ADRI

Asbestos Diseases Research Institute

ANNUAL REPORT 2016

CONTENTS

ABOUT US

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.

WHO WE ARE

The Asbestos Diseases Research Institute (ADRI) is the first stand-alone research institute tackling the current epidemic of asbestos-related diseases. The ADRI was established and is governed by the Asbestos Diseases Research Foundation (ADRF), a charitable, not-for-profit organisation. The ADRI is located in the ADRF's Bernie Banton Centre on the Concord Hospital campus which was officially opened in January 2009 by the then Prime Minister, the Hon. Kevin Rudd.

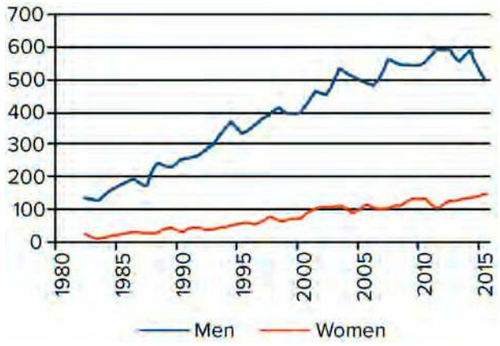
WHAT WE DO

The ADRI's primary objective is to make asbestos-related disease history, and to provide a better future for all those unfortunate Australians exposed to asbestos.

K EY STATISTICS

INCIDENCE*

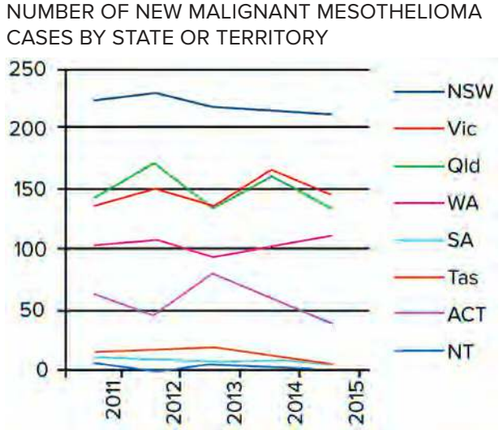
NUMBER OF NEW MALIGNANT MESOTHELIOMA CASES ACROSS AUSTRALIA



Between 1982 and 2015, a total of 15,884 people were newly dignosed in Australia with malignant mesotelioma with women making up 17% of all cases.

The rate of malignant mesothelioma in the Australian population was 2.3 per 100,000 in 2015. The highest rate of 3.2 per 100,000 occurred in 2003.

NUMBER OF NEW MALIGNANT MESOTHELIOMA CASES BY STATE OR TERRITORY

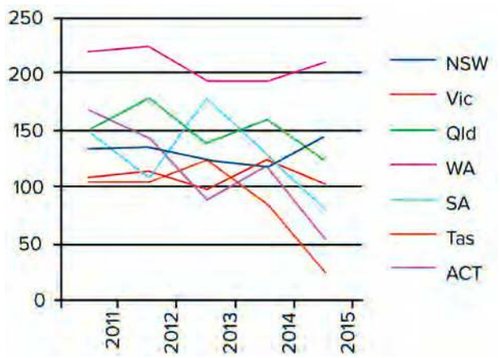


Around a third of all cases diagnosed in 2015 occured in New South Wales.

Cases in Queensland and Victoria made up about 20% each of all cases diagnosed in 2015.

Western Australian cases made up 17% of all cases diagnosed in 2015.

RATE OF NEW MALIGNANT MESOTHELIOMA CASES IN THE POPULATION



Western Australia has the highest rate of malignant mesothelioma across all the Australian states and territories.

In 2015, the rate in Western Australia was 4.2 per 100,000.

A stabilisation or decline in the rate of mesothelioma in the Australian population is occurring.

ASBESTOS EXPOSURE*

By 1 April 2016, 582 people completed the asbestos exposure data questionaires available through the Australian Mesothelioma Registry.

Around 60% of those people were assessed as having possible or probable occupational asbestos exposure, and of these, 286 also had indications of possible or probable non-occupational exposure.

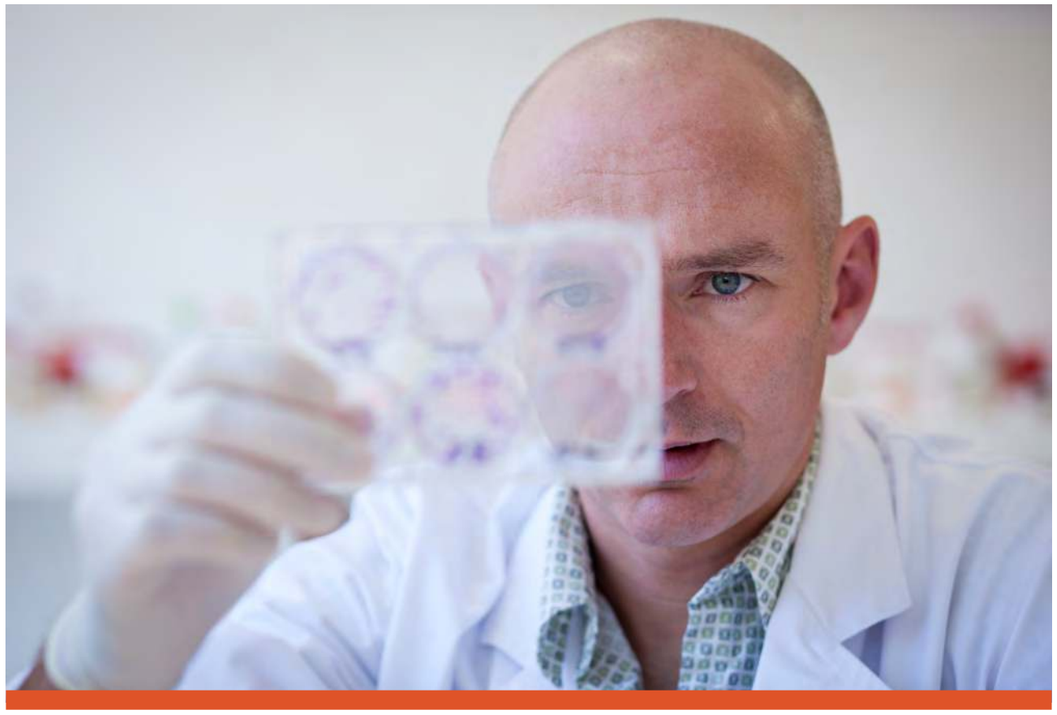
A third of people had indicatons of non-occupational exposure but not occupational exposure.

No information was found to indicate asbestos exposure in either occupational or non-occupational spheres for 6% of participants.

TYPES OF ASBESTOS EXPOSURE BY GENDER*		
Occupational exposure only	64	1
Non-occupational exposure only	98	99
Both occupational and non-occupational exposure	279	7
Niether occupational and non-occupational exposure	23	11
Total	464	118

*All data extracted from the Australian Mesothelioma Registry 5th Annual Report ‘Mesothelioma in Australia 2015’ published September 2016.

2016 HIGHLIGHTS



ADRI'S NEW TREATMENT CONCEPT IN THE CLINIC

In 2016 the phase I activities, testing nano-cells loaded with tumour suppressive microRNA mimics, have continued and in November sufficient data had been collected to close this first in human study. Although phase I studies are primarily dedicated to dosing and safety issues, clear clinical activity has been noticed among the 28 patients included in the study. A priority after the completion of this study is the exploration of loco regional drug administration. It is estimated that administration of carriers of microRNA mimics directly in the intrapleural space (the space between the thoracic wall and lung) will provide a unique opportunity to establish high drug concentrations and avoid some of the (inflammatory) toxicities noticed when the microRNA mimics packaged in minicells were introduced directly in the circulation.

FUNDING SUPPORT FOR ADRI'S RESEARCH

Donor support continues to make a major contribution to research activities at ADRI. In 2016 the Asbestos Diseases Foundation of Australia (ADFA) funded a PhD scholarship and Tom Johnson became the inaugural ADFA PhD Research Fellow. The Jim Tully Fellowship continues to provide support to ADRI, and now funds Dr Karin Schelch's post-doctoral research. In response to a Special Appeal aired in December on Channel 9's A Current Affair, The Asbestos Diseases Support Society (ADSS) along with many hundreds of individuals made generous donations that will ensure that ADRI's clinical development of new therapeutic approaches for mesothelioma can continue.

DEEPENING INSIGHT INTO microRNA BIOLOGY

Preclinical research at ADRI in 2016 has made an invaluable contribution to the increasing insight in the important and complex regulatory roles microRNA play in asbestos cancers. The research started with the microRNA-15/16 family but has expanded to other miRs with tumour suppressive activities and important interactions with tumour growth factors and immune recognition factors have been convincingly made. These outcomes reveal the power of well-designed translational research efforts and underline the importance of close interaction between molecular biologists and disease oriented clinicians.

ADRI RESEARCHERS AWARDED

Special moments in 2016 were the invited (international) lectures by A/Prof. Glen Reid, who is increasingly recognised as a world expert in the altered biology of microRNAs in cancer, and the highlighting of the new treatment opportunities to the general public on Channel 9's A Current Affair Special Appeal on December 5th. It is important to also mention the travel grants awarded to ADRI scientist including Mr Kadir Sarun, Dr Karin Schelch and Dr Yuen Yee Chang. Mr Sarun was awarded the Young Investigator Award by the International Association for the Study of Lung Cancer (IASLC) and the Local Organising Committee of the 17th IASLC World Conference on Lung Cancer (WCLC) which was presented at the IASLC Business Meeting in Vienna on the 6th December 2016. Mr Sarun was also awarded a Concord Repatriation General Hospital Research Travel Scholarship. Dr's Schelch and Chang were both awarded an Australian Lung Foundation Travel Award for the WCLC 2016.

ADRF CHAIR'S REPORT

It is my privilege once again to report on the activities of the Asbestos Diseases Research Foundation (ADRF) for 2016. This year the Board has focused on two key issues: safeguarding the intellectual property developed through the ADRI's research; and recruiting the next Research Director of the ADRI.

The MesomiR 1 phase 1 clinical trial, using microRNA, is soon to be completed. This novel therapy developed by ADRI for thoracic cancers, particularly malignant mesothelioma, is a world first. The clinical trial explored safe dose levels of TargomiRs, antibody-targeted minicells loaded with a microRNA construct. The intellectual property associated with the development of this novel therapy is complex and, even though the observations made in MesomiR 1 are promising, they will need to be confirmed. It is hoped that MesomiR 2, which will focus on efficacy and optimal dosing of TargomiRs, will commence next year.

The other major focus of the Board during the year has been the selection of the next Research Director of the ADRI. We were pleased to announce in October that Professor Ken Takahashi had been appointed as the next Director. He is the Professor of Environmental Epidemiology and Director of the WHO Collaborating Centre for Occupational Health at the University of Occupational and Environmental Health (UOEH) in Japan. Professor Takahashi 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 will take over from Professor Nico van Zandwijk in February 2017.

There has been a number of changes on the Board during the year. Mr Paul Bastian resigned in February having served on the Board for nine years as the Unions NSW nominee. Paul has been replaced by Dr Deborah Vallance. Dr Vallance has worked as a medical practitioner and since 2009 has been the National Health & Safety Coordinator of the AMWU. Another long-time member, Ms Rita Mallia, resigned in June. Rita was the Workers' Compensation Dust Diseases Board (DDB) of NSW nominee. Rita has been replaced by Ms Anita Anderson as the now Dust Diseases Authority (DDA) nominee.

Dr Tim Sinclair also resigned from the Board during the year as representative of the Sydney Local Health District. Tim has been replaced by Dr Katherine Moore, Director of Clinical Governance and Risk from the Sydney Local Health District. On behalf of the Board I would like to thank Paul, Rita and Tim for their invaluable contributions.

Uncertainty continues regarding both state and federal research funding as it is spread ever more thinly. The ADRF is extremely grateful to our donors who are very generous; their ongoing support is vital for our research which allows us to continue to facilitate a comprehensive research approach to asbestos-related diseases. On behalf of the ADRF Board I thank you for your support and generosity.

The Foundation looks forward to a new and exciting era of ADRI's development research in 2017, with a change in focus to more of prevention of asbestos-related diseases. Professor Takahashi epidemiology research focuses on occupational diseases, with a special interest in occupational lung diseases, and in particular asbestos-related diseases.

I would like to express my thanks to members of the Board for their contributions to deliberations throughout the year. On behalf of the Board, I would like also to thank Professor van Zandwijk for his tireless work over the last eight years. As the inaugural Research Director of the ADRI, he has established and equipped a vibrant and productive research team at the ADRI. We wish him well for his retirement.

John O'Meally AM RFD
Chair

ADRI DIRECTOR'S REPORT

2016 was full of research activities. The early clinical trial, testing the new treatment concept for mesothelioma developed at ADRI in cooperation with EnGeneIC Ltd, made excellent progress. After accrual of 28 patients the trial was closed for patient entry on November 24th, 2016. The analysis of the data collected from more than 270 treatment weeks is a formidable task and will provide the basis for a report to be published in a major oncological journal. So far it is evident that the microRNA mimics packaged in antibody-guided nanocells are rather well tolerated and quite capable of curtailing the tumour growth. It will be a challenge to identify the factors able to predict a positive response to our new treatment concept. At the same time we are trying hard to allocate the financial resources needed for the next research stage and it would be exciting to see ADRI contributing to the long-awaited success of gene therapy.

In 2016 Dr Matthew Soeberg was able to finalise a number of important epidemiological publications, showing that the mesothelioma epidemic in Australia is close to its peak and that cancer registries in developing countries may constitute an important tool in identifying mesothelioma diagnoses.

By combining clinical and preclinical data A/Prof Glen Reid, Dr Steven Kao, Dr Yuen Yee Cheng and PhD student Marissa Williams were able to uncover that the microRNA-16 family is involved in the regulation of immune checkpoints. PD-L1 expression in mesothelioma tissues and cell lines were closely associated with microRNA levels. These findings create new opportunities for combined therapies and are expected to influence ADRI research in the years to come. Marissa presented her work at the International Mesothelioma Interest Group (iMiG) conference in Birmingham.

Dr Karin Schelch, a Post-doc Fellow provided new information on the growth control of mesothelioma cells at the 17th World Conference on Lung Cancer Conference in Vienna by revealing that the tumour suppressor microRNA-15/16 family is closely aligned with signalling of the fibroblast growth factor (FGF). In other words, the microRNA-15/16 family is capable of repressing hyper-activated FGF signals. At the same conference Kadir Sarun presented data revealing that the source of one of the dysregulated microRNAs in mesothelioma (miR-223) is found in the tumour stroma, allowing a more accurate picture of the role of microRNAs in asbestos carcinogenesis. Dr Anthony Linton concentrated on geographical and socioeconomic factors with a potential contribution to treatment choices made in a large group of patients compensated by the Dust Diseases Board. Although conclusions are somewhat limited by the retrospective nature of this study it is clear that geographical remoteness and socioeconomic status may influence therapy choices.

Health and Safety delegations from Indonesia and Cambodia visited ADRI during November which is Asbestos Awareness month. Supported by the Australian People for Health, Education & Development Abroad (APHEDA) and the Asbestos Safety and Eradication Agency (ASEA), they took part in awareness events organised in Australia. At ADRI, we were able to highlight how keen we are to assist people from developing countries to learn from Australia's asbestos legacy and similar tragedies. The ADRI *Guidelines for the diagnosis and treatment of malignant pleural mesothelioma*, approved by the National Health & Medical Research Council of Australia, were provided to the delegations and it is hoped that this will assist local governments to adapt laws and prevent asbestos from further disturbing health and societies.

At the national level ADRI continued to support the Asbestos Education Committee and 'Betty' the ADRI (asbestos) house that continues to travel extensively in Australia and to raise awareness of the dangers of asbestos. Distribution of the second print run of the consumer guidelines (Understanding Pleural Mesothelioma. A guide for people with cancer, their families and friends, by Cancer Australia) is ongoing. Jocelyn McLean, ADRI's mesothelioma support coordinator, has comprehensively studied the needs of different patient categories and carers, and finished the year with an excellent number of support meetings. Regional meetings were successful and provided patients and carers with important information and much needed support.

In 2016 research papers were published in 15 peer-reviewed journals with another two accepted for publication. We continued to profit from the excellent advice and monetary help from many supporters. On Memorial Day, a scholarship for PhD studies was presented by the Asbestos Diseases Foundation of Australia (ADFA) to Tom Johnson. Members of ADFA continued to participate in 'quality-of-life' studies for which we are very grateful. Asbestos awareness ambassador, Don Burke made an exceptional contribution by hosting a Channel 9 produced documentary on ADRI's clinical trial. The consequences were many positive reactions and a large amount of donations to be used solely for clinical trial activities.

To give recognition and thanks to our donors an Honour Wall was unveiled with the names of organisations and individuals who have made a major contribution to ADRI. Unfortunately, it is not possible list all our wonderful supporters.

Finally, it is an honour and great pleasure to announce that Professor Ken Takahashi has accepted the invitation from The University of Sydney's selection committee and the ADRF Board, to become ADRI's new Research Director. Ken will join ADRI on February 1st 2017. We are looking forward to his arrival. Ken is an expert in Occupational Health and Epidemiology, and has all the capacities to make a great contribution to an expanding ADRI.

I have no doubt that you will enjoy reading about the 2016 research progress at ADRI.

Nico van Zandwijk MD PhD FRACP FCCP
Director

ADRF BOARD

MR JOHN O'MEALLY AM RFD
Independent Chair

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.
Appointed: 22 February 2012

MS SYLVIA KIDZIAK AM
Deputy Chair
Nominated by the Dust Diseases Board

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.
Reappointed: 16 May 2012

MS RITA MALLIA
Nominated by the Dust Diseases Board

Ms Mallia is the President of the Construction, Forestry, Mining and Energy Union (CFMEU) (NSW Branch), Construction and General Division. Prior to 2011 she was Senior Legal Officer of the Union. Rita is a former member of the NSW Workers Compensation Dust Diseases Authority and is a Director of United Super Pty Ltd, ACIRT Pty Ltd and Uplus Pty Ltd.
Reappointed: 20 August 2009
Resigned: 16 June 2016

MS ANITA ANDERSON PSM
Nominated by the Dust Diseases Authority

Ms Anderson is the Executive General Manager of the Workers Compensation Dust Diseases Authority and since 2008 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.
Appointed: 20 June 2016

PROFESSOR MARK COOPER
Nominated by The University of Sydney

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.
Appointed: 21 October 2015

EMERITUS PROFESSOR ROBERT LUSBY AM
Nominated by the ANZAC Health and Medical Research Foundation

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.
Appointed: 3 August 2012

DR TIM SINCLAIR

Nominated by the Local Health District

Dr Tim Sinclair is the General Manager of Concord Repatriation General Hospital, Sydney Local Health District. He holds a Doctor of Business Administration, a Masters in Health Services Management and a Bachelor of Applied Science (Health Information Management). Tim also successfully completed the Graduate Health Management Training Program. Prior to that appointment he was the General Manager at Balmain Hospital and he has previously held a number of senior positions with the then Sydney South West Area Health Service including the Associate Director of Clinical Operations and the Manager, Operational Initiatives. He is also a Director on the ANZAC Health and Medical Research Foundation and an Advisory Board Member of the Australian Institute of Health Services Management. In 2013 Tim was also the recipient of the Institute of Public Administration Australia award for Individual Excellence and the Anthea Kerr Award.
Appointed: 31 October 2013
Resigned: 18 August 2016

DR KATHERINE MOORE

Nominated by the Sydney Local Health District

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. She is a member of the Australian Institute of Company Directors.
Appointed: 12 December 2016

MR BARRY ROBSON

Nominated by the Asbestos Diseases Foundation of Australia Inc.

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.
Reappointed: 8 October 2014

MR PAUL BASTIN

Nominated by Unions NSW

Paul Bastian was appointed National Secretary of the Australian Manufacturing Workers' Union in March 2012, having previously held the position of National President since January 2010. Paul commenced his employment with the AMWU in 1981 and in 1997, was elected State Secretary of the NSW Branch. He is a shipwright by trade and completed a Law Degree while studying part time at the University of Technology, Sydney. Paul has worked throughout the manufacturing industry, in the construction, shipbuilding and metals industries, in both metropolitan and regional areas of the state. He represents the AMWU on a number of Boards/Committees including ACTU Executive and, AustralianSuper. Paul was on the Asbestos Management Review Advisory Group, as well as once being on the Boards of APHEDA, the NSW Manufacturing Council and the NSW Workers Compensation Advisory Council. He has a long history of involvement with community and union campaigns against asbestos and has represented the AMWU and IndustriALL Global Union (previously known as the International Metalworkers Federation at numerous international asbestos Conferences.
Appointed: 28 November 2007
Resigned: 16 February 2016

DR DEBORAH VALLANCE

Nominated by Unions NSW

Since 2009 Dr Vallance is 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.
Appointed: 18 April 2016

MR SEAN O'SULLIVAN

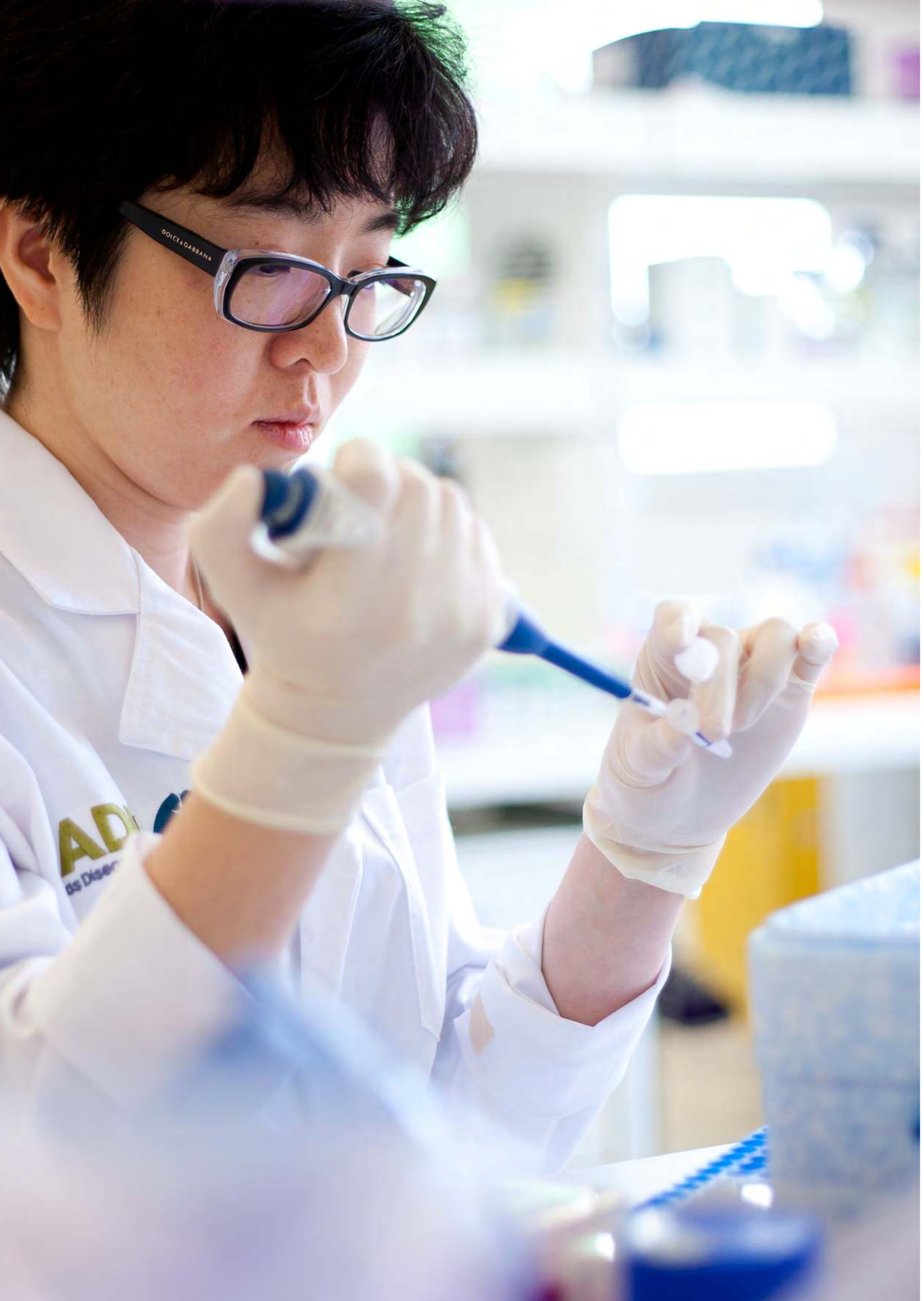
Representing the interests of past and present manufacturers and suppliers of Dust-containing goods

Sean O'Sullivan joined James Hardie as Vice President – Investor & Media Relations in December 2008. In this role Sean is responsible for matters relating to the corporate affairs for the group including government relations. Sean is a member of the James Hardie's Corporate Management Team. For the eight years prior to joining James Hardie, Sean was Head of Investor Relations at St. George Bank, where he established and led the investor relations function. Sean's background includes thirteen years as a funds manager for GIO Asset Management managing domestic and global asset portfolios. Mr O'Sullivan's final position at GIO was General Manager of Diversified Investments where his responsibilities included determining the asset allocation for funds under management. After leaving the GIO, Sean worked for Westpac Banking Corporation in funds management sales. He has a Bachelor of Arts majoring in economics from Sydney University and an MBA from Macquarie Graduate School of Management.
Appointed: 19 October 2011

DR CHRISTOPHER CLARKE

Invited by the Board

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 now works 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.
Appointed: 13 March 2014



DR ANDREW PENMAN AM

Invited by the Board

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.
Appointed: 8 October 2014

PROFESSOR NICO VAN ZANDWIJK

Research Director

Nico van Zandwijk earned his medical degree at the University of Amsterdam, The Netherlands, in 1973 and wrote his thesis on "Pulmonary injury elicited by blood" in 1976. He was editor of the Haematology section of Excerpta Medica until 1980, and received licences in internal medicine and pulmonary medicine in 1979 and 1981, respectively. In the same year he was appointed Assistant Professor of the Academic Medical Centre, Amsterdam and became Consultant Physician at the Netherlands Cancer Institute, Amsterdam. From 1985 to 2008 he was Head of the Department of Thoracic Oncology at that Institute. Professor van Zandwijk has served as Secretary (1982-1988) and Chair (1988-1994) of the European Organisation for Research and Treatment of Cancer (EORTC) Lung Cancer Group. He has chaired a number of boards and committees including: the Scientific Board of the clinical section of the Netherlands Cancer Institute; a National Advisory Board for new lung cancer medications, and a State Council on asbestos related disease. He has also been a member of the Advisory Board of the Thoracic Section of the French National Cancer Institute (INCA). Professor van Zandwijk was a Board Director of the International Association for the Study of Lung Cancer (2005-2009) co-chaired the World Lung Cancer Conference (WLCC) 2011 and, was a Member of the Core Program Committee for the WCLC 2013. He was a member of the national Asbestos Management Review Panel and was Study Coordinator of several international studies. He is a member of the Dust Diseases Board advising the Dust Diseases Authority of NSW. He authored or co-authored more than 300 peer-reviewed international papers and chapters. In 2007 the Asbestos Diseases Research Foundation, Bernie Banton and the University of Sydney recruited Nico van Zandwijk to the position of ADRI Director and Professor, Sydney Medical School.
Appointed: 29 July 2008

MR COLIN GOLDRICK

Company Secretary

Colin is a past Partner and now Special Counsel with the legal firm of Goldrick Farrell Mullan, heading up 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 15years in a variety of roles.
Reappointed: 16 May 2012

NEW GRANTS IN 2016

DUST DISEASES AUTHORITY

Micromanaging microRNAs to treat malignant pleural mesothelioma.
Reid G, Cheng YY

MicroRNAs are a class of short gene regulators that are frequently dysregulated in cancer, contributing to the growth of tumour cells. We have identified microRNAs present at reduced levels in malignant pleural mesothelioma (MPM), and have shown that some act as tumour suppressors. This project will systematically test all downregulated microRNAs to describe the full repertoire of tumour suppressor microRNAs in MPM. We will then test, both in vitro and in vivo, combinations of mimics of downregulated microRNAs for their ability to synergistically inhibit cell growth by coordinately re-exerting control over multiple dysregulated pathways. With the use of in vivo-jetPEI from Polyplus to deliver nucleic acids already in clinical trial, this approach has the potential to be rapidly tested in the clinic as a treatment for MPM patients.

ON-GOING GRANTS IN 2016

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.
Kao S, van Zandwijk N, McCaughan B, et al.

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. Thoracic cancers including lung cancer and mesothelioma are an under-researched group, and a biobank is the first step towards improving research capacity in this area. ADRI already has an established biobank collecting biospecimens and clinical data from mesothelioma patients, but there is currently no dedicated repository of similar samples and data from lung cancer patients. By ear-marking the available capacity of the ADRI biobank and database, and building on the collaborative network of clinicians and scientists already in place, increased collection of samples from mesothelioma patients and rapid collection of samples from lung cancer patients will be possible. These collections will quickly grow into a resource available for cancer researchers across NSW.

CANCER COUNCIL NSW

MicroRNA replacement: A novel therapeutic approach for malignant mesothelioma.
Reid G, van Zandwijk N, Macdiarmid J, Brahmbhatt H

MicroRNAs are short ribonucleic acids (RNAs) that regulate gene expression. Their expression is altered in tumours, with evidence suggesting a characteristic pattern of expression in malignant pleural mesothelioma (MPM). This project will build on initial observations from MPM tumour specimens, cell lines and xenograft tumour models, revealing that expression of miR-16 and related microRNAs is greatly reduced in all MPM tumour samples and MPM cell lines. This work will be carried out together with scientists from the biotech company EnGeneIC, with whom ADRI have been collaborating.

SYDNEY CATALYST

Correcting aberrant microRNA expression as a therapeutic approach in MPM.
Williams M

miR-15a/16-1, miR-15b/16-2 and miR-193a-3p are tumour suppressor microRNAs that have been shown to be downregulated in malignant pleural mesothelioma (MPM) tumours. The mechanisms driving the downregulation of these microRNAs are unknown. To understand the processes involved, the different stages of microRNA biogenesis are being investigated in this project.

CANCER COUNCIL NSW - TRANSLATIONAL PROGRAM GRANT

Translating malignant mesothelioma research into better outcomes for patients and their families
van Zandwijk N, Reid G, Vardy J, Kao S, Pavlakis N

This program grant brings together an experienced multidisciplinary research team dedicated to improving health outcomes for patients with mesothelioma. It involves epidemiological studies, basic research, and clinical approaches all aiming to provide better outcomes for malignant mesothelioma patients. Progress in this program has been made in many of the projects. Results from this project were presented at the International Association for the Study of Lung Cancer (IASLC) 17th World Conference on Lung Cancer in Vienna.

PHILANTHROPIC AND CORPORATE FUNDING

JAMES HARDIE

James Hardie Industries plc continued to provide untied support for research into the diagnosis and treatment of asbestos–related disease during 2016. This support is significantly important to ADRI's research program as it provides a level of flexibility for potential pilot studies. James Hardie have also provided support for the TargomiRs clinical trial.

CSR LIMITED — BIOBANK

The ADRI biobank is an invaluable collection providing the research team with a range of specimen types, including: fresh frozen tumour tissue, DNA and RNA samples derived from tumour tissue and matched bloods from mesothelioma patients, control tissue samples and a series of formalin-fixed tumour tissues. Thanks to CSR's co-support of the biobank, it continues to grow and is an important resource for the ADRI's on-going research program into asbestos-related diseases.

During 2016 work has focused on upgrading standard operating procedures (SOPs) as part of the NSW Health Pathology (NSWHP) Biobank Certification Program. Following registration of our biobank, for the second phase of the program we must supply NSW Health Pathology with key documents (including detailed SOPs) to demonstrate that our methods have been adapted to the best practice standards. This next phase is scheduled for 2017.

TURNER FREEMAN SCHOLARSHIP - MESOTHELIOMA SUPPORT COORDINATOR

McLean J

Turner Freeman Lawyers continued to provide support to ADRI so that we could provide much needed assistance and support to those people that have been diagnosed with asbestos-related diseases, their families and friends.

MR JIM TULLY FELLOWSHIP

Schelch K

Karin Schelch completed her PhD in Vienna and returned to the ADRI in early 2016 to take up a post-doctoral position. Dr Schelch's main research focus is to investigate dysregulated signalling pathways in mesothelioma with the aim of identifying new targets for therapy. Dr Schelch will be co-supported by the Mr Jim Tully Fellowship. Dr Schelch presented this work at the 17th World Conference on Lung Cancer in Vienna, December 2016.

ADFA SCHLOLARSHIP

Johnson T

Tom Johnson started at ADRI as a summer student at the end of 2014 and completed his Honours in 2015. He has now enrolled in 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 malignant pleural mesothelioma patient outcomes in the development of future drugs. Tom presented this work as a Poster at the 17th World Conference on Lung Cancer in Vienna, December 2016.

CLINICAL RESEARCH PROJECTS

CLINICO-PATHOLOGICAL REVIEW OF ASBESTOS-ASSOCIATED LUNG CANCER FROM DUST DISEASES AUTHORITY

Investigators: Kao S[1,3], Lin RCY[1,7], Hannaford-Turner K[2], Hyland R[1], Cooper W[4], Klebe S[5], Reid G[1,6], van Zandwijk N[1,6]
1. Asbestos Diseases Research Institute, 2. Dust Diseases Authority, 3. Chris O'Brien Lifehouse, 4. Royal Prince Alfred Hospital, 5. Flinders University, 6. University of Sydney, 7. University of New South Wales

Lung cancer is the fifth most common cancer in Australia and is predicted to remain the leading cause of all cancer deaths in 2016. The majority of lung cancers are diagnosed at an advanced stage resulting in limited treatment options and poor prognosis. Tobacco smoke is thought to be responsible for over 90% of lung cancer cases. The strength of this association and the prevalence of smoking have contributed to enduring difficulties assessing other causative factors including the impact of occupational-related exposures with known carcinogenic potential in the lung. Asbestos has been long recognised as responsible for the development of lung cancer however unlike mesothelioma, asbestos related lung cancer (ARLC) has been widely acknowledged to be underreported in many countries who have historically been high users of asbestos products, Australia included. Research suggests that there may be two ARLC for every case of malignant mesothelioma and this ratio may increase in occupations with heavy exposure.

Due to recognised challenges in identifying ARLC and limited access to significant sized cohorts of diseased population, questions still stand regarding its clinical profile. The current literature suggests there are no defining clinical features unique to ARLC in terms of presenting symptoms, cell type or tumour location. However survival outcomes have not been well researched. Thus the intention of the research was to compare clinical characteristics of ARLC to mainstream lung cancers in a cohort of known occupationally exposed workers from NSW and to contribute to the body of knowledge that surrounds this still under-researched occupational lung disease.

A total of 607 lung cancer cases presenting to the NSW Workers Compensation Dust Diseases Authority (DDA) between 2002 and 2014 as claims for lung cancer attributed to asbestos exposure were reviewed. De-identified data was entered into a custom built access database. Source documents in patient's files included, x-ray, CT and PET reports, pathology reports, GP and specialist referral letters, oncologist letters, hospital admission notes, asbestos fibre count assessments, and in a minority of cases autopsy reports and medical reviews by expert pathologists or respiratory physicians with specialist knowledge in assessment of asbestos related diseases. In some instances DDA files were missing clinical attributes that were intended to be collected. This was more likely the case for lung cancers not awarded, and thus not followed up beyond the application. Follow up of missing data was done by contacting treating physicians and reviewing medical records from treating hospitals. A disappointing, and frequently encountered, obstacle for patients in the earlier years was the retirement of treating doctors or the archiving or destroying of old patient files in hospitals. A total of 55 (9%) workers were lost to follow-up and were excluded and a further 23 (4%) were identified as not being primary lung cancer, bringing the total cohort in the analysis to 529 workers.

As we did not seek to use compensation outcomes as a marker of adequate exposure, lung cancer patients in this study population were assigned to the group of ARLC if they met any of the Helsinki Criteria. The Helsinki Criteria remains the gold standard reference tool for the identification and diagnosis of asbestos related lung cancer.

The fulfilment of the Helsinki Criteria is related to a 2-fold risk of lung cancer. The Helsinki criteria includes the following:

• The presence of asbestosis (diagnosed clinically, radiologically or histologically) or

• A count of 5000 to 15000 asbestos bodies (ABs) or more per gram dry lung tissue (/g dry), or an equivalent uncoated fibre burden of 2.0 million or more amphibole fibres (>5µm in length)/g dry, or 5.0 million or more amphibole fibres >1µm in length/g dry; this tissue count of ABs is also roughly equivalent to 5-15 ABs/mL of broncho-alveolar lavage (BAL) fluid. The criteria also recommend that when the AB concentration is < 10000/g dry, the count should be supplemented by an uncoated fibre burden analysis using electron microscopy. Occupational histories (fibre-years exposure) are considered probably to represent a better indicator of lung cancer risk from chrysotile than fibre burden analysis, or

• Estimated cumulative exposure to asbestos of 25 fibre/ml-years or more, or

• An occupational history, that only means whereby latency can be evaluated, of 1 year of heavy exposure to asbestos or 5-10 years of moderate exposure. A 2-fold risk of lung cancer can be reached with exposures less than 1 year in duration if the exposure is of extremely high intensity, and

• A minimum lag-time of 10 years from the first asbestos exposure to cancer diagnosis.

Workers who did not have asbestosis, bilateral diffuse pleural thickening or sufficient fibre counts, required a repeat independent assessment of cumulative asbestos exposure in order to assign them to the high or low exposure cohort. This work was done by the DDA Research and Education Unit. The DDA follows a standard published approach to perform exposure reconstruction but also uses a unique data set of industrial/company information pertaining to asbestos use which includes industrial processes, work practices, products (and composition), tools, workplace ventilation conditions, engineering controls, static and personal measurements. Exposure variables identified in patient's work histories were evaluated in the context of this company information. Using their technique patients were assigned to either meeting or not meeting the Helsinki Criteria for the attribution of asbestos exposure to lung cancer.

To briefly summarise our findings to date, over 95% of the cohort was deceased at the time of analysis. Less than 1% of the cohort was female and the average age at diagnosis for the whole cohort was 70 years. Nearly 70% of the cohort were stage III or greater at diagnosis. A total of 338 (64%) workers in the cohort were assigned as having met the Helsinki Criteria (i.e. ARLC) and 191 did not meet the Criteria (non-ARLC). Over 90% of workers in each group had a smoking history. We are currently finalising our analysis of survival differences between the two groups and drafting a manuscript for publication early next year.

THE IMPACT OF GEOGRAPHIC AND SOCIO-ECONOMIC FACTORS UPON MPM INCIDENCE AND PROGNOSIS IN MPM

Investigators: Linton A[1], Soeberg M[1,2], Broome R[3], van Zandwijk N[1,2]
1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. Public Health Observatory

The impact of clinico-pathological factors such as age, gender, and histological subtype on the prognosis of malignant pleural mesothelioma (MPM) is well documented. However, socio-economic and geographic factors and their impact on survival have been studied to a lesser extent. Whilst the majority of Australians live in major metropolitan centres, a significant proportion of the population reside in smaller regional centres and surrounding areas. As such access to clinical services including specialist oncological units may be limited. Furthermore, socio-economic factors may further impact on service access, treatment provision and prognosis. With the cooperation of the NSW Dust Diseases Authority and oncology and thoracic units across NSW, we performed one of the largest analyses to date of Australian patients diagnosed with MPM. Gathering data from the medical and surgical records of 910 patients diagnosed between 2002 and 2009, we assessed the impact of socio-economic advantage and disadvantage, proximity to an oncological multi-disciplinary team meeting and geographic remoteness upon treatment utilisation and survival. Our work provided evidence for differences in treatment and survival according to socio-economic status for MPM patients in NSW, whilst revealing a trend to lower survival in patients residing in more regional and rural locations. We intend to undertake prospective research examining additional explanations for the differences noted, by comparing treatment outcomes of compensated and non-compensated cases, including co-morbidity, individual socio-economic factors and patient and physician preferences.

PATTERNS OF CARE AND SURVIVAL IN ELDERLY AND VERY ELDERLY PATIENTS WITH MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Linton A[1], van Zandwijk N[1,2]
1. Asbestos Diseases Research Institute,
2. University of Sydney

Elderly patients comprise a significant proportion of individuals diagnosed with malignancy in Australia, however they are frequently under-represented in clinical trials. Care for elderly patients often deviates from evidence-based guidelines with a reduced use of chemotherapy and surgical interventions. Due to the prolonged latency period from first asbestos exposure to diagnosis, malignant pleural mesothelioma (MPM) is typically associated with an elderly population. With the co-operation of the NSW Dust Diseases Authority, we are currently investigating the records of patients diagnosed with MPM between 2002 and 2009, assessing the impact of advancing age on treatment utilisation and the potential associations between age and clinico-pathological factors. Preliminary data suggests a marked decline in the use of chemotherapy and surgical interventions in elderly (over 70 years) and very elderly (over 80 years) populations while markers of frailty seem to be present in a greater proportion of patients.

MESOMIR 1: THE PHASE I STUDY TESTING TARGOMIRS IN PATIENTS WITH RECURRENT MALIGNANT PLEURAL MESOTHELIOMA

Investigators: van Zandwijk N[1,2], Pavlakis N[4], Clarke S[4], Bailey D[3], Kao S[1,5], Boyer M[5], Fulham M[7], Linton A[1,6], Cooper W[7], Huynh Y[1], Reid G[1,2]
1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Royal North Shore Hospital,
4. Northern Cancer Institute, 5. Chris O'Brien Lifehouse, 6. Concord Repatriation General Hospital,
7. Royal Prince Alfred Hospital

After studying different drug doses and administration schedules of TargomiRs (Epidermal Growth Factor Receptor (EGFR) antibody targeted EnGeneIC Delivery Vesicles (EDVs) packaged with microRNA mimics) in 28 patients, an accurate picture of drug-associated reactions has emerged. TargomiRs continue to be rather well tolerated. Side effects are mainly associated with the inflammatory response elicited by intravenous administration of EDVs. Almost all patients experience a degree of transient shivering/rigor, and temperature elevation, sometimes accompanied by discomfort/pain in the diseased chest. Early signs of clinical activity (reduction/stabilisation of tumour size) of TargomiRs has been noted in several patients. The necessity of corticosteroid premedication was tested in the last patient cohort. Tapering of the dexamethasone dose to 1 mg was accompanied by stridor and desaturation in one patient. This anaphylactoid reaction was quickly reversible with the administration of extra corticosteroids. Therefore, complete elimination of immune-suppressive premedication before TargomiR administration will not be possible. The study was closed for patient entry on November 24th. An analysis of trial data including independent response review will be completed early in 2017. Interim results of the MesomiR 1 study were presented at COSA, the International Mesothelioma Interest Group (iMig) and the Lung Cancer Trials Group Australia.

PRECLINICAL RESEARCH PROJECTS

EXPLORING MECHANISMS OF miRNA DOWNREGULATION IN MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Williams M[1,2], Cheng YY[1], Reid G[1,2]
1. Asbestos Diseases Research Institute,
2. University of Sydney

The dysregulation of microRNA profiles is a common event in many cancer types and has been found to contribute profoundly to the malignant phenotype, through control of mRNA targets with oncogenic or tumour suppressor activity. While some investigations report upregulation of microRNAs in tumours, there is a global trend toward microRNA downregulation in malignant pleural mesothelioma (MPM) and other malignancies, including, breast, prostate and ovarian cancers. miR-15a/16-1, miR-15b/16-2 and miR-193a-3p are tumour suppressor microRNAs that have been shown to be downregulated in MPM tumours and cell lines compared to normal controls. The mechanisms driving the downregulation of these microRNAs are unknown. To understand the processes involved, the different stages of microRNA biogenesis are being investigated in this project. This involves determining whether defects exist at the genomic region of microRNA coding genes, in epigenetic and transcriptional regulation or during post-transcriptional processing of the microRNAs. This study has shown, that in MPM, unlike other cancers, the downregulation of miR-15a/16-1 and miR-15b/16-2 appears to be due to transcriptional changes rather than deletion or promoter hypermethylation. The c-Myc oncogene has previously been shown to repress miR-15a/16-1 expression in B-cell Lymphoma and is upregulated in MPM. Knockdown of c-Myc in MPM cell lines caused upregulation of microRNA primary transcript levels suggesting that c-Myc transcriptionally represses the miR-15/16 family. Similarly, miR-193a loss in MPM appears to be due to LOH rather than epigenetic silencing. A thorough understanding of these mechanisms and the mediators that influence them could allow direct targeting of the constituents involved in the complicated network of microRNA dysregulation as a therapeutic approach in MPM.

INVESTIGATING DRUG RESISTANCE IN A 3D MODEL OF MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Cheng YY[1,2], Sarun KH[1], Kirschner MB[3], Pellegrini L[4], Yang H[4], Carbone M[4], Mutti L[5], van Zandwijk N[1,2], Lin RCY[1,6] , Reid G[1,2]
1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. University Hospital Zurich, 4. University of Hawai'i Cancer Center, 5. University of Salford, 6. University of NSW

Previous studies have used 3D spheroid cultures to investigate drug response in MPM. We have shown that microRNAs are important players in MPM biology and that they contribute to the response of MPM cells to some chemotherapy drugs. In this multicentre collaborative project we are investigating the role of microRNAs in the drug resistance of a 3D spheroid model of MPM. In our adapted model of 3D cell growth, MPM cell lines form spherical 3D structures, in contrast to the donut shapes reported with other models. MPM cells in these spheroids were more resistant to cisplatin and gemcitabine when compared to cells grown in 2D cultures. In addition to a clear hypoxic gradient, spheroids also exhibited a significant up-regulation of microRNAs. We are investigating the ability of microRNA inhibitors to reverse the drug resistance in spheroids. Our spheroid model reveals a clear impact of hypoxia on gene expression in MPM cells, and suggests a link between hypoxia, microRNAs and drug resistance in MPM.

REGULATION OF PD-L1 EXPRESSION BY microRNAS IN MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Williams M[1,2], Kao SC[1,2,3], Cooper WA[2,4,5], Kirschner MB[10], Madore J[2,6], Lum T[4], Linton A[1,7], McCaughan B[2,8], Klebe S[9], van Zandwijk N[1,2], Scolyer RA[2,4,7], Boyer MJ[2,3], Reid G[1,2]
1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Chris O'Brien Lifehouse,
4. Royal Prince Alfred Hospital, 5. Western Sydney University, 6. Melanoma Institute Australia,
7. Concord Cancer Centre, 8. Sydney Cardiothoracic Surgeons, 9. Flinders Medical Centre, 10. University Hospital Zurich

Cancer immunotherapy, particularly using immune checkpoint blocking antibodies, is leading to long-term responses in some cancer patients. The interaction between programmed death 1 (PD-1) and its ligand PD-L1 are one such target, as they play a significant role in suppressing host immune response in many cancer types. Although PD-L1 expression is upregulated and associated with poor prognosis in malignant pleural mesothelioma (MPM), the mechanisms causing its dysregulation are poorly understood. We have found reduced microRNA expression to be related to elevated PD-L1 levels in the MPM patients, with previously identified tumour suppressor microRNAs in MPM showing downregulation in PD-L1 positive tumours. Our study confirms that PD-L1 is an adverse prognostic indicator in MPM. Elevated PD-L1 expression in MPM patient samples correlates with downregulation of tumour suppressor microRNAs that were in turn shown to directly regulate PD-L1 expression in vitro. The relationship between miR-193a-3p and PD-L1 was shown to be due to an unusual interaction between the microRNA and a site in the PD-L1 mRNA. This work was presented at the 2016 International Mesothelioma Interest Group iMig conference, and is under review for publication.

miR-137-3P: A NEW TUMOUR SUPPRESSOR microRNA IN MALIGNANT PLEURAL MESOTHELIOMA BIOLOGY

Investigators: Johnson T[1,2], Cheng YY[1], McCaughan BC[3], Klebe S[4], van Zandwijk N[1,5], Williams M[1,5], Lin RCY[1], Reid G[1,5]
1. Asbestos Diseases Research Institute,
2. University of Technology Sydney, 3. Sydney Cardiothoracic Surgeons, 4. Flinders Medical Centre,
5. University of Sydney

Chromosomal deletion of sites encoding tumour suppressor genes is a major contributing factor in the oncogenesis of malignant pleural mesothelioma (MPM), notably 1p21-23, which occurs in 74-85% of MPM cases. This region encodes the tumour suppressor miR-137, a site which is coincidentally also commonly hyper-methylated due to the presence of a large CpG site in its promoter. miR-137 is known to target a number of oncogenic factors such as AKT2, CDK6 and importantly, YB-1. This project set out to characterise the expression patterns and roles of miR-137 and YB-1 in MPM.
Data from this project has been presented at the International Mesothelioma Interest Group, Birmingham 2016, the Sydney Cancer Conference, 2016 and at the World Conference on Lung Cancer, 2016. A manuscript is close to completion and will be submitted in the near future.

USING ARTIFICIAL miRS TO CONTROL THE GROWTH OF MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Winata P[1,2], van Zandwijk N[1,2], Lin R[1,3], Reid G[1,2]
1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. University of NSW

Most cancer chemotherapy is based on 'one therapy, one target' model. Through this principle single gene or secondary pathway mutations can lead to loss of drug efficacy and resistance to therapy. Therefore, a therapy that has more than one target pathway has potential advantages. MicroRNAs have this property as they control expression of multiple genes across different pathways. Given the sequence-specific interaction of natural microRNAs with the 3' untranslated region of their target mRNAs, it is possible to use this principle to design artificial microRNAs that control expression of pre-selected target genes. In theory, controlling multiple genes across different pathways has the potential to avoid resistance associated in a single gene therapy. We have successfully applied an artificial microRNA concept to target genes in multiple pathways in MPM, and continue to develop this concept in preclinical models.

THE CONTRIBUTION OF STROMAL CELLS TO microRNA EXPRESSION IN MESOTHELIOMA

Investigators: Sarun K[1], Cheng YY[1], Kirschner MB[2], van Zandwijk N[1,3], Lin RCY[1], Reid G[1,3]
1. Asbestos Diseases Research Institute, 2. University Hospital Zurich, 3. University of Sydney

In this study, being carried out by Kadir Sarun as an MSc project, we have identified several microRNAs that are significantly upregulated in experimental tumours derived from human MPM cell lines when compared to the levels found in the MPM cell lines grown in the laboratory. A similar observation was made in experimental mouse tumours. In particular, mouse pri-miR-223, previously linked to a role in MPM, was up-regulated in both xenograft and syngraft, implicating a high stromal contribution of miR-223 in the tumour microenvironment. Recent in situ hybridisation work has demonstrated a clear expression of this microRNA in stromal cells. This work was presented at World Conference on Lung Cancer 2016, and Kadir received a prestigious IASLC Young Investigator Travel Award.

CO-STIMULATION OF THE IMMUNE SYSTEM TO IMPROVE CHEMOTHERAPY FOR MALIGNANT MESOTHELIOMA

Investigators: Leygo C[1,2], Cheng YY[1,2], van Zandwijk N[1,2], Webster G[3], Reid G[1,2],
1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. Innate Immunotherapeutics

Only 40% of MPM patients receiving the standard of care (palliative platinum-pemetrexed chemotherapy) respond to treatment and combined-modality treatment (with curative intent) is followed by prolonged survival in selected cases only. Currently, there is no defined second-line treatment and the need for efficient therapies for MPM remains unfulfilled. Recent research has focused on immunotherapy, to harness the immune system as a novel therapeutic approach. Minor impacts on tumour growth have been demonstrated in animal studies following immunotherapy alone, however, when combined with chemotherapy, clear shrinking of tumours was visible. Moreover, following treatment with immunotherapy, mice implanted with a secondary challenge of MPM exhibited tumour inhibition compared to mice who were not treated with immunotherapy. Clinical studies, with antibodies blocking immune checkpoints have shown dramatic responses in melanoma and non-small cell lung cancer. Efficacy of immune checkpoint blockade has also been noted in a relatively small series of MPM patients but so far the responses observed were less impressive than in patients with melanoma and non-small cell lung cancer. Thus the development of new treatment approaches for MPM remains vitally important and immune stimulation in combination with existing (chemotherapy) treatment warrants further exploration. In collaboration with New Zealand biotech company, Innate Immunotherapeutics, we are investigating the ability of a microparticulate immune response modulator, currently in clinical trial for other indications, for its ability to stimulate the immune system and improve response to chemotherapy.

IDENTIFYING microRNAS WITH THERAPEUTIC POTENTIAL IN MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Reid G[1,2], Della Gatta A[2], Suh H[2], Williams M[1,2], Cheng YY[1], Lin R[1], van Zandwijk N[1,2]
1. Asbestos Diseases Research Institute, 2. University of Sydney

We and others have shown that multiple microRNAs have tumour suppressor activity in MPM cell lines when the levels are restored using mimics. Results from our lab have led to MesomiR 1, the world's first clinical trial of a microRNA replacement strategy (TargomiRs) in mesothelioma patients, currently nearing the end of Phase I. In this project we are have carried out a head-to-head comparison of microRNA mimics, both singly and in combination, to identify the most promising microRNAs for future development as therapeutic agents. The initial experiments in this project were carried out by Andrew Della Gatta and Hyerim Suh, two students from last summer's Studentship program at The University of Sydney. This work continues as part of Marissa Williams' PhD project.

THE microRNA-15/16 FAMILY REGULATES TUMOUR CELL GROWTH VIA FIBROBLAST GROWTH FACTOR SIGNALS IN MALIGNANT PLEURAL MESOTHELIOMA

Investigators: Schelch K[1], Kirschner MB[2], Williams M[1,3] Cheng YY[1], Lin R[1,4], Grusch M[5], van Zandwijk N[1,3] and Reid G[1,3]
1. Asbestos Diseases Research Institute,
2. University Hospital Zurich, 3.Sydney Medical School, 4.University of New South Wales, 5. Institute of Cancer Research, Vienna

As shown in previous projects, fibroblast growth factor (FGF) signals play important roles in mesothelioma cell growth and malignant behavior and their inhibition leads to reduced tumor growth in vitro and in vivo. MicroRNAs (miRNAs) are conserved noncoding RNAs controlling gene expression via translational repression of target mRNAs. The miR-15/16 family is downregulated in MPM and has tumor suppressor functions. Several FGFs/FGFRs are predicted mir-15/16 targets. In this study, we explore the link between the miR-15/16 and the FGF/R family in mesothelioma and characterize its malignant potential. The data have been presented at several national and international conferences (Australian Lung Cancer Conference, Sydney Cancer Conference and the World Conference on Lung Cancer 2016) and a manuscript will be submitted in early 2017.

QUALITY OF LIFE RESEARCH

AN OBSERVATIONAL STUDY OF HEALTH RELATED QUALITY OF LIFE IN PEOPLE WITH MALIGNANT MESOTHELIOMA (MM)

Investigators: Vardy J[1,2], Kao S[3,4], Dhillon H[2], Price M[2], Fowler J[2,3], Warby A[2,3], Tan C[1], McLean J[3]
1. Concord Repatriation General Hospital, 2. University of Sydney, 3. Asbestos Diseases Research Institute, 4. Chris O'Brien Lifehouse

This multi-site, observational, longitudinal study aims to explore the patient experience of people diagnosed with malignant mesothelioma (MM). The project examines health related quality-of-life, unmet care needs and anxiety and depression in people after a diagnosis of MM. It includes a number of optional sub-studies examining associations between these variables and other prognostic indicators such as inflammatory biomarkers, nutritional status and functional status. As of December 2016, site-specific ethics approval has been received for 15 participating hospitals and cancer institutions across New South Wales, Queensland, South Australia and Victoria. s. Recruitment commenced in April 2014 at approved sites and via self-referral recruitment strategies involving the Dust Diseases Board and the Asbestos Diseases Foundation of Australia. To date, 85 participants have consented to be part of the study. Preliminary study data has been presented at both national and international conferences and publications have been submitted or are in preparation, reporting quality-of-life and nutritional risk following extrapleural pneumonectomy (EPP) surgical treatment along with a review of Quality of Life measurements.

EPIDEMIOLOGY

Epidemiology is the corner stone of public health and helps to answer questions about the causes and patterns of disease in specific populations.

MALIGNANT MESOTHELIOMA IN AUSTRALIA 2015: CURRENT INCIDENCE AND ASBESTOS EXPOSURE TRENDS

Investigators: Soeberg MJ[1], Leigh J[1], van Zandwijk N[1]
1. Asbestos Diseases Research Institute

Australia is known to have had the highest per-capita asbestos consumption level of any nation, reaching a peak in the 1970s. Although crocidolite was effectively banned in the late 1960s, and amosite use ceased in the mid 1980s, a complete asbestos ban was not implemented until 2003. This resulted in an epidemic of asbestos-related disease, which has only now reached its peak. Between 1982 and 2011, 13,036 individuals were newly diagnosed with malignant mesothelioma, with 690 diagnosed in 2011. A further 778 cases were identified between 1945 and 1981 from retrospective searches and the first 2 years of the Australian Mesothelioma Program. The age- standardized malignant mesothelioma incidence rate has leveled off in the last 10 years (2.8 per 100,000 in 2011). There has been a marked increase over time in the age-specific incidence rates for individuals aged 75 years or older. Data from the current Australian Mesothelioma Registry on asbestos exposure history in Australia is available for 449 subjects diagnosed between July 1, 2010, and April 1, 2015. This asbestos exposure history data show that 60% (n = 268) of cases had probable or possible occupational asbestos exposure, with trade-based jobs being the most frequent sources of occupational asbestos exposure. In addition, out of the 449 cases, 377 were recorded as having probable or possible nonoccupational asbestos exposure. Continuous vigilance toward changes over time in the settings in which people are exposed to asbestos and in the descriptive epidemiology of malignant mesothelioma is recommended to enable a comprehensive understanding of the current and future impact of asbestos-related diseases in Australia. This study was recently published in the Journal of Toxicology and Environmental Health Part B.

ESTIMATING THE INCIDENCE OF MALIGNANT MESOTHELIOMA IN VIETNAM: A PILOT DESCRIPTIVE CANCER REGISTRATION STUDY

Investigators: Soeberg MJ[1], Luong MA[2], Tran VT[3,5], Tran AT[2], Nguyen TTH[2], Bui D[5], Nguyen THN[5], Takahashi K[4], van Zandwijk N[1]
1. Asbestos Diseases Research Institute, University of Sydney, Sydney, NSW, Australia, 2. Health Environment Management Agency, Hanoi, Vietnam, 3. National Institute for Cancer Control, Hanoi Vietnam, 4. University of Occupational and Environmental Health, Fukuoka, Japan, 5. National Cancer Hospital, Hanoi, Vietnam

Global asbestos consumption has shifted toward lower income countries, particularly in the Asian region including Vietnam where asbestos and asbestos-containing products have been imported since the late 1960s. This pilot descriptive epidemiological study aimed to provide contemporary estimates of malignant mesothelioma incidence (histological subtype M9050/3; ICD-O-3) by gender and age group as recorded across nine cancer registries in Vietnam. We identified 148 incident cases of malignant mesothelioma during 1987–2013. The majority of cases were recorded in the Hanoi region (n = 93) and were aged 55 years or older (n = 96). By carefully reviewing existing cancer registry records in Vietnam, we identified a larger number of malignant mesothelioma cases than previously estimated. We recommend the use of cancer registry data in tracking future asbestos-related disease in Vietnam. This study was recently published in the International Journal of Occupational and Environmental Health.

SECOND PRIMARY CANCER RISK ASSOCIATED WITH MALIGNANT MESOTHELIOMA

Investigators: Soeberg MJ[1], Youlden D[2], Baade P[2], Aitken J[2], Cust A[3], Klebe S[4], van Zandwijk N[1]
1. Asbestos Diseases Research Institute. 2. Cancer Council Queensland. 3. Sydney School of Public Health. 4. Flinders University

Around 12,500 people were newly diagnosed with malignant mesothelioma during 1982-2010. There is little data quantifying the risk of developing a second primary cancer after a first primary malignant mesothelioma. There has also been no systematic analysis in Australia of people diagnosed with malignant mesothelioma as a second primary cancer. Although asbestos exposure is the primary causal factor for malignant mesothelioma, this study has the potential to uncover important insights into the occurrence of malignant mesothelioma either interacting with asbestos exposure or as an independent causal factor. For example, there is increasing evidence for genetic susceptibility to malignant mesothelioma and a number of other cancers such as uveal (eye) and cutaneous (skin) melanoma. Also, international data suggests that there is an elevated risk of developing malignant mesothelioma after receiving high-dose radiation therapy for a number of cancers including Hodgkin and non-Hodgkin lymphoma as well as for testicular, breast and prostate cancers. Understanding the magnitude of these risks at the population level will provide important baseline data for future studies where we will be able to measure genetic factors and treatment received to more precisely understand malignant mesothelioma occurrence in Australia. This study is in the early stages and its completion is subject to funding.

OTHER ACTIVITIES

MESOTHELIOMA SUPPORT CO-ORDINATOR

Coordinator: McLean J[1]
1. Asbestos Diseases Research Institute

Another 12 months of providing support for mesothelioma patients. As of 1st December 2016 there are 210 people on the database consisting of: 87 people living with mesothelioma having palliative treatment (66 males, 21 females); 17 people are surviving after radical trimodality therapy (16 males, 1 female); 86 bereaved families; and 20 others with either benign disease or not requiring support.

Three identified groups continue to require specific support:
1. Patients receiving standard (palliative) care;
2. Patients who underwent radical (combined-modality) treatment; and
3. The bereaved - struggling with grief and loss.

The three identified subcategories also remain the same: 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.

We have again attempted to meet the needs of carers, and families of patients and the bereaved through the following services:

1. Telephone calls (around 800 per year) and emails to provide a communication link between the patients 'world of living with mesothelioma' to the clinical and research 'mesothelioma world'. The topics range from information that is helpful at the time of a new diagnosis through to accessing help and services and sensitively prompting discussion about issues related to end of life.

2. Focused education and support sessions in metropolitan, rural and coastal health regions of NSW. Meetings were held at Taree (2015), Liverpool (3 times), Wollongong, and Macksville with attendances ranging from 4 to 24 people. A clear message from the rural folk was that they felt forgotten and they were the groups that best supported our visit.

3. Face to face support groups. Two groups are continuing:
a. The EPP well living group for patients, who have had trimodality therapy, and their carers meet 3-4 times a year. At the November meeting 28 people attended (including speakers). This group continues to use a private Facebook page to keep connected.
b. The Liverpool group meets on a 2-3 monthly basis and will continue through 2017. When a guest speaker attends, and where appropriate, all patients and carers are invited to these meetings.

4. Activities specifically for the bereaved have been therapeutic, and well attended. Michael Nash (Concord Bereavement Counsellor) and Tanya Segelov (Lawyer) facilitated a 'no time to grieve' workshop; a morning tea at the Museum of Contemporary Art at Circular Quay, followed by the Carers week 'Thank-you day' in October which provided an opportunity to share stories, support each other, and generate friendships.

5. Teleconferencing has not been taken up by the groups, although it still has the potential to provide group communication and connect those living with similar experiences, thus reducing the isolating impact of distance and rarity of the disease.

Other activities:
As ADRI's Mesothelioma Support Coordinator I attended the International Mesothelioma Interest Group (iMig) Conference in Birmingham and presented a poster titled:
Personalised support for patients with malignant pleural mesothelioma (MPM) in New South Wales, Australia.

I have also taken up opportunities to promote this service, the work of ADRI and raise awareness about the risks of asbestos to the public through:
• Participating on 'Betty the ADRI model house' at the Sydney Royal Easter Show;
• Attending a golf day dinner in memory of Mr Morrie Lucas at the Russell Vale Golf Club and accepting a donation on behalf of the ADRI; and
• Attending the Kiama VIEW Club meeting in September as guest speaker at the invitation of a bereaved carer.

Plans for 2017:
There is a need make education a focus and also to bring the mesothelioma families closer together- if they wish too. I would like to provide an opportunity for both of these by:

1. Holding a memorial, awareness, and fundraising walk around a Concord Park, to be followed the next day by:

2. An education day for patients, carers, families, and possibly include health providers such as nurses and allied health.

The fundraising would provide financial support to the work of supporting mesothelioma patients and carers. A long term future aim is to secure ongoing funding for a dedicated Mesothelioma Nurse.

ADRI BIOBANK

Officers: Hyland R[1], Chen K[1]
1. Asbestos Diseases Research Institute

ADRI Biobank provides investigators and collaborators with biospecimens and accompanying clinical data for research projects that will lead to a better understanding of disease. The overall goal of this work is the procurement of high quality samples and the collection of accurate, reliable and standardised clinical data which are critical to the success of the translational research work undertaken at ADRI.

The biobank contains fresh frozen tumour tissue, DNA and RNA samples derived from tumour tissue and matched bloods from mesothelioma patients, control tissue samples and a series of formalin-fixed tumour tissues. During 2016 we continued to contribute high quality blood and tumour samples and also pleural fluids from consenting patients undergoing diagnosis or surgical treatment of their asbestos related cancers. In April we received ethics approval to begin the collection of fresh frozen lung cancer specimens from consenting patients undergoing surgery at the RPAH. Since then these collections have been running smoothly alongside our longstanding mesothelioma and healthy normal control tissue collections, which we also receive from patients attending surgery at Strathfield Private Hospital. Our purpose-built clinical database (CANSTO) received an upgrade mid-year in order to adequately capture the data associated with these new collections.

We have also been focussing our efforts on upgrading our standard operating procedures (SOPs) as part of the NSW Health Pathology (NSWHP) Biobank Certification Program. Phase one of this initiative involved the registration of our Biobank to the programme and the completion of online introductory overview education modules by our biobanking staff. Certification is the second phase of the program whereby the organisation must supply NSW Health Pathology with key documents (including detailed SOPs) to demonstrate that our methods have been adapted to the best practice standards. Also as part of phase two our biobanking personnel will be required to complete further online education modules and undergo knowledge tests at the completion of the course. This is scheduled for 2017.

PREVENTION THROUGH EDUCATION

Investigators: van Zandwijk N[1,2], Soeberg M[1,2]
1. Asbestos Diseases Research Institute, 2. University of Sydney

In 2016 the ADRI staff continued to participate in various government and community activities to raise the awareness of the dangers of asbestos. On an international level, Professor van Zandwijk and Dr Soeberg continued to advise the Government of Vietnam on asbestos awareness education and why a total asbestos ban is so much needed. Delegations from Indonesia and Cambodia visited ADRI in November 2016.

AUSTRALIAN MESOTHELIOMA REGISTRY

The Australian Mesothelioma Registry (AMR) is a stand-alone database that contains information about people with mesothelioma. Since the 1st July 2010 the AMR receives notification of all new cases of mesothelioma diagnosed in Australia. In addition, this registry collects information about asbestos exposure from people with mesothelioma through a postal questionnaire and telephone interview. The organisations involved in the AMR, funded by Safe Work Australia and Comcare include: Cancer Institute NSW; Monash Centre for Occupational and Environmental Health; Hunter Research Foundation; Asbestos Diseases Research Institute; University of Sydney; Western Australia University, and Dust Diseases Board of NSW. The information collected is being used to draft a careful picture of the Australian mesothelioma epidemic and to assist governments to develop policies to best deal with the asbestos ubiquitously present in Australia, with the aim of reducing mesothelioma incidence in the future. In September 2016, the AMR published their fifth annual report providing data on malignant mesothelioma in Australia during 2014.

https://www.mesothelioma-australia.com/home
https://www.mesothelioma-australia.com/media/12513/mesothelioma-in-2015-final.pdf

PUBLICATIONS, PRESENTATIONS AND AWARDS

PEER REVIEWED ARTICLES

1. Williams M, Cheng YY, Blenkiron C, Reid G. Exploring Mechanisms of MicroRNA Downregulation in Cancer. MicroRNA. 2016. In press

2. Linton A. Geographic and socioeconomic factors in patients with Malignant Pleural Mesothelioma in New South Wales and their impact upon clinical outcomes. Respirology. 2016: In Press.

3. Manegold C, Dingemans AC, Gray JE, Nakagawa K, Nicolson M, Peters S, Reck M, Wu YL, Brustugun OT, Crino L, Felip E, Fennell D, Garrido P, Huber RM, Marabelle A, Moniuszko M, Mornex F, Novello S, Papotti M, Perol M, Smit EF, Syrigos K, van Meerbeeck JP, van Zandwijk N, Chih-Hsin Yang J, Zhou C, Vokes E. The potential of combined immunotherapy and antiangiogenesis for the synergistic treatment of advanced NSCLC. Journal of Thoracic Oncology. 2016: In press.

4. Soeberg MJ, Leigh J, van Zandwijk N. Malignant mesothelioma in Australia 2015: Current incidence and asbestos exposure trends. Journal of Toxicology and Environmental Health, Part B - Critical Reviews. 2016;19(5-6):173-89.

5. Hoda MA, Dong Y, Rozsas A, Klikovits T, Laszlo V, Ghanim B, Stockhammer P, Ozsvar J, Jakopovic M, Samarzija M, Brcic L, Bendek M, Szirtes I, Reid G, Kirschner MB, Kao SC, Opitz I, Weder W, Frauenfelder T, Nguyen-Kim TD, Aigner C, Klepetko W, van Zandwijk N, Berger W, Dome B, Grusch M, Hegedus B. Circulating activin A is a novel prognostic biomarker in malignant pleural mesothelioma - A multi-institutional study. European Journal of Cancer. 2016 Aug; 63:64-73.

6. Driml J, Pulford E, Moffat D, Karapetis C, Kao S, Griggs K, Henderson DW, Klebe S. Usefulness of Aquaporin 1 as a prognostic marker in a prospective cohort of malignant mesotheliomas. International Journal of Molecular Sciences. 2016 Jun;17(7), 1041.

7. Bremnes RM, Busund LT, Kilvaer TL, Andersen S, Richardsen E, Paulsen EE, Hald S, Khanehkenari MR, Cooper WA, Kao SC, Donnem T. The role of tumor-infiltrating lymphocytes in development, progression, and prognosis of non-small cell lung cancer. Journal of Thoracic Oncology. 2016 Jun;11(6):789-800.

8. Soeberg MJ, Creighton N, Currow DC, Young JM, and van Zandwijk N. Patterns in the incidence, mortality and survival of malignant pleural and peritoneal mesothelioma, New South Wales, Australia, 1972-2009. Australian and New Zealand Journal of Public Health. 2016 Jun;40(3):255-62.

9. Cheng YY, Wright CM, Kirschner MB, Williams M, Sarun KH, Sytnyk V, Leshchynska I, Edelman JJ, Vallely MP, McCaughan BC, Klebe S, van Zandwijk N, Lin RCY, Reid G. KCa1.1, a calcium-activated potassium channel subunit alpha 1, is targeted by miR-17-5p and modulates cell migration in malignant pleural mesothelioma. Molecular Cancer. 2016 Jun 1;15(1):44.

10. Lin RCY, Kirschner MB, Cheng YY, van Zandwijk N, Reid G. MicroRNA gene expression signatures in long-surviving malignant pleural mesothelioma patients. Genomics Data. 2016 9:44-9.

11. Reid G, Kao SC, Pavlakis N, Brahmbhatt H, MacDiarmid J, Clarke S, Boyer M, van Zandwijk N. Clinical development of TargomiRs, a miRNA mimic-based treatment for patients with recurrent thoracic cancer. Epigenomics. 2016;8(8):1079-85.

12. Soeberg MJ; Luong MA; Tran VT; Tran AT; Nguyen TTH; Bui D; Nguyen THN; Takahashi K; van Zandwijk N. Estimating the incidence of malignant mesothelioma in Vietnam: a pilot descriptive cancer registration study. International Journal of Occupational and Environmental Health. 2016 Apr;22(2):167-72.

13. Kao SC, Boyer MJ. Evolving landscape of epidermal growth factor receptor tyrosine kinase inhibitors. Journal of Clinical Oncology. 2016;34(27):3233-4.

14. Kao SC, Kirschner MB, Cooper WA, Tran T, Burgers S, Wright C, Korse T, van den Broek D, Edelman J, Vallely M, McCaughan B, Pavlakis N, Clarke S, Molloy MP, van Zandwijk N, Reid G. A proteomics-based approach identifies secreted protein acidic and rich in cysteine as a prognostic biomarker in malignant pleural mesothelioma. British Journal of Cancer. 2016 Mar 1;114(5):524-31.

15. van Zandwijk N, Soeberg M, Reid G. Using a multidisciplinary approach to combat the burden of asbestos-related disease. The Medical Journal of Australia. 2016 Feb 1;204(2) : 52.

16. Soeberg M J, Leigh J, Driscoll T, Armstrong B, Young JM, van Zandwijk N. Incidence and survival trends in malignant pleural and peritoneal mesothelioma, Australia, 1982-2009. Occupational & Environmental Medicine. 2016 Mar;73(3):187-94.

BOOK CHAPTERS

1. Soeberg M, van Zandwijk N. Chapter 9: Asbestos and malignant pleural mesothelioma. In: Mineo TC (ed) Malignant pleural mesothelioma: Present status and future direction. Benthem Science Publishers; 2016 (eBook). Chapter 9; p115-128.
eISBN 978-1-68108-193-9. ISBN 978-1-68108-194-6

INVITED PRESENTATIONS

1. Kao S. Immunotherapy management of lung cancer. Current Practice. ALTG Lung Cancer Symposium. Sydney, 12 November 2016.

2. van Zandwijk N. Advances in the biology and treatment of mesothelioma. ALTG Lung Cancer Symposium. Sydney, 12 November 2016.

3. van Zandwijk N. Mesothelioma treatment/research. Asbestos Disease Support Society (adss) Symposium 2016 Asbestos Related Diseases Here and Now, Brisbane, 19 October 2016

4. van Zandwijk N. MicroRNA based therapy in thoracic tumors: personal experience. The 8th Chinese-German Lung Cancer Forum. Dresden, Germany, 8-10 September 2016.

5. Reid G. Clinical development of TargomiRs, a microRNA mimic-based treatment for patients with malignant pleural mesothelioma. QMB Cancer Biology Satellite Meeting. Nelson, New Zealand, 28-29 August 2016.

6. van Zandwijk N. Translating malignant mesothelioma research into better outcomes for patients and their families. Sydney Catalyst Members' Meeting and Research Showcase. Education Centre, Chris O'Brien Lifehouse, 11 August 2016.

7. Reid G, Tissue-based biomarkers. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

8. van Zandwijk N, Advances in malignant pleural mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

CONFERENCE PRESENTATIONS

1. Dong Y, Zhang H, Schelch K, Klikovits T, Stockhammer P, Jakopovic M, Samarzija M, Brcic L, Reid G, Kirschner MB, Kao S, Opitz I, Weder W, Frauenfelder T, Nguyen-Kim TDL, Klepetko W, van Zandwijk N, Hegedus B, Berger W, Dome B, Laszlo V, Grusch M, Hoda MA. Circulating fibroblast growth factor 18 is elevated in malignant pleural mesothelioma patients - a multi-institutional study. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

2. Kirschner MB, Vrugt B, Friess M, Meerang M, Wild P, van Zandwijk N, Reid G, Weder W, Opitz I. Refinement of the prognostic miR-Score for use in diagnostic specimens from chemo-naïve malignant pleural mesothelioma patients. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

3. Sarun KH, Cheng YY, Kirschner MB, van Zandwijk N, Lin R, Reid G. Expression of miR-223 in mesothelioma xenografts originates from stromal cells in the tumour microenvironment. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016. (Awarded the Young Investigator Award by the International Association for the Study of Lung Cancer (IASLC) and the Local Organising Committee of the 17th IASLC WCLC presented at the IASLC Business Meeting Vienna 6th December 2016 and a Concord Repatriation General Hospital Research Travel Scholarship.)

4. Schelch K, Kirschner MB, Williams M, Lin R, Cheng YY, Grusch M, Berger W, van Zandwijk N, Reid G. The microRNA-15/16 family regulates tumour cell growth via fibroblast growth factor signals in malignant pleural mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016. . (Awarded Australian Lung Foundation Travel Award – WCLC 2016)

5. Cheng YY, Sarun KH, Kirschner MB, van Zandwijk N, Reid G, Lin RCY. Investigating the role of microRNAs in drug resistance of mesothelioma cells using a 3D spheroid model. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

6. Despotovski A, Della-Gatta A, Lin RCY, van Zandwijk N, Cheng YY, Reid G. Comparing tumour suppressing activity of microRNA mimics in malignant pleural mesothelioma. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

7. Kao S. Combination therapies in immunotherapy. 6th Australian Lung Cancer Conference, Melbourne, 18-20 August 2016.

8. Sarun KH, Cheng YY, Kirschner MB, van Zandwijk N, Lin RC, Reid G. The expression of miR-223 in malignant pleural mesothelioma xenograft tumour samples originates from stromal cells. 6th Australian Lung Cancer Conference: 33, Melbourne, 18-20 August 2016.

9. Schelch K, Kirschner MB, Williams M, Sarun K, Winata P, Johnson T, Cheng YY, Grusch M, van Zandwijk N, Reid G. Fibroblast growth factor signals and their connection to the microRNA-15/16 family in malignant pleural mesothelioma. 6th Australian Lung Cancer Conference: 37, Melbourne, 18-20 August 2016.

10. van Zandwijk N. Mesothelioma treatment in 2016 - What's new? Where are we? Australian Lung Cancer Conference, Melbourne, 18-20 August 2016.

11. Winata P, Lin RCY, van Zandwijk N, Reid G. Using artificial miRs to control growth of cancer cells. 6th Australian Lung Cancer Conference: 33, Melbourne, 18-20 August 2016.

12. van Zandwijk N. MicroRNA therapy: first clinical evidence. 8th European Regional Conference on Thoracic Oncology: Innovative diagnostics and precision oncology in lung cancer. Bialystock, Poland, 17 June 2016.

13. Linton A, Soeberg MJ, Broome R, van Zandwijk N. The impact of geographic and socioeconomic factors on prognosis and treatment provision in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

14. Reid G, Della Gatta A, Suh H, Williams M, Cheng YY, Lin R, van Zandwijk N. Identifying microRNAs with therapeutic potential in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

15. van Zandwijk N, Pavlakis N, Kao S, Clarke S, Linton A, Boyer M, Brahmbhatt H, McDiarmid J, Huynh Y, Leslie F, Foster H, Pattison S, Reid G. Phase 1 experience with TargomiRs in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

16. Williams M, Kao S, Cooper WA, Cheng YY, Kirschner MB, Madore J, Lum T, Linton A, McCaughan BC, Klebe S, van Zandwijk N, Scolyer RA, Boyer M, Reid G. Tumour suppressor microRNAs regulate PD-L1 expression in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

CONFERENCE POSTERS

1. Cheng YY, Wang Y, Sarun KH, Kirschner MB, Pellegrini L, Yang H, Carbone DP, Mutti L, van Zandwijk N, Lin R, Reid G. Hypoxia-induced changes in microRNA levels contribute to drug resistance in a 3D model of malignant pleural mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016. (Awarded Australian Lung Foundation Travel Award – WCLC 2016)

2. Johnson TG, Schelch K, Cheng YY, Sarun KH, Williams M, Lin R, van Zandwijk N, Reid G. miR-137 acts as a tumour suppressor via the down-regulation of YB-1 in malignant pleural mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

3. Lin R, Reid G, Mutti L, Ryan AW, Nicholson S, Leonard N, Young V, Ryan R, Finn SP, Cuffe S, Gray SG. circRNAs: potential novel biomarkers for the early detection of lung cancer. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

4. Linton A, Soeberg M, Kao S, Broome R, van Zandwijk N. The influence of geographic and socioeconomic factors on prognosis and treatment provision in malignant pleural mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

5. Schelch K, Wagner C, Lang E, Hoda MA, Janovjak H, Lin R, Berger W, Klepetko W, van Zandwijk N, Reid G, Grusch M. Inducible changes in cell morphology and gene expression reflecting the histological subtypes of mesothelioma. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016. (Awarded Australian Lung Foundation Travel Award – WCLC 2016)

6. Schelch K, Ingles-Prieto A, Reichhart E, Kainrath S, Hoda MA, Berger W, Janovjak H, Grusch M. Optical control of growth factor receptors to advance signal transduction research and drug screening. IASLC 17th World Conference on Lung Cancer 2016, Vienna, 4 - 7 December 2016.

7. Johnson T. MicroRNA miR-137 acts as a tumour suppressor in malignant pleural mesothelioma. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

8. Schelch K, Wagner C, Lin R, Hoda MA, Berger W, Janovjak H, Klepetko W, van Zandwijk N, Grusch M, Reid G. Growth factor-induced phenotypical changes reflecting the histological subtypes in mesothelioma cells. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

9. Sarun KH, Cheng YY, Kirschner MB, van Zandwijk N, Lin RCY, Reid G. MiR-223 in malignant pleural mesothelioma xenograft tumour samples originates from mouse stromal cells. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

10. Williams M. Multiple mechanisms cause loss of tumour suppressor MicroRNAs in malignant pleural mesothelioma. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

11. Winata P, Lin RCY, van Zandwijk N, Reid G. Using artificial miRs to control growth of cancer cells. Sydney Cancer Conference, Australian Technology Park, Sydney, 22-23 September 2016.

12. Cheng YY, Sarun KH, Kirschner MB, van Zandwijk N, Reid G, Lin RCY. Investigating the role of microRNA s in drug resistance of mesothelioma cells using a 3D spheroid model. 6th Australian Lung Cancer Conference: 40, Melbourne, 18-20 August 2016.

13. Williams M, Cheng YY, Lin R, van Zandwijk N, Reid G. Multiple mechanisms cause microRNA downregulation in malignant pleural mesothelioma (MPM). 6th Australian Lung Cancer Conference: 34, Melbourne, 18-20 August 2016.

14. Cheng YY, Wright CM, Kirschner MB, Williams M, Sarun KH, Edelman JJ, Vallely MP, McCaughan BC, Klebe S, van Zandwijk N, Lin RC, Reid G. KCNMA1 is targeted by miR-17-5p and modulates cell migration in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016. (Awarded Concord Repatriation General Hospital Research Travel Scholarship.)

15. Cheng YY, Sarun K, Kirschner MB, van Zandwijk N, Reid G, Lin RC. Utilising microRNAs to sensitise mesothelioma to cisplatin and gemcitabine. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016. (Awarded Concord Repatriation General Hospital Research Travel Scholarship.)

16. Johnson T, Cheng YY, Williams M, McCaughan BC, Klebe S, van Zandwijk N, Lin RC, Reid G. Tumour suppressor microRNA-137-3p targets onco-protein YB-1 in malignant pleural mesothelioma. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

17. McLean J, van Zandwijk N. Personalised support for patients with malignant pleural mesothelioma (MPM) in New South Wales, Australia. International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016. (Awarded Slater & Gordon Health Project and Research Fund -2015. Australian Communities Foundation. Travel Fellowship)

18. Soeberg MJ, Leigh J, Driscoll T, Armstrong B, Young J, van Zandwijk N. Increasing age at diagnosis in the Australian malignant pleural mesothelioma population: what are the potential implications? International Mesothelioma Interest Group (iMig) 2016, Birmingham, 1-4 May 2016.

19. Cheng YY, Sarun KH, Kirschner MB, van Zandwijk N, Reid G, Lin RCY. The role of microRNAs in drug resistance of mesothelioma cells. 28th Lorne Cancer Conference, Lorne, 11-13 February 2016 (and invited flash talk).

AWARDS

1. van Zandwijk N. Certificate for Highly Cited Research in Clinical Lung Cancer Awarded December, 2016. In recognition of the contribution to the quality of the journal made by: Kao SC, Vardy J, Chatfield M, Corte P, Pavlakis N, Clarke C, van Zandwijk N, Clarke S. Validation of prognostic factors in malignant pleural mesothelioma: a retrospective analysis of data from patients seeking compensation from the New South Wales Dust Diseases Board. Clinical Lung Cancer. 2013 Jan;14(1):70-7.

2. Sarun KH. Awarded the Young Investigator Award by the International Association for the Study of Lung Cancer (IASLC) and the Local Organising Committee of the 17th IASLC World Conference on Lung Cancer for the abstract “Expression of miR-223 in mesothelioma xenografts originates from stromal cells in the tumour microenvironment”. The award is to be presented at the IASLC Business Meeting Vienna 6th December 2016.

FINANCIAL SUMMARY 2016

PROFIT AND LOSS STATEMENT	2015-16	2014-15
Revenues		
Research	2,228,390	2,130,790
Fundraising	694,119	239,815
Interest	160,669	185,803
Total	3,083,178	2,556,408
Expenses		
Employee Benefits	2,041,165	1,989,551
Research consumables/equipment	387,338	246,702
Office expenses	418,999	268,912
Depreciation	420,352	356,204
Total	3,267,854	2,861,369
Surplus / Deficit for the period	- 184,676	- 304,961

BALANCE SHEET	30/06/2016	30/06/2015
Assets		
Cash and cash equivalents incl. Term Deposits	5,385,391	6,068,640
Trade and other receivables	126,671	76,712
Property Plant and Equipment	8,884,032	8,735,292
Total	14,396,094	14,880,644
Liabilities		
Trade and other payables	819,458	1,165,680
Employee provisions	207,860	161,512
Total	1,027,318	1,327,192
Net Assets	13,368,776	13,553,452

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

COMMUNITY SUPPORT

ASBESTOS DISEASES RESEARCH FOUNDATION'S HONOUR WALL UNVEILED

On the 4th April 2016 the Asbestos Diseases Research Foundation's Honour Wall was unveiled. The Honour Wall was designed by the Bernie Banton Centre's architect, Mr Mark Willett, and is located in the foyer honouring our major supporters.

The occasion gave the ADRI staff the opportunity to speak to some of the people who have so generously supported their research. Unfortunately we were unable to invite all our donors who have all contributed greatly to our research. Without this generous support we may not have been able to further our research. On behalf of everyone at the Institute, please accept our sincere thanks.

'BETTY THE ADRI HOUSE' AT THE SYDNEY ROYAL EASTER SHOW

'Betty the ADRI house' was again on show at this year's Sydney Royal Easter Show at Homebush. Betty is the first of her kind in Australia, and the world. She is a purpose built, mobile model house the size of a caravan designed to demonstrate the multiple locations where asbestos might be found in any brick, weatherboard, fibro or clad Australian home built or renovated before 1987.

Since 'Betty' was launched in 2012, Betty has travelled more than 35,000 kilometres throughout NSW, Victoria, Queensland, Northern Territory and South Australia educating Australians about the dangers of asbestos and how to manage it safely.

Because there's no known safe level of exposure to asbestos fibres, 'Betty', together with a comprehensive online national asbestos information resource, asbestosawareness.com.au website forms Australia's first line of defence in prevention against the dangers of asbestos-related diseases in Australia.

ASBESTOS AWARENESS MONTH

November is Asbestos Awareness Month and many councils, companies and stakeholder groups across Australia support the Asbestos Awareness Campaign by holding events to raise awareness of the dangers of asbestos. The 'Get to kNOw Asbestos this November' campaign aims to educate Australians about the dangers of asbestos in and around homes because Australia has one of the highest rates of asbestos-related diseases in the world.

On Tuesday 22nd November the ADRI presented lunch time information sessions to Concord Hospital staff not only to raise awareness of the dangers of asbestos but to also inform them of the latest treatment options for mesothelioma and research into asbestos-related diseases at ADRI.

The information sessions were presented by Professor Nico van Zandwijk, Dr Anthony Linton and Associate Professor Glen Reid. Attendees were rewarded with a special Asbestos Awareness cupcake and a take home brochure.

For more information visit the Asbestos Awareness website at:
http://asbestosawareness.com.au/

ADFA'S MEMORIAL DAY 2016

Each year the Asbestos Diseases Foundation of Australia (ADFA) holds a Memorial Day at the end of Asbestos Awareness month to remember all those who have been lost to asbestos-related diseases. The Memorial Day was attend this year by His Excellency General The Honourable David Hurley AC DSC (Ret'D) Governor of New South Wales, Mrs Hurley and Mrs Barbara Hall, ADFA Patron.

ADFA launched their new asbestos awareness video which will be available on their website www.adfa.org.au to raise awareness of the dangers of asbestos. Mr Barry Robson, President of the ADFA, generously presented Professor van Zandwijk with a cheque for $30,000.00. These funds are the first tranche of a $90,000.00 PhD scholarship for Mr Tom Johnson. Tom started as a summer student at ADRI and is now doing his PhD. 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.

VOLUNTEERS

JENNY WEISMANTAL

Jenny has been supporting ADRI for many years spending three afternoons a week assisting the admin team. For a not-for-profit research institute where budgets are often tight this form of assistance is greatly appreciated. Jenny has become a valuable member of the team and her support is greatly appreciated.

SUZANNE MOUTHAAN

Sue has also been with us for a number of years assisting Professor Janette Vardy's admin team at the Sydney Survivorship Centre at Concord Hospital. She has assist on a number of other projects from time to time, including a number of fundraising events for the Survivorship Centre.

Both women chose to volunteer their time as a way of contributing to the progress of medical research into asbestos-related diseases. From the team at ADRI we thank both Jenny and Sue for their continued support.

GEOFF AND KAREN WICKS - BETTY THE ADRI HOUSE CURATORS AND CHAPERONES

This year Geoff and Karen Wicks, 'Betty the ADRI House' Curators and Chaperones, are to be congratulated on being finalists in The Centre for Volunteering 2016 Volunteer of the Year Awards as a Team in the Sydney (City and East) region. Betty the model house and asbestos awareness couldn't achieve the level of success it does if it were not for the generosity of Geoff and Karen's tireless efforts. For Asbestos Awareness Month (1-30 November) Geoff and Karen took Betty on her longest tour (distance wise) travelling from Darwin to Adelaide stopping at over 30 key regions along the way in Northern Territory and South Australia before heading to Sydney via Bourke, Broken Hill and Cobar. To see the photos of their travels raising awareness of the dangers of asbestos visit Betty's Facebook page. https://www.facebook.com/BettytheADRIhouse

Once again, a big thank you to Geoff and Karen for the enormous numbers of hours you have dedicated to showcasing Betty and to raising awareness of the dangers of asbestos around Australia.

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THANK YOU TO ALL OF THOSE WHO HAVE GENEROUSLY SUPPORTED ADRI THROUGHOUT 2016.

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Asbestos Diseases Research Institute
Gate 3 Hospital Road,
Concord Hospital, NSW 2139 Australia

PO BOX 3628, Rhodes,
NSW 2138 Australia

T 61 2 9767 9800
F 61 2 9767 9860
E info@adri.org.au
W www.adri.org.au