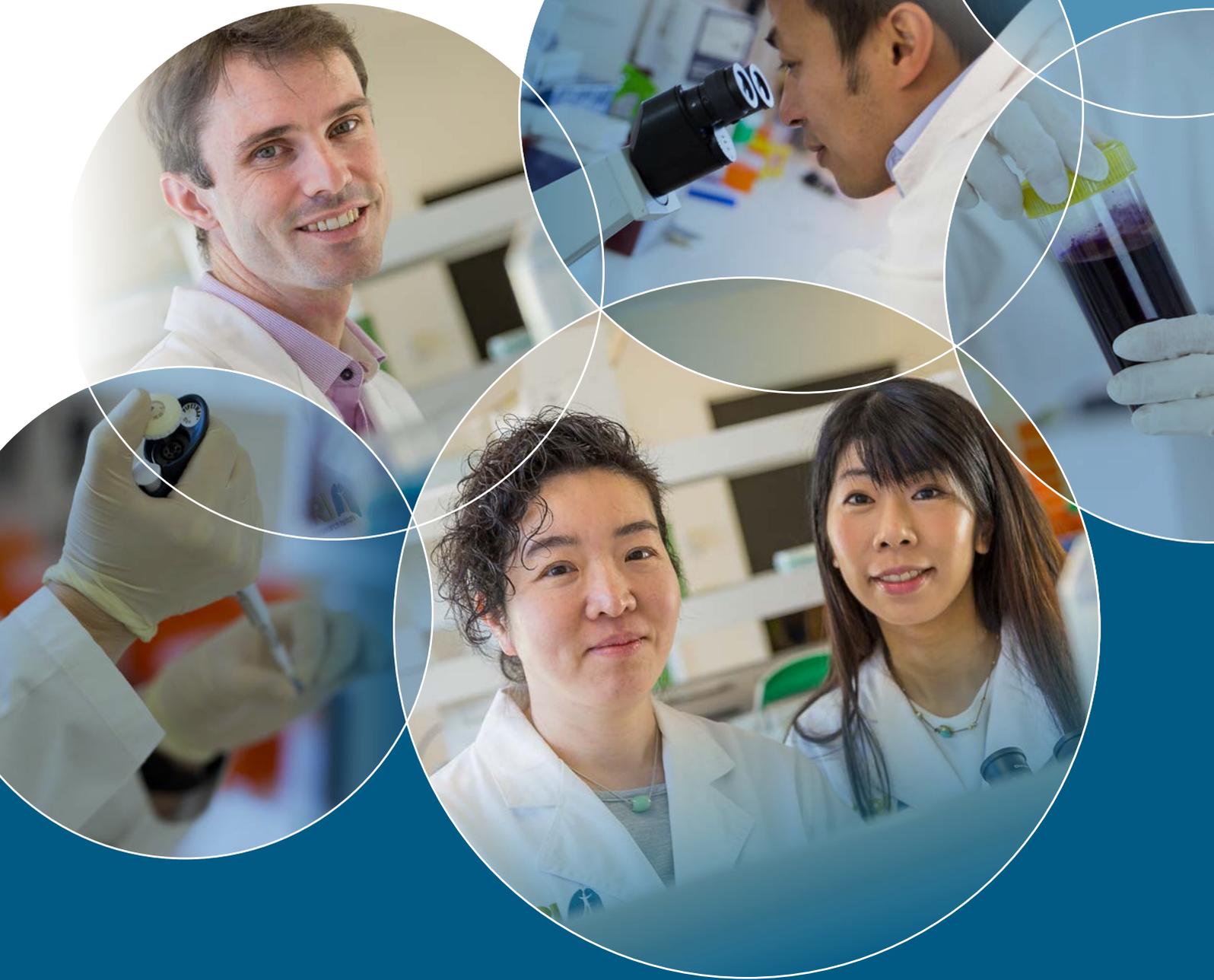


ADRI



Asbestos Diseases Research Institute



ANNUAL REPORT 2019



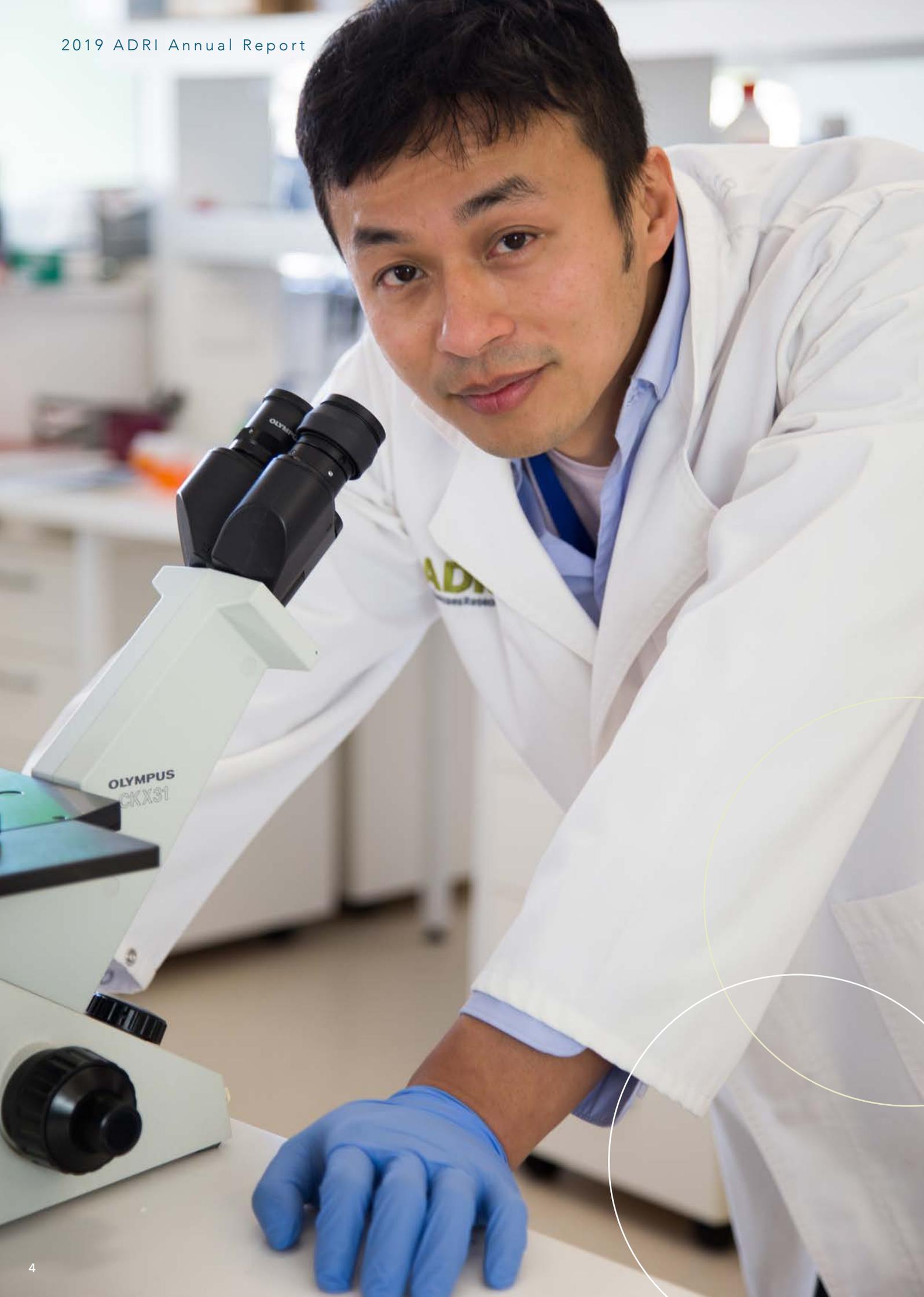
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Mission

The Asbestos Diseases Research Institute aims to improve the diagnosis and treatment of asbestos-related diseases and at the same time to contribute to more effective measures to prevent exposure to asbestos.

Australian malignant mesothelioma statistics

Key Facts



- Approximately 18,200 people have been diagnosed with malignant mesothelioma in Australia since 1982. Most people are aged 70 years or more at the time of diagnosis. Men make up over 80% of all cases. **(Figure 1)**



- New South Wales has the largest number of people diagnosed with malignant mesothelioma followed by Victoria, Queensland and Western Australia **(Figure 2)**



- The percent growth in the cumulative number of cases was highest in the 1980s. For example, a jump from 50 cases in one year to a combined figure of 100 cases in the next year represents a 100% percent growth in the cumulative number of cases each year. More recently, the cumulative number of new cases increased by about 5% per year. **(Figure 3)**

Figure 1.

Number of malignant mesothelioma cases in Australia, 1982-2018

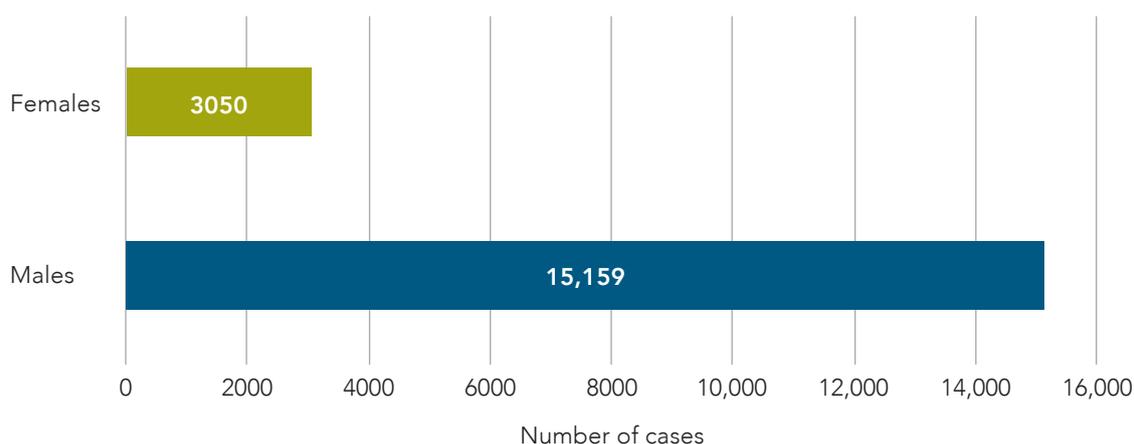


Figure 2.

Cumulative number of malignant mesothelioma cases in Australia, 1982-2015, by jurisdiction

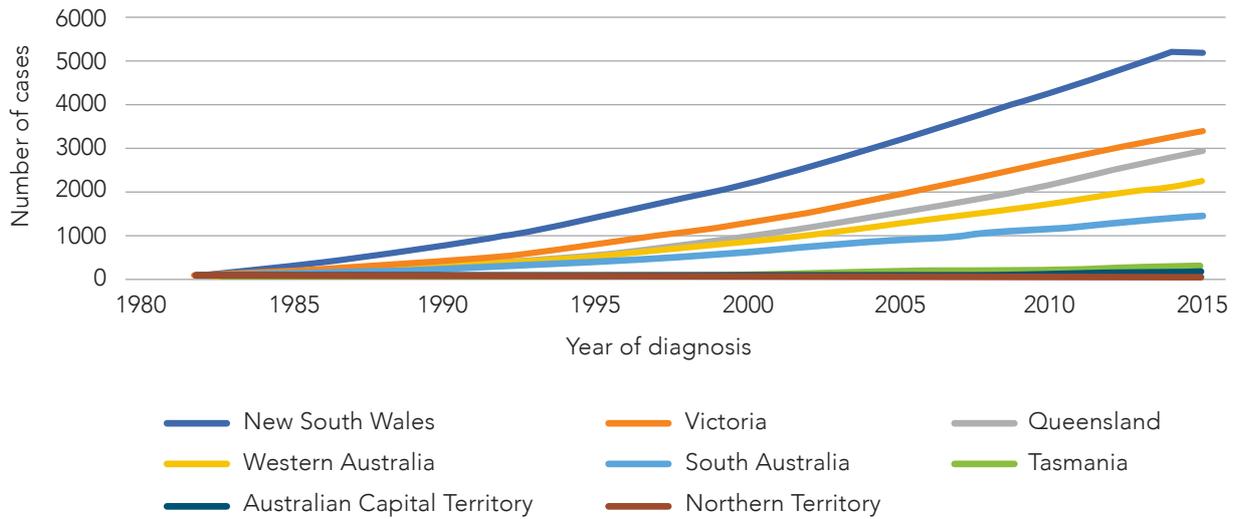
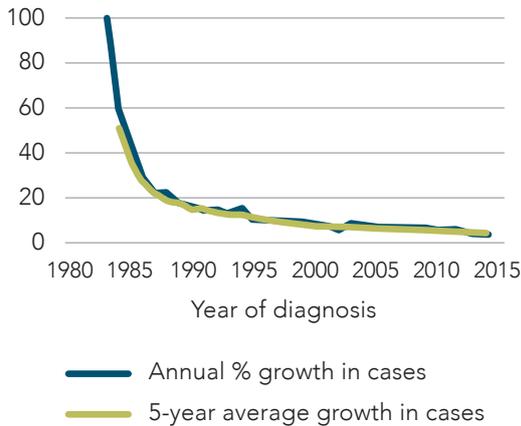
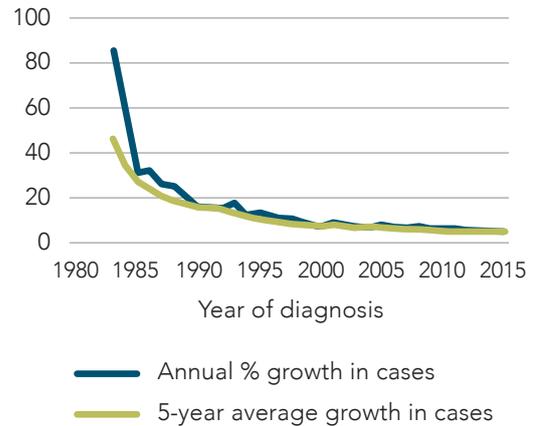


Figure 3.

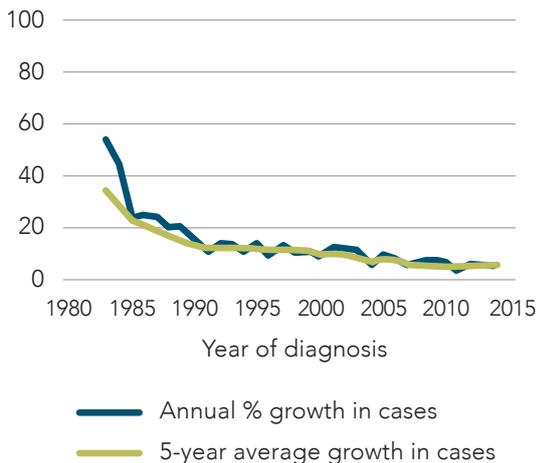
Percent growth in the cumulative number of male malignant mesothelioma cases in New South Wales, 1982-2015



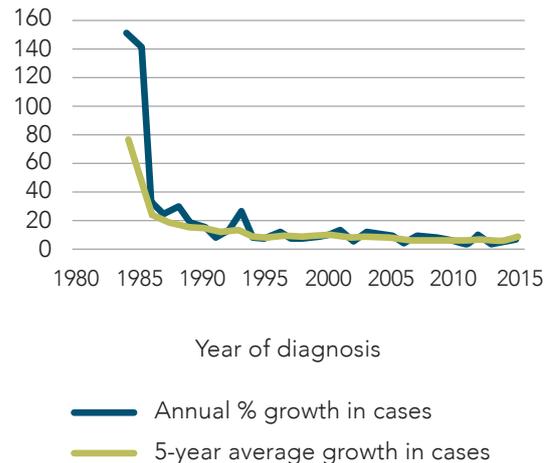
Percent growth in the cumulative number of male malignant mesothelioma cases in Western Australia, 1982-2015



Percent growth in the cumulative number of female malignant mesothelioma cases in New South Wales, 1982-2015



Percent growth in the cumulative number of female malignant mesothelioma cases in Western Australia, 1982-2015



ADRF Chair's Report



Early in 2019 I joined the ADRF Board having retired as CEO of the Commonwealth Government's Asbestos Safety and Eradication Agency (ASEA). At ASEA we established and implemented the first National Strategic Plan for the management and eradication of asbestos and asbestos containing material. I have had a long career in occupational health and safety including issues associated with asbestos; I am very passionate about the need for a stand-alone research institute for asbestos. The achievements and continued viability of an Asbestos Diseases Research Institute as a disease specific medical research facility is essential in the fight to support those exposed and their families. It is important to continue to support research into asbestos-related diseases as there are currently over 700 Australian's diagnosed each year with mesothelioma, and

global research indicates more than 4000 Australians die from asbestos cancers each year. Asbestos diseases are preventable man-made diseases, still with a poor prognosis and few treatment options available. To tackle this issue ADRI's research strategy encompasses a wide spectrum of prevention/public health, laboratory and clinical research as highlighted in this report.

Throughout 2019 ADRI's research intersected from prevention/ public health, laboratory and clinical with staff from these three areas participating in the Regional Collaboration Programme workshops. This programme aims to share preventive technologies to abate asbestos, reduce asbestos-related diseases and transition to an asbestos-free society. iCare, Dust Diseases Care continued to fund the Mesothelioma Support Service which provides evidence-based information to mesothelioma patients and their families. This service is vitally important as it fills a much need gap in the support of mesothelioma patients.

We are extremely grateful for the philanthropic support during the year. This valuable funding has supported areas of greatest need including early career researchers and pilot studies which have then contributed to peer-reviewed grant applications for further funding. Thank you to all our supporters for your ongoing generosity.

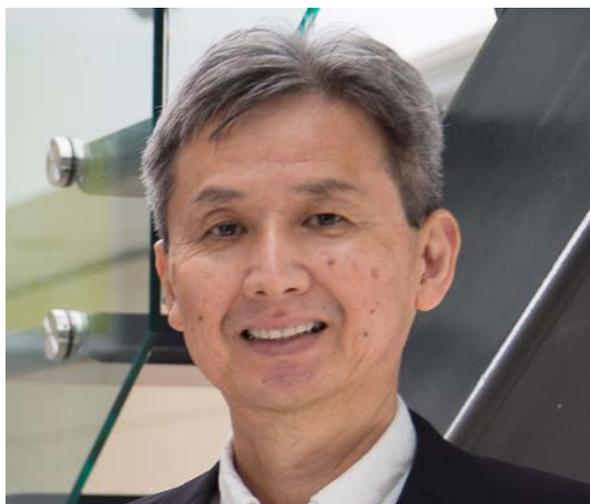
During the year, the Board farewelled two long standing members, Ms Sylvia Kidziak AM and Mr Barry Robson. Sylvia and Barry both joined the permanent Board when it was established in 2007 and were nominees of the Dust Diseases Board and the Asbestos Diseases Foundation of Australia, respectively. Dr Deborah Vallance, a nominee of Unions NSW also left the Board and on behalf of the Foundation I would like to thank them for their enormous input over many years. We welcomed Ms Tanya Buchanan as Vice Chair, during the year, Tanya brings expertise in leadership and governance to the Board. I am very grateful to all our Board of Directors, who offer their expertise and valuable time to the ADRF on a voluntary basis to further the mission of the Foundation.

A handwritten signature in black ink, appearing to read 'Peter Tighe'.

Mr Peter Tighe
Chair



ADRI Director's Report



Australia records one of the world's highest rates of mesothelioma and much of the asbestos used in the past remains in our community. Globally, many developing countries, including those near Australia, continue to use asbestos and are starting to experience mesothelioma. The founders of ADRI set a high and far-reaching goal for those to follow: *'to make asbestos-related diseases history.'* On the other hand, ADRI has throughout been one of the smallest medical research institutes (MRI) in Australia. David-and-Goliath is a case in point.

ADRI's mission is to pursue this goal and my task is to optimise resources towards the goal. For sure ADRI should not overcommit or overstretch the limited resources, and efficiency should be enhanced. However, unlike most MRIs, ADRI has no scale-merit nor able to function as a composite of specialized teams. With our level of

scale (currently 14 staff), we can only function as *'one team.'* As the theme of asbestos-related diseases warrants, our team must adhere to an interdisciplinary approach, that is, to boldly cross-over disciplines and effectively collaborate with external partners.

In last year's report, I wrote that ADRI staff began to embrace the strategy and direction based on the three pillars of research: biomedical, clinical and public health, which in turn, reflected the *'objects'* of our Constitution. This year I am happy to report that ADRI's core activities have purposely embodied this strategy and direction. I commend our staff and members for being open-minded and adaptive and I encourage them to push ahead on this path.

This year's pinnacle events in this regard were the ADRI-led international training workshop in the Philippines and Fiji. Implementing training

workshops in developing countries traditionally belongs to the realm of public health. Nevertheless, all ADRI researchers and staff came together under the theme of *'improvement of mesothelioma diagnosis and management.'* Incentives grew to seek viable intersections across the research pillars. Existing partnerships were strengthened, and new partnerships were born.

To our friends, colleagues and stakeholders, ADRI is one team keenly aware of our goal and mission. We are firmly on track but could use a bit of momentum. Kindly lend us a hand.

A handwritten signature in black ink, which reads "Ken Takahashi". The signature is written in a cursive, flowing style.

E/Professor Ken Takahashi,
MD, PhD, MPH
Director



*Improvement
of mesothelioma
diagnosis and
management.*

ADRF Board



Mr Peter Tighe

Independent Chair
Invited by the Board

Appointed: 25 February 2019

Peter Tighe was the CEO of the Asbestos Safety and Eradication Agency (ASEA), appointed by the Minister of Employment as Statutory Officer for a period of five years until August 2018. ASEA was established to implement the first National Strategic Plan for the management

and eradication of asbestos and asbestos containing material. Peter was National Secretary of the Communications Electrical and Plumbing Union (CEPU) and Divisional Secretary of the Electrical Trades Union (ETU). Peter was an Executive member of the Australian Council of Trade Unions (ACTU) and a ministerial appointee to Safe Work Australia. He has also served on a variety of vocational boards including the Central Trades Committee of Training Recognition Australia and was a committee member of the Ministerial Council for Tertiary Education and Employment Apprentices Action

Group. He was also a member of the Climate Change and Energy Efficiency's NGO Climate change roundtable. Peter was the Chair of the National Electrical and Electronic Industry Training Council and E-Profiling Pty Ltd; Chair and Deputy Chair of Connect Superannuation (now merged with C+Bus); and Trustee and Director on the Board of the Investment Committee of CBUS Superannuation. He is currently Deputy Chair of EE-Oz Energy Skills Australia and a member of the Board of Exemplar Systems Pty Ltd and Exemplar Learning Pty Ltd.

Ms Tanya Buchanan

Vice-Chair
Invited by the Board

Appointed: 23 July 2019

Tanya Buchanan is the Chief Executive Officer of the Thoracic Society of Australia and New Zealand (TSANZ), the peak professional body for health professionals and researchers working in respiratory health. She has extensive senior executive and governance experience in Australia and the United Kingdom. Tanya started her health career in nursing. She has a passion for, and a commitment to, improving respiratory health. In 2011 she was awarded membership of the UK Royal College of Physicians, Faculty of Public Health by Distinction and was the winner of the Leading Wales award for her commitment to leadership in the voluntary sector. Tanya holds an MBA majoring in health services administration and is currently completing a PhD in tobacco control. She has been a reviewer for academic journals and has held advisory positions on government bodies with respect to tobacco control and public health. Tanya is also an avid fencer in her spare time and enjoys competing and coaching.

Ms Sylvia Kidziak AM

Nominated by the Dust Diseases Board

Appointed: 27 November 2007 Acting Chair: 31 October 2018 Resigned: 24 May 2019

Ms Kidziak is Managing Director of SL Engineering, a Councillor on the NSW Business Chamber Eastern Sydney Regional Advisory Council and held the position of Principal Consultant, Occupational Health, Safety and Environment Policy at Australian Business Ltd for 26 years. She is a member of the Dust Diseases Board of NSW and was previously a member of the Board of Directors of the Workers Compensation (Dust Diseases) Board of NSW and Chair of the Research Grants and Corporate Governance Committees. Ms Kidziak held the position of Chair of the ARPANSA Radiation Health and Safety Advisory Council for 12 years and the Nuclear Safety Advisory Committee for 3 years. She was formerly a Member of the NSW Workers Compensation and Workplace Occupational Health and Safety Advisory Council, a Commissioner on the Australian Safety and Compensation Council and the National Occupational Health and Safety Commission, Board Member of the NSW Cancer Council, a Director on the NICNAS Industry, Government Consultative Committee, Chair of the Occupational Health, Safety and Rehabilitation Council of NSW and Chair or Member of various other state and federal government Councils and Committees concerned with health safety and environmental matters. Ms Kidziak has received several awards for her work which has included extensive advice on policy and technical issues relating to health and safety, medical research and specifically asbestos.

Professor Laurent Rivory

Nominated by The University of Sydney

Appointed: 7 December 2018

Professor Rivory is the Pro-Vice-Chancellor (Research) at the University of Sydney. His role focuses on the areas where cross-faculty engagement and external partnerships are integral to the academic enterprise. His responsibilities include large-scale collaborations such as the Charles Perkins Centre and the Brain and Mind Centre, the Core Research Facilities and the management of external partnerships, particularly in health. Professor Rivory is widely recognised for his research in cancer drug pharmacology and has extensive experience in the management of key research programmes in virology, immunology, cancer, RNA therapeutics and diagnostics. He has served as Senior Research Director, Research and Development, at Johnson and Johnson Research and was Director of the Research Strategy Office at the University of New South Wales. He has also had previous appointments as Clinical Senior Lecturer at the University of Sydney and as Head of the Pharmacology Laboratory, Sydney Cancer Centre at Royal Prince Alfred Hospital.

Emeritus Professor Robert Lusby AM

Nominated by the ANZAC
Health and Medical
Research Foundation

Appointed: 14 August 2012

Professor Lusby is the former Head of the Clinical School at Concord Repatriation General Hospital and also former Associate Dean of the Sydney Medical School, University of Sydney. Professor Lusby was a Colonel in the Royal Australian Army Medical Corps and has served in Rwanda with the United Nations Peacekeeping Force; in Bougainville with the Peace Monitoring Group and in 1999 he served with the INTERFET forces in East Timor. In addition, he was the Consultant Surgeon to the Australian Army and the Australian Defence Force. Professor Lusby is Chair of the ANZAC Medical Research Institute and has previously served on the Macquarie and Northern Area Health Service boards. He is the proprietor of Tintilla Estate Hunter Valley Vineyard and Winery.

Dr Teresa Anderson AM

Nominated by the Sydney
Local Health District

Appointed: 21 May 2018

Dr Teresa Anderson is the Chief Executive of Sydney Local Health District, one of the leading public health services in Australia. She has more than 35 years of experience as a clinician and health service executive. She has a well-established reputation for implementing strategies to foster innovation and best practice, supporting collaboration and building partnerships. She is an internationally recognised Speech Pathologist and is passionate about developing programs and services to support and improve the health and wellbeing of all people in the community. In 2018 Dr Anderson was appointed a Member of the Order of Australia (AM). Dr Anderson is a Vice President and has been made a Fellow of the NSW Institute of Public Administration Australia, is a member of seven Medical Research, Health and PHN boards and is an active member of the Sydney Health Partners Governing Council and Executive Management Group, one of the first four centres in Australia designated by the NHMRC as an Advanced Health Research Translation Centre.

Mr Barry Robson

Nominated by the
Asbestos Diseases
Foundation of Australia Inc.

Appointed: 27 November 2007
Resigned: 26 November 2019

Barry Robson is the President of the Asbestos Diseases Foundation of Australia (ADFA) and President of the Blacktown and Mt Druitt Cardiac Support Group. He is a life member of the Maritime Union of Australia and the St Mary's Baseball Club. Member of the National Taskforce Asbestos in Telstra Pits and Member of the Council for the Asbestos Safety and Eradication Agency.

Dr Deborah Vallance

Nominated by Unions NSW

Appointed: 18 April 2016

Resigned: 21 November 2019

Dr Vallance is the Senior Policy Officer, Work Health and Safety for the Australian Council of Trade Unions. From 2009 -2019 Dr Vallance was the National H&S Coordinator of the AMWU. The majority of her working life has been spent in health and safety roles in the union movement, including the participation in tripartite bodies and meetings at State, National and international levels. Deborah previously worked as a medical practitioner, has undertaken health and safety policy and project work for government and has worked in population health research.

Dr Christopher Clarke

Invited by the Board

Appointed: 13 March 2014

Christopher Clarke commenced practice as a Consultant Thoracic Physician in 1976. His special interest has been occupational lung disease. He has held appointments at a number of public hospitals in Sydney including Visiting Medical Officer in the Department of Thoracic Medicine at Concord Hospital until December 2008. Dr Clarke visited Aboriginal

Medical Centres in far western NSW until 2016 under the MSOAP-ICD program as a thoracic physician. He was the employee nominated member on the Medical Authority of the DDA as it is now known until December 2018. He is an Authorised Medical Specialist for the NSW Workers Compensation Commission. He is a past President of the Thoracic Society of Australia and New Zealand. He now has a Marine Engine Drivers 2 Certificate of Competency (steam) and is a Chief Engineer on ST Waratah one of the vessels run by the Sydney Heritage Fleet. This has given him first-hand experience of the trades and processes that exposed workers to occupational hazards. He did not expect to see the reoccurrence of some occupational lung diseases, the cause and prevention of which were well known when he commenced practice.

Dr Andrew Penman AM

Invited by the Board

Appointed: 8 October 2014

Andrew Penman is a public health physician whose career has been focussed on the application of health and medical research in effective public policy and health programs. From 1984 to 1998 he held a succession, of senior positions as Regional Director of Public health, Pilbara Health Region, Assistant Commissioner and Chief Health Officer, WA Health Department, Director of Disease Prevention and Health Promotion, and Deputy Chief Health Officer, NSW Health. In these

positions he initiated or led campaigns for example in control of sexually transmitted diseases, environmental health improvement in indigenous communities, expansion of hereditary disease services, improved parenting to reduce conduct disorder, alcohol harm minimisation, and expanded vaccination. Since 1996, he has been Chief Executive Officer of the Cancer Council NSW. In this position he has grown the organisation's revenue, and scale and scope of programs, and initiated innovative programs in liver cancer prevention, tobacco control among disadvantaged people, tobacco retail reform and expanded support services for cancer patients. He was Chair of the Steering Committee to develop guidelines for the management of malignant mesothelioma under the auspices of the Asbestos Diseases Research Institute. His work in cancer control was recognised by his appointment as a Member in the Order of Australia in 2010. His writing has been largely in the realm of departmental or organisational policy and strategy papers, and advocacy documents such as Health Goals and Targets for Western Australia and improving Radiotherapy services. These interests are reflected in his publication record.

Emeritus Professor Ken Takahashi

Research Director

Appointed: 1 February 2017

Ken Takahashi was Professor of Environmental Epidemiology and Director of the WHO Collaborating Centre for Occupational Health at the University of Occupational and Environmental Health (UOEH), Japan. Ken graduated from the School of Medicine, Keio University in 1983 (MD), and after completing a 2-year residency in surgery, he received a PhD from UOEH and MPH from the University of Pittsburgh. He engages in epidemiologic research of occupational diseases, with special interest on occupational lung diseases, and asbestos-related diseases in particular. He served as consultant/ advisor to the WHO and ILO on a number of occasions, examiner/advisor to academic institutes in several Asian countries, is a former Board Member of the International Commission of Occupational Health and former President of the Asian Association for Occupational Health. He currently serves as the WHO Expert on Chemical Safety/Environmental Epidemiology (International Health Regulations) and is an elected Fellow of the Collegium Ramazzini. He received the Jorma Rantanen Award from the Finnish Institute of Occupational Health in 2011 and the Irving Selikoff Lifetime Achievement Award from the Asbestos Disease Awareness Organization (USA) in 2014. Ken is Research Director (Director of ADRI) since Feb 2017 and was Professor at the University of Sydney, Concord Clinical School Feb 2017 – May 2018.

Ms Victoria Keena

Interim Company
Secretary

Appointed: 15 April 2019

Ms Victoria Keena, is the Interim Company Secretary of the Asbestos Diseases Research Foundation (ADRF) and Executive Officer the of Asbestos Diseases Research Institute (ADRI). She joined the ADRI in 2008 and has over 30 years' experience and knowledge of medical research institutes, supporting researchers, managing corporate governance, infrastructure, finances and fundraising. At the ADRI she assists the Director in the management and development of the Institute in order to achieve the strategic and operational objectives of the Foundation. She was a founding staff member and the General Manager of the Woolcock Institute of Medical Research until 2007.





ADRI Staff

Mrs Vesna Aleksova
Biobank Officer

Ms Diana Arachi
International Liaison (August 2019-)

Dr Yuen Yee Cheng
Principal Scientist

Mr Ross Flemons
Accountant

Ms Kim Hadley
Receptionist/EA

Dr Ben Johnson
Post-doc Fellow (June 2019 -)

Dr Steven Kao
Oncologist

Ms Victoria Keena
Executive Officer

Mrs Jocelyn McLean
Mesothelioma Support Coordinator

Mrs Joanne Roseman
Mesothelioma Support Coordinator

Dr Matthew Soeberg
Research Fellow

E/Prof Ken Takahashi
Director

Mrs Jenny Weismantel
Volunteer

Dr Marissa Williams
Post-Doctoral Fellow (-2019)

Mr Ta-Kun Yu
Research Assistant (July 2019-)

Mrs Ari (Man Lee) Yuen
Industrial Hygienist

Mrs Ling Zhuang
Technical Officer (February 2019-)



ADRI Students

Mr Tom Johnson
*PhD Fellow,
The University of Sydney*

Miss Fanny Colard
*Bio-engineer and Computer Scientist Intern
Université de Poitiers, France*

Miss Amanda Purcell
*Summer Student,
University of Technology Sydney*

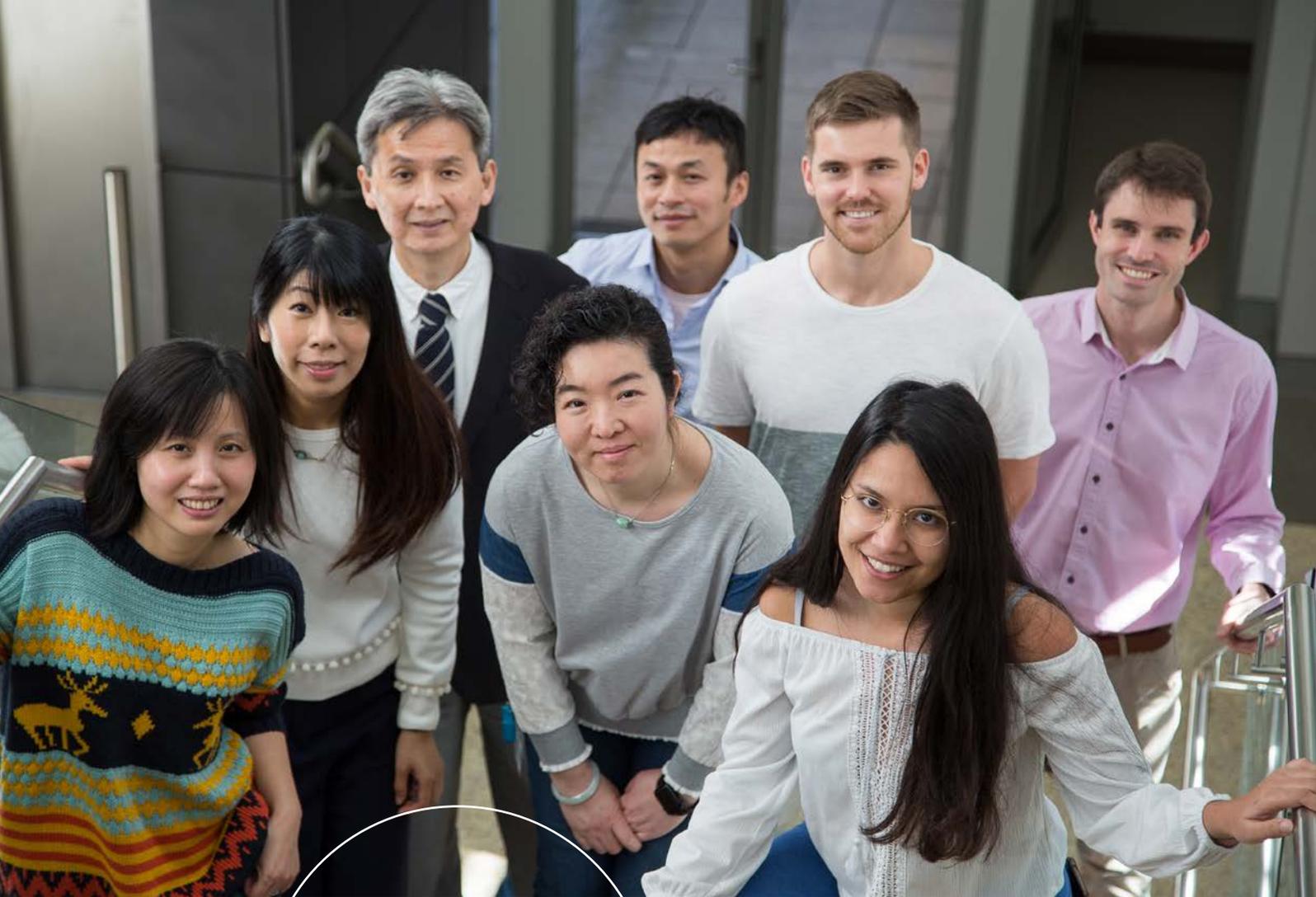
Mr Mark Viller
*Summer Student,
University of Technology Sydney*

Volunteer

Jenny Weismantel

Jenny has been working with ADRI as a volunteer since 2011 and continues to be an invaluable team member. She has become our Endnote and reference manager expert and supports various admin functions for the research team. We are forever appreciative of Jenny's hard work, attention to detail, good humour and continuing support.





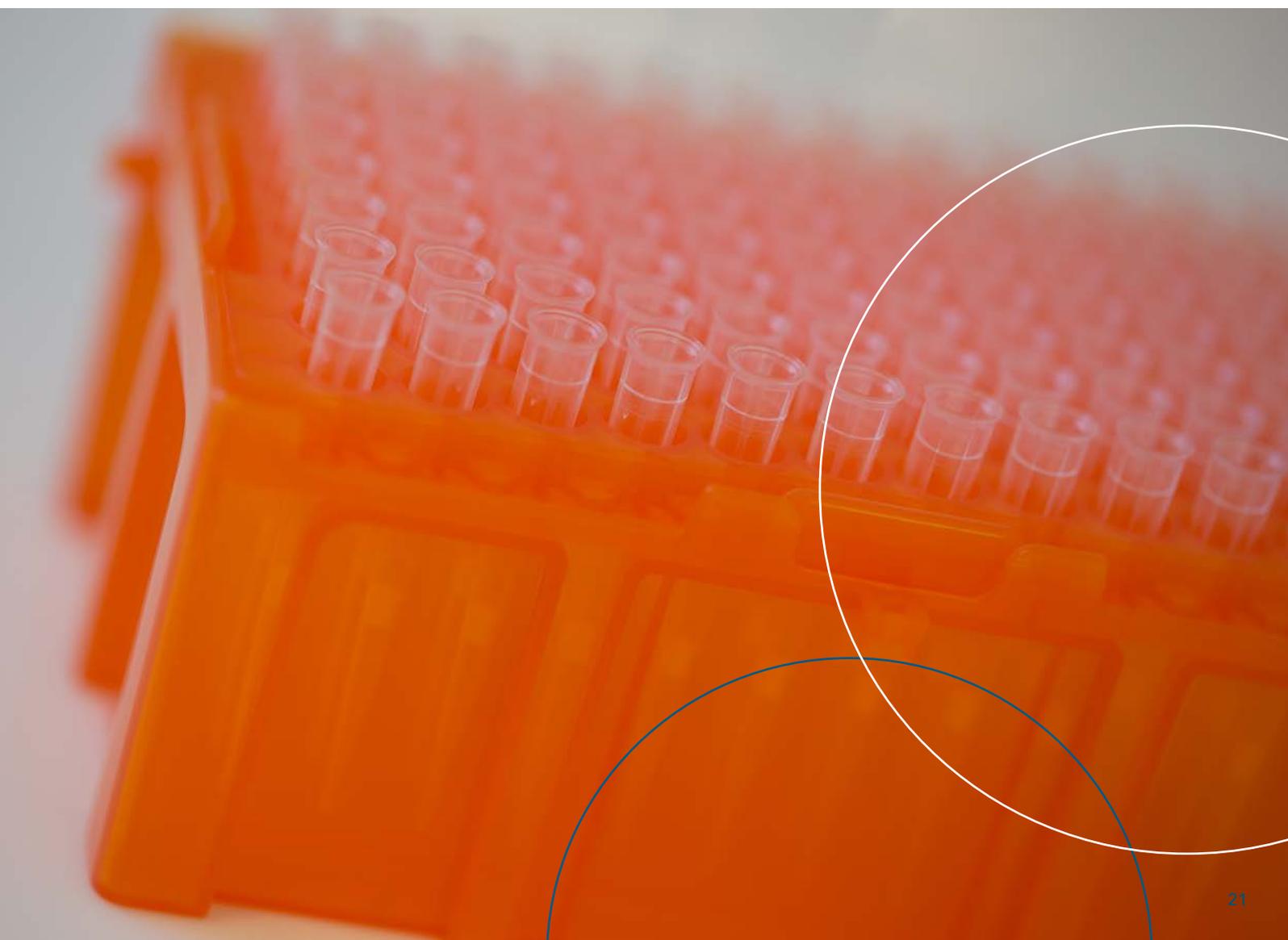
Research into asbestos-related diseases to improve methods of prevention, diagnostics and treatment.

Research

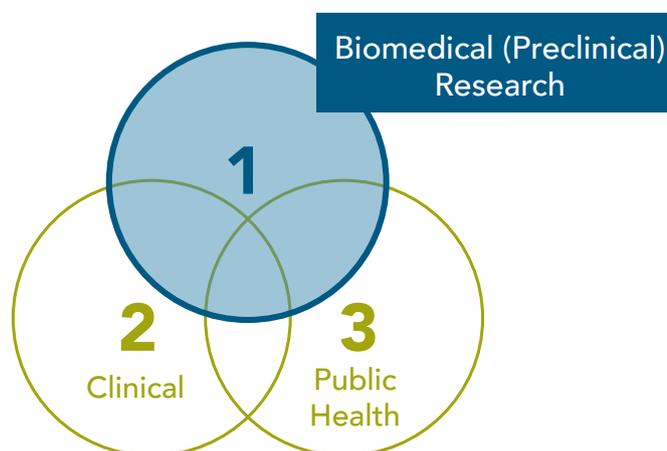
The ADRI continues to conduct biomedical (preclinical), clinical and public health research into asbestos-related diseases with findings enabling improved methods of prevention, diagnostic, therapeutic procedures and treatments. As one of the smallest independent medical research institutes (iMRI) in Australia, ADRI aims to create momentum by crossing disciplines internally and collaborating externally.

Our **biomedical (preclinical) research** focuses on a variety of molecular and biological techniques. These techniques are being applied to blood and tissue specimens stored in the **ADRI Biobank** with promising new diagnostic/therapeutic approaches being converted into **clinical** practice to tackle asbestos-related disease. Our **patient support** reaches out to mesothelioma patients who are undergoing therapy or post-therapy

in the community, thereby integrating **clinical** and **public health** approaches. Biomedical (preclinical) research is conventionally conducted in the context of **translational research**, i.e. "from bench to bedside" to which ADRI gives major emphasis. At ADRI, we aspire to add another dimension to translational research, i.e. the public health/preventative dimension. We call this "from bench to the public."



1. Biomedical (Preclinical) Research



Biomedical (Preclinical) research is the first pillar of ADRI research with focus on the following:

- knowledge of disease mechanisms
- biomarker discovery and development
- development of novel treatment strategies.

Aim

Pulmonary diseases related to human exposure to asbestos are becoming an increasingly common major health concern, both in Australia and worldwide. It is now widely understood that asbestos fibres are highly pathogenic, capable of causing a number of different asbestos-related diseases (ARDs) in humans, including asbestosis, lung cancer and malignant pleural mesothelioma (MPM). MPM is an aggressive ARD, with global incidences rising steadily over the past decade. Due to the long latency period from exposure to the onset of symptoms, it is challenging to diagnose MPM at an early stage. Consequently, prognosis is typically poor, with median survival ranging from just 9 to 12 months once a patient has been diagnosed with MPM. There is a combination of factors that can be attributed to the inadequate diagnosis and treatment of MPM in the clinic. These include

a lack of existing knowledge on the molecular mechanisms that lead to the development and progression of the disease, a lack of existing biomarkers to facilitate an early and accurate diagnosis, as well as a lack of effective treatment strategies. Therefore, the main aim of pre-clinical research undertaken in ADRI's laboratories is to improve the following key areas in relation to ARDs; 1) knowledge of disease mechanisms, 2) biomarker discovery and development, and 3) development of novel treatment strategies.

Impact

The biomedical research being carried out at ADRI utilises cell lines and patient-derived biospecimens sourced from ADRI's continually expanding and extensive biobank; which includes (but is not limited to) over 130 cell lines, and more than 600 matched MPM tumour tissue and blood samples. Conducting experiments

on these valuable biospecimens ensures that the data gained from our investigations are biologically relevant and provides us with a reliable indication of how the novel biomarkers and treatment strategies would perform when translated to the clinical setting. We anticipate that by successfully addressing the three key objectives (mentioned in our aims above), in combination with the biospecimens procured from ADRI's extensive biobank, ADRI's pre-clinical research will lead to novel diagnostic and treatment strategies that have the potential to progress to the clinical setting. Additionally, we have successfully established an MPM-specific genetic testing laboratory which has been **co-funded by Mrs Lyn Bursill**. Currently we are in the process of seeking NATA accreditation for the MPM-specific genetic test and have successfully fulfilled the requirements for the first advisory visit and external quality assessment; both of which are important milestones towards receiving full NATA accreditation. We are looking forward to completing the NATA accreditation process in 2020. The successful attainment of NATA accreditation will enable us to carry out molecular testing on clinical specimens obtained from medical practitioners in the near future, and in doing so will broaden ADRI's network with Australia's public healthcare system.

Research Projects

A novel 3D model for drug screening in mesothelioma

As the median survival for MPM is 9-12 months with most patients confronting drug resistance and recurring disease, finding more effective treatment strategies is therefore urgently needed for mesothelioma. In December 2019 we were awarded an iCare grant to accelerate drug screening into the clinic, using a model we have developed using porcine lung as a 3D scaffold. One of the major advantages of this scaffold is that it provides a biocompatible adhesive architecture for cells to grow. Most current drug screening systems rely on a 2D culture system where cells are grown as a single layer attached to a plastic surface. This is not an adequate model, as the behaviour and characteristics of cells can be very different to the actual behaviour of cells in a natural tumour microenvironment. To create a microenvironment akin to that of a tumour, we developed a novel 3D tumour model using decellularised porcine lung seeded with cancer cells. When compared to 2D culture, cells grown in this 3D model exhibited markers and expression levels comparable to that of real tumours. Over the next three years of this project we plan to further characterise the cancer biology and drug responses of this 3D model.

Transcriptional suppression of the miR-15/16 family by c-Myc in malignant pleural mesothelioma.

In this study we were looking at the molecular mechanisms that leads to the development and progression of the disease and we know that microRNA is frequently downregulated in MPM, but the mechanisms responsible for the loss of tumour suppressor microRNA miR-15/16 and miR-193a has not been explained and were investigated in this study. In tumour samples, a strong correlation was observed between the expression of miR-15b and 16, but not miR-15a and 16. From our data it suggests that in MPM, the downregulation of miR-15/16 is due to transcriptional repression by c-Myc, a family of regulator genes, primarily via control of the miR-15b/16-2 locus, while miR-193a-3p loss is due to genomic deletion. The results were published by Dr Marissa Williams and the team in *Oncotarget* in June 2019. This project was **co-funded by the Mr Jim Tully Fellowship** and follow-up studies will continue in 2020.



Genomic stratification and liquid biopsy in a rare adrenocortical carcinoma (ACC) case, with dual lung metastases.

In this collaborative project ADRI contributed Droplet Digital Polymerase Chain Reaction or ddPCR to detect their novel biomarkers. Adrenocortical carcinoma (ACC) is a rare malignancy with a poor prognosis and few treatment options. The molecular characterization of this cancer remains limited. Dr McCabe and colleagues at the Garvan Institute of Medical Research were presented with a case of ACC in a 37-year-old female, with dual lung metastases identified one year following the commencement of therapy. As standard therapeutic regimens are often unsuccessful in ACC, they undertook a comprehensive genomic study into this case to identify treatment options and monitor disease progress. They performed targeted and whole-genome sequencing of germline, primary tumour, and both metastatic tumours from this patient and monitored recurrence over two years using liquid biopsy for circulating tumour DNA and steroid hormone measurements. The molecular signatures in this ACC case suggested immunotherapy in the event of disease progression; however, the patient remains free of cancer. The extensive molecular analysis from this study was published in April 2019 by McCabe et al., and can now be applied to other rare and/or poorly stratified cancers to identify novel or repurpose existing therapeutic options, thereby broadly improving diagnoses, treatments, and prognoses.

Roles of methylated DNA biomarkers in patients with colorectal cancer

Dr Yuen Yee Cheng supervised Daisy Ma, an exchange student from the Hong Kong University to investigate the role of methylated DNA biomarkers in patients with colorectal cancer. Globally, colorectal cancer (CRC) is a leading cancer and therefore, early diagnosis and surveillance of this cancer is vitally important. Current methods to diagnose CRC rely heavily on endoscopy and radiological imaging. Non-invasive tests, including serum detection of the carcinoembryonic antigen (CEA) and faecal occult blood testing (FOBT) are associated with low sensitivity and specificity, especially at early stages. DNA methylation biomarkers have recently been found to have higher accuracy in CRC detection and enhanced prediction of prognosis and chemotherapy response. The most widely studied biomarker in CRC is methylated septin 9 (SEPT9), which is the only FDA-approved methylation-based biomarker for CRC. Apart from SEPT9, other methylated biomarkers including tachykinin-1 (TAC1), somatostatin (SST), and runt-related transcription factor 3 (RUNX3) have been shown to effectively detect CRC in a multitude of sample types. The results of this study were published as a review article in Disease Markers in March 2019 on the performances of various methylated biomarkers used for CRC diagnosis and monitoring, when used alone or in combination.

Epigenetic modification in mesothelioma

Epigenetic modifications are the key processes of cellular development and carcinogenesis. These modifications are considered a hallmark of cancer and have attracted considerable attention over the past decade for developing biomarker detection methods and therapeutic discovery for various malignancies. The advantage of using epigenetic modifications as biomarkers is their stability and availability in many sample types. They are useful in non-invasive biospecimens such as blood plasma and serum and for treatment discoveries, as different malignancies present different epigenetic signatures and, therefore, reversal of this phenotype offers a targetable therapy. Currently, there is no blood-based detection method for mesothelioma and diagnosis relies on a tumour biopsy. Previous studies have demonstrated that epigenetic dysregulation is a common event in mesothelioma and may represent critical events in the malignant transformation of the disease following asbestos exposure. Although DNA methylation is a common feature in mesothelioma, previous DNA methylation discovery approaches have been unsuccessful. Given this, investigations focusing on the application of epigenetic modifications as biomarkers, or as targets for therapeutics in mesothelioma, have the potential to produce high impact in the field and were published in Frontiers Research Topics in 2019.

Circulating RNAs for the early identification of asbestos-related cancer (ARC) including malignant mesothelioma

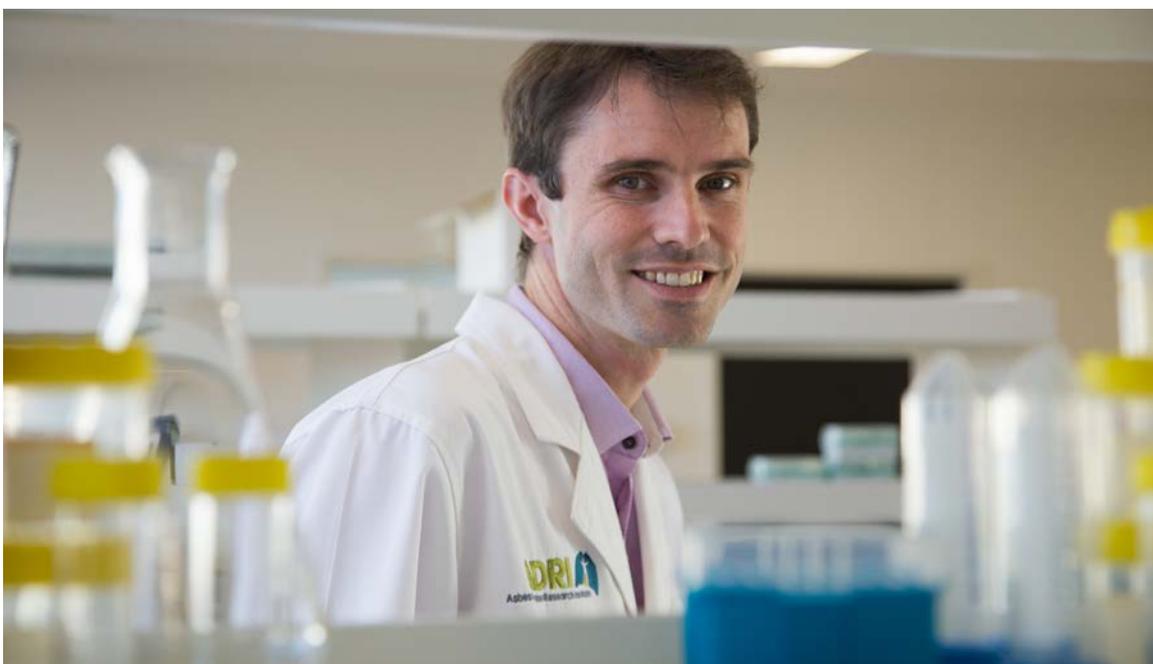
With no effective treatment options for malignant mesothelioma (MM) a timely diagnosis is critical to prolong survival. Currently, there is no early detection and/or diagnostic biomarkers available for the early identification of asbestos-related cancer (ARC). The discovery of circulating RNAs, a genetic marker which can be found in the blood, is an attractive and innovative option to consider in ARC research due to their stability and substantially in blood circulation; allowing them to potentially identify this fatal disease at an early and potentially treatable stage. To study circulating RNAs in ARC patients, the ADRI will utilise our ARC Biobank collection, the largest available collection in Australia. This ongoing study is **supported by the Revesby Workers Club Bill Bullard Charity Foundation Fellowship**. We anticipate that this project will lead to the discovery of early biomarkers for identification of ARC.

Discovery of the epigenome to facilitate Malignant Mesothelioma diagnosis

Malignant mesothelioma (MM) is difficult to diagnose because the symptoms resemble those from other lung cancers and because an invasive biopsy is needed for confirmation. Epigenetic variations, the biological mechanisms that switch genes on and off, could potentially be used to identify biomarkers in blood samples for cancer due to their accuracy, specificity and ease of collection. In this ongoing study we will determine the potential of epigenetic (DNA methylation) biomarkers as early detection tools for MM that build on our previous studies and preliminary data. We will also systematically analyse data sets from The Cancer Genome Atlas (TCGA), Gene Expression Omnibus (GEO) and our methylation profiling data set will be used to select candidate epigenetic biomarkers. Based on these data, candidate epigenetic biomarkers will be validated using our large MM tumour cohort and their clinical significance will be determined.

Circular RNA expression as potential biomarkers for mesothelioma

Currently an invasive tumour biopsy is needed to confirm a diagnosis of malignant pleural mesothelioma (MPM). Circular RNAs (circRNAs) are non-coding competitive endogenous RNAs (ceRNAs) that originate from within and interact with microRNAs as 'sponges' via direct binding, subsequently leading to their repression. CircRNAs are dysregulated in cancer and are cell-type specific, thermodynamically stable and highly conserved; thus, serve as potential blood-based biomarkers for detection of MPM. This study investigated circRNA gene expression patterns using MPM cell lines to identify potential candidates towards MPM diagnosis. We have identified the upregulation of 290 circRNAs in MPM cell lines. We have previously found the downregulation of some microRNAs to be associated with MPM and considering the selected candidate circRNAs host genes that have predicted binding sites related to these microRNAs, we can infer that circRNAs may have similar potential as diagnostic biomarkers in MPM. The validation of



their expression in MPM plasma (blood) samples were performed to test their potential as less-invasive biomarkers for the diagnosis of MPM. Dr Ben Johnson has further optimised the detection method of circRNA utilising ADRI Biobank samples, and we anticipate the results from this project will yield significant data to be published in a high impact journal in MPM research.

E-cadherin is down regulated in malignant pleural mesothelioma (MPM) and the expression of CDH1 in MPM leads to FAK inhibitor resistance

Focal adhesion kinase (FAK) inhibitors have been shown to efficiently suppress malignant pleural mesothelioma (MPM) cell growth and it has been proposed that the level of E-cadherin (a cell adhesion molecule) expression could potentially play a role in FAK inhibitor resistance in MPM. However, this area remains largely unexplored in MPM. In this study we utilised a large collection of MPM cell lines, including established and in-house primary MPM cell lines from patient samples, to study the role of E-Cadherin and FAK inhibitor in MPM. We found that the presence of CDH1 mRNA, the gene that provides instruction for making the protein E-Cadherin, is associated with resistance to FAK inhibitor PND-1186 only in MPM cells, regardless of E-Cadherin protein expression measurements by immunohistochemistry. For non-MPM cancer cell lines, neither E-cadherin mRNA, nor protein expression, appeared to play a role in FAK inhibitor resistance. This study will be completed in 2020 and submitted for publication.

CDKN2A and MTAP are useful biomarkers detectable by droplet digital PCR to identify mesothelioma from activated mesothelial phenotype

There is an urgent need to identify highly specific and sensitive biomarkers to detect MPM less invasively. Currently there are more than 15 biomarkers used in the clinic to differentially identify MPM, but none are highly specific nor sensitive. The co-deletion of the genes CDKN2A and MTAP, has been shown by researchers as a highly specific characteristic of MPM, which can potentially be utilized in the development of a less-invasive method to diagnose MPM. We have previously shown that deletion of CDKN2A (p16INK4a) is detectable by the droplet digital PCR (ddPCR) technique. In this study we aim to utilise ADRI's extensive MPM biospecimen collection to validate the detection of both CDKN2A and MTAP loss by ddPCR, which in turn could potentially be used in developing a less-invasive method of biomarker detection for MPM from cell-free tumour DNA. Our results indicate that the co-deletion of CDKN2A and MTAP is a frequent occurrence in MPM. Detection by ddPCR shows high concordance with the current utilised fluorescence in-situ hybridization (FISH) analysis and immunohistochemistry method. DdPCR can potentially be utilised for the future development of a less-invasive MPM-specific detection technique on MPM tumour DNA. This project is co-funded by the late Mr William Jupp and the first paper will be submitted to *Frontiers in Oncology* in 2020.

Exploring microRNA and exosome involvement in drug resistant malignant pleural mesothelioma

In the treatment of malignant pleural mesothelioma (MPM) combination chemotherapy, consisting of cisplatin and pemetrexed, remains the most widely used first-line treatment regimen for patients with unresectable MPM, but its clinical efficacy is hampered by drug resistance issues. Previously we have shown that MPM cell lines transfected with microRNA-16 (miR-16) induces an enhanced sensitivity to chemotherapy drug treatment, however further investigation into cellular targets to enhance MPM sensitivity to chemotherapy is warranted. Abnormal microRNA (miRNA) expression, survivin over-expression and exosome up-regulation are well known factors associated with drug resistance in many cancers, but their role in MPM drug resistance is largely unexplored. Therefore, in this project we explored the involvement of miRNA, survivin and exosomes in drug resistant MPM cell lines. We found that the restoration of miR-16 expression, in combination with the small molecule inhibitor (YM155) enhanced the sensitivity of the MPM cell lines to the chemotherapeutic agents. This suggests that both a loss in miR-16 and expression of survivin play a role in MPM drug resistance. Exosome involvement was not found to be associated with MPM drug resistance. The result from this project will be published in 2020.

The relationship of molecular biomarker detection and DNA isolation

Deoxyribonucleic acid (DNA) extraction using a Formalin-Fixed Paraffin-Embedded (FFPE) block is a frequent practice in pathological diagnosis and medical research. The extracted DNA, which is the targeted end-product for further molecular genetic analysis, depends on the ratio of tumour cells to normal cells. Theoretically, the same tissue sample would give an identical genetic detection result. However, the variable percentage of tumour cells and normal cells influences this theoretical result, therefore potentially influencing the final interpretation of this genetic testing result. The aim of this study was to investigate the relationship between DNA isolation and biomarker detection. We found that DNA isolated from leftover tissue contains a higher ratio of normal cells compared to tumour cells. DNA isolation factors can influence the interpretation of genetic alternation detection results. Therefore, we suggest that DNA extracted from leftover tissue samples cannot be used for genetic alternation detection by ddPCR as it may cause the incorrect calculation of copy number variation of the samples. Results from this study will be published in Biomedical Journal of Scientific & Technical Research.

YB-1: A central player in the carcinogenesis and malignant behaviour of MPM

Y-box binding protein-1 (YB-1) is a multifunctional transcription and translation factor of the cold-shock protein family and is an overexpressed oncogene with prognostic relevance in malignant pleural mesothelioma (MPM). The underlying mechanism of YB-1-driven in MPM was unclear. In this study we investigated the roles of YB-1 in driving the proliferation of MPM cells and considered the potential of YB-1-targeting drug development.

The Asbestos Diseases Foundation of Australia (ADFA) supported Tom Johnson's scholarship to enable him to submit his PhD thesis to The University of Sydney in 2020 focusing on the involvement of YB-1 in the drug resistance of MPM cell lines. Tom's research will further the understanding of chemo-resistance in this disease and therefore has the potential to improve MPM patient outcomes in the development of future drugs. Results from this study was published as a review paper in *Frontiers in Cell and Developmental Biology*.

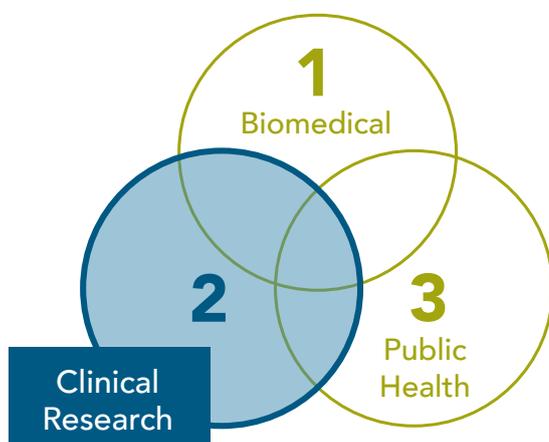
Other Research Outputs

ADRI Laboratory Educational Videos:

In June 2019, the ADRI lab group filmed and produced a series of educational videos to document the key laboratory features and molecular biology techniques that are required for biomedical research aimed to improve the diagnosis and treatment of ARDs. A total of five videos were filmed to provide a visual representation of the routine laboratory techniques carried out on a daily basis in the ADRI research facility; namely cell culture, drug treatments, polymerase chain reaction (PCR), western blotting and video microscopy. Additionally, a shortened summary video was produced, which showcased a summarised version of all five techniques. These six videos were presented at two international asbestos related diseases training workshops held in the Philippines and Fiji in July and December of 2019, respectively. These video presentations were well received by an audience comprised of public health representatives, medical practitioners, researchers and members of the general public. Based on the positive reception to these videos at the 2019 workshops, we will continue to present them at future conferences and ARD training workshops, including the upcoming workshop to be held in Thailand. Furthermore, these videos have now become a key display feature of the entrance foyer of the ADRI building and serve as a useful educational tool for prospective students, visiting scientists and other visitors.



2. Clinical Research



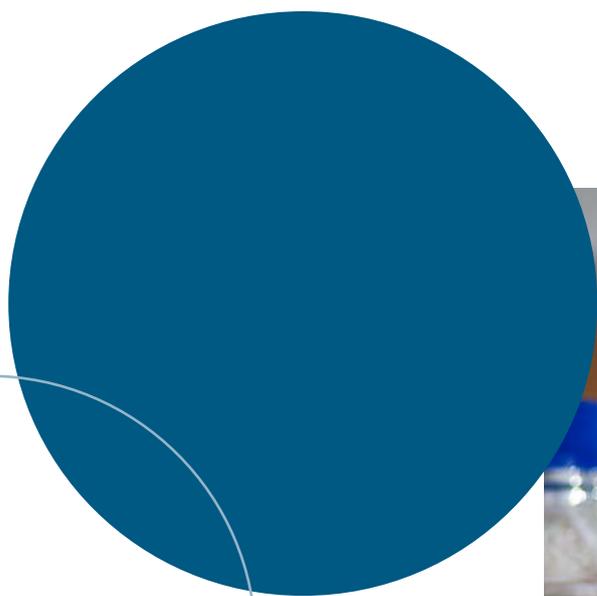
Clinical research is the second pillar of ADRI research with focus on the following:

Aim

To discover promising new therapeutic approaches to convert into clinical practice to improve outcomes for patients diagnosed with asbestos-related disease.

Impact

Treatment options for mesothelioma patients are limited and in clinical research we aim to determine the safety and effectiveness of medications, devices, diagnostics, and treatment regimens for mesothelioma patients. These may then be used for prevention, diagnosis, relieving symptoms, or treatment.



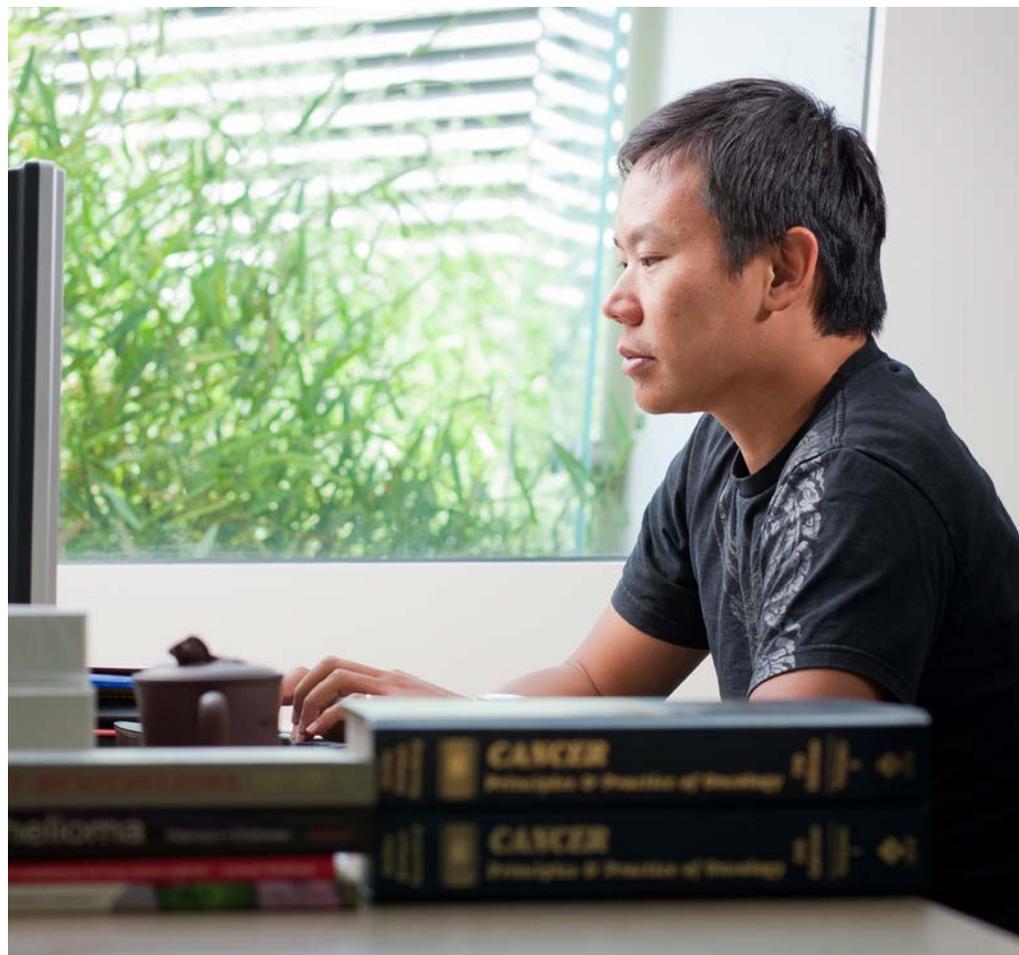
Research Projects

Retrospective evaluation of the use of Pembrolizumab in malignant mesothelioma on the DDA Compassionate Access Scheme

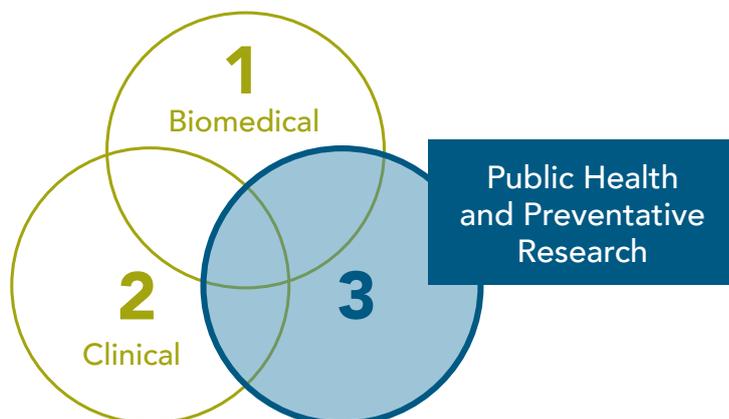
This project was **funded by iCare, Dust Diseases Authority** and we investigated the efficacy and toxicity of pembrolizumab, a type of immunotherapy, commercially known as Keytruda, in mesothelioma patients. Mesothelioma patients who were treated with pembrolizumab as part of the iCare NSW compensation scheme were included in the study. The aim of the study was to determine clinical factors and predictive biomarkers that could help select patients that were likely to benefit from pembrolizumab. Immunotherapy can be a reasonable treatment option for mesothelioma patients. Our results are comparable to other clinical trials investigating pembrolizumab in mesothelioma in terms of response. Factors such as good performance status and occurrence of immune-related adverse events may help select patients that are likely to benefit from pembrolizumab. The results of this project will be presented by Dr Steven Kao at the next International Mesothelioma Interest Group conference.

Highlight

Dr Steven Kao participated in the training workshop on the diagnosis of asbestos-related diseases in Fiji in December 2019. The workshop was delivered by ADRI in association with the World Health Organization (WHO), Country Office of Fiji, and hosted by College of Medicine, Nursing and Health Sciences, Fiji National University. It provided a unique opportunity for ADRI to share expertise aimed at advancing Fiji's capacity to detect, diagnose and treat cases of asbestos-related diseases, including mesothelioma.



3. Public Health and Preventative Research



Public Health is the third pillar of ADRI research with focus on the following:

- Quantifying the burden of asbestos-related diseases (ARDs)
- International cooperation on asbestos and ARDs
- Developing and applying public health/epidemiologic indicators
- Assessing the hazard and risk of asbestos exposure, e.g. epidemiologic studies

Aim

ARDs have unique aspects that arise from being an industrial, man-made, disease. By nature, they are 100% preventable. While we need to continue the search for effective diagnostic and treatment modalities to help patients, it is equally important to prevent the unnecessary burden from happening in the first place. The saying: “prevention is better than a cure” cannot be overemphasized. Contributing to the banning of asbestos in industrialising countries, will be of benefit to Australia by preventing asbestos-containing products slipping through our borders as well as alleviating the risk of Australians being exposed whilst travelling overseas. The aim of public health/preventative research at ADRI is to provide novel perspectives and scientific evidence that can lead to the prevention, and ultimately the elimination of ARDs.

Impact

In tackling ARD prevention, ADRI is closely collaborating with United Nations (UN) organisations such as the World Health Organization (WHO), the UN Environmental Programme (UNEP), and the International Labour Organization (ILO). Based on an unrivalled track record, ADRI awaits to be officially designated as a WHO Collaborating Centre. Moreover, this pillar provides context to the pillars of biomedical and clinical research, from the standpoint of public health and prevention, and allows us to identify research themes that are relevant and beneficial to the community, nationally and internationally.



Research Projects

Quantifying the Burden of Asbestos-Related Diseases (ARDs)

ADRI researchers continue to assess the burden of ARDs, e.g. mesothelioma, at national, regional and global levels based on internationally standardized as well as originally developed methods. We are a regular contributor to the internationally acclaimed Global Burden of Disease (GBD) study series. This year E/Prof Takahashi was among the co-authors of the GBD study on cancer published in the journal JAMA Oncology. In October, he was an invited speaker to the 13th Indonesian Occupational Medicine Conference and presented on the global situation of ARDs.

International Cooperation on Asbestos and ARDs

2019 was a seminal year in regard to international cooperation: ADRI directly organised international training workshops: 1) the Philippines and 2) Fiji; 3) supported a mini workshop on mesothelioma pathology in Indonesia; and 4) cooperated on a field study of a disaster relief project in Indonesia.

1) The Philippines Training Workshop was conducted in Manila 10-12 July and **funded by the Regional Collaborations Programme** which

aimed to advance the capacity to detect, diagnose and treat cases of ARD, with particular emphasis on mesothelioma. The Australian team comprised eight ADRI staff/associates and was joined by the Asbestos Safety and Eradication Agency (ASEA) and industrial partners, EnviroScience and Frontier Microscopy. The workshop was sponsored by The UNEP and the WHO and ILO participated.

From the Philippines Training Workshop local practitioners later referred to the ADRI for consultation several cases suspected of having mesothelioma, these were based on clinical data and pathological samples. The ADRI alliance with NSW Health Pathology assessed the cases and reported back to the local practitioners. Such referrals are a welcomed outcome of the workshop as it opened the door to continued opportunities for collaborative research via sharing clinical data and biospecimens.

2) With a similar objective, the ADRI conducted the Fiji Training Workshop in Suva 2-3 December with **funding from the Regional Collaborations Programme**. The Workshop was hosted by the College of Medicine, Nursing and Health, Fiji National University and implemented under the auspices of the WHO. The Australian team comprised eight ADRI staff/associates and an ASEA representative.

Post-workshop, the ADRI alliance with NSW Health Pathology was consulted for a local case suspected of mesothelioma in line with the project goals. Based on joint examination of clinical data and pathological samples, the search for the first case of mesothelioma in Fiji is underway. Fiji has a population of less than a million but is also the gateway to the many Pacific Island Countries. As at the end of 2019, preparation was underway for another training workshop in Thailand, in March 2020, under the auspices of the Basel, Rotterdam and Stockholm Convention Secretariat of the UNEP and co-sponsored by the WHO.

3) Associate Professor Kenneth Lee, Head of Department and Clinical Director of Anatomical Pathology at Concord Hospital and ADRI Honorary Associate, conducted the 'Mini-workshop on the Pathological Diagnosis of Mesothelioma', at the Persahabatan Hospital, Jakarta, Indonesia, 26-27 November.

Funded by the Regional Collaborations Programme grant, ADRI sponsored the event with the cooperation of Indonesian colleagues.

4) See below Assessing the Hazard and Risk of Asbestos Exposure

Developing and Applying Public Health/ Epidemiologic Indicators

With an aim to identify factors that predict the banning of asbestos by countries, the national status of adoption of asbestos-related international conventions and government effectiveness scores were assessed. After controlling for government effectiveness, countries that ratified both the ILO Asbestos Convention and the Basel Convention (on the Control of Transboundary Movements of Hazardous Wastes and their Disposal) had higher probability of banning asbestos. Agreements on international programmes and government commitments were deemed important factors for countries to move towards an asbestos ban. This research was published in The Lancet Planetary Health (see the publications list)

Assessing the Hazard and Risk of Asbestos Exposure, e.g. Epidemiologic Studies

E/Prof Takahashi joined the 16-20 July field study of the post-disaster response in Lombok, Indonesia, to advise on the assessment of asbestos contamination. He worked with Mr. Dave Hodgkin of the International Federation of Red Cross, Shelter Adviser to the Indonesian National Shelter Sub-Cluster, Indonesia.

ADRI's Industrial Hygienist, Ms Ari Yuen, and Research Assistant, Mr Ta-Kun Yu, collaborated with EnviroScience to analyse samples for asbestos content/contamination collected from Lombok. A joint paper is planned.

Research Highlights

Grant acquired from the Australian Academy of Science

In April, ADRI acquired a competitive grant 'the Regional Collaborations Programme' administered by the Australian Academy of Science and supported by the Department of Industry, Innovation and Science of the Commonwealth of Australia. The programme encourages Australian organisations to collaborate with regional and international science, research and innovation partners on solutions to shared regional challenges within the Asia-Pacific region.

The programme is entitled 'Sharing preventive technologies to abate asbestos, reduce asbestos-related diseases and transition to an asbestos-free society.' It covers the period April 2019 until the end of 2020 with a budget of \$300K combining the grant and matched funds. ADRI researchers are collaborating with researchers in Fiji (Fiji National University), South Korea (Kosin University), Japan (University of Occupational and Environmental Health), New Zealand (Massey University), the Philippines (Occupational Safety and Health Center), Thailand (Khon Kaen University) and Vietnam (Ministry of Health) as well as with industrial partners (EnviroScience, Frontier Microscopy).

Main activities of the programme comprise the implementation of training workshops on ARDs with emphasis on the diagnosis of mesothelioma and the production of an action toolkit for the elimination of ARDs. ADRI is collaborating with

the United Nations organisations, including the WHO, the ILO and the Basel, Rotterdam and Stockholm Convention Secretariat of the UNEP. In late 2019, ADRI was invited by the WHO-Western Pacific Regional Office to submit a formal application for designation as a WHO Collaborating Centre (WHO-CC). It will be assessed by the WHO-CC screening committee in February 2020. This application was prepared by ADRI's International Liaison, Ms Diana Arachi.

New Grant from the DDB on Silicosis

In late 2019, Dr. Matthew Soeberg, ADRI's Epidemiologist, acquired a new grant from iCare's Dust Diseases Board on the emerging theme of silicosis. The project is entitled: APC (Age Period Cohort) of Australia's silicosis epidemic using national hospital and mortality data. The objective of this project is to estimate the burden of silicosis in the Australia by analysing national and NSW data on hospitalisations and deaths caused by silicosis. Risk will be analysed by age group (A), the period when the silicosis was treated or diagnosed (P), and the cohort in which a person with silicosis was born (C). This project will be completed in 2020.

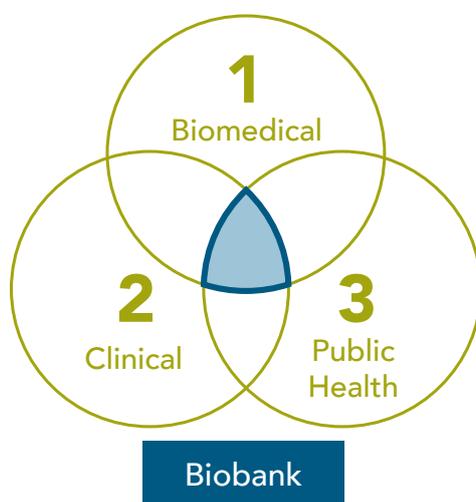
Publication in The Lancet Planetary Health

The article 'A global comparison of the implementation of national policies for a total asbestos ban' was first authored by Dr. Ro-Ting Lin from the China Medical University and ADRI Honorary Associate, and E/Prof. Ken Takahashi was the last and supervising author.



“The main purpose of workshops is to elicit an awareness of mesothelioma within these communities in the hope that they will utilise this knowledge to facilitate an improved, multi-disciplined and collaborative response to combat the rising incidence in mesothelioma.”

4. ADRI Biobank



The ADRI Biobank intersects research pillars 1 Biomedical 2 Clinical and 3 Public Health and Prevention.

Aim

The aim of the ADRI Biobank was to establish a national tissue bank for malignant mesothelioma (MM) of considerable size leading to optimal biological and molecular insight, paving the way for new treatments.

Established in 2010, ADRI's Biobank is now a unique collection and a vital resource of ethically approved high-quality biospecimens and accurate, reliable, and standardised clinical data, contributing to asbestos-related diseases research. However, the continued collection of well-characterized fresh-frozen tumour (biopsies) and blood samples is a formidable task. The Biobank relies on a consortium of clinicians (including specialists in respiratory medicine, medical oncology, surgery, and pathology) involved in diagnosing and treating MM patients who consent to participate and the ongoing funding from CSR Limited and a CINSW grant. The CINSW grant (2015-19) allowed for the expansion of the collaborative network to increase the collection

of samples from mesothelioma patients. Biospecimens are collected from Strathfield Private, Royal Prince Alfred and Concord Hospitals and the associated clinical data from a variety of sources, with governance approval we have expanded to Westmead, Blacktown and The Sydney Adventist Hospitals and are in the process of obtaining approval for Royal North Shore Hospital.

Impact

Australia has one of the world's highest incidences per capita of malignant mesothelioma with more than 700 new cases diagnosed each year due to the widespread use of the known carcinogen, asbestos. Malignant mesothelioma is predicted to cause over 1 million deaths world-wide over the next 30 years. Alarming, ~1/3 of older Australian houses are estimated to be significantly contaminated with asbestos because of its common historical use as a building material. Besides the direct human and medical cost, malignant

mesothelioma is predicted to cost the Australian economy ~\$8.4 billion and the global economy over \$300 billion in direct costs over the next 30 years. Thus, malignant mesothelioma has major economic as well as health impacts, and has unfortunately been understudied.

ADRI's Biobank is not only contributing to our research but with a formal governance in place it has allowed biospecimens to be used by other research groups at Royal Prince Alfred Hospital, Flinders Medical Centre, Lung Institute of Western Australia, as well as international groups in Dublin, Vienna and Zurich. These collaborative efforts have yielded multiple peer-reviewed publications, as listed below.

Research Projects

In 2019 ADRI researcher's utilised clinical samples stored in the ADRI Biobank to investigate the potential of oncogene c-Myc and the relationship of miR-15/16 family in mesothelioma (William et al., 2019). Oncogene c-Myc contribute to the genesis of many human cancers and recent insights into its expression and function have led to new cancer therapeutic opportunities. miR-15/16 are microRNA tumour suppressor genes which stop the growth of mesothelioma cells. Data from this study suggests that the alteration of miR-15/16 may be an important contributor of the Myc oncogenic activity in malignant mesothelioma.

The ADRI team has developed mesothelioma cell lines with acquired resistance to chemotherapy which have been included in the Biobank cell line repository and serve as a valuable tool to study drug resistance. As well as providing integral data for primary ADRI investigations, the Biobank has also served as a collaborative resource for research groups within Australia and internationally. The ADRI team also utilised the data generated from the ADRI Biobank to present on biomarker detection in mesothelioma as an invited speaker at various international workshops (Cheng 2019).

Highlights

Cancer Institute NSW – Research Infrastructure Grant - Expanding the Asbestos Diseases Research Institute (ADRI) biobank to create a state-wide repository for research into thoracic cancers.

This CINSW infrastructure grant was completed in June 2019 and allowed ADRI to further expand the collection of biospecimens and clinical data from consenting mesothelioma and lung cancer patients. Thoracic cancers including lung cancer and mesothelioma are a much under-researched group, and a biobank such ADRI's is a very important resource to improve the research capacity in these areas. This project was supported by our collaborative network of surgeons, clinicians and scientists and will ensure that it continues to be a unique national resource.

Australasian Biospecimen Network Association (ABNA) Conference

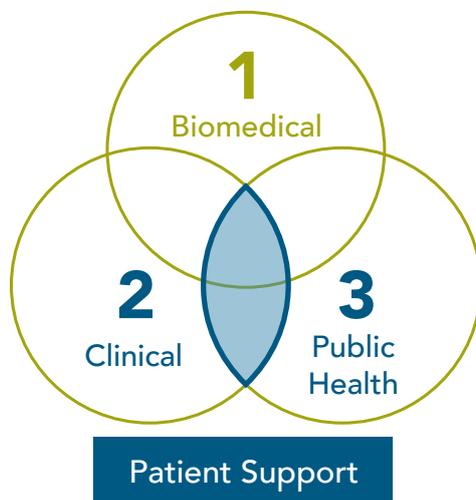
As a member of the ABNA, ADRI's Biobank Officer, Mrs Vesna Aleksova attended the 17th Annual Conference of the ABNA in Cairns in October 2019 and at this conference she was invited to make a presentation on ADRI's unique biobank. The ABNA promotes biobanking throughout Australia, New Zealand and Asia to ensure high quality biospecimens are provided to support high quality research.

Biobank Video

ADRI's Biobank Officer, Vesna Aleksova recently led the production of an educational video on biobanking at Strathfield Private Hospital and ADRI. This video will be used at international workshops to provide an overview of the standard operating procedures of how ADRI's Biobank is collecting and storing biospecimens and to provide researchers with high quality biospecimens and data in order to improve the diagnosis and treatment of asbestos-related diseases.



5. Patient Support



The national focus on public health and prevention includes patient support, advocacy and increasing awareness aimed at preventing future exposure to asbestos in the workplace, community and the home. Patient support intersects research pillars 2 Clinical and 3 Public Health.

Aim

The aim of ADRI's Mesothelioma Support Services is to provide support and advise to patients and their families who have been diagnosed with mesothelioma.

Impact

Through ADRI's Mesothelioma Support Services we have identified three groups and provide specific support to:

1. Patients receiving standard (palliative) care;
2. Patients who have undergone radical (combined modality) treatment; and
3. The bereaved - struggling with grief and loss.

Within groups 1 and 2 there are three subcategories:

1. Patients who are newly diagnosed and hope to receive clinical information and empathetic support;
2. Patients in a stable condition, who want to live a 'normal' life as much as possible; and
3. Patients with progressive (symptomatic) disease and complex medical and psychological needs.

This integrated service also conducts educational and group meetings with guest speakers and targeted group sessions on all aspects of mesothelioma management from diagnosis to bereavement.

Support Service

In 2019 our services have provided:

1. Telephone calls and emails (1606): to and from patients/families which provided a vital communication link between the patient's world of living with mesothelioma and the clinical and research world of mesothelioma.
2. Face-to-face support: The group meetings have been recognised by patients and carers as being an invaluable source of evidence-based clinical information and support. During the year there were over 155 attendances at the following group meetings:
 - a. The Liverpool Group – at Revesby Workers Club; and The City Group – iCare Medical Clinic meets 2nd monthly. Rural Group – Club Taree, co-facilitated with HNEH Manning Oncology and Palliative Care coordinator and Lung Cancer Care Coordinator, Calvary Mater Newcastle.
 - b. The EPP (extra pleural pneumonectomy) Well Living Support Group established in 2012 meets three times a year at Drummoyne Sailing Club. A guest speaker provides up to date information on topics relevant to the group which is then followed by lunch, conversation and intergroup support.
 - c. The Bereaved Group – met twice during the year and participants also attended the general and EPP group meetings as well as the Carers Day.
3. As part of the National Carers Week, the **Carer's 'Thank You' Day** was held on the 22nd October 2019 and is always well attended, and much appreciated by participants. This year the lunch and program provided carers with an opportunity to participate in 'Tech Savvy Seniors' to learn more about IT and better wellbeing through movement, as well as getting together to share their stories, support each other and generate friendships.
4. The annual **Meso March in May** was held on Sunday 5th May 2019. The walk acknowledges and supports people living with mesothelioma and remembers those who have lost their life to this terrible disease. It was a wonderful day and it was fantastic to see so many people out exercising, and many with their dogs. The morning tea following the walk was supported by **icare Dust Disease Care**.
5. **Education Webinar – The Mesothelioma Journey**

On Monday 6th May 2019 patients and their families had the opportunity to learn more about what to expect on the mesothelioma journey. An expert panel talked about how to minimise symptoms, maximise support and plan for increased care needs. The panel also discussed the hard questions when treatment stops working and how to prepare to say goodbye. The panel was chaired by Ms Jocelyn McLean RN, ADRI's Mesothelioma Support Coordinator and attended by: Dr Judith Lacey, Supportive and Integrative Oncology Specialist; Ms Joanne Roseman RN, Mesothelioma Support Service; Ms Theresa Smeal, SWSLHD Clinical Consultant Palliative Care; and Ms Fran Ferguson, Rural Cancer Nurse Coordinator, Central West Cancer Care Centre. The session was live-streamed as a webinar and can be view at: <http://adri.org.au/watch-the-qa-adri-style-event-monday-6th-may-2019/>.

The Coordinators also provide support and advice to people seeking information on other dust-related diseases, lung cancer and asbestos exposure.



Highlights

The work of the Support Coordinators has expanded over the past year with a grant from iCare, Dust Diseases Care, a Support Organisation Funding Program Grant, which has enabled the Support Service to increase to a full-time position and develop several supportive and educational programs. The grant supported Ms Joanne Roseman, a Registered Nurse.

There is no greater highlight for the year than the positive responses received by the Support Team from the people they support. Here is just an example of their responses:

"I can't thank you enough for your assistance and guidance in a very confusing world and confronting situation."

"Such a courageous group of women-and you've obviously been a huge support to many of them."

"Me and my family really appreciate the time you have taken to give us your advice, which was very helpful! It is really nice not to receive just a simple response but some reasoned advice - thank you so much!"



"We are extremely grateful and appreciative for your newsletter and follow up correspondence"

"Thank you very much for all the check-ups and support. It really does mean a lot."

"I would like to thank you for all the support you have given me when my husband was ill. It was much appreciated especially when I was living in a new area and trying to get my way around the medical world, I found myself in was at times a little over whelming, so it was great to have someone to speak to. I am now finding that I am coping well and being back near family and friends has been a good move. I feel now you can take me off the mailing list and devote the email time to the ones that need it."



PUBLICATIONS

1. Williams M, Cheng YY, Kirschner MB, Sarun KH, Schelch K, Winata P, McCaughan B, Kao S, Van Zandwijk N, Reid G. Transcriptional suppression of the miR-15/16 family by c-Myc in malignant pleural mesothelioma. *Oncotarget*. 2019 Jun 25;10(41):4125-38. doi: 10.18632/oncotarget.27010. PMID: 31289611
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9. Warby A, Dhillon HM, Kao S, Vardy JL. A survey of patient and caregiver experience with malignant pleural mesothelioma. *Support Care Cancer*. 2019;27(12):4675-86. doi: 10.1007/s00520-019-04760-x. Epub 2019 Apr 3. PMID: 30944991
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CONFERENCE POSTERS

1. Johnson T, Schelch K, Sarun K, Williams M, Cheng YY, Lasham A, Reid G. YB-1: an important driver of malignant pleural mesothelioma drug resistance and a potential novel therapeutic target. 2019 Sydney Catalyst International Translational Cancer Research Symposium, Sydney 19 September 2019.
2. Johnson T, Schelch K, Williams M, Cheng YY, Grusch M, Reid G, Burgess A. Y-box binding protein-1, a potential target in malignant pleural mesothelioma drives growth through distinct mechanisms. IASLC 2019 World Conference on Lung Cancer, Barcelona, Spain, 7-10 September 2019.
3. Johnson T, Schelch K, Sarun K, Williams M, Cheng YY, Lasham A, Reid G. YB-1: an important driver of malignant pleural mesothelioma drug resistance and a potential novel therapeutic target. 8th Annual Sydney Catalyst Postgraduate & Early Career Researcher Symposium, Sydney 26 June 2019.
4. Johnson T, Schelch K, Williams M, Cheng YY, Grusch M, Reid G, Burgess A. The potential target Y-box binding protein-1 drives the proliferation of malignant pleural mesothelioma cells in vitro and in vivo. Australian Cell Cycle Community Meeting 2019, Sydney 17-19 June 2019.

CONFERENCE/ WORKSHOP PRESENTATIONS

1. Takahashi K. Global situation on asbestos-related diseases: where are we headed? Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
2. Johnson B. Mesothelioma/ asbestos-related diseases – the biological perspective. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
3. Lee K. Mesothelioma – the clinical perspective - Diagnosis. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
4. Kao S. Mesothelioma – the clinical perspective - Treatment. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
5. Cheng YY. Mesothelioma – the research perspective. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
6. Cheng YY. ADRI Biobank. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
7. Lee K. In-depth session – Pathological diagnosis. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
8. Kao S. Treatment. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
9. McLean J. Supporting patients and carers. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
10. Keena V. Role of support organisations. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
11. Takahashi K. Next steps for Fiji. Training Workshop on the diagnosis of asbestos-related diseases (ARD's). Suva, Fiji, 2-3 December 2019.
12. Lee K. Pathological diagnosis of mesothelioma. Workshop. Jakarta, Indonesia 26-27 November 2019.
13. Takahashi K Global Situation on Asbestos-Related Diseases (ARD): Where are We Headed? The 2nd International Conference on Mining & Energy OSH and The 13th Indonesian Occupational Medicine Updates. Bali, Indonesia, 6-8 October 2019.
14. Cheng Y. Biomarkers in Mesothelioma. Institute of Biomedical Device and Joint Research Centre (IBMD and JRC Workshop 2019), China, Fuzhou, 17th September 2019.
15. Roseman J. Living and dying with grief and loss. 2019 Care and Community Conference; Parkroyal, Parramatta NSW, 15 August 2019.
16. Roseman J. Research and Support for Dust Diseases. 2019 Care and Community Conference; Parkroyal, Parramatta NSW, 15 August 2019.

17. Takahashi K. Global situation on asbestos-related diseases: where are we headed? Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019.
18. Johnson B. The pathogenesis of asbestos-related disease and biomarker discovery for the development of a non-invasive diagnostic technique. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
19. Lee K, Linton A, The clinical perspective. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
20. Cheng Y. The research perspective. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
21. Soeberg M. A public health perspective on asbestos-related diseases. Asbestos/Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
22. Yuen A. Recap of Day 1 training topics Questions and comments from training participants. Introduction of Day 2 training topics. Asbestos/Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
23. Lee K. Pathological Diagnosis of Mesothelioma. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
24. Linton A. Treatment of Mesothelioma. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
25. Soeberg M. Disease Registry, Data Compilation. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
26. Cheng Y. Recent research directions and findings. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
27. Yuen A. Setting up a laboratory dedicated to the identification and analysis of asbestos fibres. Asbestos/Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
28. McLean J. Care and support needs of the mesothelioma patients and families. Asbestos/ Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019
29. Takahashi K, Lee K, Linton A, Soeberg M, Cheng Y. An integrated approach to ARD (Combining prevention, diagnosis, treatment and support services). Asbestos/Mesothelioma Training Workshop for the Philippines, Manila 10-12 July 2019.

WEBINAR

1. McLean J, Rosman J, Q&A Part 2. What happens when treatment stops working. Medical Education Centre, Concord. 6 May 2019. <http://adri.org.au/watch-the-qa-adri-style-event-monday-6th-may-2019/>

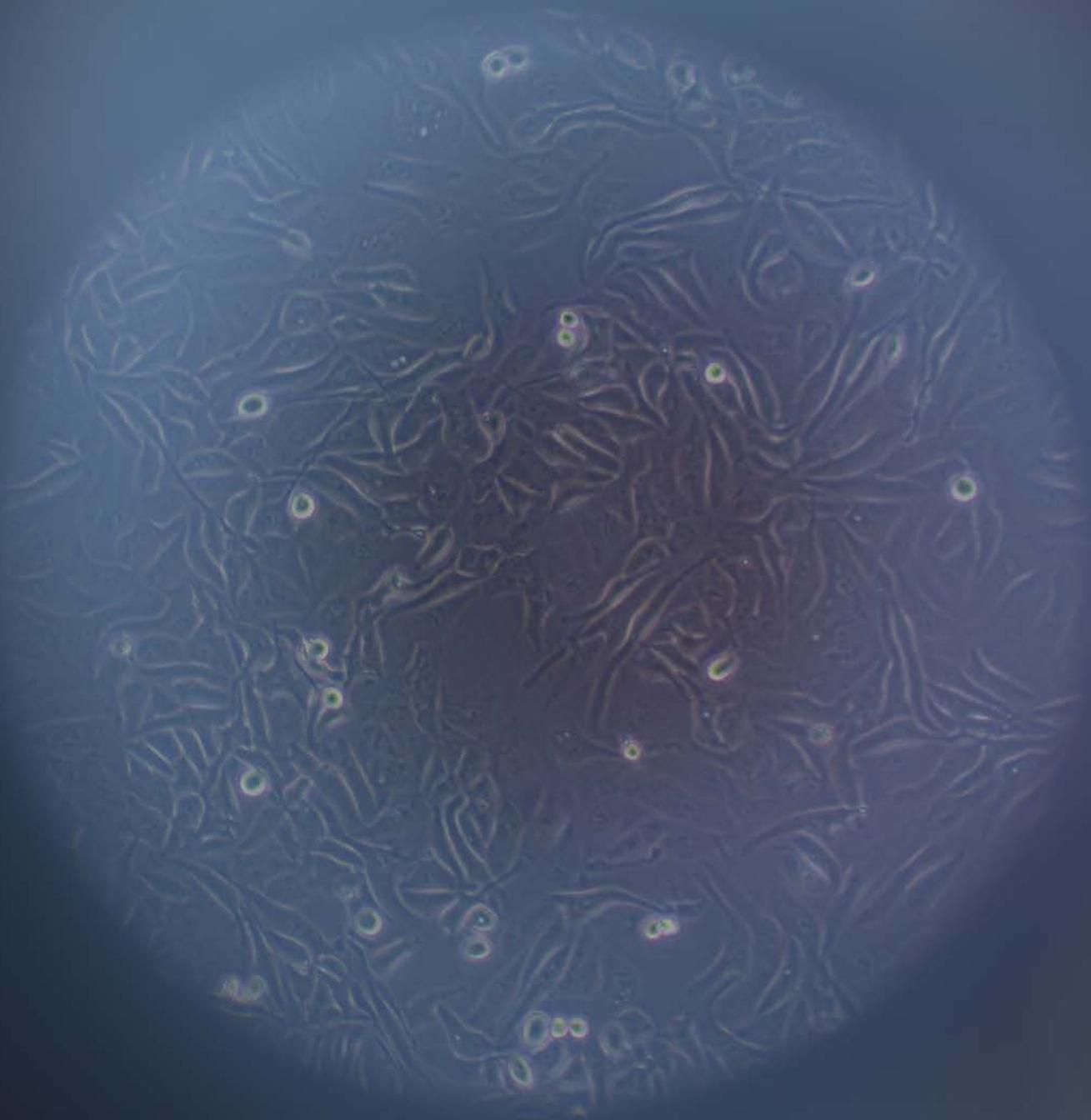


ADRI
Alzheimers Disease Research Institute

Financial Summary

Profit and Loss Statement	2018-19	2017-18
Revenues		
Research	633,682	1,274,450
Fundraising	410,796	540,177
Interest	105,170	114,529
Total	1,149,648	1,929,156
Expenses		
Employee Benefits	1,379,251	1,628,135
Research consumables/equipment	142,575	184,309
Office expenses	321,573	400,286
Depreciation	424,986	450,377
Finance costs	685	
Total	2,269,070	2,663,107
Surplus / Deficit for the period	-1,119,422	-733,951
Balance Sheet	30/06/2019	30/06/2018
Assets		
Cash and cash equivalents incl Term Deposits	3,902,897	4,618,471
Trade and other receivables	24,254	256,411
Property Plant and Equipment	7,589,703	8,014,691
Total	11,516,854	12,889,573
Liabilities		
Trade and other payables	213,329	484,169
Employee provisions	147,164	129,621
Total	360,493	613,790
Net Assets	11,156,361	12,275,783

The figures above have been extracted from the audited Financial Statements of ADRF for the relevant periods.
The full audited financial statements are available from info@adri.org.au



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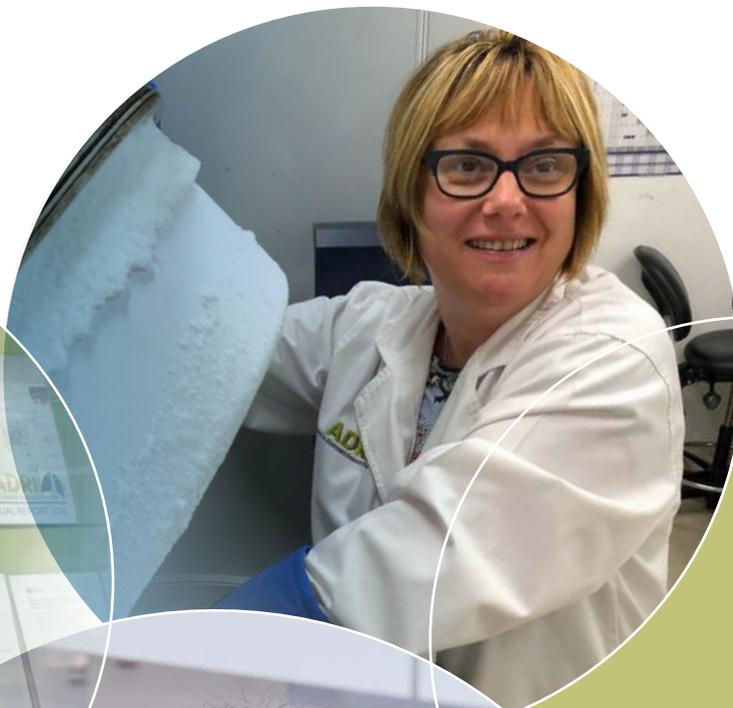
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