



ADRI



Asbestos Diseases Research Institute

2014 Annual Report



Asbestos Diseases Research Institute

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 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.



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ADRI COMMUNITY

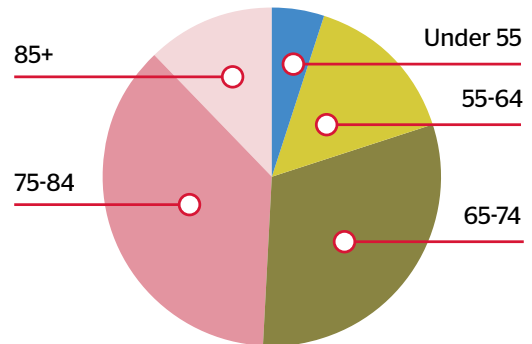
Supporters	43, 46
Volunteers	45
In memory of	47

Key statistics

Malignant Mesothelioma in 2013

This section provides an overview of malignant mesothelioma in Australia, focusing on people diagnosed in 2013, as illustrated in pie charts. Recent data about the mesothelioma epidemic in Australia is available from the Australian Mesothelioma Registry (AMR). Data from the AMR including the number of people diagnosed and – where possible – information about asbestos exposure is available from July 2010. A rapid notification system is in place for the AMR meaning that information about new mesothelioma cases are always being added. Information about the number of new cases in 2013 is accurate as at 31 May 2014. Asbestos exposure information is collected from people diagnosed with mesothelioma after consent is sought from their doctor. Asbestos exposure information reported here is accurate as at 30 April 2014. More in-depth data is contained in the ADRI's 2013 Annual Report and the reports of the AMR.

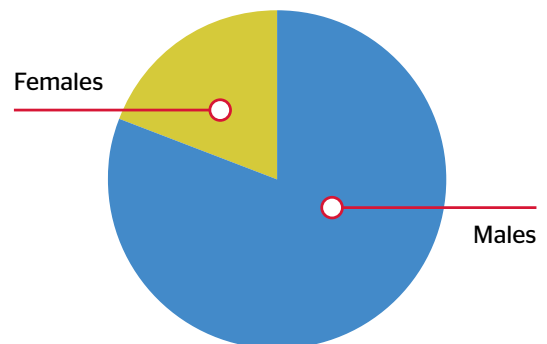
Age group



Almost half of all people diagnosed with mesothelioma in Australia in 2013 were aged 75 years or older.

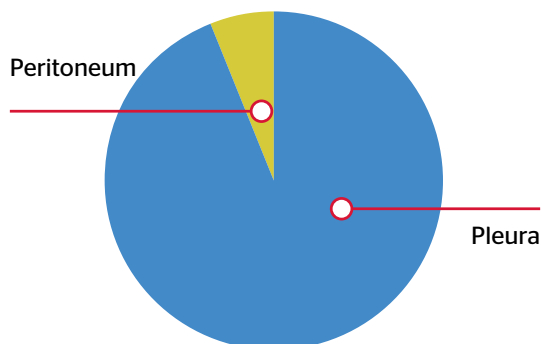
Over time in Australia, the number of older people (aged 65 years and older) diagnosed with mesothelioma has increased while the number of younger people (aged below 65 years) has decreased.

Gender



While most mesothelioma cases occurred in men (81% of cases), women made up 19% of all mesothelioma cases diagnosed in Australia in 2013.

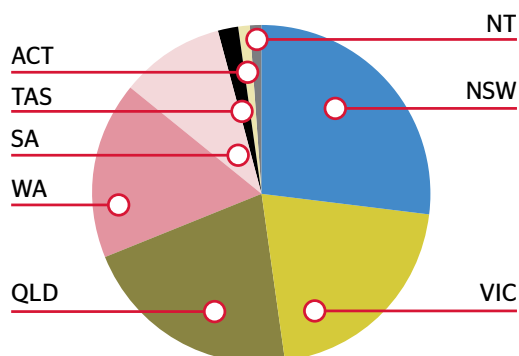
Tumour location



The majority of people diagnosed with mesothelioma in Australia, 2013, had pleural mesothelioma (94%).

In New South Wales between 1972 and 2009, the number of people with pleural mesothelioma has increased over time with little change in the number of people with peritoneal mesothelioma.

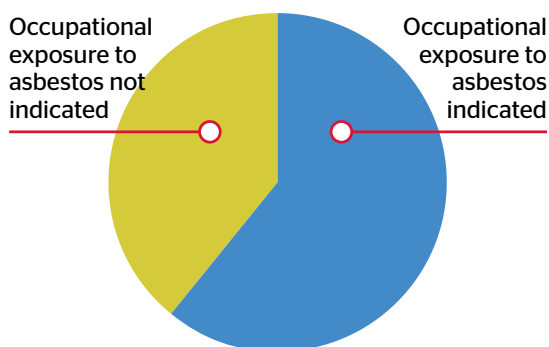
State and territory differences



70% of all mesothelioma cases in 2013 were diagnosed in either New South Wales (27%) Victoria (21%) or Queensland (21%).

17% of mesothelioma cases in 2013 were diagnosed in Western Australia. However, the incidence rate of mesothelioma in Western Australia is still the highest compared with all other states. The incidence rate compares the number of people with mesothelioma to the overall population in each state or territory.

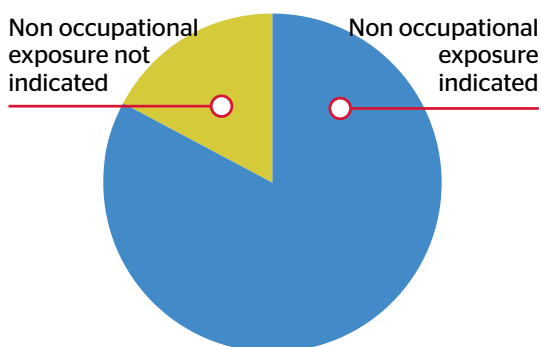
Occupational asbestos exposure



Between July 2010 and April 2014, complete information about asbestos exposure for 350 people was collected by the Australian Mesothelioma Registry.

A total of 213 (61%) people were assessed as having possible or probable occupational asbestos exposure, including five females.

Non occupational asbestos exposure



Between July 2010 and April 2014, 137 (39.1%) people provided no information to suggest they had occupational exposure.

Of those, 114 people (54 males and 60 females) reported previous asbestos exposure in non-occupational settings.

23 people provided no information to suggest they had asbestos exposure above background levels in either occupational or non-occupational settings.

2014 highlights

ADRI's Clinical Trial begins

MesomiR-1 is the name of the ADRI trial that was activated in three Sydney hospitals during the last semester of 2014, testing a new medication for malignant pleural mesothelioma (MPM) and non-small cell lung cancer (NSCLC). Thanks to the hard work of the ADRI and EnGeneIC Ltd staff important research outcomes were swiftly translated into the first-in-man clinical trial testing microRNA-based therapy. In less than 3.5 years after the discovery of an important deficiency of a microRNA family in MPM, the first clinical (safety) observations with this new treatment approach were made. It was encouraging to see that the first doses of the new medication were rather well tolerated. In 2015 we will continue to invest significant amounts of time and effort into this trial, aiming to improve the treatment outcomes of mesothelioma and lung cancer patients.

ADRI awarded the 2014 Cancer Institute NSW Premier's Award for Excellence in Translation Cancer Research

The Cancer Institute NSW Premier's Award for Outstanding Cancer Research is an annual event that celebrates excellence and innovation in cancer research. Seven awards were presented in August 2014 to those leading the way in their field. A/Prof. Glen Reid, from the Asbestos Diseases Research Institute, accepted the '2014 Excellence in Translational Cancer Research Award' (\$20,000) – on behalf of a team from:

- Asbestos Diseases Research Institute
- EnGeneIC Ltd
- Royal Prince Alfred Hospital
- Strathfield Private Hospital
- Royal North Shore Hospital
- Concord Repatriation General Hospital

The multidisciplinary team of scientists, clinicians and biotech experts from these six organisations concentrated on the development of a new treatment approach for malignant

pleural mesothelioma (MPM). Beginning with tumour samples stored in the ADRI biobank, one of Australia's largest repositories of MPM samples, a consistent change in the levels of a particular family of microRNA genes in MPM was identified and when corrected, stopped the cancer cells growing in different experimental settings. In 2014, three and a half years after the discovery of abnormal gene function in MPM, these research findings have been translated into the clinic. As indicated above the MesomiR-1 trial started in the last months of 2014 and explores the optimal dose of a new medication that is able to restore microRNA levels in MPM and NSCLC, two asbestos-related cancers, for which few treatment options exist.

An MoU between the ADRI and the Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Japan

Whilst attending the 21st Asian Conference on Occupation Health in Fukuoka City, Japan at the end of August, Professor Nico van Zandwijk had the opportunity to reinforce the collaboration and sharing of information on scientific topics relating to asbestos-related diseases with the Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, (IIES, UOEH) in Kitakyushu City. A Memorandum of Understanding (MoU) was signed formalising a closer collaboration, combining efforts to promote common research aims and the exchange of information between these Institutes.

ADRI's Mesothelioma Support Coordinator

During 2014 ADRI was fortunate to attract Jocelyn McLean as the Mesothelioma Support Coordinator, addressing the needs of mesothelioma patients and their carers.



The Federal Treasurer visited Concord Campus

The Hon. Joe Hockey MP, and Mr Craig Laundy, Federal MP for Reid, visited Concord Hospital's medical research institutes on the 10th June 2014. Mr Hockey was given an overview of the research conducted on the Concord Campus and a vision for future development by Dr Teresa Anderson, Chief Executive of the Sydney Local Health District. Professor van Zandwijk was given the opportunity to discuss the progress of ADRI's MesomiR 1 trial. The Treasurer noted that this type of research is exactly why Australia needed a Medical Research Fund, so we can put significant dollars into institutes like this which are at the forefront of global technology and development.

Jocelyn has worked for many years at Royal Prince Alfred Hospital providing care and support for patients who underwent radical surgery by A/Prof. Brian McCaughan. In that role, Jocelyn explored and reported on the recovery of mesothelioma patients and the needs of their carers. She developed a 'well living support programme' for survivors and carers, and co-authored, with A/Prof. McCaughan, a book entitled: 'Diagnosis & Treatment: The Journey of a Patient with Malignant Pleural Mesothelioma'. Jocelyn also worked with the national team of experts in the development of evidence based Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma developed by ADRI.

Launch of the National Asbestos Awareness Campaign

On behalf of the Asbestos Education Committee (AEC), the ADRI hosted the launch of Asbestos Awareness Month

campaign on 31st October 2014. In 2011, the AEC, in partnership with ADRI, started a NSW-based campaign to educate homeowners about the dangers of asbestos when renovating or maintaining homes. Following the success of the 2011 Asbestos Awareness Campaign, the AEC and ADRI promoted a national campaign in 2012 and in 2013. In 2014 the Asbestos Awareness Campaign was extended to incorporate trades and handymen and Mr Don Burke, Mr John Jarratt, and Mr Barry Du Bois, greatly supported the campaign as asbestos awareness ambassadors. The slogan for 2014 was 'Don't play renovation roulette. Get to kNOW asbestos this NOVember by visiting asbestosawareness.com.au because it's not worth the risk!'

ADRF chair's report

On behalf of the Asbestos Diseases Research Foundation Board, I have much pleasure in presenting the 2014 Annual Report. The Board of Directors has continued to work tirelessly to support the research effort and provide the Asbestos Diseases Research Institute (ADRI) with strong governance.

Joining the Board this year was Dr Christopher Clarke, who was a Visiting Medical Officer in the Department of Thoracic Medicine at Concord Hospital until December 2008. He has a special interest in occupational lung disease and is the employee nominated member on the Medical Authority of the Workers Compensation (Dust Diseases) Board of NSW. He brings tremendous experience in asbestos-related diseases to the Board. Also joining the Board was Dr Andrew Penman, who was CEO of the Cancer Council of NSW for 16 years. The organisation grew under his leadership and he initiated many of the successful pioneering programs, which are the signature of the Cancer Council of NSW today. Dr Penman's public health experiences are a huge asset to the ADRF Board.

At the meeting in March, the Board voted on a change of auditors as Mr David Gallery, who had been with Nexia Court for many years, was leaving. Mr Joseph Santangelo was advocated as Mr Gallery's successor. The Board thanks Mr Gallery for his services and wishes him the very best for his future.

The ADRI is located on the ground floor of the Bernie Banton Centre on the Concord Hospital Campus. The ADRF has a close relationship with Concord Hospital and the Sydney Local Health District. During the year a Service Agreement was signed between the Concord General Repatriation Hospital and the ADRI to work as partners to ensure the provision of corporate and clinical support services meets the needs of both organisations.

The Governor of NSW, the His Excellency General The Hon. David Hurley AC DSC (Ret'd) has been invited and has agreed to become a Patron of the ADRF. An invitation has been extended to him to visit ADRI and we are looking forward to his visit in 2015.

I would like to thank the Asbestos Diseases Foundation of Australia and all their members.

They have kindly donated over \$60k this year which has allowed ADRI to purchase much needed equipment. ADFA members have also participated in quality-of-life and various other questionnaire-based studies conducted by the Institute for which we are grateful.

On behalf of the Board I would like to commend the leadership of Professor Nico van Zandwijk and congratulate him and the ADRI consortium for being awarded the Cancer Institute of NSW 2014 Premier's Award for Excellence in Translation Cancer Research. I would also like to thank the scientific staff, administration, volunteers and all our donors for their contributions, large and small, towards combating asbestos-related diseases.



John O'Meally AM RFD
Chair



cancer
institute
NSW



2014
PREMIER'S
FOR OUTSTANDING
CANCER RESEARCH



PREMIER'S AWARDS
FOR OUTSTANDING
CANCER RESEARCH



cancer
institute
NSW



2014
PREMIER'S
FOR OUTSTANDING
CANCER RESEARCH

cancer
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NSW



Associate Professor Glen Reid
accepts the Cancer Institute
of NSW 2014 Premier's Award
for Excellence in Translation
Cancer Research on behalf of
the ADRI consortium

PREMIER'S AWARDS
FOR OUTSTANDING
CANCER RESEARCH



2014
Premier's Awards
for Outstanding Cancer Research

**Excellence in
Translational Cancer
Research**

Presented to a
multidisciplinary team from:
Asbestos Diseases Research Institute,
EnGeneC Ltd, Royal Prince Alfred Hospital,
Strathfield Private Hospital, Royal North Shore
Hospital, Concord Repatriation General Hospital

Sponsored by
SIRTeX

NSW cancer
institute
NSW

Director's report

It gives me great pleasure to present the 2014 Annual Report. 2014 has been a special year as the ADRI research team has been able to bring a novel method to stop the proliferation of experimental tumours into the clinical trial phase. The treatment concept applicable to malignant mesothelioma and non-small cell lung cancer is based on the discovery by ADRI researchers of a profound and consistent change in a particular family of genes - known as microRNAs - in asbestos-related cancer. When this abnormality was corrected in cell cultures and animal models, tumour growth could be stopped. In close cooperation with EnGeneIC, the Sydney-based biotech company that has developed an antibody-guided drug carrier (antibody-guided EDVTM nanocells) the new treatment concept, resembling the Trojan horse story, where tumour cells absorb the microRNA (mimics) delivered by EDVTM nanocells and become unable to continue growth, was further developed. The 'MesomiR-1' trial is the world's first to test this microRNA-based therapy in malignant pleural mesothelioma and non-small cell lung cancer, two thoracic tumours for which no, or very few, curative treatment options exist. On August 22nd A/Prof. Glen Reid received on behalf of the multidisciplinary team consisting of ADRI, EnGeneIC Ltd, Royal Prince Alfred Hospital, Strathfield Private Hospital, Royal North Shore Hospital and Concord Repatriation General Hospital, the Cancer Institute NSW Premier's Award for the 2014 Excellence in Translation Cancer Research for the rapid development of this exciting new treatment concept. The MesomiR-1 trial is establishing the optimal and safe dose of the new medication. Five patients participated in the trial in 2014, receiving 8 weeks of protocol treatment and more patients will follow in 2015.

The ADRI has been active on an international level advising the Ministry of Health in Vietnam about ways to start tackling the huge asbestos problems this country is facing. This was done by contributing to workshops on asbestos hazards and drafting a report on the key issues including the most urgent need for a total asbestos ban. An ADRI guided exploration of major Vietnamese

Cancer registries uncovered a significant number of mesothelioma registrations underlining undeniable association between asbestos consumption and disease.

At the 21st Asian Conference on Occupational Health, 2014 (ACOH-2014) in Fukuoka, ADRI received the honour to deliver the key-note presentation focused on the alarming shift in asbestos consumption from developed countries to Asia. The current situation in Asia was described as a time-bomb with a long fuse. At this conference I had the opportunity to formalise the scientific collaboration between ADRI and the Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, (IIES, UOEH) Fukuoka, Japan.

At a national level ADRI supported the Asbestos Education Committee to launch the asbestos awareness campaign for 2014 incorporating awareness among relevant trades and handymen. 'Betty, the ADRI house' travelled to Victoria and was also present at the Asbestos Safety and Eradication Agency's 1st international conference in Melbourne. Guidelines (for the diagnosis and treatment of malignant pleural mesothelioma) for consumers were drafted on the basis of the NHMRC Guidelines that appeared in 2013.





Distribution of these guidelines, made possible by a grant received from WorkCover NSW is expected to start early next year.

ADRI is honoured by an excellent relationship with victim support groups, in particular the Asbestos Diseases Foundation Australia (ADFA) and the Asbestosis & Mesothelioma Association of Australia (AMAA). Research updates were presented at scientific meetings and the ADRI was able to contribute to ADFA's memorial service on the last Friday of November dedicated to Australians who have lost their battle with asbestos. Our organisation is so much aware of the importance of effective communication between a disease-oriented research institute and the victim and their families. ADRI is keen to foster this excellent relationship and feels very much privileged by the wonderful financial support provided again in 2014 by the victim support groups.

In 2014 we have again lost several good friends as the ultimate consequence of asbestos-related disease. A very close friend and ADRI supporter was Mrs Carol Klintfält.

For so many years Carol was the example of a successful fight against malignant mesothelioma. Her personal fight inspired other victims and induced researchers to work even harder. Unfortunately in the spring of 2014 she was confronted with the return of disease which eventually led to her death on the 7th November. We wish the wonderful Klintfält family the strength to overcome this enormous loss.

Coming back to ADRI's 2014 Annual Report, you will notice again that ADRI is active on different fronts, keen to build a better future for all those affected by Australia's major asbestos legacy. I do hope you will enjoy reading about our progress.

Professor Nico van Zandwijk
Director

Patron of the Asbestos Diseases Research Foundation

His Excellency General The Honourable David Hurley AC DSC (Ret'd) Governor of New South Wales

His Excellency General The Honourable David Hurley AC DSC (Ret'd) is the 38th Governor of NSW. He commenced his five-year tenure in October 2014. Prior to his appointment as Governor, His Excellency served for 42 years in the Australian Army, concluding his service as the Chief of the Defence Force. His Excellency was awarded a Companion of the Order of Australia in 2010 for eminent service to the Australian Defence Force and a Distinguished Service Cross for his leadership during Operation SOLACE in Somalia in 1993. His Excellency is married to Linda and has three adult children: Caitlin, Marcus and Amelia. He has a wide range of interests in the arts and in sport.

As Governor of New South Wales, His Excellency intends to support the people and community organisations of New South Wales, through:

- assisting programs and organisations that promote inclusiveness, diversity and active citizenship
- recognising innovation, achievement and excellence
- promoting industry and regional development
- providing support in times of adversity
- advocating for marginalised members of our community.





Back row: Mr Colin Goldrick (Company Secretary), Dr Andrew Penman AM, Mr Paul Bastian, Mr John O'Meally AM RFD (Chair), Prof Nico van Zandwijk (ADRI Director)
Front row: Dr Tim Sinclair, Col. Prof Robert Lusby, Ms Sylvia Kidziak AM (Deputy Chair), Dr Christopher Clarke, Mr Sean O'Sullivan

Asbestos Diseases Research Foundation

The Asbestos Diseases Research Foundation (ADRF) established in 2006 as a charitable, not-for-profit organisation, is dedicated to assist and support the research efforts of the Asbestos Diseases Research Institute. The Foundation built and operates the Bernie Banton Centre on the Concord Hospital campus which houses the Asbestos Diseases Research Institute (ADRI). The ADRF continues to support ADRI by attracting financial support from companies and individuals.

ADRF Board

The Board of the Asbestos Diseases Research Foundation consists of the independent chairperson, two members from the Workers Compensation Dust Diseases Board; nominees from the University of Sydney, ANZAC Health & Medical Research Foundation, Sydney Local Health District, Asbestos Diseases Foundation of Australia Inc., Unions NSW, and past and present manufacturers and suppliers of asbestos or dust-containing goods. In addition, the Board has appointed further members including the Research Director of the Institute.

The 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 member of the Council of the Australian Section of the International Commission of Jurists (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 Sydney North Regional 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 Board of Directors of the Workers Compensation (Dust Diseases) Board of NSW, Chair of the Research Grants and Corporate Governance Committees and is Chair of the ARPANSA Radiation Health and Safety Advisory Council. Ms Kidziak 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 and safety 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

Mr Paul Bastian

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.
Reappointed: 11 June 2014

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 Walgett, Brewarrina and Bourke. 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.

Appointed: 13 March 2014

Col. Professor Robert Lusby

Nominated by the ANZAC Health and Medical Research Foundation

Professor Lusby is Head of the Clinical School at Concord Repatriation General Hospital and Associate Dean of the Sydney Medical School, University of Sydney. In addition, he is the Head of Vascular Surgery at Concord Hospital. Professor Lusby is a Colonel in the Royal Australian Army Medical Corps, now on the inactive reserve list. He has served in Rwanda with the UN 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 Defence Force.

Appointed 3 August 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 member of the NSW Workers Compensation Dust Diseases Board and is a Director of United Super Pty Ltd, ACIRT Pty Ltd and Uplus Pty Ltd.

Reappointed: 20 August 2009

Mr Sean O'Sullivan

Representing the interests of past and present manufacturers and suppliers of Dust or 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 Management Team and reports to the company's CEO. 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 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 (2011-2014). 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

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

Dr Tim Sinclair

Nominated by the Area Health Service

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

Professor Nico van Zandwijk

ADRI 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 Member of the Core Program Committee for the WCLC 2013 & 2015. He was a member of the national Asbestos Management Review Panel and was Study Coordinator of several international studies, and has authored or co-authored more than 250 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 15 years in a variety of roles.

Reappointed: 16 May 2012

ADRI STAFF

Research Staff

Professor Nico van Zandwijk — ADRI Director
A/Prof. Glen Reid — Senior Scientist

Mr Kan Chen — Biobank Officer
Dr Yuen Yee Cheng — Research Fellow
Dr Ngan Cheng — Research Fellow (- to March 2014)
Ms Kim Griggs — Laboratory Technician
Mrs Rebecca Hyland — Biobank Data Officer
Mrs Yennie Huynh — Clinical Trials Monitor
Dr Steven Kao — Medical Oncologist
Dr Michaela Kirschner — Postdoctoral Fellow (- to October 2014)
Dr James Leigh — Advisor
Ms Felicity Leslie — Clinical Trials Monitor
Dr Ruby Lin — Senior Researcher (May 2014 to -)
Dr Anthony Linton — Medical Oncologist
Ms Jocelyn McLean — Mesothelioma Support Coordinator
Dr Matthew Soeberg — Epidemiologist
Miss Subothini Srikanan — Research Assistant (- to March 2014)
Ms Anne Warby — Research Officer
Ms Marissa Williams — Research Assistant
Dr Casey Wright — Postdoctoral Fellow

Students

Mr Andrej Despotovski — UTS Summer Student
Mr Jason Fowler — PhD Research Fellow
Mr Tom Johnson — UTS Summer Student
Ms Nicole Khor — University of Sydney Summer Student
Mr William Lukito — University of Sydney Summer Student
Mr Kadir Sarun — UTS Summer Student
Mr David Truong — UTS Summer Student
Mr Patrick Winata — UTS Summer Student

Administrative Staff

Mr Justin Crosbie — IT Officer
Mr Ross Flemons — Accountant
Ms Kim Hadley — Administrative Assistant
Ms Victoria Keena — Executive Officer



Dr Ruby Lin



Mrs Yennie Huynh



Mr Ross Flemons



Ms Marissa Williams



Dr Steven Kao



Dr Anthony Linton



Ms Anne Warby



A/Prof. Glen Reid



Dr Yuen Yee Cheng



Ms Jocelyn McLean



Mrs Rebecca Hyland



Ms Victoria Keena



Dr Matthew Soeberg



Ms Felicity Leslie



Mr Kan Chen



Mr Justin Crosbie

New grants in 2014

CANCER COUNCIL NSW

MicroRNA replacement – a novel therapeutic approach for malignant mesothelioma

Reid G, van Zandwijk N, MacDiarmid J, Brahmhatt 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.

PFIZER AUSTRALIA

Retrospective clinico-pathological review of patients with asbestos-related lung cancer versus non-asbestos-related lung cancer – cohorts from the Dust Diseases Board

Kao S, Hannaford-Turner K, Boyer M, Horvath L, Cooper W, Klebe S, Reid G, van Zandwijk N.

This study will review a retrospective cohort of New South Wales workers with lung cancer who have applied for compensation through the Dust Diseases Board (DDB) between 2002 and 2011. This project aims to investigate whether the spectrum of clinico-pathological characteristics and molecular mutations differ between patients with heavy asbestos exposure and those with insufficient and/or no asbestos exposure. The intention is also to determine whether there are any lung cancer biomarkers that are associated with asbestos exposure.

JOHN T REID CHARITABLE TRUSTS

Phase 0,I clinical trial of an experimental therapy – TargomiRs – for malignant pleural mesothelioma patients

van Zandwijk N.

The treatment concept of this study is based on ADRI's discovery that a specific family of microRNAs (cellular housekeepers) is almost completely lost in mesothelioma and lung cancer cells. As this particular family of microRNAs is controlling cellular growth and death, restoring their levels offers an opportunity to regain control over uninhibited tumour cell growth. ADRI is fortunate to have joined forces with EnGeneIC, the biotech company that has developed an efficient antibody-guided carrier ('minicells') for microRNA therapy - TargomiRs. The concept of the new treatment resembles the Trojan horse story, where tumour cells absorb the microRNA (mimics) delivered by minicells thereby slowing/stopping tumour growth. The phase 0,I clinical trial is currently in its first stage to establish the optimal safe dose of the new medication. The next stage of clinical experimentation will focus on efficacy and we are currently seeking funding to enable us to make a smooth transition from phase I to II. The obvious goal of our clinical studies is to eventually add a new form of treatment to the limited therapeutic arsenal for malignant mesothelioma and non-small cell lung cancer, two cancer diagnoses associated with asbestos exposure.



WORKCOVER AUTHORITY
OF NEW SOUTH WALES

Dissemination of the guidelines for the diagnosis and treatment of malignant pleural mesothelioma and to develop and disseminate consumer guidelines for patients and their carers
van Zandwijk N.

The diagnosis of malignant pleural mesothelioma is difficult and treatment practices are not equally distributed, with considerable expertise concentrated in some hospitals and lacking in others. As there were no guidelines in Australia that are specifically for the diagnosis and treatment of this almost invariably fatal disease, ADRI and a national team of experts developed guidelines in accordance with the National Health and Medical Research Council (NHMRC) standard. This project will disseminate these evidence based guidelines to support informed decision making about the diagnosis and treatment of malignant pleural mesothelioma and from these guidelines develop and disseminate a booklet for patients and their carers.

WORKCOVER AUTHORITY
OF NEW SOUTH WALES

The MesomiR 1: A Phase 0, I study of TargomiRs as 2nd or 3rd line treatment for patients with recurrent MPM and NSCLC clinical investigation
van Zandwijk N.

TargomiRs have been the product of a successful cooperation between ADRI and EnGeneIC, a Sydney-based biotech company. TargomiRs are minicells (nanotechnology) loaded with a microRNA (mimic) that is almost absent in MPM cells. This microRNA (family) has important tumour suppressor functions. Experimental (MPM) tumours stopped growing/regressed upon intravenous administration of TargomiRs and this research is being translated into the clinic. New drug development protocols are being followed with initial studies establishing an optimal/safe dose and pharmacokinetics/dynamics. Phase II studies are planned following successful completion of the Phase 0/I assessment.

On-going grants in 2014

SYDNEY CATALYST

Mutation profiling study of cancer genes in malignant pleural mesothelioma

Wright C, Reid G, van Zandwijk N, McCaughan B, Caramins M, Kao S.

This pilot study aims to identify somatic cancer-gene mutations in MPM tumour tissue. The project seeks to determine the population frequency of mutations in cancer-related genes for MPM that would support pre-selection of patients for specific targeted therapies and to determine the types of mutations altered in cancer-related pathways in MPM. Sequencing is now complete and data is being analysed.

CANCER INSTITUTE NSW TRANSLATIONAL PROGRAM GRANTS

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 Mesothelioma Interest Group Conference, and published in the journal of Molecular of Oncology.

COMCARE ASBESTOS INNOVATION FUND

MicroRNAs as biomarkers to aid in the diagnosis of malignant pleural mesothelioma

Reid G.

This project was completed early in 2014. It aimed to identify novel microRNA markers for early diagnosis of MPM. On-going experiments will compare the performance of microRNAs with currently used protein-based biomarkers such as mesothelin in the same sample, using ELISA as well as novel proteomic quantification methods we are developing in a separate project.

DUST DISEASES BOARD RESEARCH & COMMUNITY SUPPORT GRANT

MicroRNAs as Biomarkers for Malignant Mesothelioma

Kirschner MB, Reid G, Birnie K, Mutsaers S.

This project investigated the use of microRNAs as biomarkers in MPM, and included analysis of patient blood, pleural effusion fluid and tumour tissue. Results obtained as part of this project were presented at 12th International Mesothelioma Interest Group Conference in Cape Town in October 2014 and were recently published in the journal of Molecular Oncology.

DUST DISEASES BOARD RESEARCH & COMMUNITY SUPPORT GRANT

Chemotherapy utilisation for malignant mesothelioma patients – optimal rate, barriers to access and patient preferences

Kao S, Ng W, Vardy J, Dhillon H, van Zandwijk N, Blinman P.

This project aims to determine the optimal chemotherapy utilisation rate in malignant pleural mesothelioma patients in NSW and investigate barriers and facilitators to potentially eligible patients receiving this treatment. Results from this study have been presented at the IASLC 15th World Conference on Lung Cancer in Sydney and the Cancer Institute NSW Innovations in Cancer Services and Care NSW Conference in 2013, and in 2014 at the Australian Lung

Cancer Conference, the Clinical Oncology Society of Australia Conference, Cancer Institute NSW Innovations in Cancer Treatment & Care Conference, and the 12th International Mesothelioma Interest Group Conference. Initial study outcomes have also been published in an article in the Asia-Pacific Journal of Clinical Oncology.

DUST DISEASES BOARD RESEARCH & COMMUNITY SUPPORT GRANT

Using proteomics to improve prognostication and prediction in malignant mesothelioma

Reid G, Molloy M, Kao SC-H,
van Zandwijk N, Clarke S.

This project aimed to identify protein-based biomarkers in the blood of patients that can be used as prognostic factors or markers to predict response to therapy. Results from this study were presented at the 12th International Mesothelioma Interest Group Conference in Cape Town in October 2014 and a manuscript is close to submission

CANCER AUSTRALIA – PRIORITY-DRIVEN STANDARD PROJECT GRANT

The use of RNAi to identify new therapeutic targets for malignant mesothelioma

Reid G, Klebe S, van Zandwijk N.

The aim of this project was to further characterise novel targets and chemotherapy combinations that potentiate drugs already in use. The identification of new and subtype-specific therapies will lead to improved outcomes for MPM patients. Results from this study were published in the British Journal of Cancer.

PHILANTHROPIC AND CORPORATE FUNDING

ANZ Trustees Foundation – Swift Family Bequest & Mr Jim Tully Fellowship

Kirschner M.

The research of Dr Michaela Kirschner was co-supported by the Swift Family Bequest & Mr Jim Tully Fellowship. The main focus of Dr Kirschner's work at the ADRI was to investigate whether microRNAs can be detected in the blood of mesothelioma patients. By assessing the microRNA content of blood from mesothelioma patients, a number of microRNAs have been identified that may act as a marker of diseases.

James Hardie

James Hardie Industries plc continued to provide untied support for research into the diagnosis and treatment of asbestos-related disease during 2014. This support is 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: tissue, plasma, serum, buffy coat and pleural fluid proteins. Kan Chen joined ADRI in 2013 as our Biobank Officer to assist with the management, maintenance and development of the biobank. During 2014 he has been busy working to enlarge the network of collection sites and has generated a number of cell lines for research use. The biobank's clinical database is being managed and maintained by an experienced team who collect and accurately document every sample. Thanks to CSR's support the biobank continues to grow and is an important resource for the ADRI's on-going research program.

Ongoing studies

Clinical, pathological and treatment factors associated with survival in MPM?

Investigators: Linton A¹, Soeberg M^{1,2}, van Zandwijk N^{1,2}.

1. Asbestos Diseases Research Institute,
2. University of Sydney

Despite therapeutic improvements over recent years, a diagnosis of malignant pleural mesothelioma (MPM) carries a grim prognosis. Nevertheless widespread variability exists as to survival outcomes, with a small percentage of patients surviving significantly longer than expected. To provide clinicians, patients and their families with accurate prognostic expectations, a number of prognostic markers (clinicopathological features assisting in the prediction of survival times), have been identified and incorporated into scoring systems. However existing models often fail to reflect current opinion on prognosis in the modern era.

With the co-operation of the NSW Dust Diseases Board and oncology and thoracic units across NSW, we have performed one of the largest analyses to date of long survivors with MPM. Gathering data from the medical and surgical records of 910 patients diagnosed between 2002 and 2009, we have confirmed the prognostic role of gender, age, histological subtype, white cell and platelet counts,

haemoglobin level, neutrophil-lymphocyte ratio and stage, and offer the first evidence of the prognostic significance of calretinin expression on immunohistochemistry in a general population.

We have utilised this data to develop a new prognostic index (PI), a score based approach predicting the likelihood of prolonged survival. We found that the PI score offered better prognostic discrimination than prior models. Future research will seek to validate this model in a prospective and independent series.

This series also allowed the opportunity to assess the impact of treatment upon survival. Whilst the use of radical surgery (in the form of an extrapleural pneumonectomy) remains controversial, our NSW series demonstrated a significant survival advantage in patients undergoing this therapy which persisted following correction for clinical factors. Of interest however, we have noted a significant



proportion of 'long survivors' who received neither chemotherapy nor radical surgery. Whilst existing factors, including histological subgroup and a favourable haematological profile differentiated the untreated long survivors from the larger untreated population, it is clear that additional factors must play a role. This is an area for future research.

The DDB case series is to date, the largest Australian series of MPM patients in the literature, for whom demographic, clinical and treatment data are available. This series will continue to be investigated and offers a unique perspective on a large general population of MPM with occupational exposure with minimal selection bias. Asbestos exposure data for each patient will be analysed as we attempt to determine an accurate exposure level for each patient and investigate the relationship between exposure and disease latency and survival.

Clinicopathological review of asbestos-associated lung cancer from Dust Diseases Board

Investigators: Kao S^{1,4}, Hannaford-Turner K², Boyer M³, Horvath L³, Cooper W⁴, Klebe S⁵, Reid G^{1,6}, van Zandwijk N^{1,6}.

1. Asbestos Diseases Research Institute, 2. Dust Diseases Board of NSW, 3. Chris O'Brien Lifehouse, 4. Royal Prince Alfred Hospital, 5. Flinders University, 6. University of Sydney

Despite the extensive epidemiological literature available, the molecular relationship between asbestos exposure and lung cancer remains the subject of controversy. Essentially, this relates to the fact that most asbestos-associated lung cancers occur in those who are also cigarette smokers, and smoking represents the strongest risk factor for lung cancer. It is estimated that asbestos-related lung cancer accounts for 4 –



12% of all lung cancers worldwide. For every case of malignant mesothelioma, there may be two asbestos-related lung cancers, and this ratio may increase in occupations with heavy asbestos exposures.

This study is a review of a retrospective cohort of New South Wales workers with lung cancer who have applied for compensation through the Dust Diseases Board (DDB) between 2002 and 2011. This project aims to investigate whether the spectrum of clinicopathological characteristics and molecular mutations differ between patients with heavy asbestos exposure and those with insufficient and/or no asbestos exposure. The intention is also to determine whether there are any lung cancer biomarkers that are associated with asbestos exposure.

This work will pave the way for identification of novel biomarkers in lung cancer tumour samples that are specifically related to asbestos exposure, thereby assisting the DDB in process of assigning asbestos dust exposure as having had material contribution to the development of lung cancer. This work will also provide an accurate overview of the clinical, pathological and molecular characteristics of asbestos related lung cancers and non-asbestos related lung cancers in NSW workers and highlight any differences that might exist between the two groups. The findings of this research will also provide valuable insight into the treatment patterns and survival outcomes of asbestos related lung cancers.

Tumour microRNAs as predictors of survival outcomes

Investigators: Kirschner MB^{1,2}, Cheng YY¹, Armstrong NJ², Lin RCY^{1,3}, Kao SC^{1,4}, Linton A¹, Klebe S⁵, McCaughan BC⁶, van Zandwijk N^{1,2}, Reid G^{1,2}.

1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. University of NSW, 4. Royal Prince Alfred Hospital, 5. Flinders Medical Centre, 6. RPA Medical Centre

The prognosis for those diagnosed with malignant pleural mesothelioma (MPM) is dismal, and most patients unfortunately die of

the disease within 12-18 months of diagnosis. The majority of patients diagnosed with MPM are eligible for palliative chemotherapy, but there is also a select group of patients who can be considered for more intensive treatment. This so-called multimodality treatment consists of chemotherapy, removal of the tumour through radical surgery and postoperative radiotherapy. Unfortunately, it has proven difficult to identify those patients who are likely to benefit from such an extensive treatment approach based on clinical factors such as the type of mesothelioma, the stage of the disease and the age of the patient. Even amongst patients selected based on these clinical factors, the survival outcomes vary considerably. But this variability can also be observed in patients not receiving radical, but rather less extensive palliative surgery.

To be able to optimally tailor the treatment to the individual patient we need factors which can help us in making the decision for or against a specific treatment based on the expected outcome of this approach. Prognostic factors which can more accurately identify patients with a good prognosis and who may be best suited for a radical treatment approach have been investigated in the past, but none of them has made it into clinical practise.

At the ADRI we have investigated whether the expression of microRNAs in the tumour can predict prolonged survival following surgical intervention in mesothelioma patients. In 2013 we performed profiling of tumour tissue from patients with long and short survival following radical surgery, and were able to identify a number of microRNAs with lower abundance in the tumour tissue of long survivors. In 2014 we performed more in-depth investigation of these microRNAs in a series of 48 tumour samples obtained from patients undergoing radical surgery (extrapleural pneumonectomy). This revealed that combining the expression of six microRNAs into a so-called signature, the miR-Score, could accurately identify those patients who survived 20 months or more following surgery. We then measured this signature in 43 tumour samples obtained from patients undergoing palliative surgery, and found that also in this group it was able to accurately identify those patients with a good

prognosis of more than 20 months survival. Taken together this study has shown that the miR-Score is able to predict prolonged survival in mesothelioma patients undergoing radical or palliative surgery. The miR-Score is the first multi-microRNA signature with broad prognostic value for malignant pleural mesothelioma.

The data from this study were presented in March 2014 as a poster at the European Lung Cancer Conference and in October 2014 as an oral presentation at the 12th International Mesothelioma Interest Group Meeting. The paper describing the miR-Score has recently been published in *Molecular Oncology*.

Building on these results, validation of the miR-Score in another independent sample series will be carried out in 2015 in collaboration with the Division of Thoracic Surgery at the University Hospital of Zurich.

Wnt signalling and malignant pleural mesothelioma (MPM)

Investigators: Cheng YY¹, Zheng Y², McLaughlin C³, McCaughan BC⁴, Jin HC⁵, Chan FKL⁶, George A³, van Zandwijk N^{1,7}, Reid G^{1,7}

1. Asbestos Diseases Research Institute, 2. ANZAC Research Institute, 3. Zhejiang University, China, 4. Royal Prince Alfred Hospital, 5. University of Technology, 6. Chinese University of Hong Kong, 7. University of Sydney

The etiology of malignant mesothelioma (MM) is closely linked with asbestos exposure. Asbestos is capable of inducing chronic inflammation which potentiates tumour suppressor gene silencing. Epigenetic silencing of the Wnt pathway, well characterized in the progression of colon cancer, is associated with chronic inflammation. As antagonists of Wnt pathways, the secreted frizzled-related proteins (SFRPs) are functional tumour suppressors of colon, gastric, breast, ovarian and lung cancers, with some of these members silenced in mesothelioma. Malignant pleural mesothelioma is a cancer closely related to asbestos exposure with limited effective treatment to date. Previous studies have

reviewed the over-expression of Wnt1, Wnt2, and Dishevelled (Dvl) in MPM cells that promote cancer cell proliferation and inhibit apoptosis. Aberrant down-regulation of the SFRP4 had been reported in MPM. In this study, we aim to investigate the importance of the SFRP tumour suppressor gene family in MPM, and the effect of Wnt inhibitors on MPM cells. The effect of long-term asbestos exposure on epigenetic alteration in MPM cells will also be examined.

Our results indicate that both SFRP2 and SFRP5 were either absent or down-regulated in MPM lines, and restored after demethylation treatment. SFRP1 and SFRP4 were highly expressed and unmethylated in all MPM lines. SFRP2 and SFRP5 were silenced and methylated in MPM patient samples. Of the 66 patient samples, 56% had SFRP2 DNA methylation and 70% had SFRP5 DNA methylation. Ectopic expression of SFRP2 or SFRP5 inhibited MPM cell growth and colony formation in both 2D and 3D culture. Wnt pathway inhibitor (LGK974) suppressed the ability of MPM cells to form colonies in a clonogenic assay. SFRP1 was down-regulated and methylated following prolonged asbestos exposure in MeT-5A cells. These findings help us to better understand the molecular background of Wnt pathway in MPM. These results were presented at the 12th International Mesothelioma Interest Group (iMig) Meeting in Cape Town, in October 2014.

Integrating multiple molecular datasets to identify new therapeutic targets for MPM

Investigators: Wright CM¹, Lin RCY^{1,2}, Williams M¹, Kirschner MB^{1,3}, van Zandwijk N^{1,3}, Reid G^{1,3}

1. Asbestos Diseases Research Institute, 2. University of NSW, 3. University of Sydney

Previous malignant pleural mesothelioma (MPM) studies have identified various molecular changes involved in MPM pathogenesis including changes in gene and microRNA expression. However, to date, no effort has been made to look for patterns of dysregulation across

multiple published studies. In this project, we mined publicly available datasets and sought to identify specific families of microRNAs whose target genes were enriched in MPM. We identified two highly enriched microRNA families, and tested their expression in MPM tumours and cell lines. One of these microRNA families was strongly down-regulated in MPM tumours compared to controls. This same family was also strongly associated with epithelioid history. Integrative analysis of microRNA and predicted target expression identified 40 mRNA targets that were differentially expressed in MPM compared to control. Correlation analyses confirmed a negative relationship between target expression and microRNA expression which was confirmed following reintroduction with microRNA mimics. One of the predicted mRNA targets was selected for further validation, as an inhibitor was currently available. Treatment with this inhibitor reduced MPM cell growth, however siRNA knockdown failed to show obvious changes in cell growth. Further functional assays are underway to confirm its role in cellular migration.

Identification of targetable mutations in MPM are accompanied by changes in gene expression

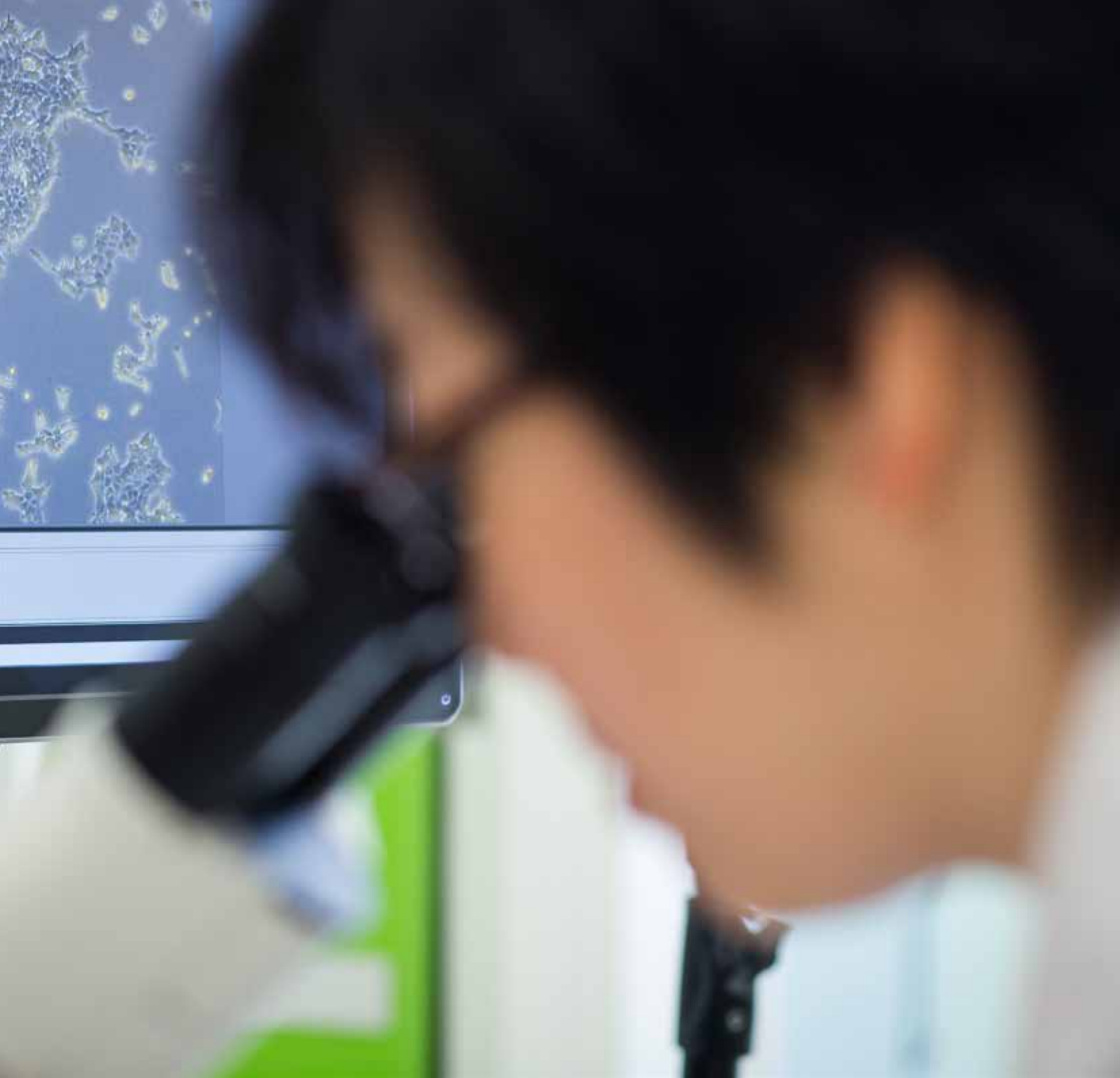
Investigators: Wright CM¹, Reid G^{1,3}, van Zandwijk N^{1,3}, McCaughan B², Caramins M³

1. Asbestos Diseases Research Institute, 2. Royal Prince Alfred Hospital, 3. University of Sydney

The identification of therapies that can be tailored to individual disease characteristics is an important goal in oncology. Currently mesothelioma is not well characterised molecularly. In this project, we aim to identify whether specific subgroups of mesothelioma patients are more likely to respond to therapy based on specific changes in their DNA. Identifying DNA changes that are likely to improve a patient's response to therapy is vitally important. Identifying specific molecular characteristics of disease will not



only assist in selecting patients for specific treatment approaches, but may also result in better tolerability of treatment. As part of the ADRI research program, we have performed a pilot study of mesothelioma cell lines to identify specific mutations that occur in cancer-related genes and pathways. In addition, we have performed RNA-seq analysis on the same cell lines to determine whether these mutations are accompanied by changes in gene expression. Candidate mutations have also been profiled in a clinical cohort of 26 tumours with matched blood. Further validation in a larger cohort is required to determine whether these mutations have an important functional



role in malignant pleural mesothelioma (MPM). We hope to extend this work to a larger panel of 30 mesothelioma tissues to identify changes that occur specifically in the tumours themselves. It is hoped that this approach will help to identify new druggable targets in MPM.

The microRNA miR-193a-3p is downregulated and has tumour suppressor activity in malignant pleural mesothelioma

Investigators: Williams M¹, Kirschner M^{1,2}, Hanh J¹, Cheng YY¹, Wright CM¹,

Linton L^{1,3}, Kao SC^{1,4}, Edelman JJB⁵, Vallely MP⁵, McCaughan BC⁶, Klebe S⁷, Lin RCY^{1,8}, van Zandwijk N^{1,2}, Reid G^{1,2}

1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. Concord Repatriation General Hospital, 4. Chris O'Brien Lifehouse, 5. Royal Prince Alfred Hospital, 6. RPA Medical Centre, 7. Flinders Medical Centre, 8. University of NSW

This project investigates the expression and functionality of microRNAs (miRNAs) in malignant pleural mesothelioma (MPM). miRNAs are small genes which have been shown to be involved in cancer progression. Specifically, their altered expression has been

directly linked to the biology of MPM and their regulation has provided alternative ways to inhibit MPM growth. Previous studies have identified a selection of miRNAs to be differentially expressed between lung adenocarcinoma and mesothelioma; forming the basis of a clinically used diagnostic test to distinguish the histologically similar cancers.

The altered expression profiles of these miRNAs have been shown to have diagnostic significance but their functionality in MPM has not been explored, as this requires comparison of their expression between MPM and normal controls.

We investigated the functional significance of these miRNAs by first determining whether their levels are altered between MPM tumour samples and normal controls. It was found that two miRNAs of this diagnostic panel were consistently expressed lower in tumour samples; miR-192 & miR-193a-3p. Their ability to distinguish tumour samples from normal controls provided evidence for their involvement in MPM tumour progression and their functionality was further explored. It was found that upon re-expression, the miRNAs inhibited cell growth, negatively regulated oncogenic targets and induced apoptosis and necrosis. Their tumour suppressor functions provide potential for use as a therapeutic target in MPM.

This work was presented at the iMig meeting in Cape Town, in October, and the Sydney Cancer Conference in November 2014. A manuscript summarising the research results has been submitted for publication.

MesomiR 1: A Phase 0, I study of TargomiRs as 2nd or 3rd line treatment for patients with recurrent malignant pleural mesothelioma and non-small cell lung cancer clinical investigation

Investigator: van Zandwijk N^{1,2}

1. Asbestos Diseases Research Institute,
2. University of Sydney

The tolerability of TargomiRs microRNA-

loaded EnGeneIC Delivery Vesicles (EDVs) is being assessed in clinical classical dose escalation (Phase 1) study. Five patients received weekly doses of 5 billion TargomiRs in 2014. This dose level was well tolerated. The most prominent side-effects of the new medication turned out to be rigor (shivering) for a relatively short period, occurring 80-90 minutes after the start of the infusion. All five patients completed an 8 week period of TargomiR treatment and prolongation of treatment is possible for patients who show signs of subjective improvement. Dose escalation will be continued in 2015 and the observations obtained in the first cohort of patients will be presented at the 13th International Congress on Targeted Anticancer Therapies (TAT) in Paris (March 2015).

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 H², Price M², Fowler J^{2,3}, Warby A^{2,3}, Tan C¹, McLean J³

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 2014, site-specific ethics approval has been received for 12 participating hospitals across Australia and approval for a further 2 sites is pending.

Negotiations regarding site-specific ethics applications are on-going for another 7 sites. 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, 25 participants have consented to be part of the study, and from these participants 49 separate assessments have been obtained.

Preliminary analyses of previously collected nutritional data for a subset of MM patients treated with extra-pleural pneumonectomy (EPP) surgical treatment have been presented at the Australian Lung Cancer Conference and the 12th International Mesothelioma Interest Group Conference in October 2014. Publications are in preparation reporting quality-of-life and nutritional risk following EPP surgical treatment.

Chemotherapy utilisation for malignant mesothelioma patients

Investigators: Kao S^{1,2}, Ng W³, Vardy J^{4,5}, Dhillon H⁵, Blinman P⁴, van Zandwijk N^{2,5}

1. Chris O'Brien Lifehouse, 2. Asbestos Diseases Research Institute, 3. Liverpool Hospital, 4. Concord Repatriation General Hospital, 5. University of Sydney

This three stage study explored perceptions of chemotherapy for malignant pleural mesothelioma (MPM), as well as potential barriers and facilitators to accessing treatment. Stage 1 determined that about 11% of people suitable for chemotherapy don't receive it. Chemotherapy is the only treatment proven to prolong overall survival in MPM therefore it is important to determine ways to reduce the gap between current practice and best evidence-based practice. In Stage 2 we conducted interviews (72 in total) with patients, caregivers, and health professionals to explore their perceptions of treatment and what influences access to chemotherapy. The results from this stage were used to develop comprehensive questionnaires to survey larger numbers from the same groups (Stage 3) to further investigate barriers and facilitators to chemotherapy treatment to guide the

development of potential interventions. The questionnaires were completed by 77 patients, 106 caregivers, 107 doctors and 19 specialist nurses.

Preliminary data analysis indicated a number of facilitators and barriers to treatment. Facilitators include discussion of MPM cases at multi-disciplinary team (MDT) meetings, treatment of MPM patients in specialist centres, policy to refer all MPM patients to a medical oncologist for an opinion on chemotherapy, and use of clinical practice guidelines. Barriers to chemotherapy can be divided into two groups: patient related and clinical/clinician related. The clinical/clinician barriers most commonly endorsed include: clinician nihilism; non-referral to medical oncologists; lack of cancer services; no MDT review; delayed diagnosis of MPM; and lack of clinician knowledge about treatment.

The most common patient-related barriers endorsed were: patient negative perception of chemotherapy regarding toxicity and impact on quality of life; patient perception of insufficient survival benefit from chemotherapy; and patient deferral of chemotherapy and then being too unwell to start. From preliminary review of the questionnaire data we anticipate key findings in the areas of unmet needs, the compensation process, decision-making around chemotherapy and issues related to diagnosis and treatment.

We have already presented findings from the project at cancer conferences in 2013 and 2014 and a number of publications are being prepared.

Epidemiology and Health Services Research @ ADRI

Epidemiology is the corner stone of public health and helps to answer questions about the causes and patterns of disease in specific populations. Health services research is a field of study that examines how people get access to health care, how much care costs, and what happens to people as a result of this care. Both epidemiology and health services research can make an important contribution to improving the outcomes for people diagnosed with asbestos-related disease in Australia as well as in countries where asbestos is still being used. This area of work is funded by the Cancer Institute NSW.

Epidemiology of malignant mesothelioma, New South Wales, 1972-2009

Investigators: Soeberg M^{1,2,3}, Young J^{2,3}, Creighton N³, Baker D³, Currow D³, van Zandwijk N^{1,2}

1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Cancer Institute NSW

High-quality cancer registration data are available over a 38-year period to better understand the patterns of malignant mesothelioma in New South Wales. The preliminary results from this descriptive epidemiological study show that over time the number of people with malignant pleural mesothelioma has increased but the age-standardised incidence rate has remained stable since the early 2000s. People diagnosed with malignant peritoneal mesothelioma make up 6% of all mesothelioma cases in New South Wales, with approximately 10-15 people diagnosed with malignant peritoneal mesothelioma each year. Survival five-years after a mesothelioma diagnosis in NSW remains poor. Preliminary results from this study were presented at the 2014 meeting of the International Mesothelioma Interest Group.

Utilisation and cost of pemetrexed, Australia, 2010-2014

Investigators: Soeberg M^{1,2,3}, Kao SC-H^{1,4}, Young J^{2,3}, Snowden K⁴, van Zandwijk N^{1,2}

1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Cancer Institute NSW,
4. Chris O'Brien Lifehouse

Chemotherapy with pemetrexed (marketed as Alimta) and cisplatin provides a survival benefit for people diagnosed with malignant mesothelioma (MM). Pemetrexed has also been shown to improve survival in people diagnosed with non-small cell lung cancer (NSCLC). Little is known about how many people are treated with pemetrexed in Australia and what the cost is for this chemotherapy treatment. This study will answer questions about how many people were treated with pemetrexed in Australia during 2000-2014, how much of the pemetrexed use in Australia is for MM compared to NSCLC, how much of the pemetrexed use was approved within the scope of PBS subsidies, and what is the cost of pemetrexed use in Australia. Data for this study has recently been obtained from records held by the Department of Human Services Pharmaceutical Benefits Scheme and will be analysed in 2015.

Estimating the incidence of malignant mesothelioma in Vietnam

Investigators: Soeberg M^{1,2}, Luong MA³, Tran VT⁴, Tran AT³, Nguyen TTH³, Bui D⁴, Nguyen HN⁴, Takahashi K⁵, van Zandwijk N^{1,2}

1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Health Environment Management Agency, Vietnam, 4. Vietnam Cancer Research Institute, Vietnam, 5. University of Occupational and Environmental Health, Japan

Vietnam is one of a number of countries in the Asian region where chrysotile asbestos is being used for the manufacturing of asbestos-containing building materials, primarily roof tiles. Asbestos use in Vietnam has the potential to lead to substantial human health, social, and economic impacts in coming decades. Here, we pilot the use of the Vietnam regional population-based Vietnam Cancer Registry data to estimate the number of incident cases of malignant mesothelioma. We identified a total of 148 incident cases of malignant mesothelioma in Vietnam between 1987 and 2013. The majority of these cases were recorded in the Ha Noi region. Men made up 53% of cases. The majority of cases were aged 55 years or older. Accurate diagnosis of malignant mesothelioma and asbestos-related lung cancers remains a challenge in low- and middle-income countries in the Asian region. As a result, the data presented here are likely to underestimate the true number of incident cases of malignant mesothelioma. Preliminary results from this study were presented at the 12th International Mesothelioma Interest Group Conference in October 2014.

Other Activities

Development of a booklet with mesothelioma information for patients and their carers

Penman A¹, McLean J¹, Keena V¹, van Zandwijk N¹

1. Asbestos Diseases Research Institute

Evidence-based Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma were approved for publication by the National Health and Medical Research Council (NHMRC) in July 2013. These guidelines support informed decision making about the diagnosis and treatment of malignant pleural mesothelioma and are being disseminated to the medical community in different formats, including: hard copy, online (see www.adri.org.au) and in a credit card style USB. From these evidence-based guidelines a new booklet has been drafted entitled Understanding Pleural Mesothelioma and will be disseminated in 2015 in collaboration with the Cancer Council NSW.

ADRI Biobank

Chan K¹, Rebecca Hyland¹

1. Asbestos Diseases Research Institute

The ADRI biobank has been established to support research into asbestos-related diseases. During 2014 additional blood and tissue specimens have been added to our collection; the biobank contains fresh frozen tumour tissue and matched bloods from mesothelioma patients, control tissue samples and series of formalin-fixed tumour tissues.

The ADRI biobank is also connected to the PRIME Study (Identification of Predictive and Prognostic Factors in Malignant Mesothelioma), which has expanded to six hospital sites in 2014, including: Concord, Royal Prince Alfred, Westmead, St George, Sutherland and the Calvary Mater. Furthermore, this year we have established a procedure that enables the collection of normal pleura tissue from consented patients undergoing cardiovascular surgery at Royal

Prince Alfred Hospital. This collection will be used to compare tissue collected from mesothelioma patients.

The biobank also collects associated clinical data on patients who donated their tissue samples and a modern data management system is used which links clinical data and biospecimen samples through a coded system to carefully protected individual patient data. Early in 2014 an audit of the biobank was conducted to ensure that all inventory records for each sample were updated.

ADRI also contributed to a major international cancer research project known as The Cancer Genome Atlas (TCGA) which is co-ordinated by the National Cancer Institute (USA). ADRI contributed several mesothelioma cases and shipped high quality frozen samples and provided comprehensive clinical data. The samples are now part of the TCGA's cancer library. Advanced genomic technologies will be utilised to generate statistically and biologically significant outcomes. The overarching goal of the TCGA is to improve the ability to diagnose, treat and prevent cancer and ADRI is very proud to be involved in this global collaborative initiative.

Significant achievements have been made in 2014 and we are looking forward to further expand the biobank study sites in 2015.

Mesothelioma Support Co-ordinator

McLean J¹

1. Asbestos Diseases Research Institute

The mesothelioma support coordinator provides support to patients, carers, families and the bereaved.

This year some of the support group meetings were characterised by a relatively small number of people attending the meetings. Frequently patients are too sick to travel (or the distance is judged too much of a burden) and therefore one-on-one support over the telephone was the preferred way of communication. Different categories of patients/carers received support including

patients that were just diagnosed, patients and families going through an active treatment phase, bereaved carers that recently lost a loved one, and past carers trying to get on with life. Teleconferencing was also used to link small groups of people to discuss similar issues and to provide support.

There was an on-going commitment with the group of patients that underwent radical surgery in the form of extrapleural pneumonectomy (EPP). The EPP group, supported by the Baird Institute, has members in Sydney as well as rural and regional NSW and Victoria. They meet at least three times a year. Because of the different nature of their treatment, the needs of the EPP group are different from other mesothelioma patients.

At a Carers Workshop held in December 2014 it became clear that more information and empathic support is needed at the time a patient learns of his/her diagnosis. From the evidence-based Guidelines for the diagnosis and treatment of malignant pleural mesothelioma an ADRI and Cancer Council NSW team is drafting a new booklet for patients and their carers, entitled: Understanding Pleural Mesothelioma which will be disseminated in collaboration with the Cancer Council NSW through their Understanding Cancer Series in 2015.

Prevention through Education

van Zandwijk N^{1,2}, Soeberg M^{1,2,3}

1. Asbestos Diseases Research Institute,
2. University of Sydney, 3. Cancer Institute NSW

Prevention of exposure to asbestos is one of ADRI's aims. If we can educate people about the dangers of asbestos we may help to prevent further exposure to this deadly carcinogen. During 2014 ADRI staff participated in various government and community activities to raise the awareness of the dangers of asbestos. Professor Nico van Zandwijk presented at a number of conferences including the Asbestos Safety and Eradication Agency's 1st international conference in Melbourne where a communique was issued outlining the way forward towards an Australia free of the risk of asbestos. On behalf of the Asbestos

Education Committee the Asbestos Awareness Campaign for 2014 was launched at ADRI incorporating awareness among relevant trades and handymen. 'Betty, the ADRI house' travelled to Victoria during the campaign.

On an international level, Professor van Zandwijk and Dr Soeberg advised the Government of Vietnam on how to start tackling the 'asbestos time-bomb'. They attended several workshops on asbestos hazards and presented a report in July summarising key findings from a five day consultancy in Vietnam regarding asbestos-related disease. Professor van Zandwijk also presented at the 21st Asian Conference on Occupational Health, 2014 (ACOH-2014) in Fukuoka, Japan summarising mesothelioma in Australia and the asbestos time-bomb, with clear lessons for the developing countries.

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.

On the 26th August 2014 the AMR published their third annual report on Mesothelioma in Australia 2013.

Publications, Presentations & Awards

Publications

Cheng NC, van Zandwijk N, Reid G. Cilengitide inhibits attachment and invasion of malignant pleural mesothelioma cells through antagonism of integrins $\alpha v \beta 3$ and $\alpha v \beta 5$. *PLoS One*. 2014; 9(3): e90374. doi:10.1371/journal.pone.0090374.

Kao SC-H, van Zandwijk N, Clarke S. Comment on 'Neutrophil to lymphocyte ratio in malignant pleural mesothelioma'. *British Journal of Cancer*. 2014; 1–2. doi: 10.1038/bjc.2014.185.

Kao SC-H, van Zandwijk N, Clarke S, Vardy J, Lumba S, Tognela A, Ng W. Estimation of an optimal chemotherapy utilization rate for malignant pleural mesothelioma: An evidence-based benchmark for cancer care. *Asia-Pacific Journal of Clinical Oncology*. 2014 Nov 10. doi: 10.1111/ajco.12306.

Kirschner MB, Cheng YY, Armstrong NJ, Lin RCY, Kao SC, Linton A, Klebe S, McCaughan BC, van Zandwijk N, Reid G. MiR-Score: A novel 6-microRNA signature that predicts survival outcomes in patients with malignant pleural mesothelioma. *Molecular Oncology*. 2014; doi: <http://dx.doi.org/10.1016/j.molonc.2014.11.007>.

Lin RCY, Ng S-F, Morris MJ. Gene expression in rat models for inter-generational transmission of islet dysfunction and obesity. *Genomics Data*. 2014; 2 (Dec): 351-353. doi:10.1016/j.gdata.2014.09.013.

Lin RCY, van Zandwijk N, Reid G. MicroRNA therapeutics – back in vogue? *Journal of Investigative Genomics*. 2014; 1(2): 00012. DOI: 10.15406/jig.2014.01.00012.

Linton A, Cheng YY, Griggs K, Kirschner MB, Gattani S, Srikanan S, Kao SC-H, McCaughan BC, Klebe S, van Zandwijk N, Reid G. An RNAi-based screen reveals PLK1, CDK1 and NDC80 as potential therapeutic targets in malignant pleural mesothelioma. *British Journal of Cancer*. 2014 Jan 21;110(2):510-9.

Linton A, Pavlakis N, O'Connell R, Soeberg M, Kao S, Clarke S, Vardy J, van Zandwijk N. Factors associated with survival in a large series of patients with malignant pleural mesothelioma in New South Wales. *British Journal of Cancer*. 2014; 111, 1860-1869. doi: 10.1038/bjc.2014.478.

Soeberg M, van Zandwijk N. The ticking time-bomb of asbestos consumption in the Asian region. *Asian-Pacific Newsletter on Occupational Health and Safety*. 2014; 21:24-27.

Book Chapters

Gulati S, Mulshine JL, **van Zandwijk N.** Chemoprevention of lung cancer and management of early lung cancer. In: Pass HI (ex. editor), Ball D, Scagliotti GV (eds.) *The IASLC Multidisciplinary Approach to Thoracic Oncology*. Aurora, CO: International Association for the Study of Lung Cancer. 2014: Chapter 9: 105-123.

Reid G, Maher SG. Chapter 4: MicroRNAs and Cancer. In: Gray S, Editor, *Epigenetic Cancer Therapy*, Elsevier. 2014: accepted.

Wright C. Chapter 5: lncRNAs and Cancer. In: Gray S, Editor, *Epigenetic Cancer Therapy*, Elsevier. 2014: accepted.

Conference Presentations

Clinical Oncology Society of Australia Annual Scientific Meeting, Melbourne, 2-4 December 2014

Fowler JM, Dhillon HM, Shaw J, Warby A, Coll J, Kao S, Vardy J. Mesothelioma from the patient's perspective: Quality of life and lived experience in people with MPM. *Asia-Pacific Journal of Clinical Oncology*. 2014; 10(Suppl 8):111.

Reid G. Repressed microRNA expression in MPM: small genes, big impact. *Asia-Pacific Journal of Clinical Oncology*. 2014; 10(Suppl 8):110.

Sydney Cancer Conference, Sydney, 26-28 November 2014

Williams M, Kirschner MB, Cheng YY, Wright C, Hanh J, Edelman J, Vallely M, Klebe S, van Zandwijk N, Reid G. Tumour suppressor functions of MIR-192 and MIR-193A-3p in malignant pleural mesothelioma. *Asia-Pacific Journal of Clinical Oncology*. 2014; 10 (Suppl. 7):21.

1st International Conference on Asbestos Awareness & Management. Asbestos Safety & Eradication Agency. Melbourne, 17- 18 November 2014

van Zandwijk N. Asbestos-related cancer research and prevention.

12th International Mesothelioma Interest Group (iMig) 2014, Cape Town 21-24 October 2014

Kao SC, Cooper W, Madore J, Linton A, McCaughan B, Klebe S, Reid G, van Zandwijk N, Scolyer R, Boyer MJ. Programmed death ligand 1 (PD-L1) expression is an independent adverse prognostic factor in malignant pleural mesothelioma (MPM).

Kao SC, Kirschner MB, Cooper W, Tran T, Burgers SA, Korse CM, van de Broek D, Linton A, Edelman J, Vallely M, McCaughan B, Pavlakis N, Clarke SJ, Molloy MP, van Zandwijk N, Reid G. Expression of Secreted Protein Acidic and Rich in Cysteine (SPARC) in malignant pleural mesothelioma (MPM) is associated with short survival.

Kirschner MB, Cheng YY, Armstrong NJ, Lin RCY, Kao SC, Linton A, Klebe S, McCaughan BC, van Zandwijk N, Reid G. Use of a 6-microRNA signature for prognosis in malignant pleural mesothelioma.

Linton A, Pavlakis N, O'Connell R, Kao S, Clarke S, Vardy J, van Zandwijk N. A prognostic index for estimating survival in a large series of patients with malignant pleural mesothelioma.

Malalasekera MA, Dhillon HM, **Warby A, Kao SC, Vardy JL.** "Mortally Wounded": stakeholder perceptions of the malignant

pleural mesothelioma diagnostic process.

Reid G, Williams M, Kirschner MB, Mugridge N, Weiss J, Brahmbhatt H, MacDiarmind J, van Zandwijk N. Targomirs: targeted delivery of a novel microRNA mimic as an approach to treating malignant pleural mesothelioma.

van Zandwijk N, Laws P, MacFarlane E, Brims F, Driscoll T, Sim MR. Mesothelioma in Australia: Data from the Australian Mesothelioma Registry.

Australian Lung Cancer Conference, Brisbane, 16-18 October 2014

Dhillon HM, Kao SC, Warby A, Vardy JL. Healthcare professional perceptions regarding chemotherapy use in treatment of Malignant Pleural Mesothelioma (MPM): quantitative survey results.

Fowler J. Nutritional risks following extrapleural pneumonectomy for malignant pleural mesothelioma.

van Zandwijk N, Soeberg M. Mesothelioma – Close to the peak?

4th International Thoracic Oncology Congress Dresden (ITOCD). Dresden, Germany, 12-14 September 2014.

van Zandwijk N. Mesothelioma Overview.

21st Asian Conference on Occupational Health, 2014 (ACOH-2014) Fukuoka, Japan, 2-3 September 2014

van Zandwijk N, Soeberg M. Asbestos a time-bomb with a long fuse.

van Zandwijk N, Laws P, MacFarlane E, Brims F, Driscoll T, Soeberg M, Sim M. Mesothelioma in Australia.

Queenstown Molecular Biology Meeting, Cancer Biology and Drug Discovery Satellite, Queenstown, New Zealand 24-25 August 2014

Reid G. Targeted delivery of a microRNA mimic as a novel approach to cancer therapy.

Poster Presentations

Sydney Cancer Conference, Sydney, 26-28 November 2014

Wright CM, Kirschner MB, Patel R, Cheng YY, van Zandwijk N, Reid G. Integrative analysis of mRNA expression profiles identifies novel targets for therapy in malignant pleural mesothelioma (MPM). *Asia-Pacific Journal of Clinical Oncology*. 2014; 10 (Suppl. 7):43

12th International Mesothelioma Interest Group (iMig) 2014, Cape Town 21-24 October 2014

Cheng YY, Zheng Y, McLaughlin C, McCaughan BC, Jin HC, Chan FKL, George AM, van Zandwijk N, Reid G. Wnt signalling and malignant pleural mesothelioma (MPM).

Fowler JM, Coll J, McLean J, McCaughan BC, Tan C, Kao S, Vardy J, Dhillon H. Nutritional risk following extrapleural pneumonectomy for malignant pleural mesothelioma

Soeberg M, Young J, Creighton N, Baker D, Aranda S, van Zandwijk N. Epidemiology of malignant mesothelioma, NSW, 1972-2009: Key information for measuring and improving mesothelioma treatment outcomes.

Soeberg M, Anh LM, Tran AT, Huyen NTT, Tran VT, Nguyen HN, Takahashi K, van Zandwijk N. Estimating the incidence of malignant mesothelioma in Vietnam: A descriptive epidemiological study using data from 9 populations-based cancer registries.

Williams M, Kirschner MB, Cheng YY, Wright CM, Hanh J, Edelman JJB, Vallely MP, McCaughan BC, Klebe S, van Zandwijk N, Reid G. Tumour suppressor functions of mir-192 and mir-193a-3p in malignant pleural mesothelioma.

Australian Lung Cancer Conference, Brisbane, 16-18 October 2014

Malalasekera MA, Dhillon HM, Warby A, Kao SC, Vardy JL. Mortally wounded: stakeholder perceptions of the Malignant Pleural Mesothelioma diagnostic process.

Cancer Institute NSW Innovations in Cancer Treatment & Care Conference, Sydney, 17 October 2014

Warby A, Kao SC, Dhillon HM, Vardy JL. Healthcare professional perceptions regarding chemotherapy use in treatment of Malignant Pleural Mesothelioma (MPM): quantitative survey results.

Basic Cardiovascular Sciences (BCVS) conference Las Vegas 14-17 July 2014

Ooi JYY, Bernardo BC, **Lin RCY,** McMullen JR. Identification of miRNA-34 networks in pathological cardiac remodelling.

WIN 2014 Symposium. Paris 23 June 2014

Reid G, Pel M, Kirschner M, Cheng YY, Mugridge N, Weiss J, **Williams M, Wright C,** Klebe S, Brahmbhatt H, MacDiarmid J, **van Zandwijk N.** Targeted delivery of a microRNA mimic as a novel approach to therapy for malignant pleural mesothelioma. (Awarded WIN 2014 Poster Award).

American Society of Clinical Oncology (ASCO) 50th Annual Meeting Chicago May 30-June 3, 2014

Kao SC-H, Kirschner M, Molloy MP, Clarke SJ, Burgers SA, Korse CM, van de Broek D, **van Zandwijk N, Reid G.** Prognostic significance of circulating secreted protein acidic and rich in cysteine (SPARC) in malignant pleural mesothelioma (MPM). *Journal of Clinical Oncology.* 2014; 32; 15s:7580.

Linton A, Pavlakis, O'Connell R, **Soeberg M, Kao SC-H,** Clarke SJ, Vardy JL, **van Zandwijk N.** Old and new prognostic factors in a series of 910 patients with malignant pleural mesothelioma (MPM). *Journal of Clinical Oncology.* 2014; 32; 15s:7586.

4th European Lung Cancer Conference. Geneva 26 -29 March 2014

Kirschner MB, Cheng YY, Kao SC, Armstrong NJ, McCaughan BC, **van Zandwijk N, Reid G.** Identification of a prognostic microRNA signature for patients with malignant pleural mesothelioma undergoing extrapleural pneumonectomy. *Journal of Thoracic Oncology,*

2014; 9 (Suppl 1-4):S50-S51. (Awarded: ESMO/ELCC travel grant & a Concord Repatriation General Hospital Research Travel Scholarship).

The Austrian Society for Haematology and Medical Oncology and the AHOP - The Hemato-oncology Nurses Association in Austria. Innsbruck 10-12 April 2014

Hoda MA, Klikovits T, **Schelch K**, Rozsas A, **Reid G**, **Kirschner M**, **Kao S**, **Hyland R**, Ghanim B, Dekan B, Laszlo V, Dome B, Grusch M, Berger W, **van Zandwijk N**, Klepetko W, Hegedus B. Activin A is a potential novel circulating biomarker in malignant pleural mesothelioma patients.

Invited Talks

van Zandwijk N. Asbestos Diseases Foundation of Australia (ADFA), Awareness Day. Maritime Museum 28 November 2014.

Reid G. MicroRNA replacement: A novel therapeutic approach for malignant mesothelioma. Cancer Council NSW. Eden Gardens, Lane Cove. 18 November 2014.

van Zandwijk N. Launch of the Asbestos Awareness Month Campaign, ADRI. 31 October 2014.

Reid G. Aberrant microRNA expression in malignant pleural mesothelioma: from biomarkers to therapeutic targets. The Garvan Institute of Medical Research, Cancer Division Seminar Series. 17 September 2014.

van Zandwijk N, **Soeberg M**. Financial burden of asbestos-related diseases: medical, compensation and environmental costs. Workshop on asbestos and community health. Ha Noi, Vietnam. 17 July 2014.

van Zandwijk N. Current asbestos research. Asbestosis & Mesothelioma Support Group (AMSG). Gold Coast. 20 June 2014.

Reid G. Restoring microRNA expression in mesothelioma: Towards a phase I clinical

trial. Woolcock Institute of Medical Research. Seminar Series. 23 May 2014.

van Zandwijk N. Tiny magic bullets. Sydney Innovation and Research Symposium 2014. Sydney Local Health District. Australia Technology Park, Eveleigh. 16 May 2014.

Soeberg M, **van Zandwijk N**. Prevention of asbestos-related diseases: an epidemiological perspective. Workshop on Asbestos and Asbestos-Related Disease organised by the Vietnam Ministry of Labours, Invalids and Social Affairs and Union-Aid Abroad (APHEDA). May 2014.

Reid G. Translation Research at the ADRI: the story so far. Keynote Presentation, Sydney Catalyst Early Career Researcher Symposium. 14th April 2014.

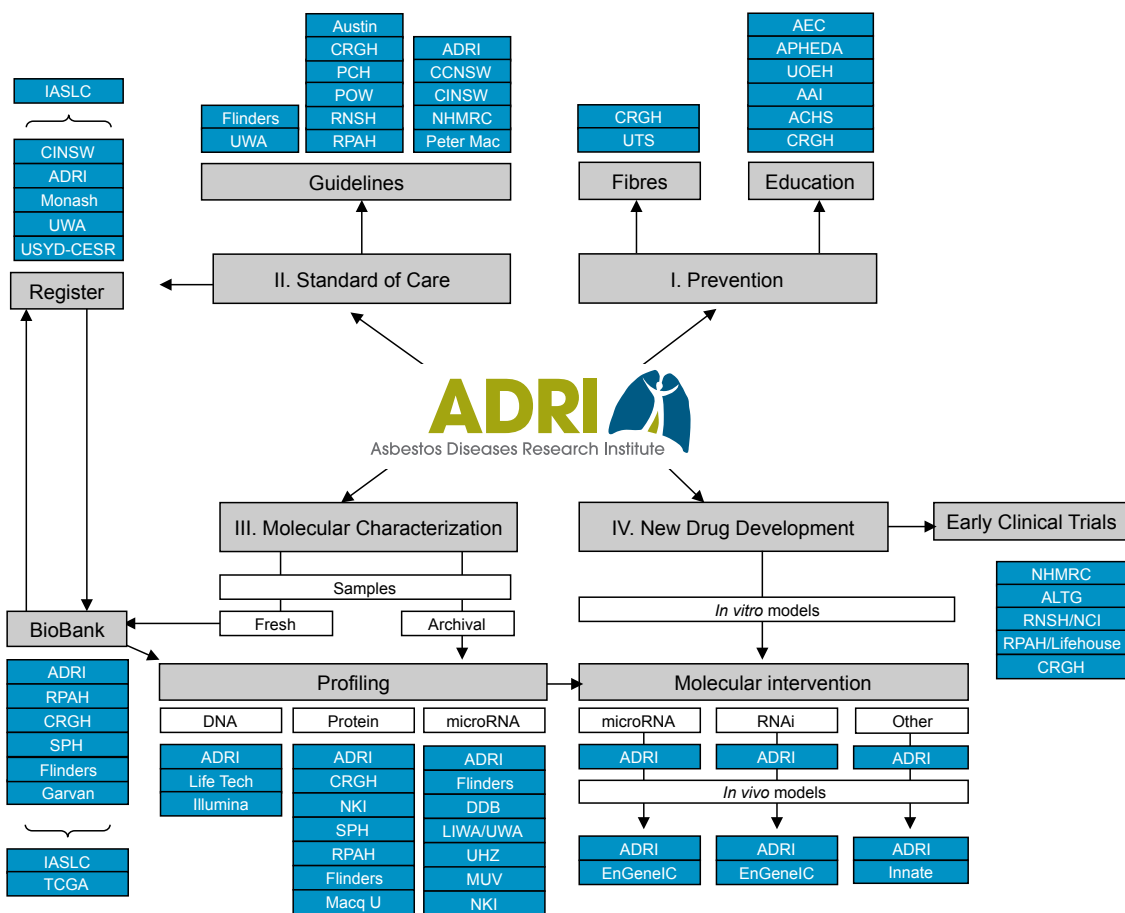
Soeberg M. Current epidemiological research in malignant mesothelioma. Presentation on current trends and directions in mesothelioma research and clinical practice at the inaugural Clinical Research Forum, Chris O'Brien Lifehouse. April 2014.

van Zandwijk N. Asbestos-related disease surveillance: International and Australian context. Asbestos hazards workshop (Union Aid Abroad-APHEDA). Hanoi, Vietnam. 25 February 2014.

van Zandwijk N. Current status of treatment and research in asbestos-related diseases. Asbestos Injuries Compensation Fund. Sydney. 20 February 2014.

Research Collaborators

The ADRI continued to strengthen its ties not only with universities (University of Sydney, UTS, Macquarie Uni), hospitals (Concord, Royal Prince Alfred, Royal North Shore) and health services (Sydney Local Health District, Northern Local Health District) private health facilities (Chris O'Brien Lifehouse, Northern Cancer Institute, Strathfield Private) and several national and international organisations including: Cancer Institute NSW (Australian Mesothelioma Registry), National Health and Medical Research Council (NHMRC) (Guidelines development), The Cancer Genome Consortium (contribution of ADRI to project on Mesothelioma genomics), the International Association for the Study of Lung Cancer, providing a direct interface between cutting-edge research (excellence) and clinical practice. These ties are illustrated below in relation to areas of research.



- AAI Asian Asbestos Initiative
- ACHS Australian Council of Health Standards
- ADRI Asbestos Diseases Research Institute
- AEC Asbestos Education Committee
- ALTG Australasian Lung cancer Trials Group
- APHEDA Australasian People for Health, Education and Development Abroad
- Austin Austin Hospital
- CCNSW Cancer Council NSW
- CINSW Cancer Institute NSW
- Lifehouse Chris O'Brien Lifehouse
- CRGH Concord Repatriation General Hospital
- DDB Dust Diseases Board of NSW
- EnGeneIC EnGeneIC Ltd (biotechnology) Sydney
- Flinders Flinders University
- Garvan Garvan Institute of Medical Research
- IASLC International Association for the Study of Lung Cancer
- Illumina Illumina Inc.
- Innate Innate Therapeutics Ltd
- Life Tech Life Technologies
- LIWA Lung Institute of Western Australia

- Macq Uni Macquarie University
- MUV Medical University of Vienna
- Monash Monash University
- NHMRC National Health & Medical Research Council
- NKI Netherlands Cancer Institute, The Netherlands
- NCI Northern Cancer Institute
- Peter Mac Peter MacCallum Cancer Centre
- PCH Prince Charles Hospital
- POW Prince of Wales Hospital
- RNSH Royal North Shore Hospital
- RPAH Royal Prince Alfred Hospital
- SPH Strathfield Private Hospital
- TCGA The Cancer Genome Atlas
- UOEH University of Occupational & Environmental Health, Fukuoka, Japan
- USYD-CESR University of Sydney, Cancer Epidemiology and Services Research
- UTS University of Technology Sydney
- UWA University of Western Australia
- UHZ University Hospital Zurich

Financial Summary

Profit and Loss Statement	2013-14	2012-13
Revenues		
Research	2,106,053	2,229,764
Fundraising	797,796	308,649
Interest	192,212	223,563
Total	3,096,061	2,761,976
Expenses		
Employee Benefits	1,846,822	1,716,838
Research consumables/equipment	367,590	355,256
Office expenses	224,517	207,463
Depreciation	403,748	424,749
Total	2,842,677	2,704,306
Surplus / Deficit for the period	253,384	57,670

Balance Sheet	30/06/2014	30/06/2013
Assets		
Cash and cash equivalents	5,765,147	4,904,982
Trade and other receivables	78,412	291,930
Property Plant and Equipment	9,021,448	9,405,196
Total	14,865,007	14,602,108
Liabilities		
Trade and other payables	921,532	916,034
Employee provisions	85,062	81,045
Total	1,006,594	997,079
Net Assets	13,858,413	13,605,029

The figures above have been extracted from the Audited Financial Statements of ADRF for the relevant periods.

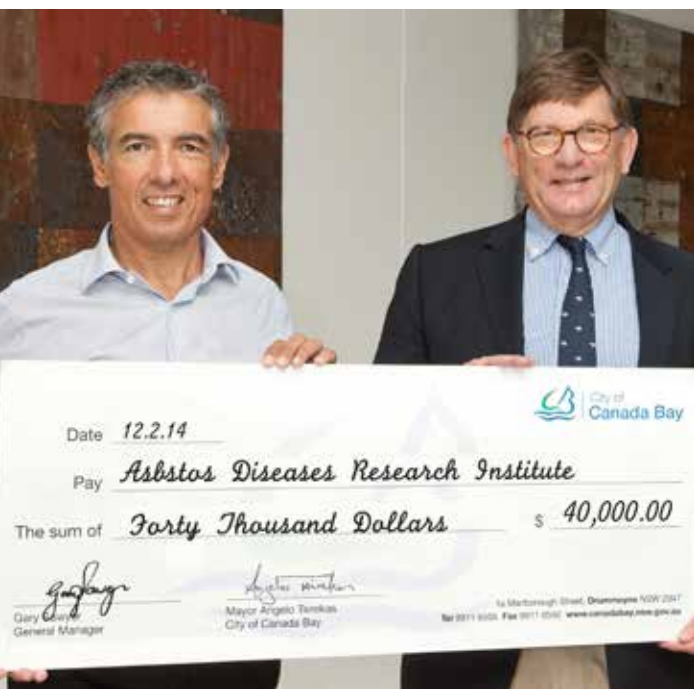
The full audited financial statements are available at www.adri.org.au

Supporters

As a diseases orientated research institute tackling an Australian legacy the ADRI welcomes visitors and greatly appreciates the community's on-going support. Fundraising for the ADRI is critically important and regardless of the size of individual donations, collectively without this support we would not be able to continue our high impact programs. We have listed below all of our donors, including some of their stories, but we would like to extend our heartfelt thanks to everyone who donated in 2014.



Turner Freeman has most generously donated \$40,000.00 to the ADRI to support a much needed position of Mesothelioma Support Coordinator. Jocelyn Mclean joined ADRI in June as our inaugural Mesothelioma Support Coordinator after working as the Case Manager for Thoracic Surgery at Royal Prince Alfred Hospital where she had been since 1994. This generous support by Turner Freeman will allow ADRI to make a positive difference to the lives of malignant mesothelioma patients and their carers. In this role Jocelyn will continue to support patients, provide professional and public education about the disease and treatment options, and contribute to the clinical research that is currently taking place within ADRI.



The Mayor of **Canada Bay Council**, Mr Angelo Tsirekas, and General Manager, Mr Gary Sawyer, presented a cheque for \$40,000.00 to ADRI on the 12th February. These funds were generously donated through the Mayor's Golf Day held each year to support a local charity and in 2013 he supported the research efforts at ADRI. The Golf Day, coinciding with the Asbestos Awareness Campaign, was held on the 22nd November 2013 at Massey Park Golf Club. The event was kindly MC'd by Mr Don Burke who is an Asbestos Awareness Ambassador. Through the Mayor and his team's expert skills \$40,000.00 was generously raised. We would like to thank all those people who made this event so successful.

Mrs Yvonne Tully in June continued her generous support of Dr Michaela Kirschner through the **Jim Tully Memorial Bequest** which commenced in 2010. Michaela came to ADRI in 2009 having completed her PhD at the Ruprecht-Karls-University Heidelberg, Germany. In the last year her work at ADRI included the identification of a combination of microRNAs which enables us to predict the survival outcomes of mesothelioma patients, in particular those undergoing surgery. In the future this microRNA signature, the miR-Score, has the potential to allow better selection of patients for surgery and therefore help to personalise treatment of mesothelioma. In October 2014 Michaela returned to Europe to join the mesothelioma research team in the Division of Thoracic Surgery at the University Hospital in Zurich and will continue to collaborate closely with the ADRI.

In July **Michelle O'Connor** took part in The RunMelbourne event to raise funds for research into asbestos-related diseases at ADRI as she lost her father, Frank Bosmans, to mesothelioma. The Age Run Melbourne is more than a fun



Emily Wong



Xiao Fang Gao opening the Andrew Lloyd Laboratory



ADFA Treasurer, Mrs Helen Davis, Prof. Nico van Zandwijk, ADRI Director, and Mr Barry Robson, ADFA President.

run as it is designed for many participants at all levels, from 3kms for kids up to a half marathon, and it is an opportunity to give back to the community by raising funds for a cause close to their heart. Michelle did the half-marathon! It is an amazing effort by most people's standards. Michelle wrote: "The day was perfect, with the sun shining and thousands of people running for a special cause. It was an amazing experience, even though it was personally challenging. I managed to complete the course in 2 hours, 1 minute, 20 seconds!" Michelle went on to say: "This was a very special journey for myself, my mum and my family as we carried dad's memory with us along the way. I am so very grateful for everyone's kindness in donating to a cause that may one day find a cure for Mesothelioma, so that others don't have to experience the protracted suffering my dad endured." We would like to thank all those people who so generously supported Michelle and donated to ADRI. Through Michelle's efforts she raised \$2852.50 – far exceeding all expectations. Thank you. Michelle's final note is: "Although I struggled

much more than I thought I would, it is amazing what the mind and body can do, when you have a reason to want to. Find meaning, and anything is possible!"

In August **Emily Wong** ran the City2Surf in memory of her uncle, Graham Weismantel who passed away from malignant mesothelioma in May 2009. Emily's aim was to raise \$350 to support research at ADRI. Emily is the niece of Jenny Weismantel who is a volunteer at ADRI. Emily not only ran the 14km to Bondi in grand style but she also managed to raise an astounding \$1,685.00. On behalf of the ADRI we would like to thank Emily, and her generous supporters, for her wonderful achievements. Well done!

On the 7th October at a small function at the ADRI the **Andrew Lloyd Laboratory** was officially opened by Andrew's partner Xiao Fang Gao, accompanied by Andrew's sister, Jennie Lloyd. The Laboratory was named in Andrew's honour because of his extraordinary generosity

to support research into asbestos-related diseases so that others may not suffer in the future. Andrew's name will be immortalised in the ADRI's history.

Many supporters participated in the **Blue Lamington Drive** during Asbestos Awareness Month (1-30 November). The Blue Lamingtons — bearing the similar colour as deadly asbestos — are intended to raise awareness of the dangers of asbestos and to generate vital funds for research into asbestos-related diseases at the ADRI. We would like to thank all those people who bravely took on the task of making blue lamingtons and collecting a gold coin donation to raise awareness with their colleagues, family and friends of the dangers of asbestos when renovating or maintaining homes.

Asbestosis and Mesothelioma Support Group, now the **Asbestosis & Mesothelioma Association of Australia (AMAA)**, offers support to victims of asbestos-related diseases on Queensland's Gold Coast, Hinterland region and NSW Tweed and Far North East Areas, which has one of the largest retiree populations in Australia. Mr Nick Bos, President of the AMAA attended the Asbestos Diseases Foundation of Australia's (ADFA) Gala Race Day at Rosehill Gardens on the 1st November where he presented a cheque for \$1,500 to Professor Nico van Zandwijk. Also at the Gala Race Day a patch quilt made and generously donated by AMAA member Kath Nolan was auctioned raising a further \$1,000.00 for research into asbestos-related diseases at ADRI.

On the 14th November **Enfield-Croydon Park Sub Branch of the RSL** continued to support research at ADRI by donating \$5,000. In 2013 they donated substantial funds which enabled us to purchase much needed equipment for the laboratory.

ADFA is a community-based group providing support for people living with asbestos-related diseases, family members, carers and friends. They have been great supporters of, and work closely with, the ADRI and at **ADFA's** Memorial Day on the 28th November, Mr Barry Robson, President, presented a cheque to Professor Nico van Zandwijk for \$45,000 to support research into asbestos-related diseases.

Volunteers

Mrs Suzanne Mouthaan joined the ADRI in 2013 as a volunteer. Previously, Sue was an executive in primary schools and the Itinerant Vision Support Service with the NSW Department of Education. She has a Bachelor of Educational Administration and graduate and post graduate studies in Hearing and Vision and Multicultural education. Sue has assisted the Administrative Team and is working with Professor Janette Vardy in the Sydney Survivorship Centre at Concord Hospital.

Mrs Jenny Weismantel (below) joined the ADRI in 2012 as a volunteer through the Concord Hospital Volunteers. Jenny has an accounting degree and her administrative skills have made her a valued member of our team. Jenny has assisted in entering retrospective data into the eTapestry and Endnote databases.



Geoff & Karin Wicks are the curators and chauffeurs of 'Betty', the ADRI model house, in collaboration with the Asbestos Education Committee. Geoff and Karen have worked tirelessly again this year, including weekends and public holidays, to raise awareness of the dangers of asbestos when renovating or maintaining the home. During the year they have travelled thousands of kilometres to many regional centres, conducting community and media events to raise awareness of the dangers of asbestos. As part of the National Asbestos Awareness Campaign they took Betty to Melbourne this year for the Asbestos Safety and Eradication Agency's 1st international conference and toured regional Victoria.

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Asbestos Diseases Research Institute

Gate 3 Hospital Road
Concord 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

ABN 79 121 168 867