNDRAISER

Over 90 people attended a movie fundraiser night at Cygnet Cinema in September. Proceeds from the night went towards supporting our doctors, scientists and nurses continue their vital work help people living with chronic respiratory conditions.

# DONORS

2018 saw members and supporters once again contribute towards the Institute's annual appeals. One of the appeals saw a story from Jenni Ibrahim (page 25) who shared her story and is a great advocate for people 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 so kindly committed their time during 2018. The main event was the Melbourne Cup Luncheon, and our passionate volunteers greatly assisted in making the day such a success. Other volunteer tasks included an endless array of administrative duties.

# WALL OF GRATITUDE

We would like to thank the following people for their support.

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D Youens

# JENNI'S STORY

My name is Jenni Ibrahim and in 1998 after a severe episode of pneumonia, I was left in a coma fighting for my life.

This year marks my 20th year of living with a chronic lung condition.

It all happened so quickly. I developed a cough and thought I was coming down with the flu or a virus. Despite being prescribed antibiotics, the following day I felt worse. I was feeling lethargic, in severe pain and struggling to breathe.

Fortunately, my neighbour checked in on me and took me straight to the hospital – possibly saving my life!

As a result, I have less than 50% lung function. I was diagnosed with bronchiolitis obliterans, bronchiectasis and fibrosis. All caused by irreversible lung damage due to the pneumonia.

After being in hospital, I started a pulmonary rehabilitation program through the Physiotherapy Department at Sir Charles Gairdner Hospital. Thanks to this program, exercise is now a crucial part of my life – regardless of how I am feeling.

Since 1999 I have been involved with and subsequently led the community support group L I F E and have been an advocate for people living with chronic lung conditions.

I also want to help educate people who don't have a lung condition. Never having smoked, I'd like people to understand that not all lung conditions are related to smoking. What it means to have a chronic cough, for example, if I'm in a lift people tend to step back thinking I'm contagious. Also why I have a disabled parking bay even though I don't look sick.

Mostly I don't get hung up about it. People react like this because lung conditions are not well understood in the community. I can help that by letting people know.

In 2017, I was diagnosed with stage four liver cancer metastases in my lungs. I am lucky to be the first person in Western Australia having access to a drug which is still in clinical trials overseas. If this doesn't work then there is nothing more, but early results look promising.

I have wound back a little but am working with the groups I lead, to help them transition to new leadership and develop greater sustainability for the future.

My message is – be active in managing your own health, and don't leave it up to others to control your health care. Look for health professionals that will answer your questions and help keep you as healthy and active as possible. Quit if you still smoke, eat a healthy balanced diet and learn everything you can about living with your lung condition.

*Jenni out walking with home visiting physiotherapist in 1998*

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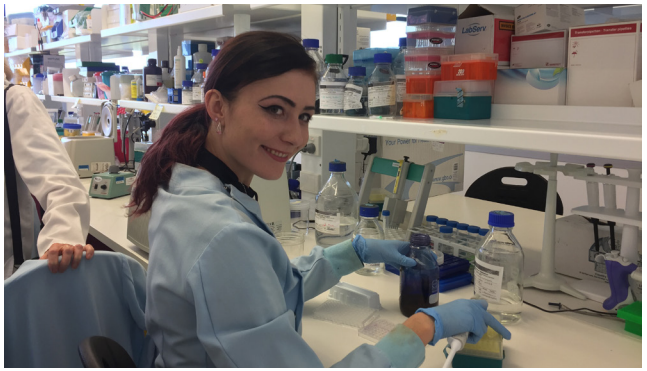

# FINANCIAL REPORT

Board members submitted the financial report of Institute for Respiratory Health (Inc) for the financial year ended 31 December 2018.

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

| | |
|---|---|
| Peter Gunzburg | Gary Lee |
| Johnson Kitto | Cecilia Prêle |
| Geoff Laurent | Sue Morey |
| Craig McGown | Anthony Fortina |
| Geoff Stewart | |

**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 2018 year amounted to $231,399.

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

G.A. Stewart

21 March 2019
Geoff Stewart, Board Member

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

# INCOME STATEMENT

## FOR THE YEAR ENDED 31 DECEMBER 2018

| | 2018 $ | 2017 $ |
|---|---|---|
| **Revenue** | | |
| Grant income | 1,462,489 | 1,525,230 |
| Research support | 245,997 | 431,221 |
| Clinical trials | 776,117 | 734,854 |
| Respirology | 295,766 | 388,996 |
| US DOD | 99,632 | - |
| Infrastructure funding | 279,881 | 114,896 |
| Fundraising income and donations | 95,521 | 128,061 |
| Corporate grants | - | 250,000 |
| Memberships income | 3,145 | 6,600 |
| Interest income | 27,696 | 26,917 |
| Other income | 1,224,280 | 454,699 |
| **Total revenue** | 4,510,524 | 4,061,474 |
| **Expenses** | | |
| Operating expenses | (991,684) | (502,209) |
| Employee benefits expense | (2,941,568) | (2,238,577) |
| Depreciation expenses | (42,291) | (22,287) |
| Finance costs | (505) | (890) |
| Other expenses | (303,077) | (327,191) |
| **Total expenses** | (4,279,125) | (3,091,154) |
| **Net current surplus** | 231,399 | 970,320 |
| **Other comprehensive income** | - | - |
| **Total other comprehensive income** | - | - |
| **Total comprehensive income attributable to members of the Institute** | 231,399 | 970,320 |
| **Surplus/(deficit) allocated to** | | |
| Restricted funds | (151,499) | 93,344 |
| Designated funds | 143,071 | 765,255 |
| Unrestricted funds | 239,827 | 111,721 |
| | 231,399 | 970,320 |

# BALANCE SHEET

## FOR THE YEAR ENDED 31 DECEMBER 2018

| | 2018<br>$ | 2017<br>$ |
|---|---|---|
| **CURRENT ASSETS** | | |
| Cash and cash equivalents | 2,775,281 | 2,324,849 |
| Trade and other receivables | 1,256,724 | 1,205,663 |
| TOTAL CURRENT ASSETS | 4,032,005 | 3,530,512 |
| **NON-CURRENT ASSETS** | | |
| Property, plant and equipment | 52,051 | 94,342 |
| TOTAL NON-CURRENT ASSETS | 52,051 | 94,342 |
| **TOTAL ASSETS** | 4,084,056 | 3,624,854 |
| **CURRENT LIABILITIES** | | |
| Trade and other payables | 393,686 | 264,770 |
| Employee provisions | 316,431 | 232,009 |
| TOTAL CURRENT LIABILITIES | 710,117 | 496,779 |
| **NON-CURRENT LIABILITIES** | | |
| Employee provisions | 53,066 | 38,601 |
| TOTAL NON-CURRENT LIABILITIES | 53,066 | 38,601 |
| **TOTAL LIABILITIES** | 763,183 | 535,380 |
| **NET ASSETS** | 3,320,873 | 3,089,474 |
| **MEMBERS' FUNDS** | | |
| Accumulated funds | | |
| Restricted | 348,006 | 499,505 |
| Designated | 2,502,902 | 2,359,831 |
| Unrestricted | 469,965 | 230,138 |
| **TOTAL MEMBERS' FUNDS** | 3,320,873 | 3,089,474 |

*institute for*
RESPIRATORY HEALTH

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We are a registered charity. All donations over $2 are tax deductible.
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