ADRI

Asbestos Diseases Research Institute

ANNUAL REPORT 2018

"ADRI aims to improve methods of preventing, diagnosing and treating asbestos-related diseases..."

ADRI
Asbestos Diseases Research Institute

Contents

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.

Overview

Australia was among the highest consumers of asbestos-containing materials globally due to our unenviable history of extensive mining and the wide-spread use of asbestos in the manufacture of thousands of products and building materials.

Although a complete national ban came into force on 31 December 2003, since the 1920s, asbestos-containing materials had been embedded in Australia's environment, concealed in schools, workplaces and in 1-in-3 Australian homes built or renovated before 1987. When these materials are exposed and disturbed, and fibres are released that can be inhaled, the health of Australian's is at risk.

With this tragic legacy signalling fears of an enduring epidemic of asbestos-related diseases, in 2009 the Asbestos Diseases Research Institute (ADRI) was established in a purpose built, state-of-the-art facility to address public health concerns surrounding the growing number of incidences of asbestos-related diseases.

Between 1982 and 2015, 15,884 Australians were diagnosed with malignant mesothelioma while tens of thousands more have been diagnosed with other forms of asbestos-related diseases (ARDs).

Today, Australia has one of the highest incidences of asbestos-related diseases in the world per capita with around 700 new cases of malignant mesothelioma recorded in Australia every year. There is no cure and current treatments to preserve and extend life are limited with the majority of patients losing their lives within nine-to-twelve months following diagnosis.

In response to this national health crisis, ADRI's ultimate goal is to save lives through investing our sustained, concerted efforts into three priority areas; laboratory research, clinical sciences, prevention and public health.

Working with medical specialists and health services, our dedicated research teams have built a formidable record for developing a best-practice diagnostic framework for earlier detection; improved understanding of mesothelioma; ground-breaking treatments to prolong life; and, invested in prevention to alert the community and the world to the risks of exposure to asbestos.

As long as asbestos remains among us posing a significant threat to public health, the ADRI will continue our pursuit in the prevention of life-threatening asbestos-related diseases and invest our concerted efforts in the development of a life-saving cure for malignant mesothelioma.

Fighting the Epidemic

With the aim of making mesothelioma history, the ADRI continues to conduct preclinical (basic), clinical and epidemiological research into asbestos-related diseases with findings enabling improved methods of prevention, diagnostic, therapeutic procedures and treatments.

In the laboratory, ADRI's researchers are working 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 and therapeutic approaches being converted into clinical practice to improve outcomes for patients with asbestos-related disease.

However, ADRI's work is not limited to the research laboratory. Our national focus on prevention and public health includes patient support, advocacy and increasing awareness aimed at preventing future exposure to asbestos in the workplace, community and the home.

Internationally regarded as a leader in our field, the ADRI contributes to the assessment of the global burden of asbestos-related diseases and advocates for an international ban on asbestos with a primary focus on the prevention of disease in developing countries.

Support

The ADRI's mesothelioma support coordinators (MSC) provide an invaluable service to people diagnosed with mesothelioma, their families and the bereaved, helping them through a very difficult time. Throughout the year, ADRI's MSC's support services also offers information and education forums in metropolitan and regional areas to address the largely unmet needs of mesothelioma patients, their families and loved ones.

Thank you

The ADRI's vital and potentially life-saving work both in the laboratory and in the community is only made possible because of the generosity of many. Thank you to the individuals and in many cases the families who have lost loved ones to asbestos-related diseases. Thank you also, to the many community groups, not-for-profit organisations, businesses and government bodies for your welcome financial contributions. And thank you to our valued volunteers for dedicating your time, effort and commitment to ADRI's mission.

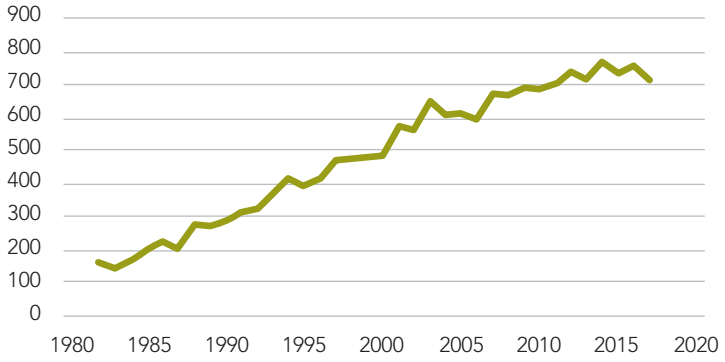
It is because of the support of many that the ADRI is able to continue our vital work. Our heartfelt thanks to you all.

Key Statistics

Three key facts about Australia's malignant mesothelioma epidemic

1. Number of new malignant mesothelioma cases*

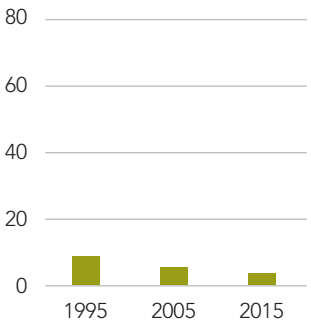
In 2017, around 710 people were newly diagnosed with malignant mesothelioma. On average, this is about 2 people per day being diagnosed with mesothelioma.



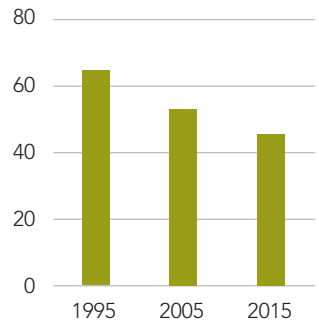
2. Age at diagnosis*

The age at which people are being diagnosed with malignant mesothelioma in Australia is changing over time. The proportion of malignant mesothelioma cases for people aged 75 years or more has almost doubled from 1995 to 2015.

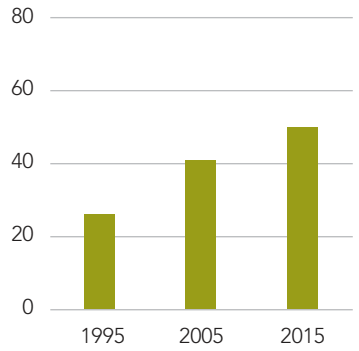
Percent of new malignant mesothelioma cases in people aged less than 54 years



Percent of new malignant mesothelioma cases in people aged between 55 and 74 years



Percent of new malignant mesothelioma cases in people aged 75 years or more



3. Type of asbestos exposure*

701 people have provided asbestos exposure data to the Australian Mesothelioma Registry between 2010 and 2016. Almost all occupational asbestos exposure occurred in men. About an equal number of men and women had non-occupational asbestos exposure.

*Data is from the Australian Mesothelioma Registry, AIHW

ADRF Chair's Report

On behalf of the Asbestos Diseases Research Foundation (ADRF) I am pleased to present the 2018 Annual Report. The past year was a year of change for the Institute, with the Board moving forward with a new Research Strategy which falls in line with ADRI's mission statement and the ADRF's Constitution. The objectives are to promote research on asbestos, asbestos-related diseases (ARDs) and other dust-related diseases encompassing a wide spectrum of activities from prevention to diagnosis and treatment. The Research Strategy emphasises the transition to achieve the ultimate balanced approach across three areas of prevention/public health, laboratory and clinical research. Until recently the ADRI focused its work and resources on laboratory work which led to the acquisition of a patent and development of a novel treatment modality tested in a phase 1 clinical trial for malignant pleural mesothelioma. The Research Strategy adds a new dimension of prevention and also public and occupational health while building on the strength of the on-going laboratory research activities.

During the year there were a number of changes to the membership of the ADRF Board with new Directors joining the Board representing the nominated bodies as stipulated in the ADRF's Constitution. Mr John O'Meally AM who served as Chair of the ADRF Board from 2012 to October 2018 also resigned. On behalf of the Board I would like to warmly thank John for his contribution over many years. I would also like to thank all members who served during the past year and to welcome the new Directors to the Board.

Support of mesothelioma patients is vitally important as a diagnosis of mesothelioma is overwhelming and confronting not only for the patient but also for their families and friends. With a grant from iCare, Dust Diseases Care the role of ADRI's Mesothelioma Support Coordinators has expanded. It has now developed into a full-time service providing support and evidence-based information, to assist patients and their families to live as well as possible after diagnosis. As part of this service, the Mesothelioma Coordinators held the annual Meso March in May. A walk to acknowledge and support people living with mesothelioma and to remember those who had lost their lives to this terrible disease. The walk was held in conjunction with a Q&A session on mesothelioma with an expert panel to discuss the latest treatments, symptom management and living with dignity. The event was live-streamed as a webinar and can be viewed on ADRI's website.

In October 2018 the ADRF commenced a review of several aspects of their operations including their corporate governance and fundraising strategy. The Board engaged the Australian Institute of Company Directors (AICD) to conduct a review of the ADRF's governance arrangements and will consider the recommendations in the coming year. The ADRF also explored the potential for further development in the fundraising portfolio and engaged More Strategic to gain a clearer picture of the net revenue opportunities that flow from good practice in fundraising, which is a critical source of support for early-career researchers at ADRI.

My heartfelt thanks go to all our donors and volunteers whose commitment and support is an inspiration to the researchers and staff of the ADRI. I take this opportunity on behalf of the Board to express gratitude to the Director Dr Ken Takahashi and staff of the ADRI for their ongoing dedication to the aims of the Institute. We look forward to making a greater impact on improving the outcomes for people affected by asbestos and other dust-related diseases.

SYLVIA KIDZIAK AM
CHAIR (ACTING)


MVE

ADRI Director's Report

This is my second year as Director of the Asbestos Diseases Research Institute and my aim was to garner understanding, earn support and achieve stability. This is still a work in progress with the Research Strategy I formulated endorsed by the ADRF Board in February 2018. The research strategy is faithfully built on the 'objects' of the Constitution of the ADRF which anticipated a balanced approach across the three areas, or pillars of research on asbestos-related diseases (ARD). The three pillars are, namely, laboratory research, clinical studies and public health/prevention. In taking this stance, I am cautious not to overcommit ourselves or overstretch limited resources. To the contrary, my hope is to better focus on our goal – ARD – and enhance efficiency in our efforts.

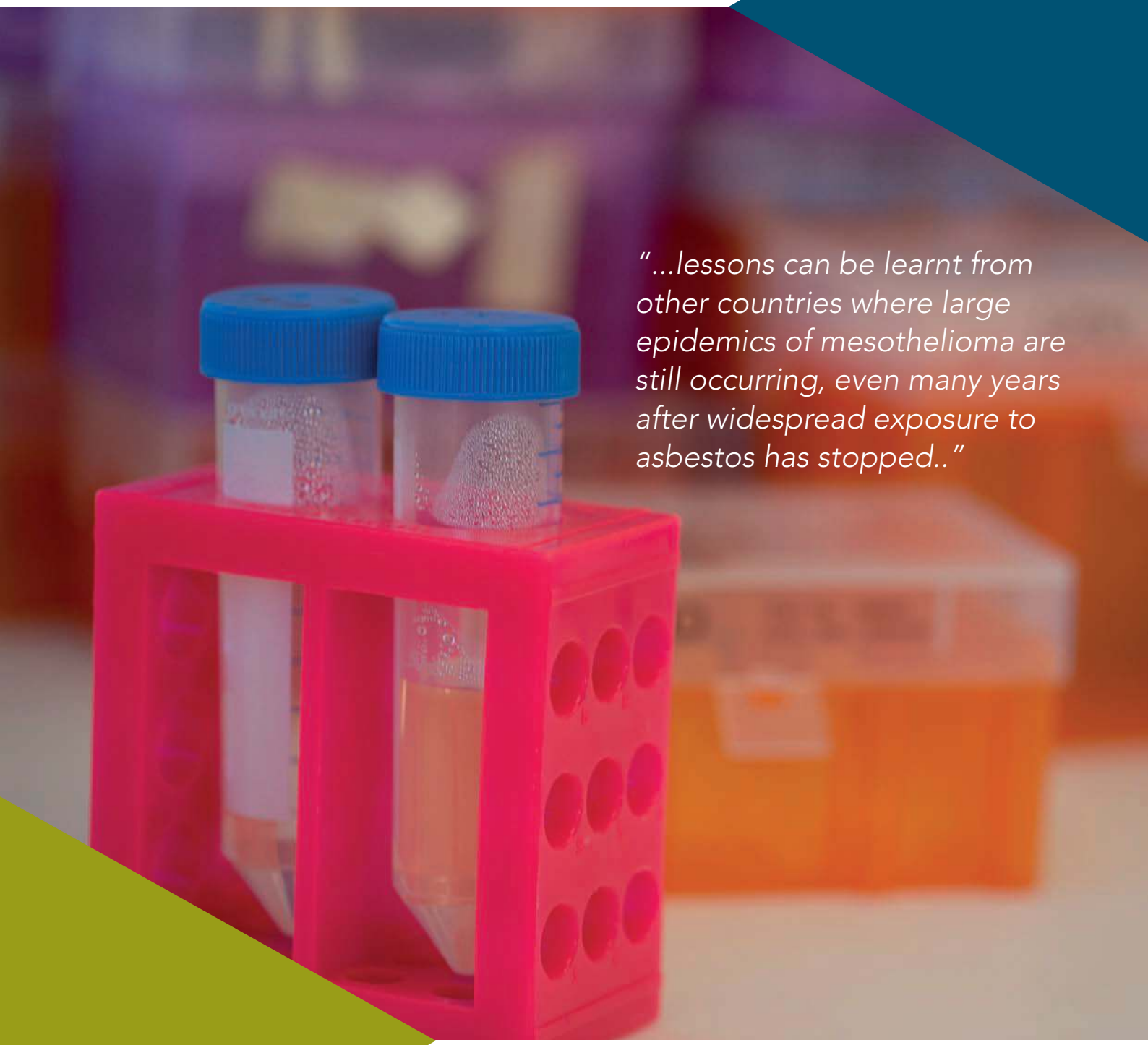
The theme of ARD warrants an inter-disciplinary approach. ARD is caused by exposure to asbestos, once an industrial commodity, and an on-going one in most parts of the world. Asbestos remains abundant in Australia and its removal will take decades. ARD patients deserve effective medical diagnosis and treatment, as much as they deserve adequate support and just compensation. The Australian public merits protection from asbestos exposure whether from domestic sources, illegal import or overseas opportunities. Therefore, insomuch as scientific evidence is needed to develop effective diagnostics or therapeutics, evidence is also needed to prevent exposure, protect the public and support policies.

The three pillars of research are necessary to reflect on the relevance and value of activities pursued by ADRI to tackle ARD. As a strategic base it can serve as reference points which can be utilized to measure progress at the level of individual staff and collectively as an organization. ADRI researchers already possess or are eager to develop solid records in their respective disciplines. I strongly encourage them to further have the flexibility to cross-over, so as to create vibrant intersections across the pillars. For example, laboratory research should intersect not only with clinical studies (that is, translational research) but also with public health/prevention. A perfect example is the development of non-invasive biomarkers and its application to screen populations.

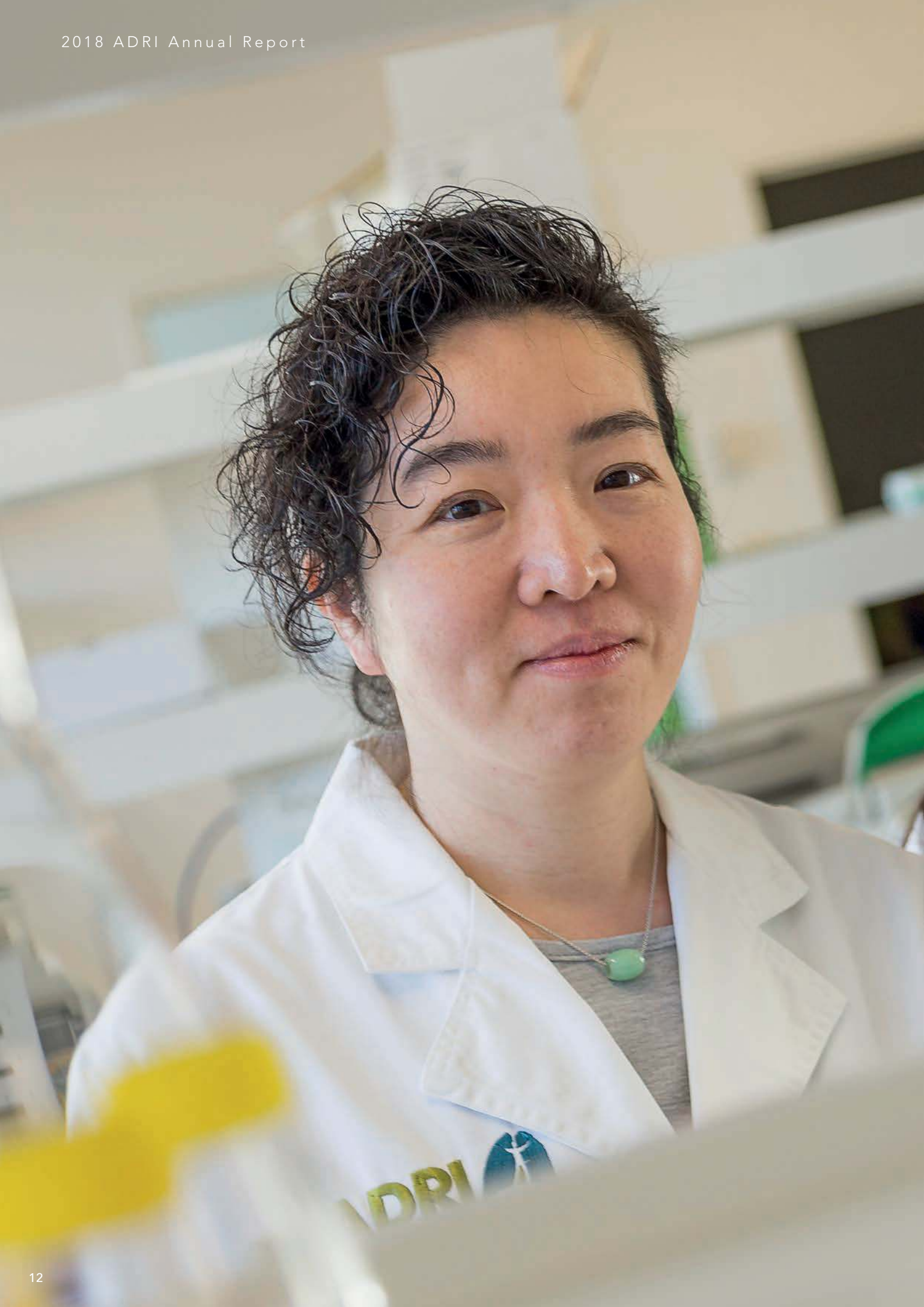
To our friends, colleagues and stakeholders, I am happy to report that ADRI staff and affiliates are starting to embrace the new strategy and direction. This manifested in last year's Conference Workshop 'Research Directions,' where ADRI researchers of laboratory research and of public health/prevention collaborated to deliver a joint presentation under the title "From Bench to Public: Another Direction of Translational Research." ADRI's aspiration to translate research to the bedside, as well as the general public, was well received. There are concrete plans and promising prospects to further this path in the coming years.

Significant challenges remain in the areas of earning wider support and achieving organizational stability. As Director I am committed to take on these challenges. I am hopeful that ADRI staff will follow with great enthusiasm.

E/PROFESSOR KEN TAKAHASHI,
MD, PHD, MPH
DIRECTOR



"...lessons can be learnt from other countries where large epidemics of mesothelioma are still occurring, even many years after widespread exposure to asbestos has stopped.."



"...the burden of asbestos-related diseases will continue to rise ...even in those countries that banned the use of asbestos many years ago"

ADRF Board

Mr John O'Meally AM RFD

Independent Chair

Appointed: 22 February 2012
Resigned: 31 October 2018

John O'Meally was appointed a judge in New South Wales in 1979. He retired as President of the Dust Diseases Tribunal and from the District Court in November 2011. Before his appointment to the bench he was an acting judge of the National Court of Papua New Guinea. He has been a judge of the High Court of Antigua and Barbuda in the Supreme Court of the Eastern Caribbean and an acting judge of the Supreme Court of NSW. Between 1995 and 2003 he was a member of the Standing Committee on Judicial Education for the Judicial Commission of NSW. He was commissioned in the Australian Army Legal Corps in 1968 and in 1979 became Chief Legal Officer (Active Reserve) of the 2nd Military District. Between 1995 and 2000 he was the Honorary Colonel of the Australian Army Legal Corps. He has been a Consultant to the Governments of St Lucia (West Indies) and Solomon Islands (Western Pacific). John O'Meally is a Commissioner of the International Commission of Jurists (ICJ), Geneva, a member of the Australian Section of the (ICJ) and President of the NSW Branch. He has been a member of ICJ Delegations to East Timor and Papua New Guinea. He is an Associate Member of the Thoracic Society of Australia and New Zealand and a member of the Australia and New Zealand Society of Occupational Medicine. In 2011 he was awarded the Thoracic Society Medal. In the same year he was appointed to the Advisory Council of the John Hulme Research Institute for Global Irish Studies at the University of NSW. He is a part time member of the NSW Civil and Administrative Tribunal and sits on the Medical Tribunal.

Ms Sylvia Kidziak AM

Nominated by the Dust Diseases Board

Appointed: 27 November 2007
Acting Chair: 31 October 2018

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.

Ms Anita Anderson PSM

Nominated by the Dust Diseases Authority

Appointed: 20 June 2016
Resigned: 10 January 2018

Ms Anderson is the former Executive General Manager of the Workers Compensation Dust Diseases Authority. From 2008 Ms Anderson was the General Manager for the Dust Diseases Board before it became part of the new Insurance and Care NSW (iCare) organisation. Ms Anderson has worked for over 20 years in senior management across all aspects of public sector administration. She began her career in the NSW Attorney General's Department in 1976 and was Director, Local Courts 2001-2003. For 5 years Anita then worked with Legal Aid NSW as Director, Strategic Planning and Policy then Grants. Ms Anderson is a Member of the Australian Institute of Company Directors.

Professor Mark Cooper

Nominated by The University of Sydney

Appointed: 21 October 2015
Resigned: 26 November 2018

Mark Cooper is the Professor of Medicine and Head of the Discipline of Medicine at the Concord Clinical School, University of Sydney. He heads the Adrenal Steroid Laboratory at the ANZAC Research Institute. Until 2012 he was a Senior Lecturer in Endocrinology at the University of Birmingham, UK. He was also metabolic bone physician at the Royal Orthopaedic Hospital, Birmingham, one of the largest orthopaedic hospitals in Europe. His clinical and research interests include adrenal steroid physiology and metabolic bone disease. In particular, he has examined the role that glucocorticoid metabolism plays in normal physiology, inflammatory arthritis and glucocorticoid induced osteoporosis. He was previously the Bertram Abraham's Lecturer in Physiology at the Royal College of Physicians of London. He continues to combine a clinical practice with a basic/translational research group.

Professor Laurent Rivory

Nominated by The University of Sydney

Appointed: 7 December 2018

Prof 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 Katherine Moore

Nominated by the Sydney Local Health District

Appointed: 12 December 2016
Resigned: 21 May 2018

Katherine is the Director of Clinical Governance and Risk for the Sydney Local Health District. Katherine has worked in the public sector of NSW Health for most of her career, working in aged care and rehabilitation. Her previous positions have included Director of Allied Health and General Manager for Community Health in Sydney South West Area Health Service. She has a doctorate in health services management. Katherine sits on the National Occupational Therapy Registration Board of the Australian Health Practitioner Regulation Agency, as well as the NSW Occupational Therapy Council of the Health Professional Council Authority.

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

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

Since 2009 Dr Vallance is the National Health & Safety Coordinator of the Australian Manufacturing Workers' Union (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.

Mr Jason Miele

Representing the interest of past and present manufacturers and suppliers of Dust or Dust containing goods

Appointed: 19 June 2017
Resigned: 15 October 2018

Jason Miele was appointed to the position of Vice President – Investor and Media Relations at James Hardie in February 2017. In this role, Mr. Miele has responsibility for overseeing the Company's investor relations strategy and successful interface with external audiences, communicating the Company's business strategy and its financial performance to various stakeholders including shareholders, investment analysts, and the financial media. Mr Miele has 19 years of relevant professional experience, including 10 years of experience with James Hardie, where he has served in various finance and operational support roles, most recently as James Hardie's Vice President - Global Controller, a position he has held since 2013. Prior to joining James Hardie in 2006, Mr Miele held finance roles at Pacificare Health Systems and PricewaterhouseCoopers LLP, both in the Los Angeles, CA, USA area. Mr Miele has a Bachelor's Degree from the University of California at Santa Barbara, where he graduated with a degree in Business Economics with an emphasis in Accounting.

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 has worked under the MSOAP-ICD program as a thoracic physician in country regions in NSW. He is the employee nominated member on the Medical Authority of the Workers Compensation (Dust Diseases) Board of NSW. 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 Chief Engineer on ST Waratah which is one of the vessels run by the Sydney Heritage Fleet. The wide range of trades represented there have given him an insight into the extensive use of asbestos in these industries.

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

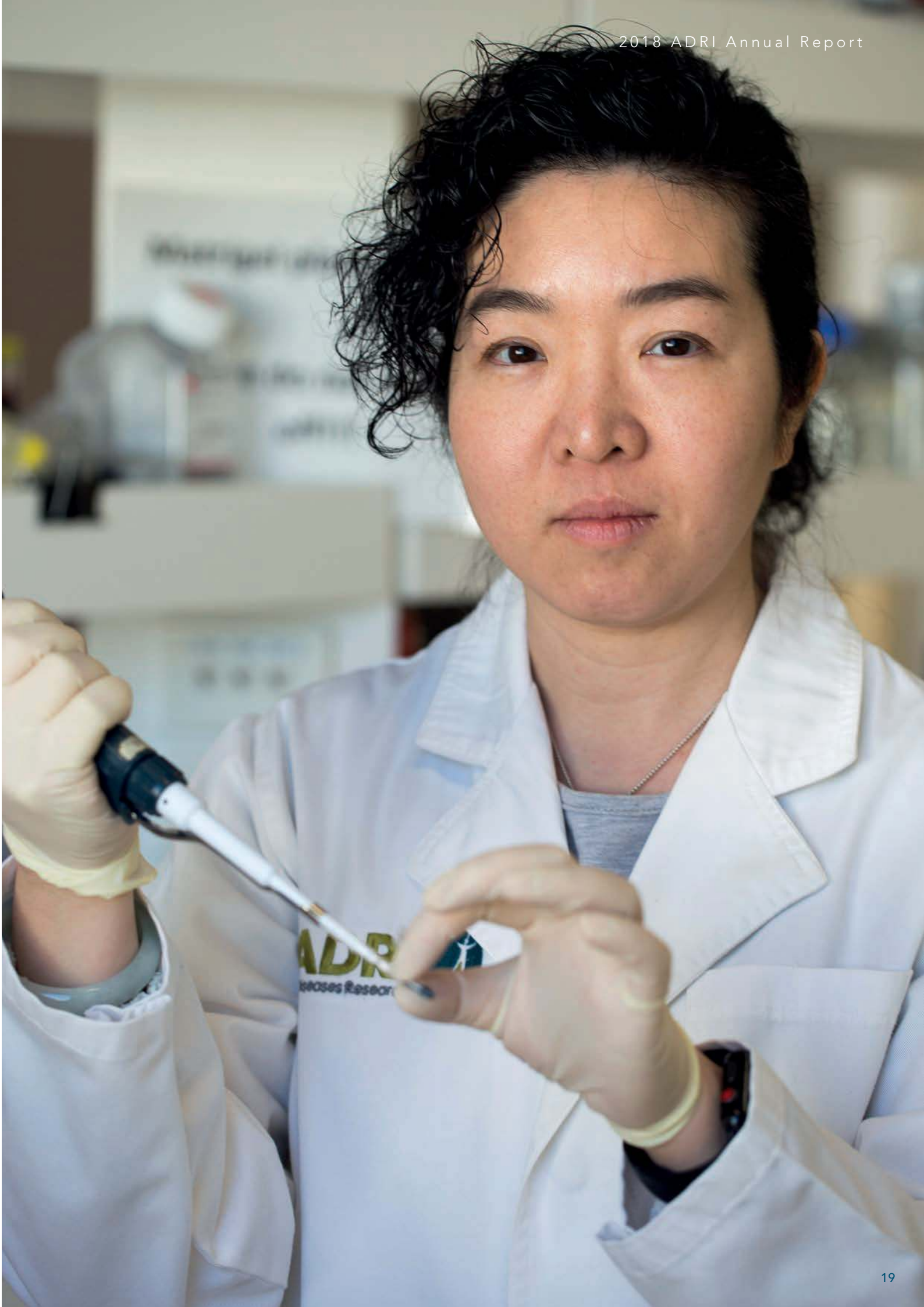
Ken Takahashi was Professor of Environmental Epidemiology and Director of the WHO Collaborating Centre for Occupational Health at the University of Occupational and Environmental Health (UOEH), Japan. Ken graduated from the School of Medicine, Keio University in 1983 (MD), and after completing a 2-year 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 a Fellow and Executive Council Member of the Collegium Ramazzini. He received the Jorma Rantanen Award from the Finnish Institute of Occupational Health in 2011 and the Selikoff Lifetime Achievement Award from the Asbestos Disease Awareness Organization (NGO in 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.

Mr Colin Goldrick

Company Secretary

Reappointed: 16 May 2012
Resigned: 18 August 2018

Colin is the Principal of Augment Legal, a specialist consulting law firm and Special Counsel with the firm of Goldrick Farrell Mullan, where he advises in their Business and Technology practice group. He also acts as legal counsel to the Foundation. Colin has been a lawyer since 1996, specialising in intellectual property, corporate advisory and commercial law, as well as compliance and governance for both commercial and not-for-profit entities. Prior to that Colin worked in the Information Technology industry for almost 15 years in a variety of roles.



ADRI Staff

2018 Staff

Mrs Vesna Aleksova
Biobank Officer (December 2018 -)

Mr Kan Chen
Biobank Officer (- October 2018)

Dr Yuen Yee Cheng
Principal Scientist

Mr Justin Crosbie
IT Manager

Mr Ross Flemons
Accountant

Ms Kim Hadley
Receptionist/EA

Mrs Rebecca Hyland
Biobank Officer (- May 2018)

Mr Thomas Johnson
PhD Fellow

Dr Steven Kao
Oncologist

Ms Victoria Keena
Executive Officer

Ms Daisy Ma
Exchange Student (- June 2018)

Mrs Jocelyn McLean
Mesothelioma Support Coordinator

Ms Monica Phimmachanh
Honours Student (August2018)

Mrs Joanne Roseman (August 2018 -)
Mesothelioma Support Coordinator

A/Prof Glen Reid
Senior Scientist (- April 2018)

Mr Kadir Sarun
Master Student/Research Assistant
(- December 2018)

Dr Karin Schelch
Post-Doctoral Fellow (- May 2018)

Mrs Karen Selmon (- July 2018)
Mesothelioma Support Coordinator

Dr Matthew Soeberg
Research Fellow

E/Prof Ken Takahashi
Director

Mrs Jenny Weismantal
Volunteer

Dr Marissa Williams
Post-Doctoral Fellow

Mr Patrick Winata
Master Student (- December 2018)

Mrs Ari (Man Lee) Yuen
Industrial Hygienist (August 2018 -)

"...ADRI aims to provide leadership and excellence in asbestos-related and dust-related diseases research..."

Meet our Students


TOM JOHNSON

Mr Tom Johnson

PhD Fellow

Tom started as a summer student at ADRI in 2015. He is now doing his PhD and his project will follow on from preliminary data conducted at ADRI which suggests YB-1 is involved in the drug resistance of malignant pleural mesothelioma (MPM) cell lines. It will further the understanding of chemo-resistance in this disease and therefore has the potential to improve MPM patient outcome in the development of future drugs. Tom was awarded a PhD scholarship by ADFA to support his studies at The University of Sydney.


KADIR SARUN

Mr Kadir Sarun

Research Assistant and Master's Student

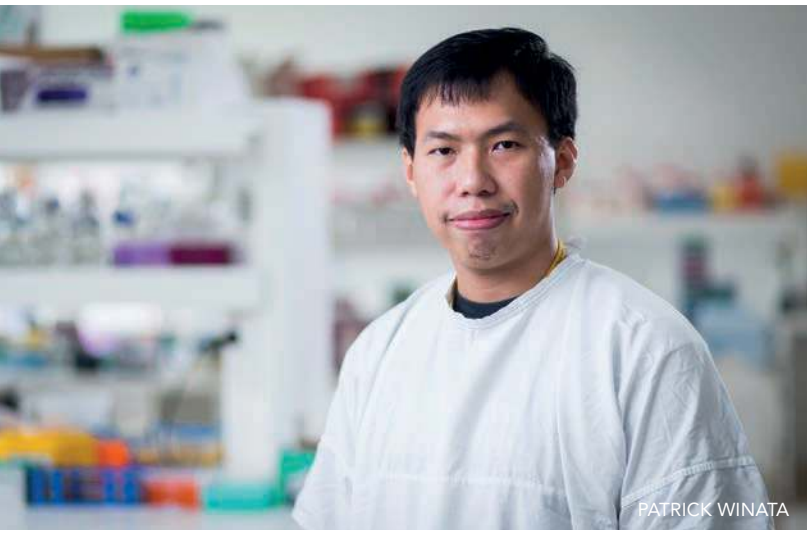
Kadir has a Bachelor of Forensic Biology in Biomedical Science from UTS (2015) and completed his Master of Science (Research) degree in December 2018. During his studies, Kadir was awarded the Young Investigator Award by the International Association for the Study of Lung Cancer (IASLC) at the 17th IASLC World Conference on Lung Cancer (WCLC) in Vienna in 2016. He was also awarded a Concord Repatriation General Hospital Research Travel Scholarship.


MARISSA WILLIAMS

Ms Marissa Williams

PhD Fellow

Marissa commenced work at ADRI in February 2012 as a research assistant and has a Bachelor of Forensic Biology in Biomedical Science from UTS (2010) and a Bachelor Science (Hons) (2011) in a project on paediatric oncology at the Tumour bank, Westmead Children's Hospital. Marissa completed her PhD through The University of Sydney in June 2018 focusing on the mechanisms driving microRNA downregulation in malignant pleural mesothelioma and their involvement in drug resistance. Marissa was awarded a PhD scholarship by Sydney Catalyst to support her studies. She was also awarded a Young Investigator Award by the International Association for the Study of Lung Cancer (IASLC) at the 18th IASLC World Conference on Lung Cancer in Yokohama, Japan in 2017 for her presentation entitled: 'Multiple mechanisms contribute to downregulation of tumour suppressor microRNAs in malignant pleural mesothelioma'.


PATRICK WINATA

Mr Patrick Winata

Master's Student

Patrick has a Bachelor of Science with First Class Honours from UTS (2015) and worked at ADRI for 6 months as a Research Assistant on a number of projects. Patrick completed his Master of Science through The University of Sydney in December 2018 focusing on noncoding RNAs (ncRNAs) as biomarkers and therapeutic targets for malignant pleural mesothelioma (MPM).

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

Research funding

New Grants in 2018

Dust Diseases Authority

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

Malignant mesothelioma (MM) is an aggressive cancer that originates in the mesothelial surfaces. Currently standard chemotherapy for MM is a combination of cisplatin and pemetrexed which provides modest prolongation of survival and temporary improvement in quality of life, however around 60% of MM patients gain little or no benefit from this therapy. Furthermore, there is no standard therapy following the failure of this chemotherapy combination and therefore there is a strong unmet clinical need to improve current second line systemic therapy in MM. This retrospective study will review patients with MM who have applied to the Dust Diseases Authority (DDA) for pembrolizumab treatment. We aim to examine the efficacy and safety results of pembrolizumab and investigate the potential predictive biomarkers for these patients.

Sydney Catalyst

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

There are only 40 % of malignant pleural mesothelioma (MPM) patients that respond to first line chemotherapies, providing an increase in median survival from 9 to only 12 months. Finding actionable targets is therefore of high importance. We recently identified Y-box binding protein-1 (YB-1), a multifunctional transcription and translation factor of the cold-shock protein family, as an overexpressed oncogene with prognostic relevance in MPM. However, the underlying mechanism of YB-1-driven malignancy in MPM remains unclear. In this study we investigated the roles of YB-1 in driving the proliferation of MPM cells. Our results have shown that YB-1 knockdown causes growth inhibition in vitro and in vivo and reduces the transcript levels of known cell cycle regulators. Live-cell imaging revealed three phenotypes of YB-1 siRNA-driven growth inhibition: apoptosis during interphase, cell cycle arrest or prolonged aberrant mitosis resulting in mitotic catastrophe and cell death. The duration of MPM cell mitosis and interphase were significantly increased, and the number of divisions overall were significantly decreased. We are awaiting RNA sequencing results of samples from YB-1 siRNA treated cells, which will further elucidate the effect of YB-1 knockdown in this disease. Understanding the underlying mechanisms of how YB-1 drives malignancy is an important consideration in future potential YB-1-targeting drug development. Our study further supports the potential of targeting YB-1 in the future and highlights its complicated nature in MPM biology.

Revesby Workers Club Bill Bullard Charity Foundation Fellowship

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. We anticipate that this project will lead to the discovery of early biomarkers for identification of ARC.

On-Going Grants in 2018

iCare, Dust Diseases Care

Mesothelioma Support

A diagnosis of mesothelioma is overwhelming and confronting for patients and their families. ADRI's Mesothelioma Support Coordinators provide support and evidence-based information to assist patients and their families to cope with this disease and to live as well as they can for as long as they can.

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 us to increase the role to a full-time position and develop several supportive and educational programs. The grant now supports Mrs Joanne Roseman, a Registered Nurse. Joanne has taken over from Mrs Karen Selmon. Joanne shares the role with Ms Jocelyn McLean who continues to be supported by Turner Freeman Lawyers.

Dust Diseases Authority

Micromanaging microRNAs to treat malignant pleural mesothelioma.

MicroRNAs are a class of short gene regulators that are frequently dysregulated in cancer, contributing to the growth of tumour cells such as mesothelioma. We have discovered that the majority of microRNAs are suppressed in malignant pleural mesothelioma (MPM) and potentially act as tumour suppressors. In this project we systematically tested all downregulated microRNAs to describe the full repertoire of tumour suppressor microRNAs and their roles in MPM. We designed experiments to test the effects of individual microRNA mimics using in vitro and in vivo models. The combination of mimics was investigated for their effect on MPM cell and tumour growth. The synergistic effects of microRNA combinations and their subsequent cellular pathway involvement were also tested. At the final stage of the project we tested how restoration of these microRNAs individually, or in combination, affected tumour growth using a newly established inter-pleural MPM model. In this model we used an in vivo-jetPEI from Polyplus to deliver the microRNAs, which has been applied in clinical trials. The outcome of this study was presented at COSA's (The Clinical Oncology Society of Australia) 45th Annual Scientific Meeting, Mesothelioma and Gastro Intestinal Cancers: Technology and Genomics in Perth, 13–15 November 2018.

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.

ADRI represents a consortium of clinicians and researchers who together aim to expand the successfully established ADRI biobank to create a state-wide repository for research into thoracic cancers. ADRI already has an established biobank, collecting biospecimens and clinical data from mesothelioma patients. We aim to further build on the collaborative network of clinicians and scientists already in place, and to increase the collection of samples from mesothelioma patients to also include samples from lung cancer patients. It is intended that it will be a growing resource for cancer researchers across NSW. Thoracic cancers including lung cancer and mesothelioma are an under-researched group, and a biobank is an important resource to improve research capacity in this area.


BEN JOHNSON

Philanthropic and Corporate Funding

James Hardie

ADRI's mission 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 is only possible with ongoing support. In 2018 James Hardie Industries continued to provide corporate untied support allowing ADRI's researchers to have the security to be able to develop ideas which often require years of work to obtain fruitful data that may then form the basis of peer-reviewed funding applications. Corporate support from James Hardie is vital for research into asbestos-related diseases and for its long-term outcomes.

CSR Limited — ADRI's Biobank

ADRI's Biobank is integral to our research into asbestos-related diseases. With CSR's on-going co-support, the biobank of high quality biospecimens has continued to grow and assist researchers to improve the diagnosis and treatment of asbestos-related diseases, including, but not limited to, malignant mesothelioma, lung cancer and fibrotic asbestos-induced lung disease (asbestosis). In December 2018, ADRI welcomed Mrs Vesna Aleksova to the team as our new Biobank Officer. Vesna has extensive experience in biochemistry and anatomical pathology having worked for many years at Royal North Shore and Sydney Adventist Hospitals as a Scientific Officer. With governance approval we are now expanding our collaborative network to increase the collection of biospecimens and clinical data.

Turner Freeman Scholarship - Mesothelioma Support Coordinator

ADRI's Mesothelioma Support Coordinators provide much needed support to people who have been diagnosed with asbestos-related diseases and to their families and friends. Turner Freeman Lawyers have kindly supported this very important role for several years and which has now grown and attracted additional funding to become a full-time integrated service. The services provide not only support but also educational sessions and group meetings.

Mr Jim Tully Fellowship -Discovery of the epigenome to facilitate Malignant Mesothelioma diagnosis

Mesothelioma 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 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.

ADFA Scholarship

The ADRI has a close relationship with the Asbestos Diseases Foundation of Australia (ADFA). In 2018 the ADRI team attended ADFA's annual fundraising event on the 3rd November, the Black and White Gala Race Day at Rosehill Gardens, and the Memorial Day on the 30 November at Revesby Workers Club. ADFA has been supporting young researchers at ADRI since 2010. The current ADFA scholar is Tom Johnson who enrolled in a PhD through The University of Sydney in 2016 focusing on the involvement of YB-1 in the drug resistance of malignant pleural mesothelioma (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.

Research Projects

Research projects

Genomic deletion of CDKN2A and BAP1 are useful markers for quality control of malignant pleural mesothelioma primary cultures

To diagnosis malignant pleural mesothelioma (MPM) the current standard test requires multiple immunohistochemical (IHC) markers on formalin-fixed paraffin-embedded tissue to differentiate MPM from other lung malignancies. To date, no single biomarker exists to definitively diagnose MPM due to the lack of specificity and sensitivity; therefore, there is ongoing research and development in order to identify alternative biomarkers for this purpose. In this study, we utilized primary MPM cell lines and tested the expression of clinically used biomarker panels, including CK8/18, Calretinin, CK 5/6, CD141, HBME-1, WT-1, D2-40, EMA, CEA, TAG72, BG8, CD15, TTF-1, BAP1, and Ber-Ep4. The genomic alteration of CDNK2Aand BAP1 is common in MPM and has potential diagnostic value. Changes in CDKN2A and BAP1 genomic expression were confirmed in MPM samples in the current study using Fluorescence In situ Hybridization (FISH) analysis or copy number variation (CNV) analysis with digital droplet PCR (ddPCR). To determine whether MPM tissue and cell lines were comparable in terms of molecular alterations, IHC marker expression was analysed in both sample types. The percentage of MPM biomarker levels showed a variation between original tissue and matched cells established in culture. Genomic deletions of CDKN2A and BAP1 however, showed consistent levels between the two. The data from this study suggests that genomic deletion analysis may provide more accurate biomarker options for MPM diagnosis. The outcomes of this project were published in the International Journal of Molecular Science.

BAMLET kills chemotherapy-resistant mesothelioma cells, holding oleic acid in an activated cytotoxic state

In this study we investigated in vitro the efficacy of BAMLET and BLAGLET, anti-cancer complexes consisting of oleic acid and bovine -lactalbumin or -lactoglobulin respectively, in killing mesothelioma cells and investigated possible biological mechanisms. We performed cell viability assays on 16 mesothelioma cell lines. BAMLET and BLAGLET have increasing oleic acid content and the ability to inhibit human and rat mesothelioma cell line proliferation at decreasing doses. Most of the non-cancer primary human fibroblasts were more resistant to BAMLET than were human mesothelioma cells. BAMLET showed similar cytotoxicity to cisplatin-resistant, pemetrexed-resistant, vinorelbine-resistant, and parental rat mesothelioma cells, indicating the BAMLET anti-cancer mechanism may be different to drugs currently used to treat mesothelioma. Cisplatin, pemetrexed, gemcitabine, vinorelbine and BAMLET, did not demonstrate a therapeutic window for mesothelioma compared with immortalised non-cancer mesothelial cells. We demonstrated by quantitative PCR that ATP synthase (energy currency of cells) is downregulated in mesothelioma cells in response to regular dosing with BAMLET. We sought structural insight for BAMLET and BLAGLET activity by performing small angle x-ray scattering, circular dichroism and scanning electron microscopy. Our results indicate the structural mechanism by which BAMLET and BLAGLET achieve increased cytotoxicity by holding increasing amounts of oleic acid in an active cytotoxic state encapsulated in increasingly unfolded protein. Our structural studies revealed similarity in the molecular structure of the protein components of these two complexes and in their encapsulation of the fatty acid and differences in the microscopic structure and structural stability. BAMLET forms rounded aggregates and BLAGLET forms long fibre-like aggregates whose aggregation is more stable than that of BAMLET due to intermolecular disulphide bonds. The results reported here indicate that BAMLET and BLAGLET may be effective second-line treatment options for mesothelioma. Data from this project has been published in PlosOne.

FGF2 and EGF induce epithelial-mesenchymal transition in malignant pleural mesothelioma cells via a MAPKinase/ MMP1 signal.

Malignant pleural mesothelioma (MPM) affects the pleural surfaces and has three main histological subtypes. The epithelioid and sarcomatoid subtypes are characterised by cuboid and fibroblastoid cells, respectively. The biphasic subtype contains a mixture of both. The sarcomatoid subtype expresses markers of epithelial-mesenchymal transition (EMT) and confers the worst prognosis, but the signals and pathways controlling EMT in MPM are not well understood. We demonstrated that treatment with FGF2 or EGF (growth factors) induced a fibroblastoid morphology change in several cell lines from biphasic MPM, accompanied by scattering, decreased cell adhesion and increased invasiveness. This depended on the MAP-kinase pathway but was independent of TGF or PI3-kinase signalling. In addition to changes in known EMT markers, microarray analysis demonstrated differential expression of MMP1, ESM1, ETV4, PDL1 and BDKR2B genes in response to both growth factors and in epithelioid versus sarcomatoid MPM. Inhibition of MMP1 prevented FGF2-induced scattering and invasiveness. Moreover, in MPM cells with sarcomatoid morphology, inhibition of FGF/MAP-kinase signalling induced a more epithelioid morphology and gene expression pattern. Our findings suggest a critical role of the MAP-kinase axis in the morphological and behavioural plasticity of mesothelioma.

Tumour suppressor microRNAs modulate drug resistance by targeting anti-apoptotic pathways in malignant pleural mesothelioma

Malignant Pleural mesothelioma (MPM) is inherently drug resistant and has limited responses to current therapies. Aberrant microRNA expression is a common event in neoplasms with many implicated in chemo-resistance, however their role in MPM drug resistance is largely unexplored. Our results indicated that the expression of miR-15a/16-1 and miR-34a was downregulated in MPM cells with acquired resistance to cisplatin, gemcitabine and vinorelbine, compared to the parental counterpart. Transfection with mimics corresponding to miR-15a/16-1 were most effective in improving sensitivity to all chemotherapeutics tested in drug resistant cell lines. In parental cell lines, miR-15a/16-1 mimic induced sensitization was also observed but restoration of miR-34a and miR-34b was also capable of improving response to cisplatin and vinorelbine. Forced miR-15/16 and miR-34a expression also sensitized both parental and resistant cell lines to cisplatin, gemcitabine and vinorelbine induced apoptosis; their ability to increase levels of drug-induced apoptosis suggest they may sensitize cells to chemotherapeutics via modulation of an anti-apoptotic mechanism involving Bcl-2. miR-15a/16-1 and miR-34a transfection caused Bcl-2 mRNA and protein reduction, confirming their regulation of Bcl-2 in MPM. Furthermore, siRNA induced knockdown of Bcl-2 also induced a modest improvement in drug sensitivity. We concluded that restoration of microRNA expression sensitised both drug resistant and parental cell lines to chemotherapeutic agents and increased levels of drug-induced apoptosis. Taken together, this data suggests that miR-15a/16-1 and miR-34a are involved in the acquired and intrinsic drug resistance phenotype of MPM cells in part by modulation of apoptotic mechanisms via targeting Bcl-2. Data from this project has been presented at IASLC 19th World Conference on Lung Cancer 2018 in Toronto, Canada in September 2018.

Combination of MicroRNAs provide a synergistic effect on growth inhibition on malignant pleural mesothelioma cells.

MicroRNAs are small non-coding RNAs that post-transcriptionally regulate gene expression. In malignant pleural mesothelioma (MPM) there is a global trend toward microRNA downregulation, some of which have a tumour suppressor function. In our previous study, we demonstrated the downregulation of the miR-16 family in MPM. Additionally, the replacement of miR-16 based microRNAs was employed as a treatment strategy for mesothelioma patients in the Phase 1 clinical trial mesomiR-1. One microRNA has many targets and therefore the combination of multiple microRNAs may lead to a synergistic tumour suppressing outcome for patients with MPM. Amongst the 75 microRNAs studied, 11 showed significant cell inhibitory response in MPM when compared to MeT-5A (an immortalised normal mesothelial cell). Results generated from CompuSyn analysis indicated that among all microRNA combinations, only miR-193a-3p and miR-16-5p demonstrated a consistent synergistic cell inhibitory response amongst all concentrations (Combination index <1), whereas others were either additive or antagonistic. Cell cycle and apoptosis analysis supported CompuSyn results and showed that combination treatment with miR-193a-3p and miR-16-5p mimics provided the most profound anti-tumour response. This study indicated that the restoration of tumour suppressor microRNAs miR-16-5p and mir-193a-3p in combination produced a synergistic anti-tumour effect in MPM cell lines compared to the normal mesothelial control MeT-5a, indicating their potential application as a therapy in MPM. Data from this project has been presented at The Clinical Oncology Society of Australia's 45th Annual Scientific Meeting on Mesothelioma and Gastro Intestinal Cancers: Technology and Genomics in Perth, Western Australia in November 2018.

The expression of miR-143, miR-214 and miR-223 in malignant pleural mesothelioma xenograft tumours is primarily from stromal cells.

Tumours consist of tumour and stromal cells that both contribute to miRNA expression. miRNAs are frequently dysregulated in cancers including MPM and play an important role in tumour biology. Hence dysregulation in tumour miRNA profiles may originate from tumour cells, stromal cells or a combination of both. This can influence the selection of candidate miRNAs and subsequently gene targets. In this project we aimed to better understand changes in microRNA expression in the MPM tumour microenvironment, the relative contributions of tumour and stromal cells to microRNA expression in tumour xenografts, and the functional activity of microRNA mimics. Our results indicated that certain microRNAs are expressed higher in xenograft models when compared to their corresponding in vitro cultured cells. Determining the species origin of these microRNAs identifies that there is a large contribution of microRNA expression from stromal cells. These microRNAs had no effect on tumour cells, therefore indicating a more likely biological relevant role in the stroma. Furthermore, this data also provides a cautionary tale for interpreting microRNA profiles where the results from a MPM biopsy may include microRNAs contributed by stromal cells. Data from this project has been presented at the Lorne Cancer Conference, Lorne, in February 2018.

Circular RNA expression as potential biomarkers for mesothelioma

Currently an invasive tumour biopsy is needed to confirm a diagnosis of malignant pleural mesothelioma (MPM). MicroRNAs are proven to be dysregulated in MPM and have a therapeutic potential for MPM. Circular RNAs (circRNAs) are non-coding competitive endogenous RNAs (ceRNAs) that 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 upregulation of 290 circRNAs in MPM cell lines. Specifically, of functional importance, upregulated circRNAs derived from host genes PHKB, SLC45A4, ARHGEF28, FBXW4,

TAF15, PLEKHM1, RALGPS1, STIL, L3MBTL4, ANKRD27, NHS, ILKAP, and PTK2 (fold change above 2; $p<0.05$) harbour predicted binding sites for tumour suppressor microRNAs miR-16, miR-15a, miR-15b, miR-34a, miR-34b, miR-34c and miR-137; which we have previously demonstrated to be downregulated in MPM tumour samples and cell lines. We have previously found downregulation of the microRNAs mentioned to be associated with MPM and considering the selected candidate circRNAs host genes have predicted binding sites related to these microRNAs, we can infer that circRNAs may have similar potential as diagnostic biomarkers in MPM. Validation of their expression in MPM plasma (blood) samples were performed to test their potential as less-invasive biomarkers for the diagnosis of MPM. Data from this project has been presented at The Clinical Oncology Society of Australia's 45th Annual Scientific Meeting on Mesothelioma and Gastro Intestinal Cancers: Technology and Genomics in Perth in November 2018.

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

MicroRNA downregulation is frequent in malignant pleural mesothelioma (MPM), but the mechanisms responsible for loss of miR-15/16 and miR-193a are yet to be elucidated and were investigated in this study. Copy Number Variation (CNV) of microRNA-coding genes was analysed in MPM cells by digital droplet PCR (ddPCR) and revealed heterozygous loss of miR-193a and miR-15a/16-1, but no change in miR-15b/16-2. Epigenetic control of microRNA expression was inferred following decitabine and Trichostatin A (TSA) treatment which did not substantially affect microRNA expression. Knockdown of c-Myc expression led to upregulation of SMC4, miR-15b and 16, and to a lesser extent DLEU2 and miR-15a, whereas c-Myc overexpression repressed microRNA expression. Chromatin immunoprecipitation (ChIP) assays confirmed the interaction of c-Myc with the DLEU2 and SMC4 promoters. Tumour microRNA expression was determined in samples from MPM patients, with samples of pleura from cardiac surgery patients used as controls. In tumour samples, a strong correlation was observed between the expression of miR-15b and 16 ($R2=0.793$), but not miR-15a and 16. Our data suggested that in MPM, the downregulation of miR-15/16 was due to the transcriptional repression by c-Myc, primarily via control of the miR-15b/16-2 locus, while miR-193a-3p loss was due to genomic deletion. The results of this project have been published in Oncotarget.

"...promising new diagnostic and therapeutic advances are being translated into clinical practice to improve outcomes for patients with asbestos-related diseases..."

Public Health and Prevention Research on Asbestos-Related Diseases

In 2018, eight peer-reviewed articles were published in the area of public health/prevention. One was first-authored by ADRI staff and another by an ADRI associate with ADRI corresponding author. Three of the six co-authored papers are the Global Burden of Disease (GBD) studies published in the prestigious journal The Lancet (E/Prof. Takahashi is a member of the GBD team with his input on the assessment of the global burden of mesothelioma). The GBD provides a tool to quantify health loss from hundreds of diseases, injuries, and risk factors, so that health systems can be improved, and disparities can be eliminated.

Late 2017 – early 2018 the Heads of Asbestos Coordination Agency (HACA) funded ADRI to lead the publication of a special issue under the theme of 'Global Panorama of National Experiences in Public Health Actions to Ban Asbestos' in the International Journal of Environmental Research and Public Health (IJERPH), with E/Prof Takahashi as Chief Guest Editor of the Special Issue. This special issue comprised of 13 articles describing the relevant national situations across different countries/ regions that can be transferred to and learnt by the currently asbestos-dependent, developing countries. In this series, the article describing Australia's ongoing legacy of asbestos was first authored by ADRI Epidemiologist Dr Matthew Soeberg in collaboration with co-authors all currently affiliated with ADRI/ADRF. E/Prof Takahashi co-authored four of the articles in the series including one in collaboration with the European Regional Office of the WHO, which found evidence that countries or regions adopting asbestos bans did not sustain losses economically or employment-wise.

ADRI was contracted by the Asbestos Safety and Eradication Agency (ASEA) to undertake a research project (June 2017 – Feb 2018) for the purpose of: i) identifying gaps in research on prevention of ARDs conducted by Australian researchers or institutions; and ii) assessing the Australian burden of non-mesothelioma ARDs. The final report was submitted to the ASEA. The main output analysed trends of all scientific literature contrasted with the ARD-related literature, finding a declining emphasis on public health in the latter, but with substantial differences on the level of emphasis across countries (published in BMJ Open).

MD Projects

ADRI continues to advise three MD students at The University of Sydney, Daniel Antaw, Joseph Hockey and Justin Phang, under the overarching topic of 'Innovative Projects for World-wide Prevention of Asbestos-Related Diseases; each with specific research subtopics, for example, public health/ prevention and the intersecting area of laboratory research and public health.

Other Activities

Mesothelioma Support Coordinator

ADRI's Mesothelioma Support Coordinators provide much needed support to people who have been newly diagnosed with mesothelioma. The Coordinators advise and support not only the patients but also their families and friends. 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.

The three groups identified requiring specific support are:

1. Patients receiving standard (palliative) care;

2. Patients who have under gone radical (combined-modality) treatment; and

3. The bereaved - struggling with grief and loss.

Within groups 1 and 2 there are three subcategories: Patients who are newly diagnosed and want clinical information and empathetic support; patients in a stable condition, who want to live a 'normal' life as much as possible; and patients with progressive (symptomatic) disease with complex medical and psychological needs.

In 2018 ADRI's Mesothelioma Support Coordinators actively supported 192 people through the following activities:

Our services have been:

1. Telephone calls and emails (1434): to and from patients/families that 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 80 attendances at the following group meetings:

   a. The Liverpool Group - meets 2nd monthly at Revesby Workers Club.

   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. The **Carer's 'Thank You' Day** is held in October each year as part of the National Carers Week. The program and lunch provides an opportunity for carers to share their stories, support each other and generate friendships. ADRI's Carer's 'Thank You' day is always well attended and is much appreciated by the participants.

4. The **Meso March in May** held on Sunday 6th May 2018 was a walk to acknowledge and support people living with mesothelioma and to remember those who have lost their life to this terrible disease. In 2018 many of the participants walked in memory of Wayne Morrow. Before he died, Wayne and his wife Carolyn had planned to see a Midnight Oil concert in the Hunter But unfortunately, Wayne was too unwell to attend. Carolyn subsequently contacted Midnight Oil who kindly donated t-shirts for all Wayne's supporters at the Meso March in May, raising over $21,000.00 for much needed medical research into mesothelioma. The morning tea following the walk was supported by **icare dust disease care.**

5. **Education Webinar**

On Monday 7th May patients and their families had the opportunity to ask questions to a large expert panel on the latest treatments and symptom management of mesothelioma and on how to live with dignity. The ADRI Q&A was moderated by Dr Antony Linton, Oncologist, and attended by: Ms Karen Dahdah, Cancer Care Coordinator; Mr Armando Gardiman, Partner, Turner Freeman Lawyers; Ms Chris Guthrie, Palliative Care Consultant; Ms Sam Khochaiche, Manager Medical Services, iCare Dust Diseases Care; Ms Julie Kurlasoy, Manager of Compensation, iCare Dust Diseases Care; Dr Judith Lacey, Supportive Care & Integrative Oncology, Lifehouse; A/Prof. Brian McCaughan, Cardiothoracic Surgeon; Ms Jocelyn McLean and Mrs Karen Selmon, ADRI Mesothelioma Support Coordinators; E/Prof. Ken Takahashi, ADRI Director; Dr MoMo Tin, Radiation Oncologist; Ms Cindy Tan, Dietician, and Ms Jane Turner, Exercise Physiologist. The Q&A session was live-streamed as a webinar and can be view at: **http://adri.org.au/watch-qa-adri-style-10am-on-monday-7th-may-livestreamed/**

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

The Mesothelioma Support service is supported by a Turner Freeman Fellowship and last year ADRI was awarded a Support Organisation Grant from Dust Diseases Care (DDC) which allowed for the service to evolve into a full-time role employing Karen Selmon to job share with Jocelyn McLean. In July 2018 Karen moved to Queensland and we then welcomed Joanne Rosman to the role. Joanne is a registered nurse with extensive experience caring for people of all ages and walks of life. She has worked in a chemotherapy unit and in critical care, as well as having a strong background in community health caring for people with chronic and complex diseases, and those requiring supportive care. Joanne has supported family members with chronic and life-limiting illnesses and so understands the impact this can have on patients, carers and loved ones.

ADRI Biobank

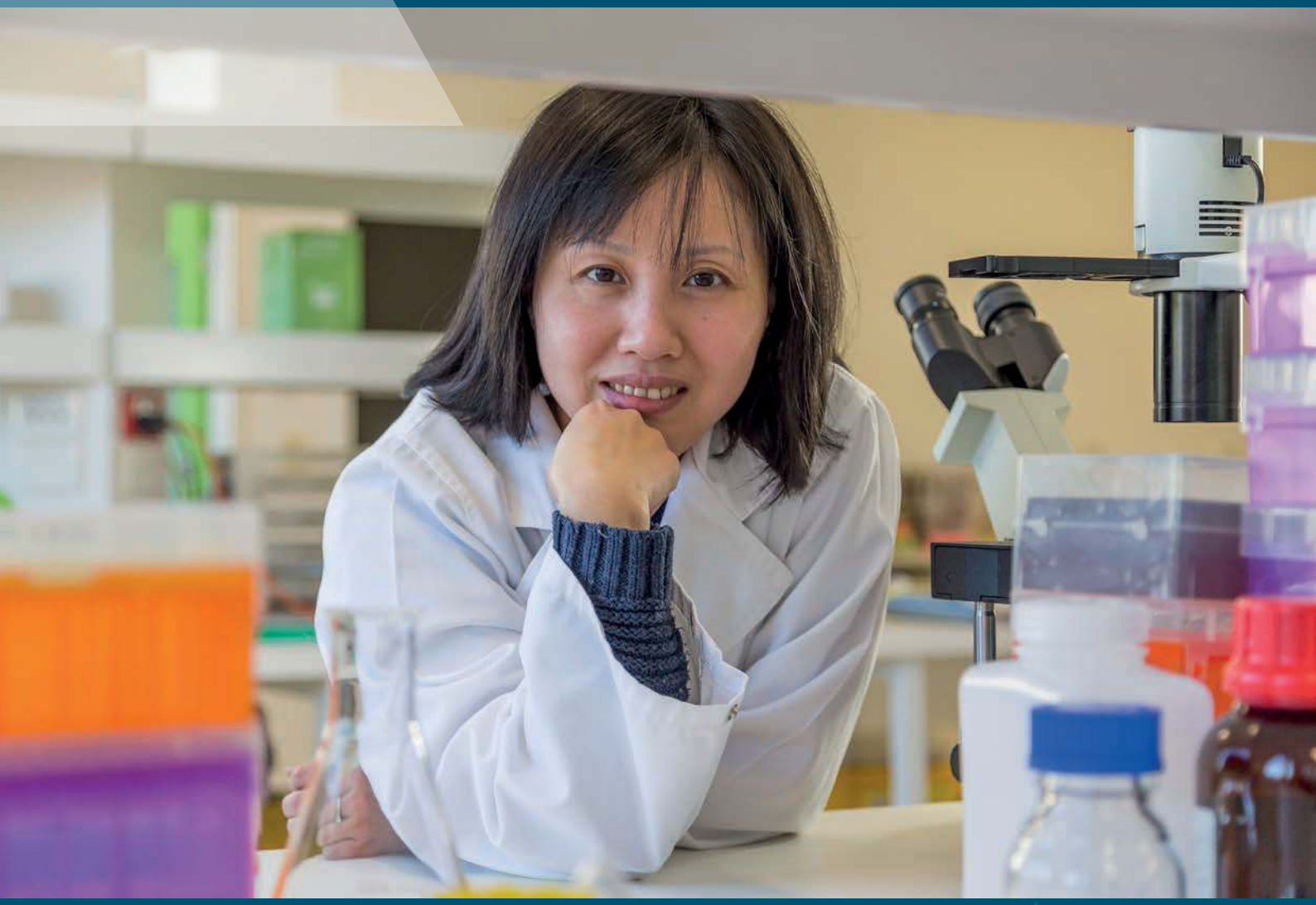
In December 2018 ADRI welcomed Mrs Vesna Aleksova to the team as our new Biobank Officer replacing Mr Kan Chen. Vesna has extensive experience in biochemistry and anatomical pathology having worked for many years at Royal North Shore and Sydney Adventist Hospitals as a Scientific Officer. Vesna's knowledge spans a broad spectrum of routine and specialised techniques with extensive practice in collecting, processing, storing and retrieving of specimens.

ADRI's established biobank collects biospecimens and clinical data from mesothelioma patients and is supported by a consortium of clinicians and researchers. We aim to further build on this collaborative network and with governance approval we have embarked on a program of expansion which should see an increase in the collection of specimens. The overall goal of this work is the ethically approved procurement of high-quality specimens and the collection of accurate, reliable and standardised clinical data which contributes to research that will lead to a better understanding of asbestos-related diseases.

International Cooperation

In 2018 Prof. Takahashi served three consultancies for the World Health Organization (WHO) to: 1) Lao PDR on 28 February – 2 March for the Workshop for Developing the National Action Plan for the Elimination of Asbestos-Related Diseases; 2) Vietnam on 11-12 October for the Consultation Meeting on White Asbestos, which was jointly organized by the WHO and the Ministries of Health and Construction of Vietnam; 3) Lao PDR on 27-29 November for the National Workshop for Moving Forward from Planning to the Implementation of the National Action Plan on Elimination of Asbestos-Related Diseases. In Vietnam, he attended the high-level meeting with the Vice Minister of Health, Vice Minister of Construction and the WHO Representative of Vietnam. In Lao PDR, he met with the Laotian Minister of Health and the Australian Ambassador. He continues to give advice on asbestos and ARD-related issues as the WHO Regional Expert and Member on the WHO Roster of Experts under the International Health Regulations.

"...Biobanking has been recognised as a critical resource for enabling twenty-first century research in an era when, increasingly, an emphasis is being placed on predictive and preventative personalised medicine...."



Publications, Presentations and Awards

Peer-Reviewed Articles

1. GBD 2017 Mortality Collaborators (incl. **Takahashi K**). Global, regional, and national age-sex-specific mortality and life expectancy, 1950–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 2018, 392 (10159): 1684-1735. doi:https://doi.org/10.1016/S0140-6736(18)31891-9

2. GBD 2017 Causes of Death Collaborators (incl. **Takahashi K**). Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 2018, 392 (10159): 1736-1788. doi:https://doi.org/10.1016/S0140-6736(18)32203-7

3. GBD 2017 Risk Factor Collaborators (incl. **Takahashi K**). Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 2018, 392 (10159): 1923-1994. doi:https://doi.org/10.1016/S0140-6736(18)32225-6

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Book Chapters

1. Winata P, Williams M, Keena V, Takahashi K, Cheng YY. DNA Methylation in Mammalian Cells. In: Uchiumi F, editor. Gene Expression and Regulation in Mammalian Cells – Transcription toward the establishment of novel therapeutics: INTECH; 2018. p. 55-76. ISBN 978-953-51-3868-6 Print ISBN 978-953-51-3867-9

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Conference Presentations

1. **Takahashi K**. Asbestos-related diseases in the global context. Asia-Pacific Journal of Oncology; 14(Suppl 7):72. COSA's 45th Annual Scientific Meeting, Mesothelioma and Gastro Intestinal Cancers: Technology and Genomics; Perth Convention and Exhibition Centre, Perth, Western Australia, 13–15 November 2018.

2. **Williams M, Cheng YY, Phimmachanh M, Winata, P, Reid G.** Tumour suppressor microRNAs modulate drug resistance by targeting anti-apoptotic pathways in malignant pleural mesothelioma (MPM). Journal of Thoracic Oncology; IASLC 19th World Conference on Lung Cancer 2018, Toronto, Canada, 23-26 September 2018.

3. **Soeberg M, Takahashi K.** An Oceanian perspective: Malignant mesothelioma and other ARDs. 14th International Conference of the International Mesothelioma Interest Group (iMig), Ottawa, Canada, 2-5 May 2018.

4. Chimed-Ochir O, **Takahashi K**, Sorahan T, Driscoll T, Fitzmaurice C, Yoko-o M, Sawanyawisuth K, Furuya S, Tanaka F, Horie S, van Zandwijk N, Takala J. Estimation of the global burden of mesothelioma deaths from incomplete national mortality data. Occupational Environmental Medicine; 75(Suppl 2): A131. 32nd Triennial Congress of the International Commission on Occupational Health (ICOH), Dublin, Ireland, 29th April to 4th May 2018.

Conference Posters

1. **Sarun K, Cheng YY**, Schelch K, Reid G. Combination of MicroRNAs provide a synergistic effect on growth inhibition on MPM cells. COSA's 45th Annual Scientific Meeting, Mesothelioma and Gastro Intestinal Cancers: Technology and Genomics; Perth Convention and Exhibition Centre, Perth, Western Australia, 13–15 November 2018.

2. **Cheng YY, Sarun K**, Lee K, Clarke C, Cheng N, **Takahashi K**. Genomic deletion of BAP1 and CDKN2A are better MM diagnostic biomarkers. Journal of Thoracic Oncology; IASLC 19th World Conference on Lung Cancer 2018, Toronto, Canada, 23-26 September 2018.

3. **Johnson T**, Schelch K, **Sarun K**, **Williams M, Cheng YY,** Lasham A, **Reid G**. YB-1: an important driver of mesothelioma drug resistance and a potential novel therapeutic target. Journal of Thoracic Oncology; IASLC 19th World Conference on Lung Cancer 2018, Toronto, Canada, 23-26 September 2018.

4. Schelch K, **Johnson T, Sarun K**, Burgess A, Lasham A, **Reid G**. YB-1 - A key factor in mesothelioma aggressive growth and behaviour. Journal of Thoracic Oncology; IASLC 19th World Conference on Lung Cancer 2018, Toronto, Canada, 23-26 September 2018.

5. **Sarun KH, Cheng YY**, Kirschner MB, Lin RCY, van Zandwijk N, **Reid G.** The expression of miR-143, miR-214 and miR-223 in malignant pleural mesothelioma xenograft tumours is primarily from stromal cells. Lorne Cancer Conference, Lorne, 8-10 February 2018.

6. **Johnson TG, Schelch K, Sarun K, Cheng YY**, Lasham A, van Zandwijk N, **Reid G**. Targeting YB-1 controls drug response via distinct mechanisms in malignant pleural mesothelioma. Lorne Cancer Conference, Lorne, 8-10 February 2018.

7. **Schelch K**, Wagner C, Reichhart E, Prieto AI, **Reid G**, Janovjak H, Grusch M. Fibroblast growth factor signals stimulate cell growth, EMT and malignant behaviour in malignant pleural mesothelioma. Lorne Cancer Conference, Lorne, 8-10 February 2018

Invited Presentations

1. **Johnson T.** Y-box binding protein-1: a novel therapeutic target in malignant pleural mesothelioma? 2018 Postgraduate and ECR Cancer Research Symposium. New Law Building, University of Sydney, 29 November 2018.

2. **Takahashi K.** Research Directions. Asbestos Safety and Eradication Summit, Sheraton on the Park, Sydney 19-20 November 2018

3. **Cheng YY.** Research Directions. Asbestos Safety and Eradication Summit, Sheraton on the Park, Sydney 19-20 November 2018

4. **Soeberg M.** Research Directions. Asbestos Safety and Eradication Summit, Sheraton on the Park, Sydney 19-20 November 2018

5. **Takahashi K.** [Plenary Speaker] Strategies and challenges towards asbestos banning. 5th Regional Conference on Occupational Health (5th RCOH) Kuala Lumpur, 13-14 September 2018.

6. **Takahashi K.** [Symposium Speaker] Asbestos-related diseases (ARDs) - Recent findings from research and current practice. 5th Regional Conference on Occupational Health (5th RCOH) Kuala Lumpur, 13-14 September 2018.

7. **Marissa Williams.** Aberrant microRNA expression in malignant pleural mesothelioma. Children's Cancer Research Unit, Weekly Seminar Series at Westmead Children's Hospital, 4 July 2018

8. **McLean J.** The evolving support service for mesothelioma patients

& their carers and obstacles to good care. Australian Lung Cancer Conference. Lung Foundation Australia, Sydney, 5-7 April 2018.

9. **Kao S.** Update on thoracic cancers and malignancies. Australian Lung Cancer Conference. Lung Foundation Australia, Sydney, 5-7 April 2018.

10. **Takahashi K.** [WHO Consultant] Asbestos: impacts on health and society. WHO Western Pacific Region. Workshop for developing National Action Plan for the elimination of asbestos-related diseases in Lao PDR. Vientiane, Laos 1-2 March 2018.

11. **Takahashi K.** [WHO Consultant] How do countries ban asbestos? A case study. WHO Western Pacific Region. Workshop for developing National Action Plan for the elimination of asbestos-related diseases in Lao PDR. Vientiane, Laos 1-2 March 2018.

12. **Takahashi K.** [WHO Consultant] Debunking lies and myths about asbestos. WHO Western Pacific Region. Workshop for developing National Action Plan for the elimination of asbestos-related diseases in Lao PDR. Vientiane, Laos 1-2 March 2018.

Webinair

1. Linton A, **Takahashi K**, McCaughan B, **Kao S**, Tin M, Dahdah K, Guthrie C, Lacey J, Tan C, Turner J, Gardiman A. Kurlasoy J, Khochaiche, **Selmon K**, **McLean J.** Q&A Adri Style. Medical education Centre, Concord. 7 May 2018.

http://adri.org.au/watch-qa-adri-style-10am-on-monday-7th-may-livestreamed/

Travel Grants

1. **Schelch K.** Early Career Researcher Conference Travel Grant, The Cancer Research Network Australia - Lorne Cancer Conference, 8-10 February 2018

2. **Cheng YY.** Slater & Gordon Health Projects & Research Fund for Continuing Education Travel Grant - 19th World Conference on Lung Cancer, Toronto, Canada, 23- 28 September 2018

3. **McLean J.** Slater & Gordon Health Projects & Research Fund for Continuing Education Travel Grant - 14th International Mesothelioma Interest Group Conference (iMig2018), Ottawa, Canada, May 2 – 5, 2018.

Financial Summary

Profit and Loss Statement

	2016-18	2016-17
Revenues		
Research	1,274,450	1,925,636
Fundraising	540,177	693,603
Interest	114,529	126,189
Total	1,929,156	2,745,428
Expenses		
Employee Benefits	1,628,135	1,995,162
Research consumables/equipment	184,309	402,214
Office expenses	400,286	247,924
Depreciation	450,377	459,170
Total	2,663,107	3,104,470
Surplus / Deficit for the period	***-733,951***	***-359,042***

Balance Sheet

	30/06/2018	30/06/2017
Assets		
Cash and cash equivalents incl. Term Deposits	4,618,471	5,241,469
Trade and other receivables	256,411	280,596
Property Plant and Equipment	8,014,691	8,459,863
Total	12,889,573	13,981,928
Liabilities		
Trade and other payables	484,169	847,496
Employee provisions	129,621	124,698
Total	613,790	972,194
Net Assets	***12,275,783***	***13,009,734***

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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ADRI
Asbestos Diseases Research Institute

Asbestos Diseases Research Institute

Gate 3 Hospital Road
Concord Hospital
Concord NSW 2139
Australia

PO Box 3628
Rhodes NSW 2138
Australia

Phone: +61 2 9767 9800
Fax: +61 2 9767 9860
Email: info@adri.org.au
Website: www.adri.org.au