

2013 annual report



Asbestos Diseases Research Institute

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Our 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 still increasing 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 Australians unfortunately exposed to asbestos.

Key statistics

Malignant mesothelioma in Australia

Measuring rates of malignant mesothelioma is an important way to assess the overall burden of asbestos-related disease in Australia. This is because there is a strong causal association between asbestos exposure and malignant mesothelioma, high-quality data at the population level are available to measure mesothelioma incidence, mortality and survival, and these data can be monitored over time.

Data on the number of people with newly diagnosed malignant mesothelioma (incidence) and the number of deaths from malignant mesothelioma (mortality) is available at the national and state- and territory-levels in Australia. From these data, it is possible to estimate the rate in the Australian population of mesothelioma incidence and mortality, most often expressed as the rate of incident cases or deaths per 100,000 people, per year.

Two sets of national data can be used to count the number of people newly diagnosed with malignant mesothelioma and the number of people who have died from malignant mesothelioma. The Australian Cancer Database contains information about each new case of mesothelioma reported in each state and territory between 1982 and 2009. Complete data on the number of deaths from mesothelioma are also available from 1997 to 2009, with provisional data available for 2010 and 2011.

Information about more recent cases of mesothelioma is available from the Australian Mesothelioma Registry. The Registry was established in July 2010 making it difficult to count the new cases of mesothelioma that occurred over that whole year. However,

the Registry contains data for people newly diagnosed with malignant mesothelioma from January 2011 to December 2012. A strength of the Australian Mesothelioma Registry is that asbestos exposure is able to be collected."

Number of people with newly diagnosed malignant mesothelioma, 1982-2009 and 2011-2012

The total number of people with newly diagnosed malignant mesothelioma from 1982 to 2009 was 11,667,¹ with men making up

85% of all incident cases. Since 2003, approximately 600 cases of newly diagnosed malignant mesothelioma cases have been reported each year. Data on the number of people with newly diagnosed malignant mesothelioma in 2010 are currently not available.

A total of 619 people from 1 January 2012 to 31 December 2012 were newly diagnosed with malignant mesothelioma in Australia. People newly diagnosed in 2012 were more likely to have pleural mesothelioma (94%), be male (79%), and be 70 years of age or older (62%). In 2011, 639 people were newly diagnosed with malignant mesothelioma bringing the total for 2011-2012 to 1,258. These numbers were based on data from the Australian Mesothelioma Registry as at 30 June 2013.²

Number of people who died from malignant mesothelioma, 1997-2009

A total of 6,492 people were recorded as having died from malignant mesothelioma from 1997 to 2009 (Figure 1).¹ In 2009, 584 people died from malignant mesothelioma. Data reported by the Australian

11,667

Number of people with newly diagnosed malignant mesothelioma, 1982-2009 and 2011-2012

6,492

Number of people who died from malignant mesothelioma, 1997-2009

639

People were newly diagnosed with malignant mesothelioma in 2011

606

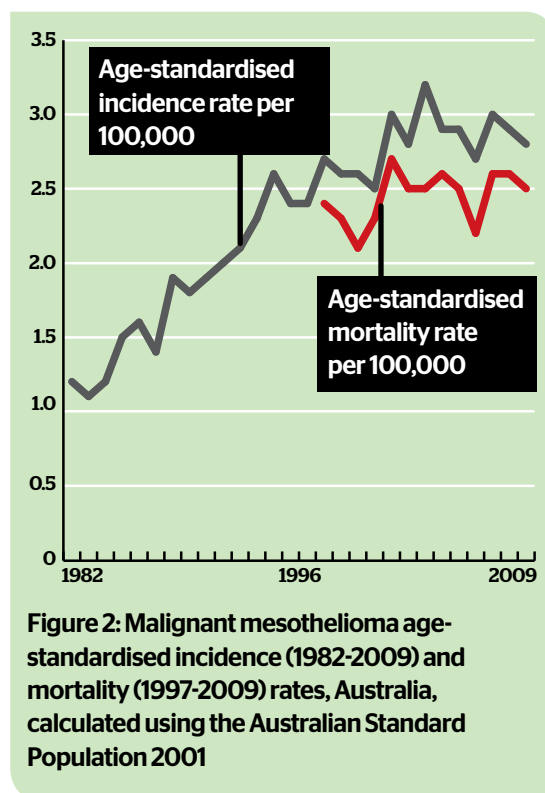
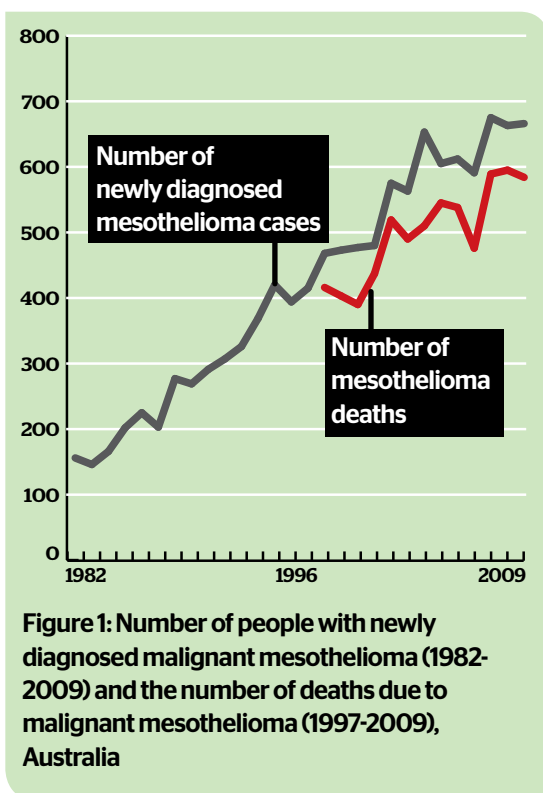
People died from malignant mesothelioma in 2011

44%

The probability of surviving up to one year after the diagnosis of malignant mesothelioma

6%

Estimate of the probability of surviving five years after a malignant mesothelioma diagnosis



Institute of Health and Welfare up to 2009 is final. Data are also available for 2010 and 2011 (634 and 606 deaths respectively)¹, but these figures are subject to revision as more up-to-date mortality data are received.

Age-standardised incidence rates, 1982-2009 and 2011-2012

The age-standardised malignant mesothelioma incidence rate in 2012 was 2.4 per 100,000.² This incidence rate applies equally across males and females and across all states and territories. When broken down by sex, the age-standardised incidence rate for men was 4.3 per 100,000 and 0.8 per 100,000 for women.

There was also variation in the age-standardised incidence rate by jurisdiction. Western Australia had a higher age-standardised incidence rate compared to other states and

territories, 4.3 per 100,000, reflecting the previously high-levels of asbestos consumption in that state.

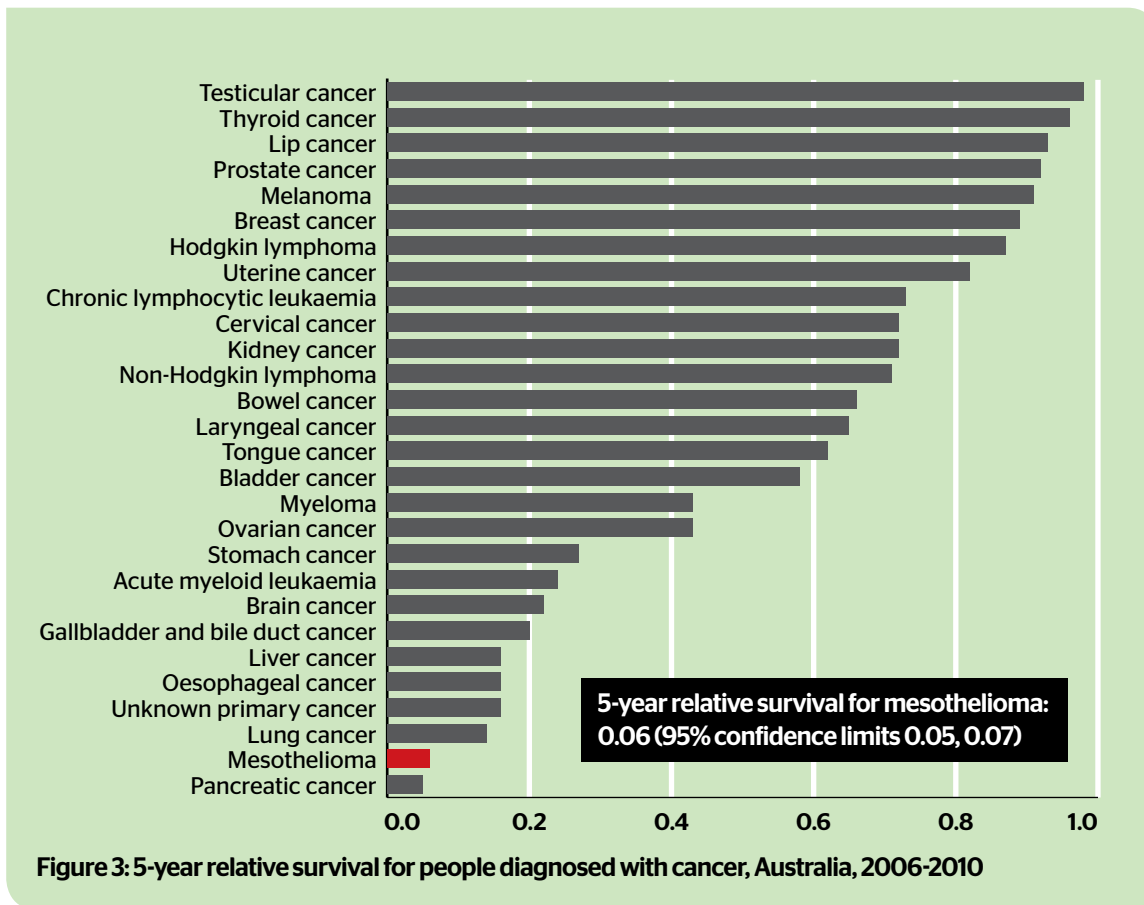
The age-standardised incidence rate was 1.2 per 100,000 in 1982 and 2.8 per 100,000 in 2009, with the increase in the rate over time being greater in the 1980s and 1990s (Figure 2).

Age-standardised mortality rate

The age-standardised malignant mesothelioma mortality rate in 2009 was 2.5 per 100,000, with a rate of 2.3 per 100,000 in 1997 suggesting little change over time in age-standardised mortality rates. The age-standardised mortality rates were similar to the age-standardised incidence rates reflecting the aggressive nature of disease progression.

References

1. Safe Work Australia 2013. Mesothelioma in Australia: Incidence 1982 to 2009, Mortality 1997 to 2011. Canberra: Safe Work Australia
2. Australian Mesothelioma Registry 2013. 2nd Annual Report Mesothelioma in Australia 2012. New South Wales: Cancer Institute NSW
3. Australian Institute of Health and Welfare (AIHW) 2012. Cancer survival and prevalence in Australia: period estimates from 1982 to 2010. Cancer Series no. 69. Cat. No. CAN65. Canberra: AIHW.



Relative survival

Compared to other cancers, people diagnosed with malignant mesothelioma are considered to have a poor prognosis with a 5-year relative survival of less than 0.10 (Figure 3).³ Relative survival is a commonly used — at the population level — to measure the probability of survival following a cancer diagnosis where non-cancer deaths have been accounted for. The probability of surviving up to 1-year following a malignant mesothelioma diagnosis in 2006-2010 was 44% (1-year relative survival of 0.44). However, the probability of surviving up to 5-years after a malignant mesothelioma diagnosis was estimated to be 6% (5-year relative survival of 0.06). There have been incremental changes in 1-year relative survival in Australia, but little change in longer-term 5-year relative survival.

Asbestos exposure

One of the objectives of the recently established Australian Mesothelioma Registry is to document asbestos or carcinogenic exposures for people with newly diagnosed

malignant mesothelioma. These data can assist in determining any shifts in the sources of exposure to asbestos or other carcinogens.

Complete asbestos exposure data from 229 people with newly diagnosed malignant mesothelioma, recorded on the Australian Mesothelioma Registry, was available as at 30 June 2013.² ‘Possible’ or ‘probable’ asbestos exposure in occupational settings was found in 144 people. An additional 80 people were identified who had no indication of occupational exposure to asbestos. From this group, 70 people had ‘possible’ or ‘probable’ exposure to asbestos in non-occupational settings. Fifteen people were identified as having no occupational or non-occupational exposure to asbestos above background exposure levels.

Ongoing collection and monitoring of asbestos exposure in people with newly diagnosed malignant mesothelioma is important in understanding how Australia should best respond to the current and future burden of asbestos-related disease, including asbestos exposure in non-occupational settings.

2013 highlights



ADRI received a bequest from Andrew Lloyd, allowing researchers to bring the new treatment approach into the clinical trial stage without any interruption.

ADRI's new treatment concept for malignant pleural mesothelioma was presented by Dr Glen Reid at the 2013 annual conference of the American Society for Clinical Oncology in Chicago.

Publication of this new treatment concept followed in the December 2013 issue of *Annals of Oncology*.

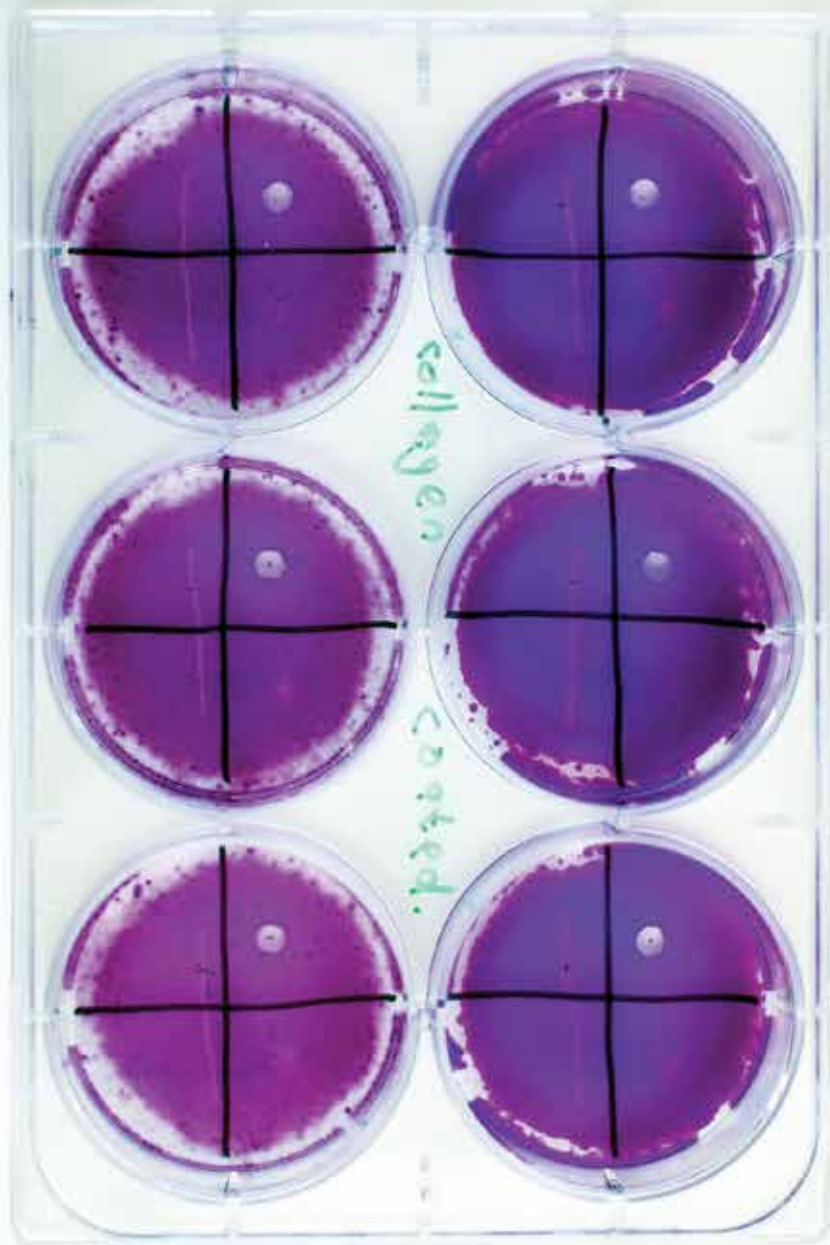
Glen Reid is pictured on the cover page and page 19


ADRI researchers were asked for expert advice on asbestos problems by the governments of Vietnam and Laos.

ADRI researcher Michaela Kirschner was invited to attend the prestigious tutorial conference on Cancer Biomarker Development organized by the European Organization for Research and Treatment of Cancer (EORTC) in Brussels.

ADRI produced a record number of 22 peer-reviewed publications.

ADRI made major contributions (including membership of the core program committee and local organizing committee, session chair and discussant) to the 2013 World Conference on Lung Cancer (WCLC).





Organisational structure

The ADRI Research Team has grown steadily since the opening of the Bernie Banton Centre in 2009. The growth of the research team is dependent on peer-reviewed grant funding. Through the hard work and dedication of the team our success is increasing. The research team is supported by a small administrative team, and both groups report to the ADRI Director, who reports to the Asbestos Diseases Research Foundation.

ADRF chair's report

I am pleased to report that Asbestos Diseases Research Foundation (ADRF) has had another successful year in 2013 in promoting and facilitating research into asbestos diseases, with the aim of assisting those who suffer as a result of exposure to asbestos. It also promotes awareness of the need for prevention of, and the risks of contracting, asbestos and other dust diseases. The Foundation is authorised to operate the Asbestos Diseases Research Institute (ADRI), and to raise funds for research and the operation of its research facilities.

The Foundation's Code of Conduct was reviewed and accepted during 2013 and a Charter formulated. Other events occurring during 2013 included the appointment of Dr Tim Sinclair, General Manager of Concord Repatriation Hospital, to the Board as the representative of the Sydney Local Health District (SLHD), replacing Mr Garry Miller who resigned from the Board in March. Dr Christopher Clarke was also invited to join the Board and will take up his position early next year. In June 2013 the ADRF signed a Tripartite Agreement with the SLHD and the Commonwealth of Australia committing \$3.3 million to the building of a Translational Research Facility on the Concord Campus.

During the year the ADRI succeeded in attracting research funding including two grants from Comcare's Asbestos Innovation Fund. One of these grants assisted in the production of much needed Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma which were accepted by the National Health & Medical Research Council of Australia in July 2013. As part of the Board's commitment to seek much needed funds to support the Institute's research activities I am pleased to report that in 2013 the ADRI received a substantial donation from the Andrew Lloyd Family.

This donation, over five years, will help to support a clinical trial into a newly developed drug therapy for the treatment of malignant mesothelioma commencing in early 2014.

Now in its fifth year of operation, the ADRI highlighted its research outcomes at its Symposium on Translational Research Progress in Malignant Mesothelioma, opened by the Minister for Health and Minister for Medical Research, The Hon Jillian Skinner, in October 2013. The Symposium coincided with the 15th World Conference on Lung Cancer held in Sydney and profited from the attending international experts.

Professor Nico van Zandwijk and his

“ The ADRI succeeded in attracting research funding including two grants from Comcare's Asbestos Innovation Fund

team of able and dedicated researchers and the administrative staff of the Foundation are worthy of gratitude and congratulations for their devotion to all aspects of its work. On behalf of the Board I convey our gratitude and congratulations.



John O'Meally AM RFD
Chair

Director's report

It gives me great pleasure to present the 2013 Annual Report. In the fifth year of ADRI's existence, important progress has been made, as shown in this report. This major progress is the direct consequence of ADRI's excellent research output. I am especially pleased to see that after five years ADRI is covering a broad research area, from molecular studies identifying basic characteristics of asbestos-related disease and new targets for treatment, to epidemiological and quality of life studies. Looking at the record number of peer-reviewed papers accepted in 2013, we may conclude that ADRI research is well focused.

“ Looking at the record number of peer-reviewed papers accepted in 2013, we may conclude that ADRI research is well focused.

Our studies investigating microRNAs in malignant mesothelioma represent one of the most important research subjects of the last five years. These studies, accurately measuring the presence of microRNAs in blood, normal and tumour cells, have not only provided a number of candidate diagnostic and prognostic biomarkers but also supplied the basis of a concept for a new treatment approach for malignant pleural mesothelioma. The drafting of a clinical research protocol for first-in-man testing was completed mid 2013 and approved by the ethics committee of Sydney Local Health District in November 2013. Excellent news came in July 2013 when a most generous bequest from the late Andrew Lloyd was announced and we realized that we are able to start clinical experimentation without major interruption.

The new TargomiR treatment concept is based on our discovery that a specific family

of microRNAs is almost completely lost in malignant pleural mesotheliomas. As this particular family of microRNAs is involved in modulating cellular growth and death, the replenishment of them seems to offer unique opportunities to regain control over uninhibited tumour cell growth. In this project ADRI is fortunate to join forces with EnGeneIC, the biotech firm that invented the minicell as an efficient drug carrier. The microRNAs lost in malignant mesothelioma cells are expected to be replenished by antibody-guided minicells. The therapy concept resembles the Trojan Horse story, where tumour cells absorbing microRNA mimics delivered by antibody-guided minicells are bound to slow or stop growing. The cooperation with EnGeneIC minicell has significantly accelerated the usual transition time from bench to bedside. We are especially excited that Dr Glen Reid, who established ADRI's microRNA research in 2013, has received a second grant to further explore how minicells can be optimally targeted towards tumour cells.

The national Guidelines for the Diagnosis and Treatment of malignant pleural mesothelioma were approved by NHMRC in July 2013 and have become available in electronic form (disc and online) and in print in September 2013. The guidelines also appeared in an article form in December. I would like to once more congratulate the members of the steering committee and the authors of the various chapters for their excellent contribution and to complete this amazing job within the allocated time. A special thank you goes to Victoria Keena, who invested many hours in this successful project.

ADRI has made a major contributions to the October 2013 World Lung Cancer Conference in Sydney through memberships of the program committee, the local organizing committee and as discussants and session chairs. In addition ADRI researchers made 10 contributions to oral and poster sessions.

On an international level, ADRI was active in advising the Governments of



Vietnam and Laos about how to start tackling the asbestos time-bomb. Epidemiological evidence, that all forms of asbestos are carcinogenic, was summarised together with Australian data pointing to the dangers of asbestos in a non-occupational situation. A complete ban is the only reasonable way forward.

ADRI also presented at the 6th Asian Asbestos Initiative (AAI) meeting in Manila, summarizing the Australian asbestos legacy, with clear lessons for the developing countries. A similar presentation was given in Christchurch for an audience directly involved in the consequences of the Canterbury earthquake. At a national level the spectrum of asbestos-related disease and state-of-the-art diagnosis and treatment of malignant mesothelioma were reviewed at the first public meeting Asbestos Safety and Eradication Agency in Sydney during Asbestos Awareness week. At a state level ADRI together with the Asbestos Education Committee was involved in the successful asbestos awareness campaign that uses "Betty, the ADRI house" to educate the public to be cautious with handling asbestos-

containing materials.

I am very pleased to see the number of friends of ADRI growing again in 2013. It was an honour to receive many donations, sometimes accompanied by a moving letter from family and friends of asbestos victims. Let me assure you once more that these wonderful contributions are well used and directly invested in ADRI's best research efforts.

The 2013 annual report provides another opportunity to thank the ADRI team that has worked so hard and well towards a better future for all of us. Thanks should also go to the ADRF board, headed by Mr John O'Meally AM RFD and Deputy Chair Ms Sylvia Kidziak AM, Sydney's Local Health District, and the new general manager of Concord Hospital Mr Tim Sinclair. They all made an important contribution to the prosperity of ADRI in 2013.

Professor Nico van Zandwijk
Director

ADRF Board

Mr John O’Meally AM RFD

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. Appointed 22 February 2012

Ms Sylvia Kidziak AM

Deputy Chair

Representative of - Workers’ Compensation Dust Diseases Board of NSW

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

Representative of - 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, AustralianSuper and Manufacturing Excellence Taskforce of Australia. Paul was on the Asbestos Management Review Advisory Group, as well as once being on the Boards of PHEDA, 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 International Metalworkers Federation (IMF) at numerous international asbestos conferences.
Appointed: 28 November 2007

Col. Professor Robert Lusby
Representative of - ANZAC Health & 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 United Nations Peacekeeping Force, in Bougainville with the Peace Monitoring Group and in 1999 he served with the INTERFET forces in East Timor. In addition, he was the Consultant Surgeon to the Australian Defence Force.
Appointed 3 August 2012

Ms Rita Mallia
Representative of - Workers' Compensation Dust Diseases Board of NSW

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 Dust Diseases Board and is a Director of United Super Pty Ltd.
Reappointed: 20 August 2009

Mr Barry Robson
Representative of - Asbestos Diseases Foundation of Australia

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.
Appointed: 28 November 2007

Mr Sean O'Sullivan
Representative of - Past & Present Manufacturers & Suppliers of Dust & 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 all matters relating to the corporate affairs for the group including government relations. Sean is a member of the James Hardie's Group 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 Tim Sinclair
Representative of - Sydney Local Health District

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

recipient of the Institute of Public Administration Australia award for Individual Excellence and the Anthea Kerr Award. Appointed: 31 October 2013

Professor Nico van Zandwijk

Foundation Nominee

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, is a Member of the Core Program Committee for the WCLC 2013. He was a member of the national Asbestos Management Review Panel and was Study Coordinator of several international studies, and has authored or co-authored more than 300 peer-reviewed international papers and chapters. In 2007 the Asbestos Diseases Research Foundation, Bernie Banton and the University of Sydney recruited Nico van Zandwijk to the position of ADRI Director and Professor, Sydney Medical School. Appointed: 29 July 2008

Mr Colin Goldrick

Company Secretary

Colin is a past Partner and now Special Counsel with the legal firm of Goldrick Farrell Mullan, heading up their Business and Technology practice group. He also acts as legal counsel to the Foundation. Colin has been a lawyer since 1996, specialising in intellectual property, corporate advisory and commercial law. Prior to that Colin worked in the Information Technology industry for almost 15 years, holding positions ranging from technical support, through to sales and business unit management. He has also worked as a management consultant with CSC, consulting with companies on implementing business change. He advises a number of companies on compliance and governance issues.

Reappointed: 16 May 2012





Our staff

Professor Nico van Zandwijk

Director

Professor Nico van Zandwijk, Director of the Asbestos Diseases Research Institute (ADRI), is Professor of Medicine at the University of Sydney. In 2007 he joined ADRI after a long career in thoracic oncology in Europe. In 1985 he founded the department of thoracic oncology at the Netherlands Cancer Institute and made major contributions to the identification of prognostic factors in lung cancer and malignant mesothelioma, to chemoprevention studies in lung cancer and major national and international clinical trials. He served as secretary (1982-1988) and chair (1988-1994) of the EORTC Lung Cancer Cooperative Group. He chaired the Dutch Guidelines Committee for Diagnosis and Treatment of Lung Cancer and State Committees on Asbestos-related diseases, and Asbestos & Lung Cancer of the Dutch Health Council (2002-08). He was a member of the Board of Directors of the International Association for the Study on Lung Cancer (IASLC) (2005-09) and the advisory board of the Thoracic Oncology Section of the French National Cancer Institute (INca) (2006-2008) and co-chaired the (IASLC) World Conference on Lung Cancer 2011 in Amsterdam and is a member of the Core Program Committee for the WCLC 2013 in Sydney. He has been plenary speaker at ASCO and IASLC meetings and currently serves on the editorial board of *Cancer Prevention Research*, a journal of the AACR. He is a member of the National Lung Cancer Advisory Group of Cancer Australia and the National Asbestos Management Review Panel. He has authored or co-authored more than 250 peer-reviewed international scientific papers and book chapters and has long-standing collaborations with investigators from other states in Australia, Europe, Canada, the US, Japan and Korea.



Research staff

Dr Glen Reid (pictured, front)

Senior Scientist

Dr Glen Reid was appointed ADRI's Senior Research Scientist in April 2009, and he established the Institute's cell and molecular biology labs. His research focuses on the identification of new markers and molecular targets for malignant mesothelioma. Previously he was Principal Investigator, Head of RNAi Product Development for Genesis Research & Development Corporation in New Zealand where he led a cancer RNAi discovery program. He was awarded a PhD from the University of Göttingen in Germany, after which completed his postdoctoral studies with Professor Piet Borst at The Netherlands Cancer Institute in Amsterdam, where his main focus was on the characterization of multidrug resistance proteins.

Dr Christopher Clarke

Senior Clinical Advisor

Dr 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, Bourke and Orange. He is the employee nominated member of 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.

Dr Steven Kao

Clinical Research Fellow

Dr Steven Kao is a medical oncologist at Royal Prince Alfred and Liverpool Hospitals. He completed his PhD at the ADRI and focused his research on predictive and prognostic factors in malignant mesothelioma. Steven has a wide clinical, translational and psycho-social research interest in thoracic cancers including malignant mesothelioma and asbestos-related lung cancers. He was awarded the Premier's Award for Outstanding Cancer Research Scholar from the Cancer Institute, NSW.



Dr Michaela Kirschner (pictured)

The Swift Family Bequest & Jim Tully Fellow

Dr Michaela Kirschner joined as a Postdoctoral Fellow in 2009. Having completed her teaching degree in biology and chemistry, Michaela performed her PhD thesis at the University of Heidelberg and the German Cancer Research Centre in Heidelberg (2005-2009). Her thesis was on preclinical studies on the anti-metastatic effects of drugs in lung cancer and the identification of potential drug target genes. The main focus of Michaela's work at the ADRI is 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. This research is supported by The Swift Family Bequest & Mr Jim Tully Fellowship.

Dr Yuen Yee Cheng

Molecular Biologist

Dr Yuen Yee Cheng joined ADRI as a Research Fellow in March 2010. She completed her PhD at the Chinese University of Hong Kong where she started her research in epigenetic alterations in gastric cancer. She then undertook two years of postdoctoral training at the University of Hong Kong. Epigenetic gene regulation has been the major focus of Dr Cheng's research efforts and her research in epigenetic alterations in cancer has been published in prestigious international journals. At ADRI, Dr Cheng continues her epigenetic study as well as focusing on microRNA profiling of malignant mesothelioma.

Dr Ngan Ching Cheng

Molecular Biologist

Dr Ngan Ching Cheng completed her PhD at the University of Amsterdam, The Netherlands, on neuroblastoma tumour suppressor genes. She then worked on mouse models of Fanconi Anaemia and Fragile X syndrome at the Free University of Amsterdam, the Netherlands Cancer Institute and Erasmus University, Rotterdam. Since her relocation to Sydney in 2001 she has been working on experimental therapies for neuroblastoma using the TH-MYCN mouse model at the Children's Cancer Institute. She is now engaged at the ADRI to work on novel treatments for mesothelioma.



Dr Anthony Linton (pictured)

Biaggio Signorelli Foundation Fellow

Dr Anthony Linton is an oncology fellow at Concord Hospital and started his PhD at ADRI building on the research success of the ADRI to identify new bio-markers and potential targets for new treatment approaches for malignant mesothelioma. Dr Linton has completed a review on the epidemiology of mesothelioma and in particular on the consequences of occupational and environmental asbestos exposure. Dr Linton is supported by the Biaggio Signorelli Foundation.

Ms Casey Wright

Biaggio Signorelli Research Fellow

Casey Wright completed her Bachelor of Science at the University of Queensland in 2004 and was awarded first class honours in 2006. In August 2007, Casey undertook a PhD program entitled "Genomic characterisation of asbestos-related lung cancer" at The Prince Charles Hospital where she was a recipient of an NHMRC Biomedical Postgraduate Scholarship. These studies focussed on investigating gene expression profiles, copy number variations and methylation profiles in asbestos-related lung cancer. Casey has presented her work at several international and national meetings and has received several prizes and awards. She has written and been involved with publications investigating asbestos fibre counting in lung cancer patients, gene expression profiles in asbestos-related lung cancers, and CYP1A1 polymorphisms in lung cancer. Casey is passionate about contributing to research that can potentially revolutionize treatment options, provide greater understanding of biology and provide better quality of life for sufferers of mesothelioma.

Ms Marissa Williams

Research Assistant

Marissa Williams joined in February 2012 as a research assistant. She completed her undergraduate degree of Forensic Biology in Biomedical Science at the University of Technology Sydney and went on to undertake an honours project in paediatric oncology at the Tumour Bank, Westmead Children's Hospital. This project was based on drug-resistance mechanisms of a childhood cancer to novel therapeutics. At ADRI she assists in the investigation of a multitude of projects, mostly looking at the effects of microRNA reintroduction into cell lines. She hopes to pursue a PhD in this area in the near future.



Miss Subothini Srikanan (pictured)

Research Assistant

Subothini Srikanan joined in February 2012. She has been investigating whether treatment of mesothelioma cell lines with small molecule inhibitors is capable of sensitizing them to currently used chemotherapeutic drugs. She is generating mesothelioma cell lines that are resistant to chemotherapeutic drugs such as Cisplatin, Pemetrexed, Gemcitabine and Vinorelbine for the DDB grant. In addition to this she is also involved in general laboratory maintenance.

Dr Matthew Soeberg

Epidemiologist

Dr Matthew Soeberg is a postdoctoral research fellow working on Part I of the ADRI's Cancer Institute NSW Translational Program Grant. He is employed through the University of Sydney's Cancer Epidemiology and Services Research (CESR) group and is based at the Cancer Institute of New South Wales. He will help to develop epidemiological research projects using mesothelioma cancer registry and other data. Matthew completed his PhD at the University of Otago, Wellington in July 2012. Matthew's PhD examined trends and inequalities in cancer survival in New Zealand, 1991-2004, using relative survival and excess mortality rate modelling with linked Census, cancer registry and mortality data. Matthew has a strong interest in maximising the relevance of epidemiological research to policy, practice and improved patient outcomes.

Dr Lauren McCann

Research Fellow

Dr Lauren McCann is a medical student at the University of Sydney, due to complete a Bachelor of Medicine and Bachelor of Surgery in 2015. She joined the ADRI in 2013 to complete a Master of Philosophy concurrently with her medical degree working on identifying new biomarkers for the diagnosis of mesothelioma and identifying molecular targets which could be used to develop new treatments for mesothelioma. She completed an Honours degree in 2003 characterising drug resistance to chemotherapeutic medications for cancer for which she was awarded First Class Honours. She then completed a PhD in 2008 developing a new methodology to — and identifying new anti-angiogenic targets for — cancer treatments in brain and breast cancer. Her research has been published in international journals and presented at international conferences. She has also worked in clinical research, having experience in various aspects of initiating and conducting trials.



Mr Jason Fowler

Research Fellow

Jason Fowler joined ADRI in February 2013 as a Research Fellow undertaking his PhD in the School of Psychology, University of Sydney. Jason completed his undergraduate and initial postgraduate education at the University of Tasmania from 1995 through to 2003. Since then he has been working as a Clinical Psychologist in mental health and has developed a variety of clinical, educational and governance projects. Jason's research project is a longitudinal study of health-related quality of life in people diagnosed with malignant mesothelioma. The project will also examine anxiety and depression, supportive care needs, nutritional status, functional status and markers of inflammation.

Mr Kan Chen (pictured on page 31)

Biobank Officer

Kan Chen joined ADRI as a Biobank Officer in 2013 on a part-time basis to assist with the management, maintenance and development of the tissue bank. He has completed his undergraduate degree of Medical Science at the University of Sydney and worked in a blood bank for a private company. Recently he has also completed a Master in Biomedical Engineering at the University of NSW; he is looking forward to complementing the current biobank system.

Mrs Rebecca Hyland

Database Coordinator

Rebecca Hyland joined the ADRI in 2012 on a part-time basis to assist with the development of the biobank database. Rebecca has a Masters of International Public Health and has experience in the management and maintenance of clinical databases. Rebecca had been the Clinical Database Coordinator of the Ovarian Cancer Study at the Garvan Institute and was a Research Officer at the Dust Disease Board of NSW. Rebecca has co-authored a number of papers asbestos-related diseases.

Ms Anne Warby (pictured)

Research Officer

Anne Warby joined the ADRI in 2013 as a research officer working with Dr Steven Kao. She is responsible for the coordination of two research studies, one investigating chemotherapy utilisation for patients with malignant mesothelioma, and the other a quality of life study in patients with malignant pleural mesothelioma. Anne has extensive experience in project management, clinical trial coordination and high-level administrative support.



Support staff

Ms Victoria Keena (pictured)

Executive Officer

Victoria Keena joined the ADRI in August 2008 as a Senior Consultant after many years as the General Manager of the Woolcock Institute of Medical Research. Victoria assisted with fitout and development of the ADRI since it opened in 2009. She has extensive hands-on experience in the administration of a medical research institute. She has been involved with a variety of funding programs and awards to support science and medical research, such as NH&MRC, ARC, and infrastructure support programs such as the NSW Medical Research Support Program. Victoria has written peer-reviewed journal articles, published annual reports, edited scientific publications and co-authored a number of books, including: Peat J, Elliott E, Baur L, Keena V. Scientific writing: easy when you know how. London: BMJ Books 2002. Victoria is also the Executive Officer for the development of Guidelines of the Diagnosis and Treatment of Malignant Pleural Mesothelioma.

Mr Ross Flemons

Accountant

Ross Flemons joined the ADRI in December 2009 as part time accountant. He was previously Finance Manager of the Woolcock Institute of Medical Research for 14 years. Ross is CPA-qualified and has vast experience with all financial matters relating to independent medical research organisations, including reporting, budgeting, payroll, compliance and financial management.

Ms Kim Mattock

Receptionist

Kim Mattock joined the ADRI in April 2010 as the Receptionist/Administrative Assistant of the Bernie Banton Centre. Kim previously worked in varied administration roles and fields, both corporate and government. Joining ADRI is a return to the Concord Hospital campus for Kim; in a 'previous life' she worked for various specialists throughout the hospital.



Mr Justin Crosbie (pictured)

IT Officer

Justin Crosbie joined ADRI in 2009 as the Information Systems Manager. He has completed a science degree in Information Technology at the University of Technology, Sydney. Justin has previous experience working an information technology consultancy firms and also works for the ANZAC Research Institute on the Concord Campus.

Mrs Jenny Weismantel

Volunteer

Jenny Weismantel joined the ADRI in 2011 as a volunteer through the Concord Hospital Volunteers. Jenny has a Bachelor of Business in accounting and has assisted the administration team in many tasks including the development of the grants calendar and cataloguing of samples from the Australian Mesothelioma Surveillance Program. Jenny has also participated in the development of the Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma as a consumer representative.

Mrs Suzanne Mouthaan

Volunteer

Sue joined ADRI in May, 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 in various tasks including revision of references for the Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma.

Mr Geoff and Mrs Karen Wicks

Volunteers

Geoff and Karen volunteered in 2012 becoming the curators and chauffeur for Betty the ADRI model house. Since her launch in November 2012 Geoff and Karen have supported the Asbestos Awareness campaign by demonstrating Betty to thousands of people around NSW including the Sydney Royal Easter Show, the HIA Sydney Home Show. They have travelled thousands of kilometre to the Hunter, New England, Mid-North Coast and other regions. They have volunteered over 1000 hours each and have helped to educate more than 20,000 people to the dangers of asbestos when renovating or maintain a home.

Our research

MicroRNAs in the blood as biomarkers for malignant pleural mesothelioma (MPM)

Michaela Kirschner

The diagnosis of MPM remains difficult even in patients with known previous exposure to asbestos. An accurate diagnosis can often only be made on a tumour biopsy, but these can be difficult to obtain, since the patient has to be well enough to undergo a thoracoscopy. Finding a biomarker, or flag, that can be measured in a blood sample, rather than in tumour tissue, will be a major step towards less difficult and faster diagnosis of MPM. Exploring biomarker candidates other than proteins, in 2012 ADRI identified the microRNA miR-625-3p as potential blood-based diagnostic marker for MPM. MicroRNAs are small pieces of genetic information that play important roles in regulating the function and life of cells. Dysregulation of microRNAs has been shown to be a major contributor to the development of cancer, and altered expression of microRNAs in tumour tissue has been found to be a useful diagnostic marker for various cancers. Most importantly it is also

possible to measure these microRNAs in the blood, making them ideal candidates for non-invasive diagnostic tests.

In the past year we have been able to validate our findings in additional samples. We have been able to see that miR-625-3p may not only be able to discriminate between patients with MPM and asbestosis or healthy individuals, but also between MPM and lung cancer. To be able to further validate these findings, we have established collaborations with researchers at the Netherlands Cancer Institute in Amsterdam and the Medical University of Vienna. Through these collaborations we have access to larger numbers of samples to measure miR-625-3p. To better use microRNAs in the blood as biomarkers, we have investigated the effect of haemolysis (bursting of red blood cells during blood collection) on the levels of biomarker microRNAs measured in the blood. This research resulted in two publications in *Frontiers in Genetics*.

The importance of tumour suppressor genes in malignant pleural mesothelioma (MPM)

Yuen Yee Cheng

MPM is an aggressive tumour strongly associated with asbestos exposure. It is well

known that inactivation (or silencing) of tumour suppressor genes, through shutting down regulatory regions by a process known as DNA hypermethylation, is crucial role in the progression of MPM.

ZIC1, a tumour suppressor gene silenced through the DNA methylation process in gastric and colorectal cancer, was expressed (present) at high levels in normal mesothelial cells. In contrast, ZIC1 was not expressed in MPM cell lines. We have investigated the molecular biology as well as the functional role of ZIC1 in MPM. Our results indicate that ZIC1 acts as a functional tumour suppressor in MPM and is closely linked to the expression of microRNAs, another class of regulatory molecules in the cell. In particular, microRNA-23a is present in higher levels in tumour samples from patients with shorter survival. We found that when we reintroduced ZIC1 in MPM cells it caused suppression of microRNA-23a expression. These findings will help us better understand the molecular background of MPM, which hopefully will lead to new treatment approaches. These results were published in *Journal of Thoracic Oncology* (2013;8: 1317-1328).

New molecular targets in malignant pleural mesothelioma (MPM)

Anthony Linton & Yuen Yee Cheng

We have assessed a number of genetic

targets involved in cell division and tumour growth, including PLK1, CDK1, NDC80, ERCC1 and Beta-3 Tubulin. In a large, surgical retrospective cohort of patients diagnosed with MPM, PLK1 expression was associated with a significant alteration in prognosis. Furthermore, inhibition of PLK1, CDC2 and NDC80 in MPM cell lines was shown to result in a marked change in cancer cell growth. Such exciting results support the further investigation of therapeutic agents targeting these in animal models and human trials. In contrast, and despite promising results in other malignancies such as NSCLC, however, neither ERCC1 nor Beta-3 Tubulin demonstrates a consistent or measurable impact on MPM cell growth, or influence on the sensitivity of chemotherapy.

MicroRNAs as therapeutic targets in malignant pleural mesothelioma (MPM)

Glen Reid

Previously we observed a significant downregulation of an entire microRNA family – the miR-15/16 group – in MPM tumours samples and cell lines. When the expression of these microRNAs was restored in cell lines using ‘mimics’, growth was inhibited and cells were sensitised to chemotherapeutic agents pemetrexed and



gemcitabine. The growth inhibition was also seen in pre-clinical models. These initial results were presented at the 2013 ASCO meeting in Chicago and published in *Annals of Oncology*. Further to this work, we developed a completely novel 'mesomiR', derived from the consensus sequence of the miR-15/16 family, which we found to have increased activity. We are now undertaking studies to understand the basis of this enhanced consensus microRNA, as well as to understand the mechanism responsible for the downregulation of these and other microRNAs in MPM.

The miR-15/16 work described above has led to the development of a clinical protocol for testing microRNA replacement in patients. The trial, "MesomiR 1: A Phase 0, I study of TargomiRs as 2nd or 3rd line treatment for patients with recurrent MPM and NSCLC", has been approved by Human Research Ethics Committee at Concord and is in the final stage of activation (patient accrual expected to begin in February/March 2014).

Health-related quality of life in malignant mesothelioma (MM)

Steven Kao, Janette Vardy, Haryana Dhillon, Jason Fowler, Jocelyn McLean, Cindy Tan, Anne Warby, Joseph Coll

This multi-site, observational, longitudinal study aims to explore the patient experience of people diagnosed with MM. The project will examine health related quality of life, unmet care needs and anxiety and depression. Optional sub-studies will examine the associations between these variables and other prognostic indicators such as inflammatory biomarkers, nutritional status and functional status.

In 2013, the research protocol for this project was finalised, and the project successfully received endorsement from relevant research cooperatives such as the Australasian Lung Cancer Trials Group and the Psycho-oncology Co-operative Research Group. Interest and participation in the study was negotiated with investigators around the country from 18 hospitals across 5 states and 1 territory.

Lead ethics approval was received from Sydney Local Health District HREC in August 2013 and site-specific approval has subsequently been granted for Concord

General and Repatriation Hospital (CGRH) and Northern Cancer Institute. Site-specific applications are currently in process for 5 out of the 18 additional research sites. Recruitment will start in March 2014.

The project was presented in poster form as part of the trial in progress session at the Clinical Oncology Society of Australia Annual Scientific Meeting in November 2013. Preliminary analyses have been conducted on previously collected quality of life data for a subset of MM patients who had received extra-pleural pneumonectomy surgical treatment. Results of these analyses have been presented at the World Conference on Lung Cancer and at the Postgraduate Cancer Research Symposium at the University of Sydney.

Inhibition of malignant pleural mesothelioma (MPM) cell growth and invasion by cilengitide, a small molecule integrin antagonist

Ngan Ching Cheng

Integrins are membrane adhesion molecules mediating cell-cell and cell-extracellular matrix interactions via binding to their ligands e.g. collagen, laminin, fibronectin, fibrinogen, vitronectin etc. They are crucial for tissue architecture and adaptation of cells to their environment. Unsurprisingly, integrins are implicated in cancer development and cancer growth (spread). Expression of integrins has been implicated in the growth characteristics of MPM. Therefore we have investigated the integrin inhibitor cilengitide from Merck Serono as a potential treatment for MPM. We have analysed the response to cilengitide in 11 MPM cell lines.

Cilengitide caused growth inhibition in MPM cells with a broad range of efficacy. Furthermore, it caused cell detachment and subsequently death of cells sensitive to anoikis (i.e. death of anchorage-dependent cells detached from extracellular matrix). Cilengitide inhibited invasion of MPM cells in monolayer and tumour spheroid cultures.

We have shown that this is mediated by inhibition of the group of 'so called' $\alpha\beta3$ and $\alpha\beta5$ integrins.

Altogether, our data imply that cilengitide may have clinical potential in the treatment of MPM.

Long Noncoding RNAs in malignant pleural mesothelioma (MPM)

Casey Wright

At present there are very few markers that can accurately diagnose or predict disease outcome in patients with MPM. Long noncoding RNAs (lncRNAs) have been found to be important in the regulation of gene expression. Recently, it has been shown that non-coding RNAs can be detected in body fluids (urine and blood). As part of the ADRI research program, we have identified a number of lncRNAs that seem to be specifically present in MPM, and that can potentially be used as a biomarker. Currently we are investigating the plausibility of detecting these lncRNAs in the blood (plasma) of MPM patients, using a cell line model. Preliminary work has shown that certain candidate lncRNAs are detectable in cell culture medium from MPM cell lines. Future work will focus on whether these lncRNAs are also found in plasma from MPM patients. If successful this could potentially lead to a screening test (e.g. a simple blood test). In addition to this work, we are also investigating the function of these lncRNAs in MPM biology. We aim to show that altering the expression of these lncRNAs can affect important cellular processes that are critical to MPM development.

Tumour microRNAs as prognostic biomarkers for surgery

Michaela Kirschner

When diagnosed with MPM, selected patients can be considered for multimodality treatment approaches consisting of chemotherapy, radical surgery and radiotherapy. However, even amongst these highly selected patients, the outcome is variable. In particular the role of radical surgery within these approaches has been controversially discussed in recent years, although it has been shown that when performed by an experienced surgeon radical surgery can result in significantly prolonged survival. Selecting those patients that are likely to benefit from surgery on clinical factors only has however proven to be difficult.

In order to identify novel markers that can aid in patient selection, we have profiled the microRNA content of tumour tissues

from MPM patients with long and short survival following radical surgery. Through this research we have found a number of microRNAs associated with longer survival if found in lower abundance in tumour tissue. These preliminary data have been presented at the World Conference on Lung Cancer held in Sydney in October 2013 and the Markers in Cancer Meeting held in Brussels in November 2013. For further validation of these promising prognostic microRNAs we have established a collaboration with surgeons and researchers at the University Hospital in Zürich, through which we will gain access to additional tumour samples from patients undergoing radical surgery.

Molecular characterisation of malignant pleural mesothelioma (MPM) to identify new biomarkers and potential targets

Lauren McCann

MPM is a disease with few treatment options, late diagnosis, few treatment options, with treatments prolonging a patient's life rather than curing them. This project is aimed at identifying molecular changes that are MPM specific, allowing these molecules to be used as biomarkers for earlier diagnosis of patients with this disease and treatment targets to offer an effective treatment. In addition, we are also aiming to determine the source of these molecules. The two main possibilities are from either the MPM tumour cells themselves or from the tissue ('stroma') that grows around the tumour and supports its growth.

So far, we have studied MPM cells, which can be grown in culture or in animal models, to identify changes in microRNA expression that are associated with MPM. Using qPCR-based microarrays, we have identified a number of microRNAs that are altered and we will investigate the cellular origin of these microRNAs using specific tests for each molecule. Understanding how these molecules may be making an impact on the tumour growth, and whether this can be altered to slow or reduce tumour growth could allow us to target these molecules. This way, we can develop new, more effective treatment approaches that could have a significant impact on patients with this disease.

Survival of patients with Malignant Pleural Mesothelioma (MPM) in NSW

Anthony Linton, Matthew Soeberg

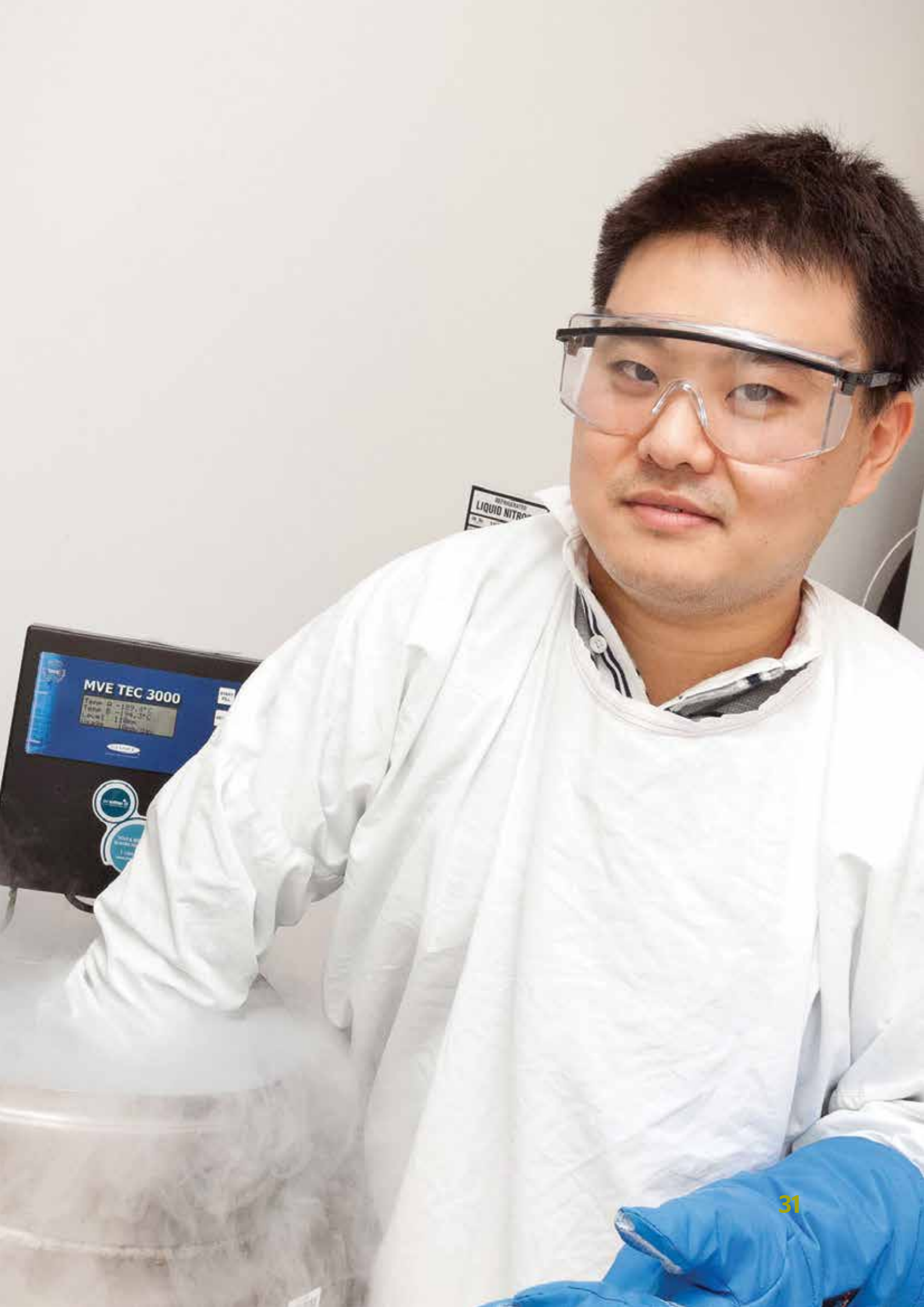
In 2013, thanks to the support of the Biaggio Signorelli Foundation, we were able to continue our laboratory and clinical research into prognostic factors in MPM. With the co-operation of the NSW Dust Diseases Board and oncology and respiratory units across NSW, we have performed one of the largest analyses of long-term survivors with MPM, comprising 910 patients diagnosed between 2002 and 2009. Individual patient data was extracted from medical and surgical records and factors associated with longer (than usual) survival were studied. Approximately 20% of patients diagnosed with MPM were found to survive beyond 20 months. We were able to validate a number of existing, and also to identify new, prognostic factors. We are currently using this data to develop a new prognostic tool to better predict survival in patients with MPM.

Identification of targetable mutations in malignant pleural mesothelioma (MPM)

Casey Wright

Selecting therapies that can be tailored to individual disease characteristics is an important goal in oncology. Currently MPM is not well characterised molecularly. In this project, we aim to identify whether specific subgroups of MPM 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 an initial pilot study of MPM cell lines to identify specific mutations that occur in cancer-related genes and pathways. We hope to extend this work to a larger panel of 30 MPM tissues to identify changes that occur specifically in the tumours themselves. It is hoped that this approach will help to identify new targets in MPM, leading to individualised therapy for MPM patients.





The Australian Mesothelioma Registry

The Australian Mesothelioma Registry (AMR) www.mesothelioma-australia.com was established to collect information about people with mesothelioma. The AMR is set up as a stand-alone database containing information about people diagnosed with mesothelioma from July 1, 2010, in Australia, including information about asbestos exposure.

The aim of the AMR is to:

- Monitor the number of new cases of mesothelioma
- Collect detailed information about people with mesothelioma and their occupational and environmental asbestos exposure.

Historically, although Australia has collected national mesothelioma incidence data for many years, the ability to estimate patterns of exposure in an “at risk population” has been limited. The AMR provides a national resource for researchers to conduct further analysis with the aim of identifying preventable risk factors to assist in reducing mesothelioma in the future.

The AMR is funded by Safe Work Australia and its development and operation is overseen by a consortium of organisations, including some of Australia’s leading experts in asbestos-related diseases and cancer registration. The Cancer Institute NSW is responsible for the management of the AMR. The AMR has developed a relationship with the Cancer Registry of each state and territory in Australia to provide the AMR with information about each person with mesothelioma.

The following organisations have a role in the AMR:

- Safe Work Australia
- Cancer Institute NSW
- The Monash Centre for Occupation and Environmental Health, Monash University
- The Hunter Valley Research Foundation
- Asbestos Diseases Research Institute
- The Cancer Epidemiology and Health Services Research Group, the University of Sydney
- The University of Western Australia and the Western Australian Cancer Registry
- Other State and Territory Cancer Registries (ACT, NSW, NT, QLD, SA, TAS, VIC).

The AMR collects information about cases of mesothelioma to:

- Better understand the relationship between asbestos exposure and mesothelioma
- Better understand the nature and levels of asbestos exposure that can result in mesothelioma
- Identify the groups of workers exposed to potentially dangerous levels of asbestos and to prevent that exposure
- Assist with the development of policies to best deal with the asbestos still present in our environment (mainly our built environment)
- Provide information to assist researchers in undertaking investigations with the aim of preventing mesothelioma in the future
- Identify other potential exposures that may cause mesothelioma.

Prevention through Education

Nico van Zandwijk, Victoria Keena and Matthew Soeberg

Part of ADRI's mission is to contribute to primary prevention - to prevent any exposure to air-borne asbestos fibres. During 2013 ADRI staff participated in various government and community group forums to raise awareness of the dangers of asbestos, including the Asbestos Safety and Eradication Agency's National Asbestos Forum and the Asbestos Diseases Foundation of Australia's Asbestos Awareness Week in November.

Australia is now one of the countries with the highest incidence of malignant mesothelioma in the world and it is hoped that the experience from our asbestos legacy will help our neighbouring countries in Asia to take preventive action. Most of them have seen a rapid increase of asbestos consumption in the last 25-35 years, which is often referred to as the 'ticking time bomb in Asia'.

In June Professor van Zandwijk and Dr Soeberg were invited to Vietnam to consult on diagnosis and registration of asbestos-related disease in that country. Following their visit they submitted a report recommending epidemiological studies be undertaken to more accurately describe the burden of asbestos-related disease in Vietnam. Professor van Zandwijk also spoke at the International Seminar on Asian Asbestos Initiative held in Manila under auspices of the World Health Organisation. This meeting aims to develop strategic approaches towards a total ban of asbestos and its products in the region. Dr Soeberg was invited to a governmental meeting in Laos and was able to underline the importance of not repeating the errors made in other countries.

In December Professor van Zandwijk travelled to New Zealand at the invitation of the Canterbury Rebuild Health and Safety



Group in Christchurch. He provided advice on the major challenges after the Canterbury earthquakes, such as managing asbestos present in most of the damaged buildings/houses.

The Asbestos Education Committee's initiative – 'Betty' the ADRI mobile model house, continued to raise awareness of the dangers of asbestos when renovating or maintaining the home. 'Betty' was on display at Sydney's Royal Easter Show, the HIA Sydney Home Show, AgQuip 2013 in Gunnedah, Parkes and Condobolin Shows. Betty travelled thousands of kilometres to many regional centres in the Hunter, New England, Mid-North Coast and Central West of NSW. During these tours the media, local council representatives and the general public were engaged to ensure the asbestos awareness message was disseminated as far and as wide as possible.

The asbestos awareness message continues to flow through the 'think smart, think safe, think asbestosawareness.com.au' website and Betty's Facebook page: <https://www.facebook.com/BettytheADRIhouse>

Research support

New grants in 2013

Comcare Asbestos Innovation Fund Production and dissemination of evidence-based guidelines for the diagnosis and treatment of malignant mesothelioma Van Zandwijk N, Penman A.

Malignant Pleural Mesothelioma (MPM) is an almost invariably fatal asbestos-induced cancer affecting the lining of the thoracic cavities. The diagnosis of MPM is difficult and treatment ranges from palliative (symptomatic) measures to radical multimodality approaches.

Chemotherapy has become more widely utilised both in treatment approaches with curative and palliative intent. Neither diagnosis nor treatment of MPM is standardised, and sometimes intensive radical treatment is provided despite unfavourable prognostic factors, while in other circumstances appropriate therapy and support that has proven benefits may not be instituted.

This project published and disseminated evidence-based guidelines that will support informed decision making about the diagnosis and treatment of asbestos-related diseases, in particular MPM.

Comcare Asbestos Innovation Fund MicroRNAs as biomarkers to aid in the diagnosis of malignant pleural mesothelioma Reid G.

Novel markers for early diagnosis of malignant pleural mesothelioma (MPM) are urgently needed. We have identified microRNAs in plasma that discriminate MPM patients from controls, potentially enabling diagnosis to be made using blood samples.

We will further validate these markers in MPM patients and high-risk groups, using our already optimised methods for ensuring sample quality, isolating RNA from plasma/serum, and quantification of microRNAs using RT-qPCR. Additional experiments will compare 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.

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 will test for 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 re-selection of patients for specific targeted therapies and to determine the types of mutations altered in cancer-related pathways for MPM.

Illumina MiSeq Pilot Grant

Transcriptome sequencing for identification of drug resistance and mesothelioma related changes

Wright C

This project will analyse mesothelioma using Transcriptome sequencing and aims to identify differential splicing events, mRNA and lncRNA expression changes that can differentiate mesothelioma and normal mesothelium, and may identify differences between parental and drug resistant MPM cell lines

Ongoing grants in 2013

Dust Diseases Board Research (DDB) & Community Support Grant

MicroRNAs as Biomarkers for Malignant Mesothelioma

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

This project is investigating the use of microRNAs as biomarkers in MPM, and includes analysis of patient blood, pleural effusion fluid and tumour tissue. Results obtained as part of this project were presented at the EORTC (European Organisation for Research & Treatment of Cancer) 'Markers in Cancer' Meeting in Brussels and at the IASLC 15th World Conference on Lung Cancer in Sydney.



Dust Diseases Board Research (DDB) & 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, N. van Zandwijk, Blinman P.

This project aims to determine the optimal chemotherapy utilisation rate in malignant mesothelioma patients in NSW. Results from this study were 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 2013.

Dust Diseases Board Research (DDB) & 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 aims 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 IASLC 15th World Conference on Lung Cancer in Sydney.

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 is 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 have been accepted for publication in the British Journal of Cancer.

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. Results from this study were presented at the American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago. Dr Reid was awarded the ADFA Travel Fellowship; Vojakovic Fellowship and the Concord General Repatriation Hospital Travel Scholarship to attend this conference. In addition the results were published in the Annals of Oncology.

Non-peer-reviewed support

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

Kirschner M.

The research of Dr Michaela Kirschner is co-supported by the Swift Family Bequest & Mr Jim Tully Fellowship. The main focus of Dr Kirschner's work at the ADRI is 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. For her research, Dr Kirschner was awarded the EORTC (European Organisation for Research & Treatment of Cancer) early career oncologist/scientist's award to attend a tutorial 'From hypothesis to product: diagnostic development tutorial' at the 'Markers in Cancer' meeting in Brussels in November 2013. She was also awarded the Asbestos Research Fund Vojakovic Fellowship to support travel to this meeting.



Biaggio Signorelli Foundation

The Biaggio Signorelli Foundation (www.biaggiosignorelli.org.au) has continued to generously support major ADRI projects during 2013:

1. Development of National Guidelines for Mesothelioma

The Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma were developed to reduce the variability of care in Australia for mesothelioma patients. They were submitted for public consultation in January 2013 and accepted for publication by the National Health and Medical Research Council in July 2013 following a rigorous approval process.

2. Fellowship – (Dr Anthony Linton)

Dr Anthony Linton, an oncology fellow, started his PhD at the ADRI in 2011 and he has continued to work on biomarkers and potential targets for new treatment



approaches for mesothelioma. In 2013 Dr Linton presented the results from his research at the IASLC 15th World Lung Cancer Conference in Sydney. Dr Linton was awarded the Best of the Best: Clinical research oral presentations at the COSA meeting for his presentation on 'Disease and patient characteristics related to survival in a large population-based cohort of patients with malignant pleural mesothelioma'. In addition, he has published his results in a number of peer-reviewed journals.

3. Fellowship – (Casey Wright)

Casey Wright submitted her PhD in early 2012 entitled "Genomic characterisation of asbestos-related lung cancer" at The Prince Charles Hospital in Brisbane where she was a recipient of an NHMRC Biomedical Postgraduate Scholarship. Since starting at ADRI, Casey has been investigating the potential of long non-coding RNAs (lncRNAs) to serve as biomarkers in malignant pleural mesothelioma. Ms Wright presented her findings at both national and international meetings including the IASLC 15th World Lung Cancer Conference in Sydney.

CSR - 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. During 2013 Kan Chen joined ADRI as a Biobank Officer to assist with the management, maintenance and development of the biobank. He has a Medical Science degree and a Masters in Biomedical

Engineering complementing the current biobank system. The collection of samples continues to be a formidable task. 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.

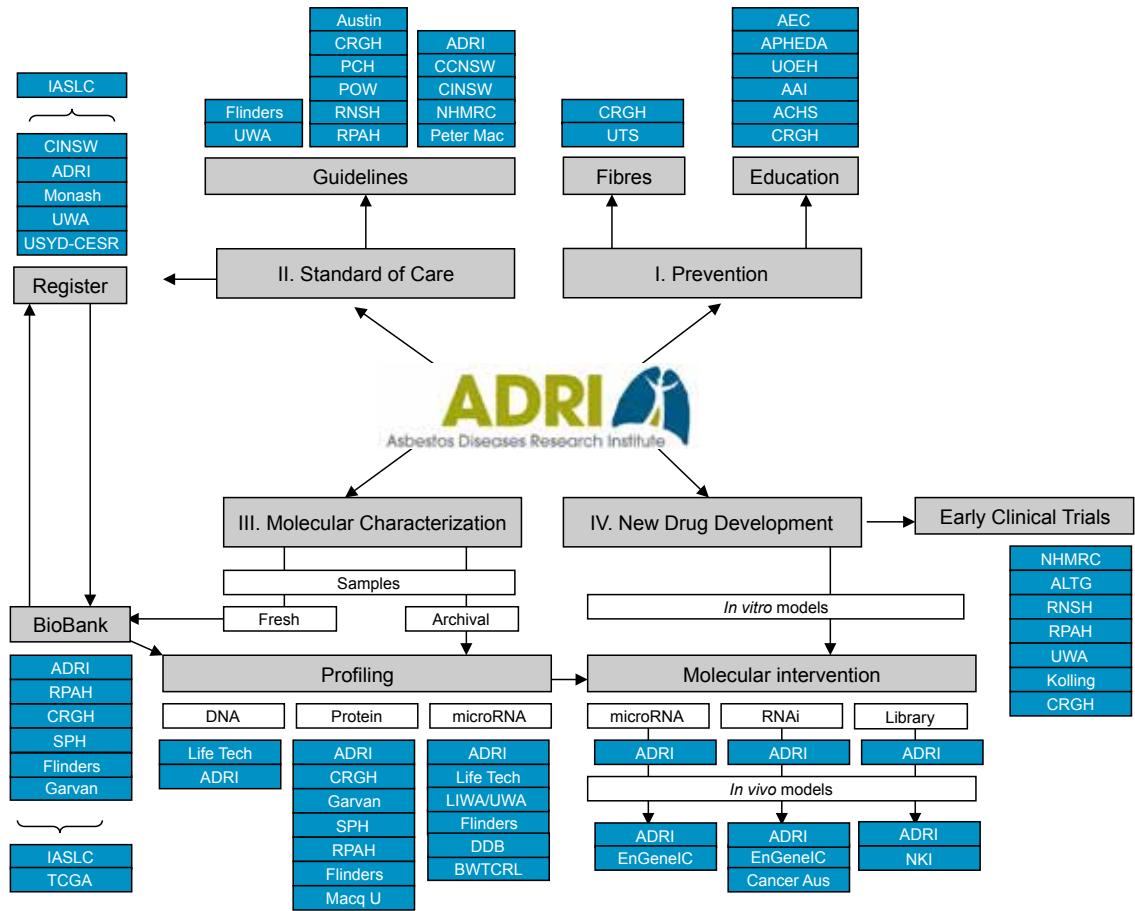
Merck KGaA Cilengitide: Pre-clinical studies in Malignant Mesothelioma

Cilengitide, a cyclic RGD peptide derivative, is an antagonist of the $\alpha\beta3$ and $\alpha\beta5$ integrins with clinical application in the treatment of glioblastoma and other solid tumours. This study aimed to characterise the expression of integrin subunits and receptors in malignant mesothelioma cell lines and to determine the effects of cilengitide treatment on malignant mesothelioma cell biology, both in vitro and in vivo.

James Hardie

James Hardie Industries SE continued to support ADRI's research into the diagnosis and treatment of asbestos-related diseases during 2013. This untied support provides important flexibility to ADRI's research program and is also a potential resource for pilot studies. Promising data from pilot studies can be used to attract further grant funding.

Collaborations



Abbreviations

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 Australian People for Health, Education and Development Abroad
 Austin Austin Hospital
 BWTCRL Bill Walsh Translational Cancer Research Laboratory
 Cancer Aus Cancer Australia
 CCNSW Cancer Council NSW
 CINSW Cancer Institute NSW
 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
 Kolling Kolling Institute

Life Tech Life Technologies
 LIWA Lung Institute of Western Australia
 Macq Uni Macquarie University
 Monash Monash University
 NHMRC National Health & Medical Research Council
 NKI Netherlands Cancer Institute, The Netherlands
 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

Publications and presentations - 2013

Peer-reviewed articles

- 1. Linton A, Cheng YY, Griggs K, Kirschner MB, Gattani S, Srikanan S, Kao SCH, 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* 2013; 110(2):510-9
- 2. Reid G, Pel M, Kirschner MB, Cheng YY, Mugridge N, Weiss J, Williams M, Wright C, Edelman JJB, Vallely MP, McCaughan BC, Klebe S, Brahmabhatt H, MacDiarmid J, van Zandwijk N.** Restoring expression of miR-16: a novel approach to therapy for malignant pleural mesothelioma. *Annals Oncology* 2013; 24(12):3128-35
- 3. van Zandwijk N.** Clinical practice guidelines for malignant pleural mesothelioma. *Journal of Thoracic Disease* 2013; 5(6):724-5
- 4. van Zandwijk N, Clarke C, Henderson D, Musk AW, Fong K, Nowak A, Loneragan R, McCaughan B, Boyer M, Feigen M, Currow D, Schofield P, Pavlakakis N, McLean J, Marshall H, Leong S, Keena V, Penman A.** Guidelines for the diagnosis and treatment of malignant pleural mesothelioma. *Journal of Thoracic Disease* 2013; 5(6):E254-E307
- 5. Majewski IJ, Mittempergher L, Davidson NM, Bosma A, Willems SM, Horlings HM, de Rink I, Greger L, Hooijer GK, Peters D, Nederlof PM, Hofland I, de Jong J, Wesseling J, Kluin RJ, Brugman W, Kerkhoven R, Nieboer F, Roepman P, Broeks A, Muley TR, Jassem J, Niklinski J, van Zandwijk N, Brazma A, Oshlack A, van den Heuvel M, Bernards R.** Identification of recurrent FGFR3 fusion genes in lung cancer through kinome-centred RNA sequencing. *Journal of Pathology*. 2013; 230(3):270-6
- 6. Wright CM, Kirschner MB, van Zandwijk N, Reid G.** Does miR-1 play a role in malignant pleural mesothelioma development and progression? *Chest* 2013; 144(6):1971
- 7. Cheng YY, Kirschner MB, Cheng NC, Gattani S, Klebe S, Edelman JJB, Vallely MP, McCaughan BC, Jin HC, van Zandwijk N, Reid G.** ZIC1 is silenced and has tumour suppressor function in malignant pleural mesothelioma. *Journal of Thoracic Oncology* 2013; 8(10):1317-28
- 8. Honeyball F, Boyer M, van Zandwijk N, Kao SC.** Malignant pleural mesothelioma. *CancerForum* 2013; 37(2):178-82
- 9. Wright CM, Kirschner MB, Cheng YY, O'Byrne KJ, Grey SG, Schelch K, Hoda MA, Klebe S, McCaughan BC, van Zandwijk N, Reid G.** Long non coding RNAs (lncRNAs) are dysregulated in malignant pleural mesothelioma (MPM). *PLoS One*. 2013; 8(8):e70940
- 10. Lim CB, Prêle CM, Cheah HM, Cheng YY, Klebe S, Reid G, Watkins DN, Baltic S, Thompson PJ and Mutsaers SE.** Mutational analysis of Hedgehog signaling pathway genes in human malignant mesothelioma. *PLoS ONE*, 2013; 8(6):e66685
- 11. Henderson DW, Reid G, Kao SC, van Zandwijk N, Klebe S.** Challenges and controversies in the diagnosis of mesothelioma: Part 1. Cytology-only diagnosis, biopsies, immunohistochemistry, discrimination between mesothelioma and reactive mesothelial hyperplasia, and biomarkers. *Journal of Clinical Pathology* 2013; 66(10):847-53
- 12. Henderson DW, Reid G, Kao SC, van Zandwijk N, Klebe S.** Challenges and controversies in the diagnosis of malignant mesothelioma: Part 2: Malignant mesothelioma subtypes, pleural synovial sarcoma, molecular and prognostic aspects of mesothelioma, BAP1, aquaporin-1 and microRNA. *Journal of Clinical Pathology* 2013; 66(10):854-61
- 13. Kirschner MB, Edelman JB, Kao SC, Vallely MP, Van Zandwijk N, Reid G.** The impact of hemolysis on cell-free microRNA biomarkers. *Frontiers in Genetics* 2013; 4:94
- 14. Kirschner MB, van Zandwijk N, Reid G.** Cell-free microRNAs: potential biomarkers in need of standardized reporting. *Frontiers in Genetics* 2013; 4:56
- 15. Kao SC-H, van Zandwijk N, Corte P, Clarke C, Clarke S, Vardy J.** Use of cancer therapy at the end of life in patients with malignant pleural mesothelioma. *Supportive Care in Cancer* 2013; 21(7):1879-84

16. Cheng ASL, Li MS, Kang W, **Cheng VY**, Chou J-L, Lau SS, EK, Yu J, Huang TH, To KF, Chan MW, Sung JY, Chan FKL. *Helicobacter pylori* Causes epigenetic dysregulation of foxd3 to promote gastric carcinogenesis. *Gastroenterology*: 2013; 144(1):122-33

17. **Kao SC**, Vardy J, Harvie R, Chatfield M, **van Zandwijk N**, Clarke S, Pavlakis N. Health-related quality of life and inflammatory markers in malignant pleural mesothelioma. *Supportive Care in Cancer* 2013; 21(3):697-705

18. **Kao SC**, Vardy J, Chatfield M, Corte P, Pavlakis N, Clarke C, **van Zandwijk N**, Clarke S. Validation of Prognostic Factors in Malignant Pleural Mesothelioma: A Retrospective Analysis of Data From Patients Seeking Compensation From the New South Wales Dust Diseases Board. *Clinical Lung Cancer* 2013; 14(1):70-7

19. **Kao SC**, Lee K, Klebe S, Henderson D, McCaughan B, Vardy J, Clarke S, **van Zandwijk N**. Excision repair cross complementation group 1 and thymidylate synthase expression in mesothelioma patients. *Clinical Lung Cancer* 2013; 14(2):164-71

20. **Linton A, Kao S**, Vardy J, Clarke S, **van Zandwijk N**, Klebe S. Immunohistochemistry in the diagnosis of malignant pleural mesothelioma: Trends in Australia and a literature review. *Asia-Pacific Journal of Clinical Oncology* 2013; Sep 9(3): 273-9

21. **Kao SC**, Clarke S, Vardy J, Corte P, Clarke C, **van Zandwijk N**. Patterns of care for malignant pleural mesothelioma patients compensated by the Dust Diseases Board in New South Wales of Australia. *Internal Medicine Journal* 2013; 43(4):402-10

BOOKS

1. Guidelines for the Diagnosis and Treatment of Malignant Pleural Mesothelioma. Asbestos Diseases Research Institute, July 2013

CONFERENCE PRESENTATIONS

1. **Nico van Zandwijk**. Preventive initiatives in a country with an extensive asbestos legacy. 6th International Seminar on Asian Asbestos Initiative. Strategic approaches towards the elimination of asbestos-related diseases. Manila 13-15 November 2013

2. **Linton A**, Pavlakis N, Kao SC, Clarke S, Vardy J, van Zandwijk N. Disease and Patient Characteristics related to Survival in a large population-based cohort of patients with Malignant Pleural Mesothelioma (MPM); Best of the Best: Clinical Research Oral Presentation COSA's 40th Annual Scientific Meeting, Adelaide, 12 - 14 November 2013.

3. **Michaela B. Kirschner**. Elevated tumour expression of miR-210 is associated with short survival in malignant pleural mesothelioma patients undergoing extrapleural pneumonectomy. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

4. **Linton A**, Pavlakis N, Kao SC, Clarke S, Vardy J, van Zandwijk N. Disease and Patient Characteristics related to Survival in a large population-based cohort of patients with Malignant Pleural Mesothelioma (MPM) (Mini-Oral Presentation) IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

5. **Nico van Zandwijk**. T1 research in mesothelioma – Restoring expression of the miR-15/16 family: a novel approach to therapy for malignant pleural mesothelioma. International Translational Cancer Research Symposium. Park Royal, Darling Harbour, 6 May 2013.

6. **Michaela Kirschner**. Cell-free microRNAs: potential novel diagnostic markers for malignant pleural mesothelioma. International Translational Cancer Research Symposium. Park Royal, Darling Harbour, 6 May 2013.

7. **Casey Wright**. Long noncoding RNAs as prognostic markers in MPM. International Translational Cancer Research Symposium. Park Royal, Darling Harbour, 6 May 2013.

8. Huang L, Laws P, Macfarlane E, Sim M, De Crespigny F, **van Zandwijk N**, Musk W, Armstrong B, Anderson A, Dalton V, Kwaan G, Forrest A. Mesothelioma in Australia 2011: Data from the new Australian Mesothelioma Registry. TSANZ Annual Scientific Meeting 22-27 March 2013 Darwin. *Respirology* 18(Suppl 2)2012: 22

9. **Wright CM**, Svarimuthu Francis SM, Sri-ram KB, Stark MS, Hayward NK, Yang IA, Bowman RV, Fong KM. Distinct profiles for

lung cancer and its major subtypes. TSANZ Annual Scientific Meeting 22-27 March 2013 Darwin. *Respirology* 18(Suppl 2)2012: 23

CONFERENCE POSTERS

1. Kirschner MB, Cheng YY, Kao SC, McCaughan BC, van Zandwijk N, Reid G. Tumour miR-210 expression is elevated in malignant pleural mesothelioma patients with shorter survival undergoing extrapleural pneumonectomy. ASCO/EORTC/NCI 2013 Markers in Cancer Meeting, Brussels, 7-9 November 2013. (Awarded: EORTC Early career oncologist/scientists award and the Vojakovic Fellowship)

2. Reid G, Williams M, Kirschner MB, Cheng YY, Mugridge N, Weiss J, Klebe S, Brahmbhatt H, Macdiarmid J, van Zandwijk N. Targeted delivery of RRM1-specific siRNA leads to tumour growth inhibition in malignant pleural mesothelioma. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

3. Fowler JM, Coll J, McLean J, McCaughan B, Kao S, Vardy J, Dhillon HM. Longitudinal observation of health related quality of life following extrapleural pneumonectomy for malignant pleural mesothelioma. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

4. Dhillon HM, Warby A, Kao S, Vardy J. Chemotherapy for mesothelioma: patient, caregiver and health professionals' perceptions of treatment and what influences access. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

5. Tognela A, Kao S, van Zandwijk N, Clarke S, Vardy J, Bray V, Lumba S, Ng W. Estimation of an optimal chemotherapy utilisation rate for malignant pleural mesothelioma: an evidence-based benchmark for patient care. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

6. Kao S, Kirschner MB, Amirkhani A, Pascovici D, Song X, Harvie R, Pavlakis N, Clarke S, Molloy MP, van Zandwijk N, Reid G. Novel plasma proteins associated with prognosis in malignant pleural mesothelioma. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

7. Wright C, Kirschner MB, Cheng YY, O'Byrne K, Gray S, Schelch K, Hoda MA, Klebe S, McCaughan B, van Zandwijk N, Reid G. Long non coding RNAs (lncRNAs) are dysregulated in malignant pleural mesothelioma (MPM). IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

8. Soeberg M, Lee LJ-H, Kao S, Van Zandwijk N, Chang Y-Y, Wang J-D. Estimates of expected years of life lost and lifetime direct medical costs for malignant pleural mesothelioma patients: data from Taiwan and New South Wales, Australia. IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

9. Soeberg M, Takahashi K, Movahed M, Jiang Y, Van Zandwijk N. Global patterns in the incidence of malignant mesothelioma, 1988-2002, using data published by the International Agency for Research on Cancer (IARC). IASLC 15th World Conference on Lung Cancer. Darling Harbour, 27-30 October 2013.

10. Warby A, Dhillon H, Kao S, Vardy J. Chemotherapy for malignant mesothelioma: patient, caregiver and health professionals' perceptions of treatment and what influences access. CINSW Innovations conference, Sydney. August 23 2013.

11. Reid G, Pel1 M, Kirschner MB, Cheng YY, Mugridge N, Weiss J, Williams M, Wright C, Edelman JJB, Valley MP, McCaughan BC, Klebe S, Brahmbhatt H, MacDiarmid J and van Zandwijk N. Restoring expression of miR-16: a novel approach to therapy for malignant pleural mesothelioma. American Society of Clinical Oncology (ASCO) Annual Meeting, Chicago May 31 – June 4 2013. (Awarded: ADEFA Travel Fellowship; Vojakovic Fellowship; CGRH Travel Scholarship)

INVITED PRESENTATIONS

1. Nico van Zandwijk. Medical research on asbestos related diseases. Asbestos Conference. Canterbury Rebuild Health & Safety Group. Ministry of Business, Innovation and Employment. Christchurch, New Zealand 3-5 December 2013

2. Nico van Zandwijk. Advance in medical research on asbestos related diseases. As-

bestos Awareness Week. Asbestos Diseases Foundation of Australia. Maritime Museum, Darling Harbour, Sydney. 29 November 2013.

3. Nico van Zandwijk. Advance in medical research on asbestos related diseases. 2013 National Asbestos Forum. Asbestos Safety and Eradication Agency. Hilton Hotel, Sydney. 25 November 2013.

4. Matthew Soeberg. Asbestos-related disease surveillance: the international and Australian context. Presentation at an inter-ministerial workshop as part of the short-term consultancy with ADRI supported by APHEDA (Union Aid Abroad) for the Vietnam Health and Environment Management Agency, Ministry of Health, 17-21 June 2013. Hanoi, Vietnam.

5. Matthew Soeberg and Nico van Zandwijk. The case for acting now: lessons from the epidemiology of malignant mesothelioma. Towards a National Strategy on Asbestos in the Lao P.D.R. A workshop hosted by the Ministry of Industry and Commerce and APHEDA (Union Aid Abroad), Vientiane, Lao PDR. 24-25 July 2013.

6. Glen Reid. Dysregulated microRNA expression in mesothelioma. NCARD Mesothelioma Symposium. Molecular mechanisms, genomics and translational implications. Novotel Darling Harbour, Sydney. 26th October 2013.

7. Glen Reid. The potential therapeutic role of restoring the miR-16 family in malignant pleural mesothelioma. Translational research Progress in Malignant Mesothelioma Symposium, Medical Education Centre, Concord Hospital, 25th October 2013.

8. Matthew Soeberg. Global and Australian patterns of mesothelioma incidence, mortality and survival. Translational research Progress in Malignant Mesothelioma Symposium, Medical Education Centre, Concord Hospital, 25th October 2013.

9. Steven Kao. Diagnostic, prognostic and predictive markers in malignant mesothelioma: an overview of ADRI research. Translational research Progress in Malignant Mesothelioma Symposium, Medical Education Centre, Concord Hospital, 25th October 2013.

10. Nico van Zandwijk. Introduction of the guidelines for malignant pleural mesothelioma. Translational research Progress in Malignant Mesothelioma Symposium, Medical Education Centre, Concord Hospital, 25th October 2013.

11. Nico van Zandwijk. Asbestos: Background and overview of the Australian setting. Better Living with Mesothelioma. A One Day Workshop for health professionals who care for mesothelioma patients - primarily aimed at nurses. Australian Technology Park, 23rd May 2013.

12. Wright C. Long noncoding RNAs are dysregulated in malignant pleural mesothelioma. Sydney Catalyst International Translational Cancer Research Symposium: short dinner presentation, 6th of May 2013.

13. Kirschner M. Cell-free microRNAs: potential novel diagnostic markers for malignant pleural mesothelioma. Sydney Catalyst International Translational Cancer Research Symposium: short dinner presentation, 6th of May 2013.

14. Matthew Soeberg. Trends in malignant mesothelioma incidence, survival and mortality in Australia: current knowledge and implications for population health and patient outcomes. Sydney Catalyst Post-Graduate Student and early-Career Researcher Symposium, Kinghorn Cancer Centre, Darlinghurst, 22nd March 2013

15. Nico van Zandwijk. Mesothelioma tissue banking. ALTG Tissue Collection Workshop – Lung Foundation Australia. Olivia Newton-John Cancer & Wellness Centre, Heidelberg, Victoria. 15th March 2013

Visitors

Turner Freeman Morning Teas

(3rd May 2013 & 8th November 2013)

Turner Freeman is one of the prominent law firms providing expert legal advice to clients with dust diseases. Through the ongoing assistance and support of their clients, informative morning teas were organised at the ADRI in May and November in 2013. These visits provide an opportunity for ADRI's research staff to showcase the latest research into asbestos-related diseases and a tour of the research facilities. The morning teas are informal and the clients and their families are able to ask questions and comment on the research.

Penrith City Sub-Branch of the National Servicemen's Association of Australia

We were delighted to meet the Veterans from the Penrith City Sub-Branch of the National Servicemen's Association of Australia on the 16th July 2013. We were pleased to inform the veterans of our latest research and show them around the Institute. Research into asbestos-related diseases is important to the veterans as asbestos and asbestos products were used in the past by the armed services which endangered the lives of servicemen and women. The Veterans generously donated \$300 towards research.

Federal Minister for Health and Medical Research announces the Andrew Lloyd bequest to support a new clinical trial

The Federal Minister for Health and Medical Research, the Hon Tanya Plibersek and a number of other VIP guests attended the announcement of the Andrew Lloyd bequest in support of a clinical trial at the ADRI on 31st July 2013. The clinical trial, based on research from the ADRI, uncovered a novel way to inhibit the growth of malignant mesothelioma. This research was presented at the American Society of Clinical Oncology in Chicago in June 2013.

Professor van Schooten visits ADRI

Prof. Dr. Frederik-Jan van Schooten, from the Department of Toxicology, Maastricht University, The Netherlands, visited the ADRI on the 8th August 2013 and gave an interesting lecture on the "Inflammation in relation to biomarkers of DNA damage and repair".

ADFA Morning Tea

Asbestos Diseases Foundation of Australia (ADFA) is a not-for profit organisation working to provide support to people living with asbestos related diseases, family members, carers and friends. ADFA is community based with support groups in different regions of NSW and the ACT including the Central Coast Asbestos Diseases Support Group (CCADS). CCADS is run by Mrs Maree Stokes who provides a sense of belonging and knowledge of not being alone during a time of great need. On the 22nd May 2013 the CCADS group visited ADRI to hear about the



latest research and for a tour of the labs. These visits are important not only to new members of ADFA but to all members as it gives them an opportunity to see what is happening with asbestos-diseases research and to ask questions and to provide feedback to the researchers.

NSW Minister for Health and Minister for Medical Research opened ADRI's Symposium

The Hon. Jillian Skinner - Minister for Health and Minister for Medical Research officially opened ADRI's symposium on the Translational research progress in malignant mesothelioma on the 25th October 2013 held at Medical Education Centre, Concord. The symposium coincided with the World Conference on Lung Cancer held in Sydney and profited from the availability of the international experts and also provided an opportunity to showcase ADRI's latest research. The Keynote speaker was Professor Dean Fennell, Chair of Thoracic Medical Oncology, University of Leicester. Professor Fennell's clinical specialisation is in thoracic medical oncology and early clinical trials, particularly for mesothelioma, with a particular interest in therapeutic targeting of the core apoptosis pathways.



(l to R) Mr Don Burke, Asbestos Awareness Patron, the Hon Tanya Plibersek MP, Minister for Health and Medical Research, and Mr John Jarratt, Asbestos Awareness Patron.

Supporters

ADFA

The Asbestos Diseases Foundation of Australia (ADFA) very generously donated \$20,000.00 toward the purchase of two -80oC freezers in 2013. ADFA continues to support ADRI in so many ways; currently they participate in and provide feedback on a number of research projects.

AMSG

Mr Nick Bos, President of the Asbestosis and Mesothelioma Support Group (AMSG) from the Gold Coast, and his wife Jenny visited ADRI on the 20th December 2013 and presented Professor van Zandwijk with a cheque for \$1,000.00. The AMSG established by volunteers offer assistance, support, information and guidance to people affected by or concerned about asbestos related diseases.

The purchase of vital equipment through generous donations

A generous donation from the Enfield-Croydon Park Sub-Branch of the RSL and from Ms Sue O'Keefe and Mr Matt Shearer, in memory of Ms Lynda Shearer, allowed for the purchase of a ViiA 7 real-time qPCR system for applied

biosystems. This instrument allows the researchers to identify genes that are important in mesothelioma biology. It can accurately measure the levels of certain genes in patients, and compare unaffected but asbestos-exposed individuals.

The Andrew Lloyd bequest

Andrew Lloyd died of mesothelioma on the 15th August 2011. Before his death he directed through his Last Will and Testament a bequest to the ADRI. On the 31st July 2013 Andrew's partner, Xiao Fan Gao, brother, Professor Christopher Lloyd, sister Jennie Lloyd, friend Mr Greg Newbury and family friend Mr Patrick Timbs supported Andrew's extraordinary generosity of \$1.2 million to the ADRI. This bequest over 5 years will support a clinical trial.

Mayor's Golf Day

The 2013 Mayor's Golf Day on the 22nd November was a huge success raising much needed funds for research into asbestos-related diseases. The Golf Day organised by Canada Bay's Mayor, Angelo Tsirekas, coincided with the Asbestos Awareness campaign which raises awareness of the dangers of asbestos.



(l to r) Mayor Angelo Tsirekas, Mr Colin Goldrick (ADRF Company Secretary), Mr Barry Robson (ADRF Board Member), Mr Don Burke (Asbestos Awareness Patron), Professor Nico van Zandwijk (ADRI Director), Mr Ross Flemons (ADRI Accountant), Dr Anthony Linton (ADRI Research Fellow)



Mr Nick and Mrs Jenny Bos (AMSG) presenting Professor Nico van Zandwijk with a cheque.



Ms Sue O'Keefe, Mr Matt Shearer and Dr Michaela Kirschner



Mr Dough Hinsfors, Mr Peter Lang, Mr John Thornton and Mr Ben Fisher from the Enfield Croydon Park Sub-Branch of the RSL.

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Susan Murone
Brian Muston
Mark Nash
National Servicemen's
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In memory of

Chris Nichols
Bethany Nicholson
Gary Oddy
Stephen Odenthal
Janet Offord
N & J Ostwald
Analisa Palmieri
Martha Panos
William Pappas
Elide Pasut
Melinda Pasut
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