ADRI

Asbestos Diseases Research Institute

Annual Report 2015

Contents


Cryo-Gloves
TEMPSHIELD


DRI

MISSION

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

WHO WE ARE

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

WHAT WE DO

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

Key Statistics

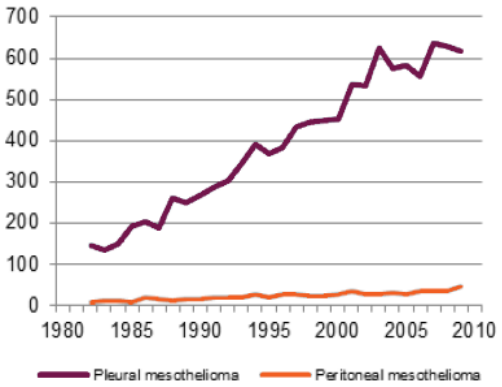
MALIGNANT MESOTHELIOMA

Malignant pleural mesothelioma is the most commonly occurring form of mesothelioma. Malignant peritoneal mesothelioma is less frequently diagnosed. International data suggest that more than 90% of reported cases of mesothelioma occur in the pleura (chest), compared with 4-7% affecting the peritoneum (abdomen).

Recent epidemiological data from Australia confirms that malignant peritoneal mesothelioma accounts for approximately 6% of all mesothelioma cases, with malignant pericardial mesothelioma being diagnosed very infrequently.

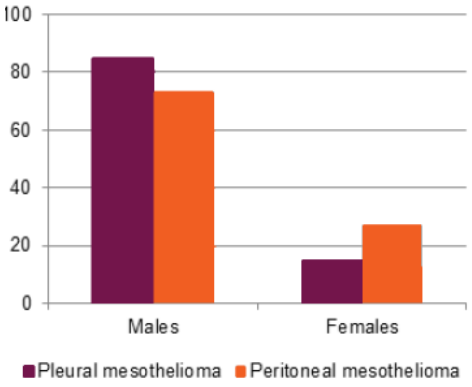
There appear to be important differences by age and gender between the incidence of malignant pleural mesothelioma and malignant peritoneal mesothelioma. Our statistics summary for 2015 highlights these differences as well as the role that histological subtype plays in survival for malignant pleural mesothelioma. This information is from our analysis of malignant mesothelioma data from the Australian Cancer Database for people diagnosed between 1982 and 2009.

NEW CASES



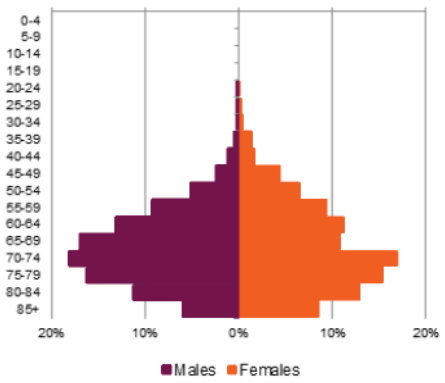
The majority of cases of malignant mesothelioma diagnosed in Australia are located in the pleura. Malignant peritoneal mesothelioma remains a rare disease with little change over time in the number of new cases since 1982. In 2009, 46 people were diagnosed with malignant peritoneal mesothelioma compared to 616 cases of malignant pleural mesothelioma.

GENDER



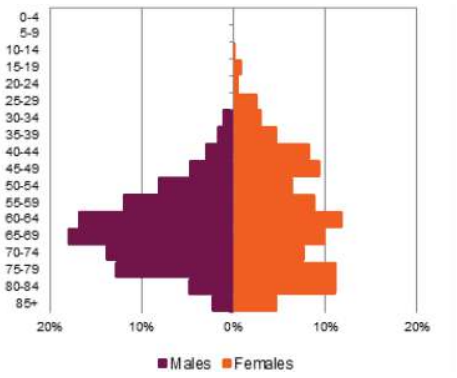
More men than women are diagnosed with malignant pleural mesothelioma, with men making up 85% of all cases diagnosed between 1982 and 2009. 73% of malignant peritoneal mesothelioma cases in Australia were diagnosed in men.

MALIGNANT PLEURAL MESOTHELIOMA BY AGE GROUP



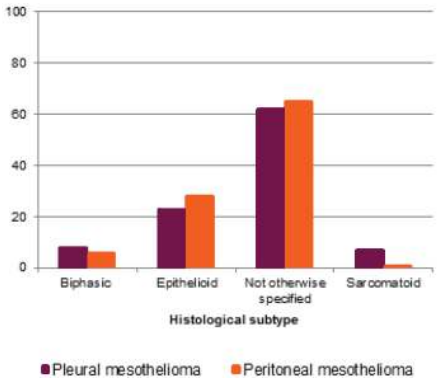
The average age at diagnosis for people with malignant pleural mesothelioma is 70 years. Between 1982 and 2009 in Australia, 66% of pleural mesothelioma occurred in people aged 65 or older.

MALIGNANT PERITONEAL MESOTHELIOMA BY AGE GROUP



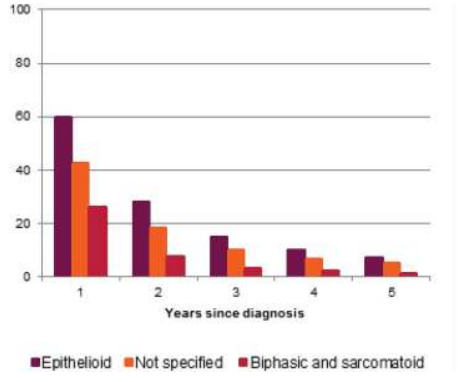
The average age at diagnosis for malignant peritoneal mesothelioma is 64 years. Just over 50% of people diagnosed with malignant peritoneal mesothelioma in Australia between 1982 and 2009 were aged less than 65.

MALIGNANT MESOTHELIOMA BY HISTOLOGICAL SUBTYPE



Most of the malignant mesothelioma cases diagnosed in Australia are recorded with a not specified histological subtype of disease. However, the ability to record this data more accurately in cancer registries across the country is substantially improving over time.

SURVIVAL DIFFERENCES BY HISTOLOGICAL SUBTYPE



Histological subtype plays an important role in survival following a malignant pleural mesothelioma diagnosis, with people with epithelioid disease having better survival compared to other histological subtypes.

2015 Highlights

ADRI'S NEW TREATMENT CONCEPT IN THE CLINIC

Early in 2015 there was positive news from MesomiR 1, the trial investigating the safety and the optimal dose of TargomiRs. The TargomiR treatment consists of nano-cells packaged with tumour suppressing microRNAs developed by ADRI and EnGeneIC, the Lane Cove-based biotech company. An impressive response was noted in the 5th patient on the trial after only 8 weekly injections of TargomiRs. After so many experiments in the ADRI and EnGeneIC laboratories a confirmation of TargomiR activity in a patient who had exhausted standard therapy was very much welcomed. We would like to express our heartfelt thanks to all patients in the MesomiR 1 trial. For the ADRI staff it is a priority to further develop this novel treatment approach for malignant mesothelioma.

INCREASING ASBESTOS AWARENESS IN AUSTRALIA AND ASIA

ADRI was privileged to contribute again to Asbestos Awareness Campaign in 2015. It cannot be underlined enough that education is such an essential element in the prevention of asbestos-induced diseases and the ADRI staff were excited to assist in activities organized by the Asbestos Education Committee. 'Betty' the ADRI's asbestos model house; a perfect platform to educate the public about the dangers of asbestos in the home, travelled all over Queensland in 2015. A Vietnamese/Laotian delegation joined ADFA's ceremony on the last Friday of November remembering asbestos victims. It was very encouraging to notice that our friends from Southeast Asia are becoming aware of the magnitude of the problems caused by asbestos and the need for a worldwide asbestos ban.

ADRI RESEARCHERS AWARDED

Special moments in 2015 included: A/Prof Glen Reid addressing a special meeting of the American Association of Cancer Research about ADRI's microRNA research; Prof Nico van Zandwijk receiving the first Dr J. Stumphius Recognition Award at the first European Asbestos Forum for his lifetime dedication to asbestos-diseases research; and Marissa Williams receiving a full scholarship from Sydney Catalyst at the beginning of her research career.

IMPORTANT FINANCIAL SUPPORT FROM VICTIM GROUPS

It was so encouraging to receive major donations from individual supporters and victim's support groups in 2015, recognizing ADRI's hard work towards a better future for all those Australians exposed to asbestos. Impressive donations received from ADSS and AMAA during Asbestos Awareness week will allow ADRI to make extra investments in promising research areas, such as our clinical trial with TargomiRs.

ADRF Chair's Report

The Asbestos Diseases Research Foundation (ADRF) aims to assist and support the research efforts of the Asbestos Diseases Research Institute (ADRI) through strong leadership and governance. One of the objects of the Foundation is to apply its research and other activities to the development of relevant products and treatments. This year the activities of the Board have been characterised by safeguarding intellectual property developed through the ADRI's research.

Even though the ADRI is a relatively small disease orientated research institute it has developed a novel therapy for thoracic cancers, in particular malignant mesothelioma. MesomiR 1, the world's first phase 1 clinical trial using microRNA, explored safe dose levels of TargomiRs, antibody-targeted minicells loaded with a microRNA construct. The intellectual property associated with the development of this novel therapy is complex. After consideration an intellectual property and commercialisation consultant was engaged to guide the Board and the Institute through this multifaceted period. Whilst the observations made in MesomiR 1 are very promising they will need to be confirmed. MesomiR 2 will focus on efficacy and optimal dosing of TargomiRs in the coming year.

The other major focus for the Board during the year was the succession planning for the next Research Director of the ADRI. The inaugural Research Director, Professor Nico van Zandwijk, appointed 2008, will be retiring in 2016. Over the last seven years he has worked tirelessly to equip and establish a vibrant and productive research team at the ADRI. We are looking to appoint a new Director in 2016 who will provide strategic insight and organisational drive to further the domestic and international standing of research outcomes, professional achievements and the business performance of the Institute through the next phase of its development.

In October 2015 Professor Mark Cooper was appointed to the Board as The University of Sydney's representative. Professor Cooper is the Professor of Medicine and Head of the Discipline of Medicine at the Concord Clinical School, University of Sydney. He heads the Adrenal Steroid Laboratory at the ANZAC Research Institute. Further changes to the ADRF Board's membership will be necessary in the New Year. Currently we have two representatives who were appointed by the Worker's Compensation Dust Diseases Board which in September 2015 was replaced by the Dust Diseases Authority as part of the new Insurance and Care NSW (icare).

During the year the Board also reviewed the compendium of existing policies and procedures and constituted an Audit and Risk Committee to ensure that the policies and procedures reflect the corporate focus and align with the Board's governance and responsibilities.

I express thanks to our Board and to those who serve on our Committees, including the Committee for the next Director of the ADRI, and the Finance and Fundraising Committee for their dedication. The ADRF is extremely grateful for the community support which allows us to continue to facilitate a comprehensive research approach to asbestos-related diseases. On behalf of the ADRF Board I thank you for your support and generosity.

The Foundation continues to be honoured to operate under the patronage of His Excellency General The Honourable David Hurley AC DSC (Ret'd) Governor of New South Wales who in March 2015 visited ADRI and toured its facilities.

John O'Meally AM RFD
Chair

ADRI Director's Report

2015 was another exciting year for the ADRI research team. Early in the year the first signs of clinical activity of the new treatment concept developed by ADRI and EnGeneIC, the Lane Cove biotech company, were noted. An impressive tumour response, together with a major improvement of quality-of-life, was reported in the fifth patient on the trial after only 8 weeks of treatment. This observation formed the basis of a case report published in the American Journal of Respiratory and Critical Care Medicine in June 2015. The report elicited wide publicity and our patient kindly confirmed his remarkable story in interviews in newspapers and TV. It was especially encouraging that he was able to continue the experimental treatment for more than 40 weeks under the close supervision of Dr Steven Kao at the Chris O'Brien Lifehouse. We are eminently grateful to all patients contributing to this trial and sincerely hope that the experimental treatment will continue to exert beneficial effects in the coming year. In the meantime 17 additional patients have received treatment with a series of different doses of microRNA-loaded antibody-guided nano-cells (TargomiRs). The results from over 220 TargomiR treatment weeks are currently being analysed and it is expected that the dose finding study will be completed in mid-2016.

In 2015 Dr Matthew Soeberg was able to finalise a number of epidemiological studies. His careful analyses of Australian data suggest that the mesothelioma epidemic in Australia has seen its largest growth. This outcome largely confirms the accurateness of predictions made several years ago by Dr Jim Leigh. It is a positive sign and it is very much hoped that the number of new diagnoses of asbestos-related cancer in Australia will now start to decline after so many years of increasing figures.

Together with the Australian People for Health, Education & Development Abroad (APHEDA) ADRI has devoted significant time to education and to establishing a better level of understanding of the dangers of asbestos in developing countries with ongoing significant asbestos consumption. The ADRI guidelines for the diagnosis and treatment of malignant pleural mesothelioma were translated into Vietnamese and we have received encouraging signs from governmental sources in Vietnam that a complete ban of asbestos and its products could become effective by the end of this decade. A Vietnamese delegation contributed to the Australian Asbestos Safety & Eradication Agency (ASEA) international conference in Brisbane and this delegation also paid a visit to ADRI after attending ADFA's memorial service at Sydney's Maritime Museum on the last Friday of November as part of Asbestos Awareness Month.

At the national level ADRI continued to support the Asbestos Education Committee that made important contributions to asbestos awareness and primary prevention through 'Betty' the ADRI house that has travelled extensively throughout Queensland this year raising awareness of the dangers of asbestos. Distribution of the consumer guidelines (Understanding Pleural Mesothelioma. A guide for people with cancer, their families and friends) through the Cancer Council started early in 2015. The fact that a re-print of these guidelines was necessary underscores that they were very much needed. A second print run is in preparation.

Several ADRI researchers made important contributions to international scientific meetings in 2015. At the first European Asbestos Forum held in Amsterdam in June I was pleasantly surprised to receive the Dr. J. Stumphius Recognition Award after presenting an overview of ADRI's research. In December A/Prof Glen Reid was invited to present at a special meeting of the American Association of Cancer Research in Boston on microRNAs in asbestos cancers dedicated to non-coding RNAs.

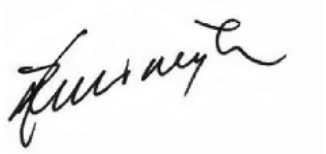
In 2015 research papers were published in 14 peer-reviewed journals with another four accepted for publication. ADRI also contributed as editor to a series of journal articles on lung cancer practice and implementing evidence around the world and to a chapter in an e-book entitled: Malignant pleural mesothelioma: Present status and future direction; confirming an excellent research output.

Marissa Williams, a Research Assistant at ADRI, was awarded a full PhD scholarship by Sydney Catalyst to support her PhD studies at The University of Sydney. This highly competitive and sought after award will allow Marissa to embark on PhD studies extending the skills and knowledge she has gained at the ADRI.

The importance of good relations with victims support groups cannot be emphasised enough. In 2015 we continued to profit from the excellent advice, participation and financial support from several groups. Wonderful contributions from the Asbestos Diseases Foundation of Australia (ADFA), the Asbestosis & Mesothelioma Association of Australia (AMAA) and the Asbestos Disease Support Society (ADSS) needs to be mentioned. ADFA members also kindly consented to participate in a number of quality-of-life studies for which we are very grateful.

During asbestos awareness month at the ADSS's inaugural Thank you event in Brisbane the ADRI was presented with a cheque for $100,000.00 and at the official opening of the AMAA headquarters on the Gold Coast we received donations totalling $14,430. We are extremely grateful for all of these most generous donations, without which the ADRI could not continue its important research. To give recognition to our major donors an Honour Wall will be unveiled in the foyer of the Bernie Banton Centre in 2016.

I do hope that you will enjoy reading about the research progress at ADRI in creating a better future for all those affected by Australia's asbestos legacy.



Nico van Zandwijk MD PhD FRACP FCCP
Director

ADRF Board

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

MR JOHN O'MEALLY AM RFD

Independent Chair

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

Appointed 22 February 2012

MS SYLVIA KIDZIAK AM

Deputy Chair

Nominated by the Dust Diseases Board

Ms Kidziak is Managing Director of SL Engineering, a Councillor on the NSW Business Chamber 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

PROFESSOR MARK COOPER

Nominated by The University of Sydney

Mark Cooper is the Professor of Medicine and Head of the Discipline of Medicine at the Concord Clinical School, University of Sydney. He heads the Adrenal Steroid Laboratory at the ANZAC Research Institute. Until 2012 he was a Senior Lecturer in Endocrinology at the University of Birmingham, UK. He was also metabolic bone physician at the Royal Orthopaedic Hospital, Birmingham, one of the largest orthopaedic hospitals in Europe. His clinical and research interests include adrenal steroid physiology and metabolic bone disease. In particular, he has examined the role that glucocorticoid metabolism plays in normal physiology, inflammatory arthritis and glucocorticoid induced osteoporosis. He was previously the Bertram Abraham's Lecturer in Physiology at the Royal College of Physicians of London. He continues to combine a clinical practice with a basic/translational research group
Appointed 21 October 2015

COL. PROFESSOR ROBERT LUSBY AM

Nominated by the ANZAC Health and Medical Research Foundation

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

Nominated by the Dust Diseases Board

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

MR PAUL BASTIAN

Nominated by Unions NSW

Paul Bastian was appointed National Secretary of the Australian Manufacturing Workers' Union in March 2012, having previously held the position of National President since January 2010. Paul commenced his employment with the AMWU in 1981 and in 1997, was elected State Secretary of the NSW Branch. He is a shipwright by trade and completed a Law Degree while studying part time at the University of Technology, Sydney. Paul has worked throughout the manufacturing industry, in the construction, shipbuilding and metals industries, in both metropolitan and regional areas of the state. He represents the AMWU on a number of Boards/Committees including ACTU Executive and, AustralianSuper. Paul was on the Asbestos Management Review Advisory Group, as well as once being on the Boards of APHEDA, the NSW Manufacturing Council and the NSW Workers Compensation Advisory Council. He has a long history of involvement with community and union campaigns against asbestos and has represented the AMWU and IndustriALL Global Union (previously known as the International Metalworkers Federation at numerous international asbestos Conferences.
Reappointed: 11 June 2014

DR CHRISTOPHER CLARKE

Invited by the Board

Christopher Clarke commenced practice as a Consultant Thoracic Physician in 1976. His special interest has been occupational lung disease. He has held appointments at a number of public hospitals in Sydney including Visiting Medical Officer in the Department of Thoracic Medicine at Concord Hospital until December 2008. Dr Clarke now works under the MSOAP-ICD program as a thoracic physician in country regions in NSW. He is the employee nominated member on the Medical Authority of the Workers Compensation (Dust Diseases) Board of NSW. He is an Authorised Medical Specialist for the NSW Workers Compensation Commission. He is a past President of the Thoracic Society of Australia and New Zealand. He now has a Marine Engine Drivers 2 Certificate of Competency (steam) and is Chief Engineer on ST Waratah which is one of the vessels run by the Sydney Heritage Fleet. The wide range of trades represented there have given him an insight into the extensive use of asbestos in these industries.
Appointed: 13 March 2014

DR ANDREW PENMAN AM

Invited by the Board

Andrew Penman is a public health physician whose career has been focussed on the application of health and medical research in effective public policy and health programs. From 1984 to 1998 he held a succession of senior positions as Regional Director of Public Health, Pilbara Health Region, Assistant Commissioner and Chief Health Officer, WA Health Department, Director of Disease Prevention and Health Promotion, and Deputy Chief Health Officer, NSW Health. In these positions he initiated or led campaigns for example in control of sexually transmitted diseases, environmental health improvement in indigenous communities, expansion of hereditary disease services, improved parenting to reduce conduct disorder, alcohol harm minimisation, and expanded vaccination. From 1996 he was Chief Executive Officer of the Cancer Council NSW until October 2012. In this position he has grown the organisation's revenue, and scale and scope of programs, and initiated innovative programs in liver cancer prevention, tobacco control among disadvantaged people, tobacco retail reform and expanded support services for cancer patients. He was Chair of the Steering Committee to develop guidelines for the management of malignant mesothelioma under the auspices of the Asbestos Diseases Research Institute. His work in cancer control was recognised by his appointment as a Member in the Order of Australia in 2010. His writing has been largely in the realm of departmental or organisational policy and strategy papers, and advocacy documents such as Health Goals and Targets for Western Australia, and improving Radiotherapy services. These interests are reflected in his publication record.

Appointed 8 October 2014

MR BARRY ROBSON

Nominated by the Asbestos Diseases Foundation of Australia Inc.

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

Reappointed: 8 October 2014

MR SEAN O'SULLIVAN

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

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

Appointed 19 October 2011

PROFESSOR NICO VAN ZANDWIJK

Research Director

Nico van Zandwijk earned his medical degree at the University of Amsterdam, The Netherlands, in 1973 and wrote his thesis on “Pulmonary injury elicited by blood” in 1976. He was editor of the Haematology section of Excerpta Medica until 1980, and received licences in internal medicine and pulmonary medicine in 1979 and 1981, respectively. In the same year he was appointed Assistant Professor of the Academic Medical Centre, Amsterdam and became Consultant Physician at the Netherlands Cancer Institute, Amsterdam. From 1985 to 2008 he was Head of the Department of Thoracic Oncology at that Institute. Professor van Zandwijk has served as Secretary (1982-1988) and Chair (1988-1994) of the European Organisation for Research and Treatment of Cancer (EORTC) Lung Cancer Group. He has chaired a number of boards and committees including: the Scientific Board of the clinical section of the Netherlands Cancer Institute; a National Advisory Board for new lung cancer medications, and a State Council on asbestos related disease. He has also been a member of the Advisory Board of the Thoracic Section of the French National Cancer Institute (INCA). Professor van Zandwijk was a Board Director of the International Association for the Study of Lung Cancer (2005-2009), co-chaired the World Conference on Lung Cancer (WCLC) 2011 and, was a Member of the Core Program Committee for the WCLC 2013 and 2015. He was a member of the national Asbestos Management Review Panel and was Study Coordinator of several international studies. He has authored or co-authored more than 350 peer-reviewed international papers, book chapters and conference presentations. 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

DR TIM SINCLAIR

Nominated by the Local Health District

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

MR COLIN GOLDRICK

Company Secretary

Colin is a past Partner and now Special Counsel with the legal firm of Goldrick Farrell Mullan, heading up their Business and Technology practice group. He also acts as legal counsel to the Foundation. Colin has been a lawyer since 1996, specialising in intellectual property, corporate advisory and commercial law, as well as compliance and governance for both commercial and not-for-profit entities. Prior to that Colin worked in the Information Technology industry for almost 15 years in a variety of roles.
Reappointed: 16 May 2012

ADRI Staff

RESEARCH STAFF

Professor Nico van Zandwijk — ADRI Director
A/Prof. Glen Reid — Senior Scientist
Mr Kan Chen — Biobank Officer
Dr Yuen Yee Cheng — Research Fellow
Mr Andrej Despotovski — UTS Student
Mr Jason Fowler — PhD Research Fellow
Mrs Rebecca Hyland — Biobank Data Officer
Mrs Yennie Huynh — Clinical Trials Monitor
Mr Tom Johnson — UTS Student
Dr Steven Kao — Medical Oncologist
Dr James Leigh — Advisor
Ms Felicity Leslie — Clinical Trials Monitor
A/Prof Ruby Lin — Senior Researcher
Dr Anthony Linton — Medical Oncologist
Ms Jocelyn McLean — Support Coordinator
Mr Kadir Sarun – Research Assistant/Student
Dr Matthew Soeberg — Epidemiologist
Ms Anne Warby — Research Officer
Ms Marissa Williams — Research Assistant
Mr Patrick Winata — Research Assistant/Student

ADMINISTRATIVE STAFF

Ms Victoria Keena — Executive Officer
Mr Justin Crosbie — IT Officer
Mr Ross Flemons — Accountant
Ms Kim Hadley — Administrative Assistant
Mrs Jenny Weismantal - Volunteer




















New Grants in 2015

CINSW - RESEARCH INFRASTRUCTURE GRANT

Expanding the Asbestos Diseases Research Institute (ADRI) biobank to create a state-wide repository for research into thoracic cancers
Kao SC-H, van Zandwijk, N, McCaughan B, Yan T, et.al.

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

CINSW - RESEARCH EQUIPMENT GRANT

Expanding Basic, Clinical and Functional Genomic Cancer Research at Concord Campus
van Zandwijk N, Reid G, Lin RCY, Seibel M, Cowley M, Bowden, Cooper W, Kao S, Horvath L, Hart D.

The aim of this proposal is to introduce the next generation of genome analysis tools to the Concord Cancer Research Consortium and collaborators engaged in basic, clinical and functional genomic cancer research. By acquiring the requested equipment, the consortium will be able to offer state-of-the-art facilities to all researchers and clinicians who are interested in the molecular basis of variations in both healthy and diseased patients, as well as disease model systems. Importantly, the costs of undertaking this type of research will be significantly reduced by the acquisition of the equipment requested.

SYDNEY CATALYST – PHD SCHOLARSHIP

Correcting aberrant microRNA expression as a therapeutic approach in malignant pleural mesothelioma (MPM)
Williams M

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

ASBESTOS SAFETY AND ERADICATION AGENCY (ASEA)

Living well with mesothelioma
McLean J

A diagnosis of malignant mesothelioma (MM) is devastating, and patients frequently report negative experiences in coping with MM. To retain some hope and obtain the best available treatment, this project aims to make living with MM more bearable.

SLATER & GORDON (AUSTRALIAN COMMUNITIES FOUNDATION)

circular RNAs (circRNAs): novel biomarkers for early detection of malignant pleural mesothelioma
Lin R

Malignant pleural mesothelioma (MPM) is an aggressive cancer with poor prognosis. Diagnosis is often difficult, especially in cases where biopsies are not available, and a new blood-borne marker would represent a significant advance. We have recently shown that molecular markers such as microRNAs have the potential to serve as diagnostic and prognostic markers for MPM patients. With the advent of next generation sequencing technology, circular RNAs (circRNAs) have been shown to compete with endogenous RNAs (ceRNAs) or microRNA 'sponges' with significant roles in gene regulation. Moreover, these molecules have been shown to play important roles in cancer. Thus the aim of this project is to examine the potential of circRNAs in early MPM diagnosis.

On-going Grants in 2015

CANCER COUNCIL NSW

MicroRNA replacement — a novel therapeutic approach for malignant mesothelioma
Reid G, van Zandwijk N, MacDiarmid J, Brahmbhatt H.

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

WORKCOVER AUTHORITY OF NEW SOUTH WALES

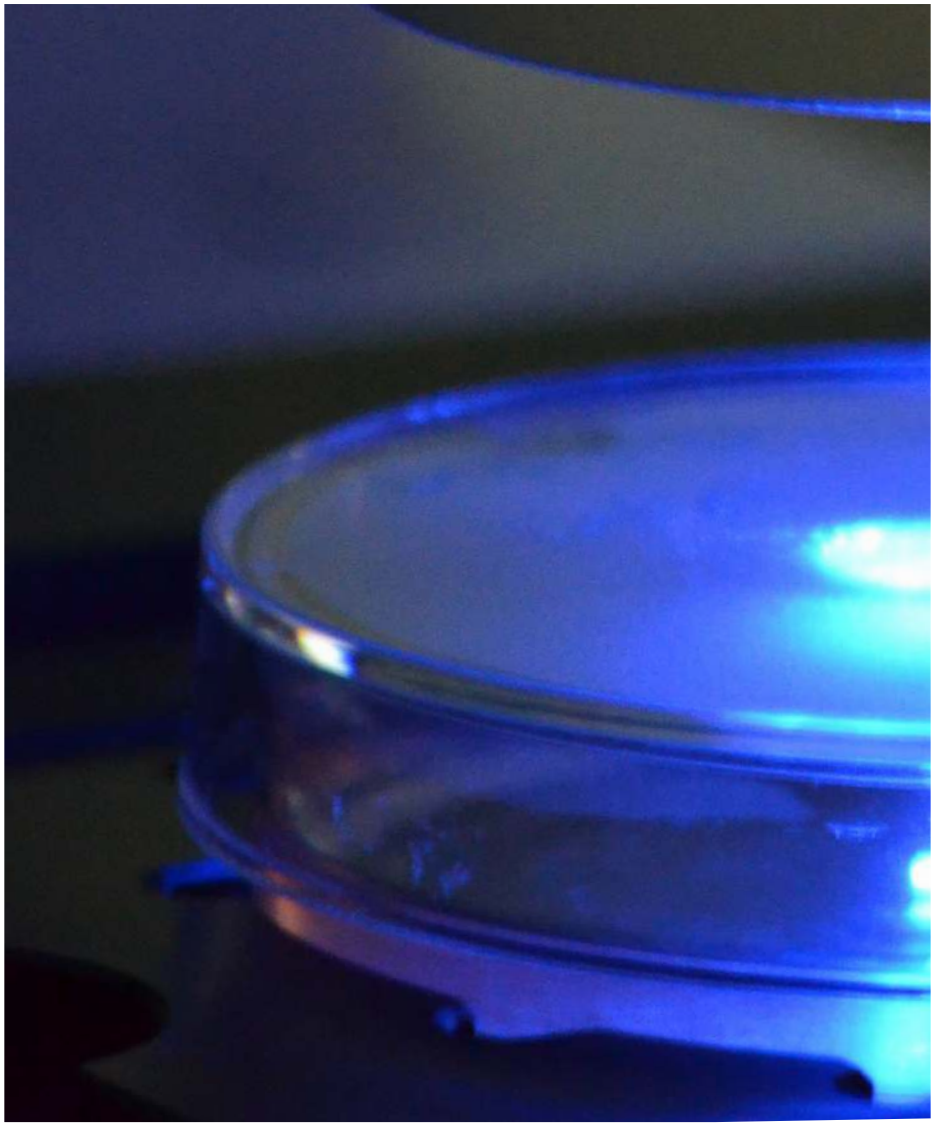
Dissemination of the guidelines for the diagnosis and treatment of malignant pleural mesothelioma and to develop and disseminate consumer guidelines for patients and their carers
van Zandwijk N.

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

WORKCOVER AUTHORITY OF NEW SOUTH WALES

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

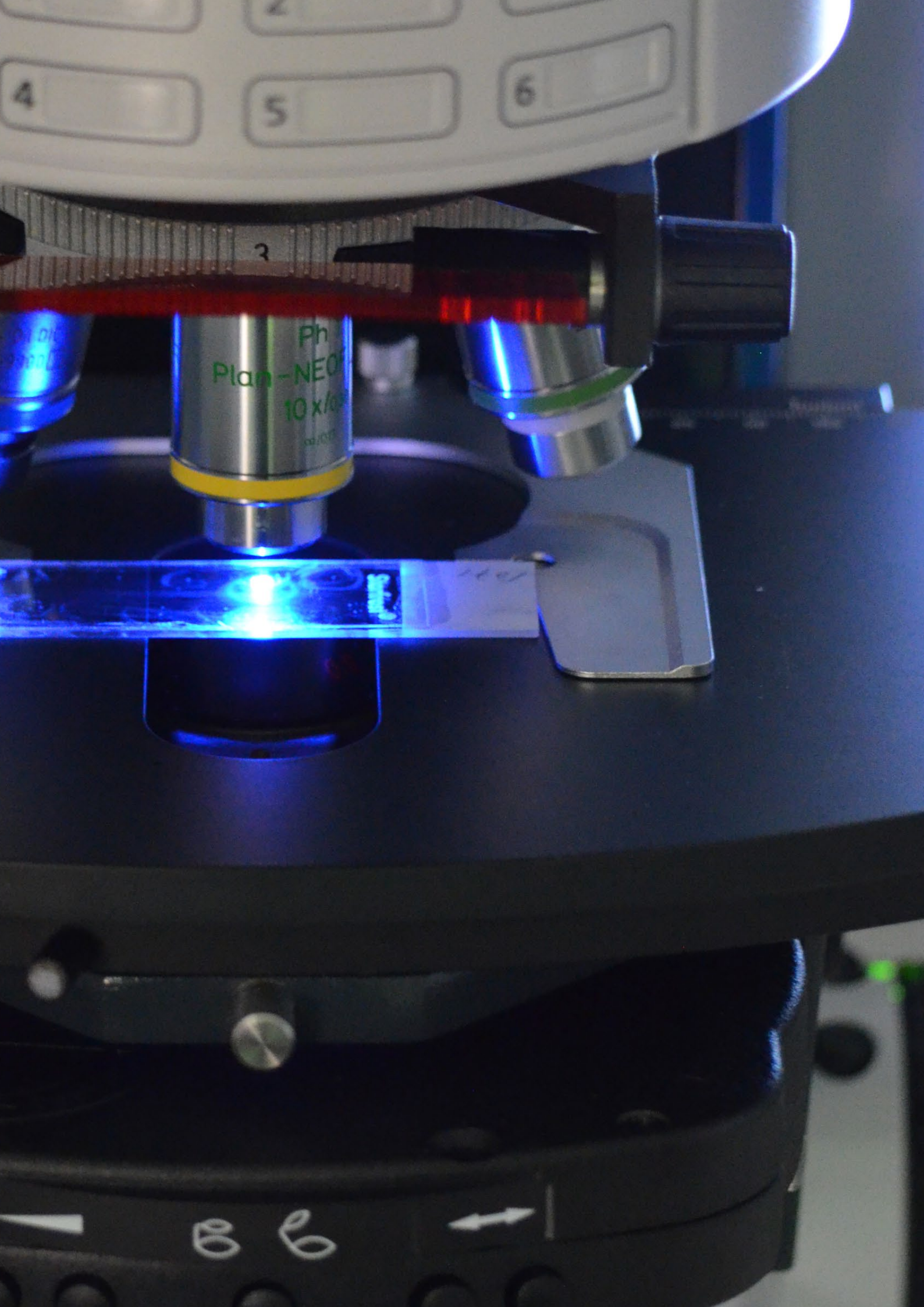
TargomiRs have been the product of a successful cooperation between ADRI and EnGeneIC, a Sydney-based biotech company. TargomiRs are minicells (nanotechnology) loaded with a microRNA (mimic) that is almost absent in MPM cells. This microRNA (family) has important tumour suppressor functions. Experimental (MPM) tumours stopped growing/regressed upon intravenous administration of TargomiRs and this research is being translated into the clinic. New drug development protocols are being followed with initial studies establishing an optimal/safe dose and pharmacokinetics/ dynamics. Phase II studies are planned following successful completion of the Phase0/I assessment.



CANCER INSTITUTE NSW - TRANSLATIONAL PROGRAM GRANT

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

This program grant brings together an experienced multidisciplinary research team dedicated to improving health outcomes for patients with mesothelioma. It involves epidemiological studies, basic research, and clinical approaches all aiming to provide better outcomes for malignant mesothelioma patients. Progress in this program has been made in many of the projects. Results from this project were presented at the International Mesothelioma Interest Group Conference, and published in the journal of Molecular Oncology.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Philanthropic and Corporate Funding

MR JIM TULLY FELLOWSHIP

Schelch K.

Karin Schelch has recently completed her PhD in Vienna and will be returning to the ADRI in early 2016 to take up a post-doctoral position. The main focus of Dr Schelch's work at the ADRI will be to investigate dysregulated signalling pathways in mesothelioma with the aim of identifying new targets for therapy. Dr Schelch will be co-supported by the Mr Jim Tully Fellowship.

TURNER FREEMAN SCHOLARSHIP

Mesothelioma Support Coordinator
McLean J

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

JAMES HARDIE

James Hardie Industries plc continued to provide untied support for research into the diagnosis and treatment of asbestos–related disease during 2014. This support is important to ADRI's research program as it provides a level of flexibility for potential pilot studies. James Hardie have also provided support for the TargomiRs clinical trial.

CSR LIMITED — BIOBANK

The ADRI biobank is an invaluable collection providing the research team with a range of specimen types, including: fresh frozen tumour tissue, DNA and RNA samples derived from tumour tissue and matched bloods from mesothelioma patients, control tissue samples and a series of formalin-fixed tumour tissues.

During 2015 work to enlarge the network of collection sites was on-going and the generation of a number of cell lines for research use. The biobank's clinical database is managed and maintained by an experienced team who collect and accurately document every sample. Thanks to CSR's co-support of the biobank it continues to grow and is an important resource for the ADRI's on-going research program into asbestos-related diseases.

Clinical Research Projects

THE IMPACT OF GEOGRAPHIC AND SOCIOECONOMIC FACTORS UPON MPM INCIDENCE AND PROGNOSIS IN MPM?

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

The impact of clinico-pathological factors such as age, gender, and histological subtype on the prognosis of malignant pleural mesothelioma (MPM) is well understood. However, socio-economic and geographic factors and their impact on survival have been studied to a lesser extent. Whilst the majority of Australians live in major metropolitan centres, a significant proportion of the population reside in smaller regional centres and surrounding areas. As such access to clinical services including specialist oncological units may be limited. Furthermore, socio-economic factors may further impact service access, treatment provision and prognosis.

With the cooperation of the NSW Dust Diseases Board and oncology and thoracic units across NSW, we have performed one of the largest analyses to date of Australian patients diagnosed with MPM. Gathering data from the medical and surgical records of 910 patients diagnosed between 2002 and 2009, we are studying the impact of socio-economic advantage and disadvantage, proximity to an oncological multi-disciplinary team meeting and geographic remoteness upon treatment utilisation and survival. Furthermore we are analysing the distribution of MPM diagnoses across NSW in comparison to those identified by the Cancer Institute NSW, to assess the appropriateness of cancer service distribution and the scope of DDB utilisation in NSW.

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

Investigators: van Zandwijk N[1,2], Bailey D[3], Pavlakis N[4], Clarke S[4], Kao S[1,5], Boyer M[5], Vardy J[6], Linton A[1,6], Blinman P[6], Cooper W[7], Klebe S[8].
1. Asbestos Diseases Research Institute, 2. University of Sydney, 3. Royal North Shore Hospital, 4. Northern Cancer Institute, 5. Chris O'Brien Lifehouse, 6. Concord Repatriation General Hospital, 7. Royal Prince Alfred Hospital, 8. Flinders University

After studying different drug doses and administration schedules of TargomRs (Epidermal Growth Factor Receptor (EGFR) antibody targeted EnGeneIC Delivery Vesicles (EDVs) packaged with microRNA mimics) in 18 patients a more accurate picture of drug-associated reactions has emerged. TargomiRs are rather well tolerated. The side effects observed are the consequence of the inflammatory response elicited by intravenous administration of EDVs and most patients experience transient shivering/rigor, and temperature elevation, sometimes accompanied by discomfort/pain at the disease site. Early signs of clinical activity (reduction/stabilisation of tumour size) of TargomiRs has been noted and one particular impressive response has been published in the American Journal of Respiratory and Critical Care Medicine (June 2015). It is expected that dose escalation studies will continue until mid-2016 and will be followed by a formal phase II study concentrating on the efficacy of TargomiRs. A detailed protocol for the execution of the phase II study is in preparation. Abstracts documenting study progress have been submitted to the International Mesothelioma Interest Group (iMiG) and the American Society of Clinical Oncology (ASCO) for presentation at their conferences in 2016.

CLINICOPATHOLOGICAL REVIEW OF ASBESTOS-ASSOCIATED LUNG CANCER FROM DUST DISEASES BOARD

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

Despite the extensive epidemiological literature available, the molecular relationship between asbestos exposure and lung cancer remains the subject of controversy. Essentially, this relates to the fact that most asbestos-associated lung cancers occur in those who are also cigarette smokers, and smoking represents the strongest risk factor for lung cancer. It is estimated that asbestos-related lung cancer accounts for 4–12% of all lung cancers worldwide. For every case of malignant mesothelioma, there may be two asbestos-related lung cancers, and this ratio may increase in occupations with heavy asbestos exposures. This study is a review of a retrospective cohort of New South Wales workers with lung cancer who have applied for compensation through the Dust Diseases Board (DDB) between 2002 and 2011. This project aims to investigate whether the spectrum of clinicopathological characteristics and molecular mutations differ between patients with heavy asbestos exposure and those with insufficient and/or no asbestos exposure. The intention is also to determine whether there are any lung cancer biomarkers that are associated with asbestos exposure. This work will pave the way for identification of novel biomarkers in lung cancer tumour samples that are specifically related to asbestos exposure, thereby assisting the DDB in process of assigning asbestos dust exposure as having had material contribution to the development of lung cancer. This work will also provide an accurate overview of the clinical, pathological and molecular characteristics of asbestos related lung cancers and non-asbestos related lung cancers in NSW workers and highlight any differences that might exist between the two groups.

So far, we have examined a cohort of 467 patients and 60% were diagnosed with stage 4 disease. We are currently finalising the asbestos exposure data and treatment details. Analyses of the clinical data is expected in 2016 and molecular characterisation will follow shortly after that.

The findings of this research will also provide valuable insight into the treatment patterns and survival outcomes of asbestos related lung cancers.

Preclinical Research Projects

EXPLORING MECHANISMS OF MIRNA DOWNREGULATION IN MALIGNANT PLEURAL MESOTHELIOMA

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

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

INVESTIGATING MICRORNA TARGET GENES AS POTENTIAL THERAPEUTIC TARGETS IN MALIGNANT PLEURAL MESOTHELIOMA

Cheng YY[1], Wright CM[1], Kirschner MB[2], Williams M[1,3], Sarun KH[1], Edelman JJ[4], Vallely MP[3,4,5], McCaughan BC[6], Klebe S[7], van Zandwijk N[1,3], Lin RCY[1], Reid G[1,3].
1. Asbestos Diseases Research Institute, 2. University Hospital Zurich, 3. University of Sydney, 4. Royal Prince Alfred Hospital, 5. The Baird Institute, 6. Sydney Cardiothoracic Surgeons, 7. Flinders Medical Centre

We and others have shown that microRNAs play an important role in mesothelioma biology and have potential as therapeutic agents. In this study we attempt to identify dysregulated microRNAs with functional roles by utilising publicly available gene expression datasets on malignant pleural mesothelioma (MPM), in combination with our transcriptomics studies. We identified enrichment of target binding sites for the miR-17 and miR-30 families in both MPM tumours and cell lines. Members of both families were significantly down-regulated in MPM tumours and cell lines. Interestingly, lower expression of miR-17-5p and miR-20a-5p was clearly associated with epithelioid histology. We interrogated the predicted targets of these differentially expressed microRNA families in MPM cell lines, and identified KCa1.1, a calcium-activated potassium channel subunit alpha 1 encoded by the KCNMA1 gene, as a target of miR-17-5p. KCa1.1 was overexpressed in MPM cells compared to the immortalised mesothelial line MeT-5A, and was also upregulated in patient tumour samples compared to normal mesothelium. Transfection of MPM cells with a miR-17-5p mimic or KCNMA1-specific siRNAs reduced mRNA expression of KCa1.1 and inhibited MPM cell migration. Similarly, treatment with paxilline, a small molecule inhibitor of KCa1.1, resulted in suppression of MPM cell migration. These functional data implicating KCa1.1 in MPM cell migration support our integrative approach using MPM gene expression datasets to identify novel and potentially druggable targets. These results will be published in the journal of Molecular Cancer in 2016.

THE ROLE OF MICRORNAS IN THE RESISTANCE OF MESOTHELIOMA CELLS TO CHEMOTHERAPY

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

Malignant pleural mesothelioma (MPM) is an aggressive asbestos-related thoracic cancer. Chemotherapy is an important palliative treatment option but almost every patient will be confronted with recurrence of disease and drug resistance. We have shown that microRNAs are involved in drug response in MPM cells. To better understand the potential role of microRNAs in drug resistance and sensitisation in MPM we have used monolayer (2D) and spheroid (3D) cell culture models and profiled microRNAs expression in these two models. Drug cytotoxic assay were also carried out to test the difference of drug resistance in 2D and 3D cultures. We confirmed that MPM cells grown as spheroids are more resistant to cisplatin and gemcitabine when compared to MPM cells grown in 2D cultures. Immunofluorescence studies showed a gradient of hypoxia from the centre of the spheroids where high Hif1 expression is observed. We also identified significant up-regulation of miR-210-3p, miR-378a-3p, miR-195-5p and miR-146b-5p, and down-regulation of miR-320b and miR-1225b-5p in 3D spheroids. Transfecting MPM cells in 2D culture with a miR-210-3p mimic resulted in increased drug resistance. Increasing the levels of miR-210 using a mimic resulted in increased resistance of MPM cells to chemotherapy, suggesting this microRNA plays a role in drug resistance observed in MPM. These results will be presented at the Lorne Cancer Conference 2016 and an abstract was submitted to the International Mesothelioma Interest Group (iMig) to be presented in May 2016.

THE ROLE OF TUMOUR SUPPRESSOR MICRORNA MIR-137-3P IN MALIGNANT PLEURAL MESOTHELIOMA BIOLOGY

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

Deletion on a number of chromosomal regions is a common characteristic observed in malignant pleural mesothelioma (MPM), notably within regions 9p21-22 and 1p21-22. Specifically, studies have shown that the deletion of region 1p21-22 occurs in approximately 74-85% of MPM cases. Since this region has been implicated in tumour suppression, we set out to investigate this phenomenon. The microRNA miR-137 resides within this region and has been shown to modulate tumour suppression in a number of cancers including breast, lung and gastric cancer. However, its role in MPM is not yet clear. In this project, which was the topic of Tom Johnson's Hons year, we have investigated whether miR-137 can act as a tumour suppressor in MPM. We are also investigating the role of miR-137 in the regulation of the oncoprotein YB-1.

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

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

Programmed death 1 (PD-1) and its ligand PD-L1 have significant roles in suppressing host immune response in many cancer types. As in other cancers, PD-L1 expression is upregulated and associated with poor prognosis in malignant pleural mesothelioma (MPM) but the mechanisms causing its dysregulation are poorly understood. Characterisation of the mechanisms leading to PD-L1 upregulation could improve the understanding of its dysregulation in MPM and give depth to its prognostic significance. We found 25% of the tumour samples from MPM patients had positive PD-L1 staining, and this was more common in the non-epithelioid subtype. Also, PD-L1 expression was associated with poor survival. Reduced microRNA expression was related to elevated PD-L1 levels in the MPM patient panel, with previously identified tumour suppressor microRNAs in MPM showing downregulation in PD-L1 positive tumours. Our study confirms that PD-L1 is an adverse prognostic indicator in MPM. Elevated PD-L1 expression in MPM patient samples was correlated to downregulation of tumour suppressor microRNAs that were shown to directly and indirectly regulate PD-L1 expression in vitro. This work will be presented at the 2016 International Mesothelioma Interest Group iMig conference.

IDENTIFYING MICRORNAS WITH THERAPEUTIC POTENTIAL IN MALIGNANT PLEURAL MESOTHELIOMA

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

MicroRNA expression is globally downregulated in cancers including malignant pleural mesothelioma (MPM). We and others have shown that multiple microRNAs have tumour suppressor activity in MPM cell lines when the levels are restored using mimics. Results from our lab have led to the world's first clinical trial of a microRNA replacement strategy in thoracic cancer patients, currently nearing the end of Phase I. In this project we are carrying out a head-to-head comparison of microRNA mimics to identify the most promising microRNAs for future development as therapeutic agents, both singly and in combination. The initial experiments in this project were carried out by Andrew Della Gatta and Hyerim Suh, two students who joined ADRI as part of The University of Sydney's Summer Studentship program.

INVESTIGATING BAMLET AS A POTENTIAL TREATMENT FOR CHEMO-RESISTANT MESOTHELIOMA

Rath EM[1], Cheng YY[2], Hudson AL[3], Weir C[3], Sarun K[2], Håkansson AP[4,5], Howell V[3], Knott RB[6], Duff AP[6], Liu GJ[6], Reid G[1,2], Church WB[1].
1. University of Sydney, 2. Asbestos Diseases Research Institute, 3. Kolling Institute, 4. Lund University, 5. University of Buffalo, 6. Australian Nuclear Science and Technology Organisation.

Together with Emma Rath from the Faculty of Pharmacy of The University of Sydney, we are pre-clinically exploring the activity of BAMLET (bovine alpha-lactalbumin made lethal to tumour cells) in mesothelioma (models). BAMLET and related HAMLET (human alpha-actalbumin version)-like complexes have demonstrated anti-cancer activity in a large number of cancer cell lines at concentrations that do not seem to harm primary and immortalised non-cancer cells. In vivo experiments with HAMLET and BAMLET in demonstrated anti-tumour efficacy in bladder cancer, colon cancer and glioblastoma models. HAMLET-like compounds have not yet been investigated in mesotheliomas. BAMLET was cytotoxic in 11 human epithelial-like and biphasic mesothelioma and rat mesothelioma cell lines at similar concentrations. Chemo-resistant rat mesothelioma cells were just as sensitive to BAMLET as the chemo-sensitive cells. Small-angle X-ray scattering (SAXS) analysis revealed that the amount of incorporated oleic acid correlated with BAMLET toxicity. These results provide the basis for future studies to determine BAMLET activity in vivo. An abstract of these results was submitted to the International Mesothelioma Interest Group (iMig) to be presented in May 2016.

THE CONTRIBUTION OF STROMAL CELLS TO MICRORNA EXPRESSION IN MESOTHELIOMA

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

To understand changes in global microRNA gene expression in the malignant pleural mesothelioma (MPM) tumour microenvironment, we investigated the contribution of microRNA gene expression from MPM tumour cells and host cells associated with the tumour. In this study, being carried-out by Kadir Sarun as an MSc project, we have found that several microRNAs were significantly upregulated in experimental tumours derived from human MPM cell lines when compared to the levels found in the MPM cell lines grown in the laboratory. A similar phenomenon was observed in experimental mouse tumours grown in mice. Interestingly, mouse pri-miR-223, previously linked to a role in MPM, was up-regulated in both xenograft and syngraft, implicating a high stromal contribution of miR-223 in the tumour microenvironment.


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Quality of Life Research

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

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

This multi-site, observational, longitudinal study aims to explore the patient experience of people diagnosed with malignant mesothelioma (MM). The project examines health related quality-of-life, unmet care needs and anxiety and depression in people after a diagnosis of MM. It includes a number of optional sub-studies examining associations between these variables and other prognostic indicators such as inflammatory biomarkers, nutritional status and functional status. As of December 2015, site-specific ethics approval has been received for 14 participating hospitals and cancer institutions across Australia with potential expansion to an additional two sites. Recruitment commenced in April 2014 at approved sites and via self-referral recruitment strategies involving the Dust Diseases Board and the Asbestos Diseases Foundation of Australia. To date, 71 participants have consented to be part of the study.

In 2015 we presented an analysis of study data looking at optimal measures for assessing health related quality-of-life in patients with MM at the International Society of Quality of Life Research 22nd annual conference in Vancouver, Canada. Publications are in preparation reporting quality-of-life and nutritional risk following extrapleural pneumonectomy (EPP) surgical treatment.

Epidemiology and Health Services

Epidemiology is the corner stone of public health and helps to answer questions about the causes and patterns of disease in specific populations. The focus during 2015 for ADRI's epidemiology work has been on analysing and publishing epidemiological studies that assist us in accurately describing the malignant mesothelioma epidemic in Australia. This area of work is funded by the Cancer Institute NSW Translational Program Grant awarded to the Asbestos Diseases Research Institute, as well as through an Academic Leader in Cancer Epidemiology awarded to the University of Sydney.

PATTERNS IN THE INCIDENCE, MORTALITY AND SURVIVAL OF MALIGNANT PLEURAL AND PERITONEAL MESOTHELIOMA, NEW SOUTH WALES, AUSTRALIA, 1972-2009

Investigators: Soeberg MJ[1,2], Creighton N[3], Currow DC[3], Young JM[1], van Zandwijk N[1,2].
1. University of Sydney, 2. Asbestos Diseases Research Institute, 3. Cancer Institute NSW.

Malignant pleural mesothelioma (MPM) and malignant peritoneal mesothelioma (MPeM) are often grouped together in descriptive epidemiological analyses, resulting in limited understanding of epidemiological patterns for these tumour types. We studied patterns in the incidence, mortality and survival of people diagnosed with MPM (n=4,076) and MPeM (n=293) in New South Wales (NSW), Australia, 1972-2009. We also calculated 5-year relative survival for people diagnosed 1972-2006 followed up to 2007. We assessed patterns for each tumour type and histological subtype, and where possible, by combination of these categories. Annual MPM cases steadily increased over time (n=208 in 2009). There was an increasing trend in the MPM age-standardised incidence rate from 1972 up to 1994. This rate increase has levelled off in the last 10 years. Since 1999, on average 11 cases of MPeM were diagnosed each year. Five-year relative survival remained stable over time for MPM and MPeM. However, 5-year relative survival in 2002-2006 was substantially higher for people with MPM epithelioid histological subtype (11.7 % (95% CI 6.8%-19.2%)) compared to all other non-epithelioid histological subtypes (6.9% (95% CI 5.0%-9.1%)), a 70% difference. Survival was also greater for women with MPM (13.4% (95% CI 8.5%-19.4%)) with MPM compared to men (7.0% (95% CI 5.1%-9.2%)). MPM incidence rates have stabilised since the mid-1990s, suggesting that maximum incidence levels have been reached. When more up-to-date data are available, survival estimates should be reanalysed to include people likely to benefit from the wide introduction of combination chemotherapy in 2007, including pemetrexed. This work was published in the Australian and New Zealand Journal of Public Health.

INCIDENCE AND SURVIVAL TRENDS FOR MALIGNANT PLEURAL AND PERITONEAL MESOTHELIOMA, AUSTRALIA, 1982-2009

Investigators: Soeberg MJ[1,2], Leigh J[2], Driscoll T[1], Armstrong B[1], Young JM[1], van Zandwijk N[1,2].
1. University of Sydney, 2. Asbestos Diseases Research Institute

Australia is known to have had one of the highest per-capita asbestos consumption rates, yet there are few contemporary reports on malignant mesothelioma (MM) trends. Data on 10,930 people with malignant pleural mesothelioma (MPM) and 640 people with malignant peritoneal mesothelioma (MPeM) diagnosed in Australia during 1982-2009 were analysed. Observed incidence rate trends were quantified. Incidence rates were projected up to 2030 using observed incident cases during 1982-2012. The relative per-decade change in excess mortality during 1999-2009 was estimated. During 1982-2009, acceleration in MPM age-standardised incidence rates were highest for women and those aged 75 years and above, with average annual percentage changes of +4.9 (95% CI 3.6, 6.2) and +7.2 (95% CI 5.4, 9.0) respectively. Age-standardised incidence rates for men with MPM aged 0-64 years decelerated rapidly during 2003-2009, an average annual percentage change of -5.1% (95% CI -7.6, -2.5). Overall, male age-specific MPM incidence rates in the 65-74 year age group during 2010-2030 are projected to decline with rates projected to increase for older men and women with MPM. There was a statistically significant 16% relative reduction in the excess mortality rate up to 5-years post diagnosis for people diagnosed with MPM and MPeM combined in 2009 compared to those diagnosed in 1999, an excess mortality rate ratio of 0.84 (95% CI 0.77, 0.92). Australia's MM incidence rates appear to have reached maximum levels but with differences over time by age, gender and tumour location. Improvements over time in survival provide a glimpse of hope for this almost invariably fatal disease. This work was published in the Journal of Occupational and Environmental Medicine.

INCIDENCE OF MALIGNANT MESOTHELIOMA IN NEW ZEALAND AND AUSTRALIA – A GLOBAL SNAPSHOT

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

There has been recent, and increasing, interest in the human health effects of occupational and non-occupational exposure to airborne asbestos fibres including the potential risk of malignant mesothelioma (MM) occurrence in New Zealand and Australia. Despite New Zealand and Australia having among the highest age-standardised incidence rates globally, there are few contemporary reports comparing malignant mesothelioma in New Zealand and Australia with data from other countries. For example, the most recent literature on the epidemiology of MM in New Zealand was published in 2004. High-quality global cancer incidence rate data published in 2013 by the International Agency for Research Cancer (IARC) can help determine where New Zealand and Australia are placed in terms of the global incidence of MM. The IARC global cancer incidence data are reported as male and female populations separately. For the purpose of this short communication, we have focused on male age-standardised MM incidence rates as men are the population group most affected by MM due to the primary mode of asbestos exposure being in occupational settings. However, non-occupational asbestos exposures for both men and women are of increasing concern, particularly in Australia. This work was published as a letter to the editor in the New Zealand Medical Journal.

ASBESTOS AND MALIGNANT PLEURAL MESOTHELIOMA

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

There is strong scientific evidence demonstrating that exposure to airborne asbestos fibres is considered to be the single major cause of malignant pleural mesothelioma (MPM). There are different aetiological explanations for MPM that remain controversial or unresolved including the role of biological gender differences, genetic risk, as well as the association between maternal asbestos exposure and subsequent mesothelioma in children. Nevertheless, MPM is an important epidemiological marker of asbestos exposure through which it is possible to track a country's current and prior asbestos consumption and current or future patterns of asbestos-related disease. Quantifying the association between population-level asbestos consumption and MPM disease trends is an important yet challenging task as the morbid effects of asbestos use remain hidden for several decades. This is due to the long latency period between first asbestos exposure and a diagnosis of MPM, with this latency period ranging between 20 and 50 years. There have been significant shifts in global asbestos consumption with the most striking change occurring in the geographical regions in which asbestos is being used. The Asian region has become by far the largest asbestos consumer today. The deleterious human health, social, economic and environmental impacts of asbestos-related disease are preventable. Implementing a universal ban on asbestos and organising comprehensive occupational health and safety programmes are top priorities. This work was published as a book chapter in the e-book: Malignant Pleural Mesothelioma: Current Status and Future Directions.

Other Activities

MESOTHELIOMA SUPPORT CO-ORDINATOR

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

Three groups of patients were identified as requiring specific support from the Mesothelioma Support Coordinator in 2015.

1. patients receiving standard (palliative) care;
2. patients who underwent radical (combined-modality) treatment; and
3. the bereaved - struggling with grief and loss

.

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

We have used multiple mediums in an attempt to tailor a service to the needs of patients, carers and bereaved which included:

1. Monthly 'meet and greet' support meetings;
2. Telephone calls and emails that provide a communication link between the patient and the clinical and research 'mesothelioma world';
3. Teleconferencing that provides group communication and connects those living with similar experiences, thus reducing the isolating impact of distance and rarity of the disease;
4. Focused education and support sessions in metropolitan, rural and coastal health regions of NSW; and
5. Social-oriented activities, such as the carer's thank-you day. This gathering provided current and past carers with opportunities to share stories, support each other, and generate friendships.

A survey of support group members revealed that Facebook was not a medium they wanted to use, but they would support and consider attending educational meetings. However, the structured educational and activity-based programme for patients undergoing radical (combined modality) treatment including extrapleural pneumonectomy (EPP) has continued to be well attended and only recently established a private 'well living' Facebook page. Anecdotal evidence suggests there are a number of barriers that impact on patients and potentially affect the uptake of our service. They include travel time that can be up to 3 hours and distances of more than 100 kms, appointments for treatment that need to be kept as well as changes in performance status that may affect their ability to travel and engage in a meeting. There are a number of patients who also prefer to avoid the confrontation with other patients and only welcome one-on-one conversations.

Through a database, our support service recorded 160 patient referrals and 824 direct contacts to patients, carers and the bereaved. We also recorded 113 enquiries directly related to the ADRI TargomiR1 trial and the role of Pembrolizumab (Keytruda) in the treatment of MPM. They were primarily from Australia and New Zealand, but also a small number from UK, Asia and Europe.

Patients and carers prefer a personalised approach to physical and emotional support. They look forward to the one-on-one phone calls and will travel to attend a specific function, so in the coming period we will continue to monitor the uptake of our service but we will also explore the addition of interactive technologies to target typical physical symptoms of malignant pleural mesothelioma (MPM) and the informational needs of patients, carers and the bereaved and translate this in a personalised approach.

ADRI BIOBANK

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

The ADRI biobank occupies a central position in ADRI's research mission, which aims to improve the outlook for all those Australians exposed to asbestos. During 2015 additional samples have been added to the ADRI collection; the biobank contains fresh frozen tumour tissue, DNA and RNA samples derived from tumour tissue and matched bloods from mesothelioma patients, control tissue samples and a series of formalin-fixed tumour tissues. The ADRI biobank is connected to PRIMe (Identification of Predictive and Prognostic Factors in Malignant Mesothelioma) a study activated at Chris O'Brien Lifehouse at Royal Prince Alfred Hospital (RPAH). Since late 2015 we are in the process of establishing a structure that will also enable the collection of fresh frozen lung cancer specimens from consenting patients undergoing surgery at the RPAH. The collection of lung cancer specimens will enable us to focus on studies investigating asbestos-related lung cancer.

Independent pathological review of existing malignant pleural mesothelioma (MPM) samples was carried out in 2015 allowing us to contribute to a whole genome sequencing project in collaboration with Nic Waddell at the QIMR in Queensland. The samples in the biobank are supplemented by accurate clinical data and a purpose built IT system (CANSTO) is in place to link coded data, ensuring the protection of the privacy of biobank donors. Early in 2015 a biobank audit was conducted to control optimal functioning of the system and to verify if the records for each sample were sufficiently updated.

ADRI also contributed high quality mesothelioma specimens to a major international cancer research project known as The Cancer Genome Atlas (TCGA) which is co-ordinated by the National Cancer Institute (USA). The samples are being used for the TCGA's library of MPM. Advanced genomic technologies will be utilised to generate statistically and biologically significant outcomes. The overarching goal of the TCGA is to improve the ability to diagnose, treat and prevent cancer and the ADRI is proud to support this global collaborative initiative. 2015 was a year with major achievements and we are looking forward to further expand the biobank study sites and activities in 2016.

UNDERSTANDING PLEURAL MESOTHELIOMA

Penman A[1], McLean J[1], Keena V[1], van Zandwijk N[1,2].
1. Asbestos Diseases Research Institute,
2. University of Sydney

This information booklet, based on ADRI guidelines, was published in June 2015 by the Cancer Council as part of their 'Understanding' series. The booklet written for patients and carers provides information about the standards of care for malignant pleural mesothelioma (MPM) and is intended to assist with optimal communication between MPM patients, carers and the doctors involved in MPM care. A reprint of the booklet was necessary after less than a year, which clearly shows the importance for well-balanced patient information. The booklet is available from the Cancer Council website as an ebook (http://www.cancer.org.au/about-cancer/cancer-ebooks.html) and from the ADRI. If you would like a copy please call ADRI 02 9767 9800.

PREVENTION THROUGH EDUCATION

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

In 2015 the ADRI staff continued to participate in various government and community activities to raise the awareness of the dangers of asbestos. On an international level, Professor van Zandwijk and Dr Soeberg continued to advise the Government of Vietnam on how to start asbestos awareness education and why a total asbestos ban is much needed in a country with ongoing asbestos consumption. ADRI, in collaboration with the Viet Nam Health Environment Management Agency and the University of Occupational and Environmental Health (Japan), has also recently published its findings from a pilot descriptive cancer registry study identifying the presence of malignant mesothelioma in Viet Nam. These data will provide an important benchmark for measuring the future incidence of asbestos-related cancer in Viet Nam as well as provide peer-reviewed scientific data for the Viet Nam government's efforts to put an asbestos ban in place in the coming years. A delegation from government and non-government officials from Viet Nam and Laos also visited Australia in November. Their trip included a presentation at ADRI focusing on new research findings and the development of the ADRI malignant pleural mesothelioma consumer guidelines.

AUSTRALIAN MESOTHELIOMA REGISTRY

The Australian Mesothelioma Registry (AMR) is a stand-alone database that contains information about people with mesothelioma. Since the 1st July 2010 the AMR receives notification of all new cases of mesothelioma diagnosed in Australia. In addition, this registry collects information about asbestos exposure from people with mesothelioma through a postal questionnaire and telephone interview.

The organisations involved in the AMR, funded by Safe Work Australia and Comcare include: Cancer Institute NSW; Monash Centre for Occupational and Environmental Health; Hunter Research Foundation; Asbestos Diseases Research Institute; University of Sydney; Western Australia University, and Dust Diseases Board of NSW.

The information collected is being used to draft a careful picture of the Australian mesothelioma epidemic and to assist governments to develop policies to best deal with the asbestos ubiquitously present in Australia, with the aim of reducing mesothelioma incidence in the future.

In August 2015, the AMR published their fourth annual report providing data on malignant mesothelioma in Australia during 2014.

Publications, Presentations and Awards

PEER REVIEWED ARTICLES

2016

1. Soeberg MJ; Luong MA; Tran VT; Tran AT; Nguyen TTH; Bui D; Nguyen THN; Takahashi K; van Zandwijk N. Estimating the incidence of malignant mesothelioma in Viet Nam: a pilot descriptive cancer registration study. International Journal of Occupational and Environmental Health. doi: 10.1080/10773525.2016.1151604 : In press 2016

2. Kao S, Kirschner M, Cooper W, Tran T, Burgers JA, Wright C, Korse CM, van den Broek D, Edelman J, Vallely M, McCaughan B, Pavlakis N, Clarke SJ, Molloy M, van Zandwijk N, Reid G. A proteomics-based approach identifies Secreted Protein Acidic and Rich in Cysteine (SPARC) as a prognostic biomarker in malignant pleural mesothelioma. British Journal of Cancer: In press 2016.

3. van Zandwijk N, Soeberg M, Reid G. Using a multidisciplinary approach to combat the burden of asbestos-related disease. Medical Journal of Australia 204 (2) 1 February 2016: 52 PMID:26821095

4. Soeberg M J, Leigh J, Driscoll T, Armstrong B, Young JM, van Zandwijk N. Incidence and survival trends in malignant pleural and peritoneal mesothelioma, Australia, 1982-2009. Occupational and Environmental Medicine: 2016;0:1-8. doi:10.1136/oemed-2015-103309 PMID: 26800709

2015

5. Soeberg M, van Zandwijk N. Incidence of malignant mesothelioma in New Zealand and Australia – a global snapshot. [Letter] New Zealand Medical Journal 2015; 128 (1427):68-71.

6. Soeberg MJ, Creighton N, Currow DC, Young JM, and van Zandwijk N. Patterns in the incidence, mortality and survival of malignant pleural and peritoneal mesothelioma, New South Wales, Australia, 1972-2009. Australian & New Zealand Journal of Public Health 2015; Online; doi: 10.1111/1753-6405.12503 PMID:26713662

7. Glover AR, Zhao JT, Gill AJ, Weiss J, Mugridge N, Kim E, Feeney AL, Ip JC, Reid G, Clarke S, Soon PS, Robinson BG, Brahmbhatt H, MacDiarmid JA, Sidhu SB. microRNA-7 as a tumor suppressor and novel therapeutic for adrenocortical carcinoma. Oncotarget. 2015 Nov 3;6(34):36675-88. PMID: 26452132

8. Kirschner MB, Pulford E, Hoda MA, Rozsas A, Griggs K, Cheng YY, Edelman JJB, Kao SC, Hyland R, Dong Y, László V, Klikovits T, Vallely MP, Grusch M, Hegedus B, Dome B, Klepetko W, van Zandwijk N, Klebe S, and Reid G. Fibulin-3 levels in malignant pleural mesothelioma are associated with prognosis but not diagnosis. Br J Cancer. 2015; 113(6): 963-9. PMID: 26263483

9. Williams M, Kirschner MB, Cheng YY, Hanh J, Weiss J, Mugridge N, Wright CM, Linton A, Kao SC, Edelman JJB, Vallely MP, McCaughan BC, Cooper W, Klebe S, Lin RCY, Brahmbhatt H, MacDiarmid J, van Zandwijk N, Reid G. miR-193a-3p is a potential tumor suppressor in malignant pleural mesothelioma. Oncotarget. 2015; 6(27):23480-95. PMID:26125439

10. Kao SC, Fulham M, Wong K, Cooper W, Brahmbhatt H, MacDiarmid J, Pattison S, Sagong JO, Huynh Y, Leslie F, Pavlakis N, Clarke S, Boyer M, Reid G, van Zandwijk N. A significant metabolic and radiological response after a novel targeted microRNA-based treatment approach in malignant pleural mesothelioma. [To the Editor] American Journal of Respiratory and Critical Care Medicine. 2015:191(12):1467-1469. PMID:26075427

11. Reid G. MicroRNAs in mesothelioma: from tumour suppressors and biomarkers to therapeutic targets. J Thorac Dis. 2015;7(6):1031-40. PMID:26150916

12. Birnie KA, Yip YY, Ng DC, Kirschner MB, Reid G, Prele CM, Musk AW, Lee YG, Thompson PJ, Mutsaers SE, Badrian B. Loss of mir-223 and JNK Signalling Contribute to Elevated Stathmin in Malignant Pleural Mesothelioma. Mol Cancer Res. 2015 Mar 30. pii: molcanres.0442.2014. [Epub ahead of print] PMID:25824152

13. Klebe S, Griggs K, Cheng Y, Driml J, Henderson DW, Reid G. Blockade of aquaporin 1 inhibits proliferation, motility, and metastatic potential of mesothelioma in vitro but not in an in vivo model. Disease Markers 2015: 286719. doi: 10.1155/2015/286719. Epub 2015 Mar 4 PMID:25821338

14. Kumarakulasinghe NB, van Zanwijk N, Soo RA. Molecular targeted therapy in the treatment of advanced stage non-small cell lung cancer (NSCLC). Fong KM, van Zanwijk N. (Series Ed.) Invited Review Series: Lung cancer practice, implementing evidence around the world. Respirology. 2015 Apr;20 (3):370-8. doi: 10.1111/resp.12490. Epub 2015 Feb 17. PMID:25689095

15. van Zandwijk N, Fong KM. Update in lung cancer: Prologue to a modern review series. Fong KM, van Zandwijk N. (Series Ed.) Series Editorial – Prologue: Lung cancer practice, implementing evidence around the world. Respirology. 2015: 20 (2):183–184 PMID:25594901

16. Kao SC-H, van Zandwijk N, Clarke S, Vardy J, Lumba S, Tognela A, Ng W. Estimation of an optimal chemotherapy utilization rate for malignant pleural mesothelioma: An evidence-based benchmark for cancer care. Asia-Pacific Journal of Clinical Oncology. 2015; Mar 11(1): 85-92. PMID:25382807

17. Kirschner MB, Cheng YY, Armstrong NJ, Lin RCY, Kao SC, Linton A, Klebe S, McCaughan BC, van Zandwijk N, Reid G. MiR-Score: A novel 6-microRNA signature that predicts survival outcomes in patients with malignant pleural mesothelioma. Molecular Oncology. 2015; 9(3):715-726. PMID : 25497279

BOOK CHAPTERS
2016

1. Soeberg M, van Zandwijk N. Chapter 9: Asbestos and malignant pleural mesothelioma. In: Mineo TC (ed) Malignant pleural mesothelioma: Present status and future direction. Benthem Science Publishers; 2015 (eBook). Chapter 9; p115-128. eISBN 978-1-68108-219-6. ISBN 978-1-68108-220-2 http://ebooks.benthamscience.com/book/9781681081939/

CONFERENCE PRESENTATIONS
2015

1. Reid G, Kao S, Marcela P, Kirschner MB, Cheng YY, Williams M, Mugridge N, Weiss J, Boyer M, Linton A, Pattison S, Leslie F, Huynh Y, Molloy M, Lin RCY, Brahmbhatt H, MacDiarmid J, Clarke S, Pavlakis N, van Zandwijk N. Development of a microRNA mimic delivered by targeted nanocells as a treatment for patients with recurrent thoracic cancer. American Association for Cancer Research. Noncoding RNAs and Cancer: Mechanisms to Medicines, Boston, 4-7 December 2015. (Awarded Slater & Gordon Asbestos Research Fund Travel Award)

2. Kirschner MB, Williams M, Burgers S, Hoda MA, Korse CM, Van Den Broek D, Klikovits T, Hegedus B, Dome B, Grusch M, Klepetko W, van Zandwijk N, Reid G. Cell-free microRNA miR-625-3p is elevated in the blood of patients with thoracic malignancies. Journal of Thoracic Oncology. 2015; 10(Suppl 2): S350. IASLC 16th World Conference on Lung Cancer, Denver, 6-9 September 2015.

3. van Zandwijk N, Pavlakis N, Kao S, Clarke S, Linton A, Brahmbhatt H, Macdiarmid J, Pattison S, Leslie F, Huynh Y, Reid G. Early signs of clinical activity of a microRNA-based therapy in a phase I study in recurrent malignant pleural mesothelioma. Journal of Thoracic Oncology. 2015; 10(Suppl 2): S224-S225. IASLC 16th World Conference on Lung Cancer, Denver, 6-9 September 2015.

INVITED PRESENTATIONS

2015

1. van Zandwijk N. A microRNA-based and immunologically active treatment approach of thoracic cancers. The 7th Chinese-German Lung Cancer Forum, Shanghai, China, 13-14 November 2015.

2. van Zandwijk N. Challenges/management of malignant pleural mesothelioma. Post-World Conference on Lung Cancer 2015. International Congress Center Dresden, Germany, 5-6 November 2015.

3. van Zandwijk N. Asbestos-related lung diseases guidelines and research advances. RMA15 Conference Workshop. Adelaide Convention Centre, 23 October 2015.

4. Reid G. RPA Institute of Academic Surgery, 4 September 2015.

5. Kao S. Welcome. Sydney Catalyst International Translational Cancer Research Symposium. Darling Harbour, Sydney, 27 July 2015

6. Reid G. Thoracic Cancer. An illustrative journey. Sydney Catalyst International Translational Cancer Research Symposium. Darling Harbour, Sydney, 27 July 2015

7. Kao S. Early signs of activity of TargomiRs (microRNA mimics delivered by nanocells) in a phase I study for patients with recurrent mesothelioma 6th International Nanomedicine Conference , Coogee, 6-8 July 2015

8. van Zandwijk N. TargomiRs in Thoracic Oncology: recent results and future prospects. Netherlands Cancer Institute, Amsterdam, 26th June 2015.

9. van Zandwijk N. Current research in mesothelioma & the mesothelioma registry. Asbestos related lung disease & malignant pleural mesothelioma health professional workshop. Medical Education Centre, Concord Hospital, 19th June 2015.

10. McLean J. Surgery – VAT, Pleurodesis, EPP. Asbestos related lung disease & malignant pleural mesothelioma health professional workshop. Medical Education Centre, Concord Hospital, 19th June 2015.

11. Linton A. Chemotherapy. Asbestos related lung disease & malignant pleural mesothelioma health professional workshop. Medical Education Centre, Concord Hospital, 19th June 2015.

12. Kao S. Welcome. From discover to recovery: examining the cancer patient's journey. 2015 International translational cancer research symposium. Sydney Catalyst, Darling Harbour 27 July 2015

13. Reid G. Lung cancer: An illustrative journey. From discover to recovery: examining the cancer patient's journey. 2015 International translational cancer research symposium. Sydney Catalyst, Darling Harbour 27 July 2015

14. van Zandwijk N. Hopeful treatment of asbestos cancers. European Asbestos Forum, Amsterdam. 27th May 2015

15. Soeberg M, van Zandwijk N. Patterns in the incidence, mortality and survival of malignant pleural and peritoneal mesothelioma, New South Wales, Australia, 1972-2009. Know Cancer Risks at Work 2015, Forum. Cancer Council Australia's Occupational and Environmental Cancer Committee. Sydney 18 May 2015.

16. Kao S. Phase II trial of nab-paclitaxel as second line chemotherapy for advanced malignant pleural mesothelioma (MPM). Australasian Lung cancer Trials Group (ALTG), Melbourne, 1 May 2015.

17. Linton A. Addition of surviving-inhibitor to 1st ling chemotherapy in pleural mesothelioma. Australasian Lung cancer Trials Group (ALTG), Melbourne, 1 May 2015.

18. van Zandwijk N. Asbestos: a time-bomb with a long fuse. World Asbestos Congress 2015.Karachi, Pakistan. 31st January – 1st February 2015.

CONFERENCE POSTERS

2015

1. Fowler JM, Vardy JL, Kao S, Coll JR, Warby A, Price MA, Dhillon H. Assessing Health Related Quality of Life (HQOL) in Mesothelioma: which measures are optimal? Quality of Life Research. 2015; 24(Suppl 1): 127-8. International Society for Quality of Life Research, 22nd Annual Conference, Vancouver BC, 21-24 October 2015.

2. Reid G, Cheng YY, Sarun K, Williams M, Kirschner MB, Despotovski A, Mugridge N, Weiss J, Brahmbhatt H, Macdiarmid J, Molloy M, Lin R, van Zandwijk N. Targeted delivery of a synthetic microRNA-based mimic to treat thoracic cancers. Journal of Thoracic Oncology. 2015; 10(Suppl 2): S426. IASLC 16th World Conference on Lung Cancer, Denver, 6-9 September 2015.

3. Kirschner MB, Pulford E, Hoda MA, Rozsas A, Griggs K, Edelman JJB, Kao S, Hyland R, Dong Y, Laszlo V, Klikovits T, Jakopovic M, Vallely M, Grusch M, Hegedus B, Dome B, Klepetko W, van Zandwijk N, Klebe S, Reid G. Fibulin-3: A potential prognostic biomarker in malignant pleural mesothelioma? Journal of Thoracic Oncology. 2015; 10(Suppl 2): S747. IASLC 16th World Conference on Lung Cancer, Denver, 6-9 September 2015.

4. Kao S, Dhillon H, Warby A, Vardy J. Healthcare professional perceptions of chemotherapy in treatment of malignant pleural mesothelioma (MPM). Journal of Thoracic Oncology. 2015; 10(Suppl 2): S629. IASLC 16th World Conference on Lung Cancer, Denver, 6-9 September 2015

5. van Zandwijk N, Pavlakis N, Kao S, Clarke S, Linton A, Boyer M, Brahmbhatt H, McDiarmid J, Pattison S, Leslie F, Huynh Y, Reid G. Early signs of activity of TargomiRs (microRNA mimics delivered by nano cells) in a Phase I study for patients with recurrent Mesothelioma. WIN 2015 Symposium, Paris, 29-30th June 2015.

6. Reid G, Cheng YY, Williams M, Kirschner M, Despotovski A, Mugridge N, Weiss J, Brahmbhatt H, MacDiarmid J, Molloy M, Lin R, van Zandwijk N. Targeted delivery of a synthetic microRNA-based mimic as an approach to treating cancer. WIN 2015 Symposium, Paris, 29-30th June 2015.

7. van Zandwijk N, Pavlakis N, Kao S, Clarke S, Lee A, Brahmbhatt H, MacDiarmid J, Pattison S, Leslie F, Huynh Y, Linton A, Reid G. MesomiR 1: A Phase I study of TargomiRs in patients with refractory malignant pleural mesothelioma (MPM) and lung cancer (NSCLC). Annals of Oncology. 2015; 26 (suppl 2):ii16. 13th International Congress on Targeted Anticancer Therapies (TAT) 2015, Paris France 2-4 March 2015. PMID:25795822

8. Reid G. Targeted delivery of a synthetic microRNA mimic as a novel approach to treating cancer. 27th Lorne Cancer Conference 2015, 12th-14th February 2015.

AWARDS

2015

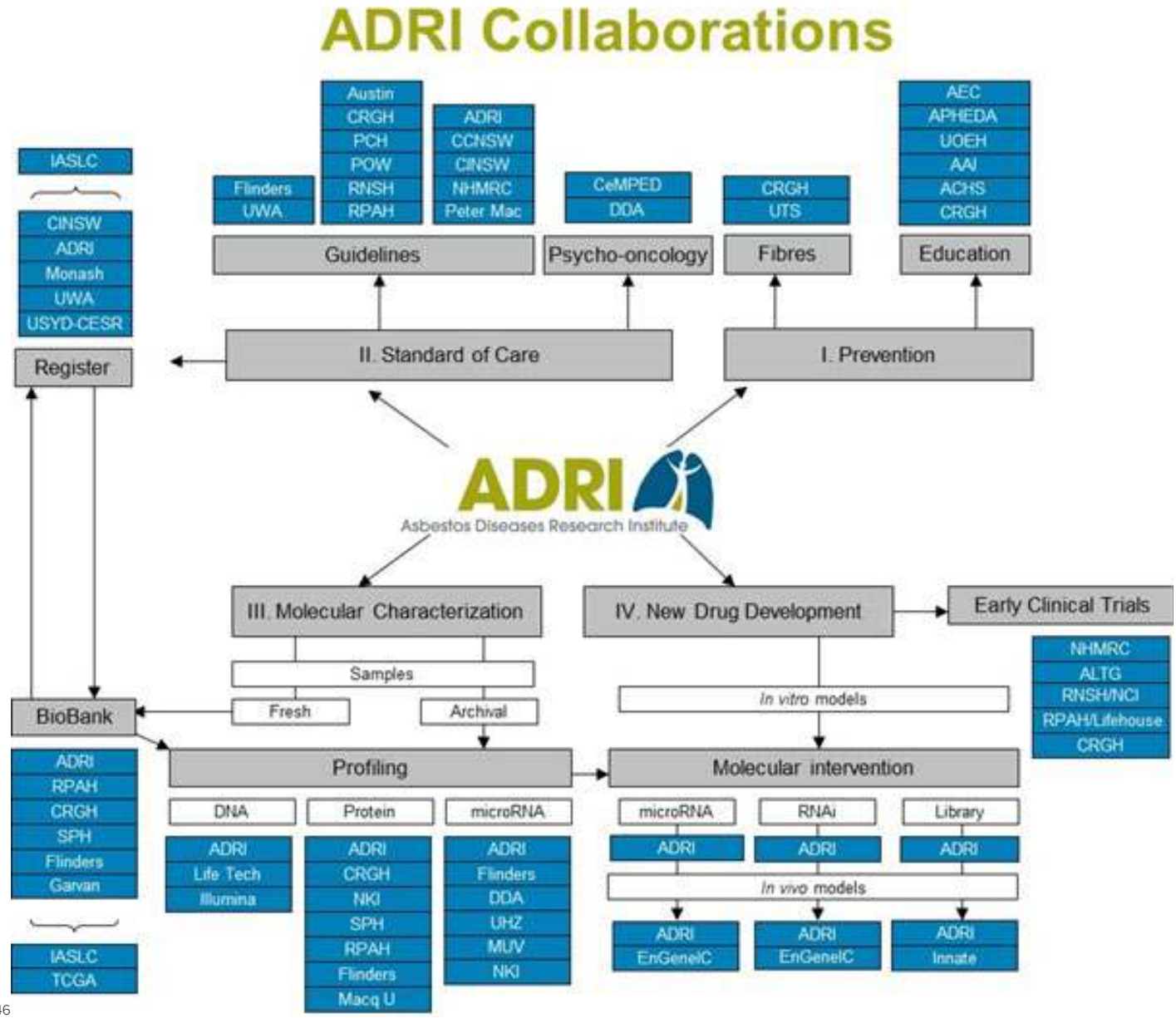
1. van Zandwijk N. Awarded The Dr J. Stumphius Recognition Award at the European Asbestos Forum, Amsterdam. 27th May 2015

TRAVEL AWARDS

1. Reid G. Slater & Gordon Health Project and Research Fund - 2015. Australian Communities Foundation. Travel Fellowship; American Association for Cancer Research. Noncoding RNAs and Cancer: Mechanisms to Medicines, Boston, 4-7 December 2015.

2. McLean J. Slater & Gordon Health Project and Research Fund -2015. Australian Communities Foundation. Travel Fellowship; The International Mesothelioma Interest Group (iMig) Conference, Birmingham, 1-4 May 2016.

Research Collaborators



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
CCNSW	Cancer Council NSW
CINSW	Cancer Institute NSW
CeMPED	Centre For Medical Psychology & Evidence-Based Decision-Making
Lifehouse	Chris O'Brien Lifehouse
CRGH	Concord Repatriation General Hospital
DDA	Dust Diseases Authority
EnGeneIC	EnGeneIC Ltd (biotechnology) Sydney
Flinders	Flinders University
Garvan	Garvan Institute of Medical Research
IASLC	International Association for the Study of Lung Cancer
Illumina	Illumina Inc.
Innate	Innate Therapeutics Ltd
Life Tech	Life Technologies
Macq Uni	Macquarie University
MUV	Medical University of Vienna
Monash	Monash University
NHMRC	National Health & Medical Research Council
NKI	Netherlands Cancer Institute, The Netherlands
NCI	Northern Cancer Institute
Peter Mac	Peter MacCallum Cancer Centre
PCH	Prince Charles Hospital
POW	Prince of Wales Hospital
RNSH	Royal North Shore Hospital
RPAH	Royal Prince Alfred Hospital
SPH	Strathfield Private Hospital
TCGA	The Cancer Genome Atlas
UOEH	University of Occupational & Environmental Health, Fukuoka, Japan
USYD-CESR	University of Sydney, Cancer Epidemiology and Services Research
UTS	University of Technology Sydney
UWA	University of Western Australia
UHZ	University Hospital Zurich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Financial Summary 2015

PROFIT AND LOSS STATEMENT	2014-15	2013-14
Revenues		
Research	2,130,790	2,106,053
Fundraising	239,815	797,796
Interest	185,803	192,212
Total	2,556,408	3,096,061
Expenses		
Employee Benefits	1,989,551	1,846,822
Research consumables/equipment	246,702	367,590
Office expenses	268,912	224,517
Depreciation	356,204	403,748
Total	2,861,369	2,842,677
Surplus / Deficit for the period	**304,961**	**253,384**

BALANCE SHEET	30/06/2015	30/06/2014
Assets		
Cash and cash equivalents incl. Term Deposits	6,068,640	5,765,147
Trade and other receivables	76,712	78,412
Property Plant and Equipment	8,735,292	9,021,448
Total	14,880,644	14,865,007
Liabilities		
Trade and other payables	1,165,680	921,532
Employee provisions	161,512	85,062
Total	1,327,192	1,006,594
Net Assets	**13,553,452**	**13,858,413**

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

Community Support

As a direct consequence of the intense use of asbestos, and its products, Australia is among the countries with the world's highest incidences of malignant mesothelioma. The ADRI was established as a response to this legacy; with an objective to make asbestos-related diseases history, and to provide a better future to those Australians exposed to asbestos. To achieve these objectives it is vital that the ADRI has the community's support and participation.

The ADRI benefits from good relations with victim support groups receiving excellent advice, participation and financial support. These groups include: Asbestos Diseases Foundation of Australia (ADFA), the Asbestosis & Mesothelioma Association of Australia (AMAA) and the Asbestos Disease Support Society (ADSS).

Mr Barry Robson, President of ADFA, and Professor Nico van Zandwijk, ADRI Director, speaking at ADFA's Memorial Day in November 2015 at the Australian National Maritime Museum, Darling Harbour. Throughout 2015 ADFA members have kindly consented to participate in a number of quality-of-life studies for which we are very grateful.

Mr Nic Bos, AMAA, presenting Professor van Zandwijk a cheque at the official opening of the AMAA headquarters on the Gold Coast in November 2015.

At the ADSS inaugural Thank You event in November 2015 Ms Amanda Richards, Chief Executive Officer, and Mr Andrew Ramsay, Chair, presented Professor Nico van Zandwijk a cheque for $100,000.00. This extremely generous donation by the ADSS will enable the ADRI to continue our research, and in particular the MesomiR clinical trial. The 'MesomiR 1' trial was the world's first trial to focus on the value of microRNA-based therapy in malignant pleural mesothelioma and non-small cell lung cancer for which essentially no curative treatment options exist.

The concept of the new medication, TargomiRs, resembles the Trojan horse story, where tumour cells absorb the microRNA (mimics) delivered by minicells thereby slowing/stopping tumour growth. Whilst the results of the MesomiR 1 trial were very exciting it was a very early observation that requires confirmation in the next phase of clinical testing. The next stage will focus on efficacy and the very generous donation by the ADSS will contribute to the transition from phase I to II. The obvious goal of our clinical studies is to eventually add a new form of treatment to the limited therapeutic arsenals for malignant mesothelioma and non-small cell lung cancer; two cancer diagnoses associated with asbestos exposure.


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Renovate
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Asbestos Disease
Support Society
25/11/2015
Pay ADRI
$100,000.00
One hundred Thousand
Asbestos Disease Support Society


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Australia Inc.
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Asbestosis & Mesothelioma
Association of Australia
AMAA
ASBESTOS DISEASES RESEARCH INSTITUTE
TWELVE THOUSAND, FIVE HUNDRED
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$12,500.00
Asbestosis & Mesothelioma Association of Australia
diseases
iation.com.au
758

Our Volunteers

Jenny Weismantal and Suzanne Mouthaan have been volunteering at ADRI for a number of years. Jenny is a wonderful asset to both ADRI's admin and research teams. Over the years, Jenny has spent three afternoons a week at ADRI and has become a valuable member of the team. Sue assists Professor Janette Vardy's admin team at the Sydney Survivorship Centre at Concord Hospital and a number of other projects from time to time. Both women choose to volunteer their time as a way of contributing to the progress of medical research into asbestos-related diseases.

Thank you to both Jenny and Sue.

Geoff and Karen Wicks are 'Betty'- the ADRI house's curators and chauffeurs. Geoff is a retired avionics engineer and DIYer, he and Karen have volunteered their time to travel thousands of kilometres up and down the eastern states of Australia, participating in numerous media events to educate the community about the dangers of asbestos. Betty is a purpose built mobile model home, designed to demonstrate where asbestos may be found in and around any Australian home built or renovated before 1987. Betty is an initiative of the Asbestos Education Committee in partnership with ADRI. Betty's mission is to educate all Australians about the dangers of asbestos. For more information visit asbestosawareness.com.au or https://www.facebook.com/BettytheADRIhouse

Thank you to Geoff and Karen for the enormous numbers of hours you have dedicated to showcasing Betty and to raising awareness of the dangers of asbestos.

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