

National Centre for Asbestos Related Diseases

an Australian Research Cooperative



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Researcher profile – Professor Jenette Creaney

The Tumour Immunology Group (TIG) is a node of NCARD based at Perth's Sir Charles Gairdner Hospital. The TIG team comprises more than 30 students and staff, and is led by four senior researchers: Bruce Robinson, Richard Lake, Anna Nowak, and Jenette Creaney.



PROFESSOR JENETTE CREANEY WITH HER COLLEAGUE PROFESSOR ANNA NOWAK

Jenette Creaney heads the Biomarkers team, and was the key leader of the group that identified and characterised the use of serum mesothelin as a biomarker in malignant mesothelioma, a test which has since been commercialised and become widely available. This work was published in prestigious journals including *The Lancet*, *Thorax* and *Chest*.

Jenette's work on the value of mesothelin for distinguishing mesothelioma from lung cancer and non-malignant pulmonary disease was so significant in changing clinical practice that it established her in international mesothelioma research, acknowledged by her being awarded Young Investigator at the International Mesothelioma Interest Group (IMIG) conference in Amsterdam in 2008.

Jenette joined the TIG research team in 1999, with a PhD in protein chemistry and molecular biology. She has focussed on improving our understanding of mesothelioma ever since.

Building networks with a multi-disciplinary team – within the State, across Australia, and internationally – is one of Jenette's fortes. She is an experienced collaborator with researchers and clinicians including medical oncologists, pulmonary medicine physicians, molecular biologists, pathologists and physicists. Among her long-time research collaborators are Steven Skates at Harvard, an eminent biostatistician in the field of ovarian cancer biomarkers; while in Perth, she has had a long association with respiratory physician Bill Musk. Recently Jenette has established a collaboration with Richard Simpson in Melbourne, a world leader in proteomics.

Jenette has executive roles with both the Australian Biospecimens Network and the Australian Lung Cancer Clinical Trials Groups. She is the Manager of the Australian Tissue Bank, and was instrumental in building the foundation of this bank through her strong working relationships with clinicians, surgeons and pathologists. This considerable bank of tissue samples forms an extraordinary resource for mesothelioma research.

Jenette has contributed to grants being awarded to the research team by the National Health & Medical Research Council (NHMRC), National Institute of Health (NIH), the Insurance Commission of WA and the Cancer Council of WA that together total more than \$8 million. Currently she is leading her team in identifying new mesothelioma biomarkers using a suite of five discovery platforms. Whilst ambitious, aspects of this work have already been reviewed and funded, and Jenette is optimistic of more breakthroughs.

TRACY HAYWARD, NCARD ADMINISTRATIVE OFFICER

Welcome to the relaunched NCARD Newsletter

Since the Asbestos Management Review's inception about 12 months ago, NCARD has been an active contributor, with Professor Bruce Robinson, the Director of NCARD, a member of the Advisory Board.

The Review, set up by the Federal Government under the chairmanship of Mr Geoff Fary, previously ACTU Assistant Secretary, accepted public submissions in 2011, and will report to Federal Parliament at the end of June 2012.

Asbestos Awareness Week ran from 21 to 27 November. Events were held around the country by Asbestos Diseases Societies and other groups. A Parliamentary Group on Asbestos Related Diseases (PGARD) was launched at Parliament House, Canberra, that week. The Asbestos Diseases Society of Australia held their annual, very moving, ecumenical service on Friday 25 November at Redemptorist Monastery, North Perth. Earlier in the week, NCARD joined with the Asbestos Diseases Society at their information stall on the Murray Street Mall in Perth.

The Executive Producer of the Australian Broadcasting Commission's current affairs programme, Four Corners, contacted NCARD regarding the re-screening of the 1988 programme on Wittenoom, "Blue Death", as part of the Four Corners 50th Anniversary celebrations. Kerry O'Brien presented an updated introduction to the programme, which had been especially chosen because of its impact and significance, with information provided by NCARD researchers. "Blue Death" screened the week after Asbestos Awareness Week, on 3 December 2011.

DR MATTHEW TILBROOK, NCARD BUSINESS MANAGER



Annual Scientific Meeting

The first of a two part Annual Scientific Meeting for NCARD was held on 17 & 18 May at the Perth Flying Squadron Yacht Club in Nedlands, Perth.

The invited speaker was Professor Frank Carbone, an NHMRC Australia Fellow from the Department of Microbiology and Immunology at the University of Melbourne.

The second part of the Annual Scientific Meeting was held on 23 and 24 August in Brisbane. The focus was on Genetics, Proteomics and Lung Cancer. Local Queensland NCARD researchers in Professor Kwun Fong's team attended as well as members of the team from Perth. Other NCARD affiliated researchers who attended were Professor Nico van Zandwijk and Dr Glen Reid from the Bernie Banton Centre, and Dr Neil Watkins from the Monash Institute of Medical Research. Professor Sean Grimmond from the Queensland Centre for Medical Genomics and Dr Greg Rice, an NHMRC Principal Research Fellow and Deputy Director (Translation) at the University of Queensland Centre for Clinical Research, were also invited to attend.

Previous NCARD Annual Scientific Meetings have been held in Perth (2007 and 2010), Melbourne (2008) and Sydney (2009).

The next Scientific Meeting will be held at the end of October 2012, again in Perth.

DR MATTHEW TILBROOK,
NCARD BUSINESS MANAGER

Research news review

Serum vs Plasma Biomarkers for diagnosis of Malignant Plural Mesothelioma.

Malignant Plural Mesothelioma (MPM) is a uniformly fatal, asbestos related cancer that arises from the mesothelial cell lining of the surface of the pleural cavity. Diagnosis of MPM is currently based on analysis of histological and cytological biopsies. However, diagnosis often occurs late, when there is already extensive tumour burden and advanced disease; a situation associated with the overall poor prognosis and limited effective treatment options for patients. Research aimed at improving early detection of MPM has received increased focus in recent years. Much of this research has focussed on identifying and validating blood or fluid-based markers for MPM, with particular interest in using osteopontin and the mesothelin family of proteins as potential useful biomarkers.

Of the four variants of the mesothelin protein, two have been investigated as potential biomarkers for MPM. The archetypal mesothelin protein is a 40 kDa cell surface protein that is often over expressed in malignant conditions including MPM, ovarian and prostate cancers, while the soluble mesothelin related protein (SMRP) with its identical N-terminal end, but unique C-terminus is shed from the cell surface. Numerous studies have detected both protein variants in the serum of patients with MPM with a high degree of

specificity and sensitivity and importantly elevated levels of soluble mesothelin have been detected in 15% of asbestos exposed individuals prior to diagnosis of MPM. In addition to soluble mesothelin, researchers have investigated the potential of osteopontin as a biomarker for MPM. Osteopontin is a secreted glycoprotein with diverse functions. It is involved in cell migration and cell matrix adhesion and, like mesothelin, is over expressed in breast, lung, prostate and ovarian cancers. Osteopontin can be detected in serum and plasma, which has led to its potential as a biomarker for early detection of MPM.

Two recent studies have looked at whether combining serum or plasma osteopontin levels with soluble mesothelin could be used to accurately diagnose MPM. Both studies used commercially available enzyme linked immunosorbent assay (ELISA) kits to assess the levels of soluble mesothelin and plasmid or serum osteopontin between their respective cohorts. The study by Cristaudo et al, published in *The Journal of Thoracic Oncology*, compared a cohort of 31 confirmed MPM patients to 111 patients with benign respiratory disease (BRD) and 93 healthy controls, and found a significant increase in the level of soluble mesothelin and plasma osteopontin in MPM in

comparison with BRD or healthy controls. A similar outcome was not observed between BRD and healthy controls. They also stated that the combination of both biomarkers resulted in improved diagnosis of MPM, and have proposed that their use as a "combined risk index" should be further investigated in a larger cohort of patients to validate their use as a biomarker for MPM diagnosis.

Creaney et al (Jenette Creaney, profiled in this newsletter), recently reported a study in the journal *Lung Cancer* in which their team investigated the diagnostic accuracy of combined osteopontin and soluble mesothelin in matched serum and plasma samples for 66 patients with MPM in comparison to 89 patients with BRD and 21 patients with non MPM lung cancer. The authors found that the level of mesothelin was significantly higher in MPM patients in comparison to controls, a result that was consistent regardless of whether mesothelin levels were assessed in serum or plasma.

DR SCOTT FISHER,
RESEARCH ASSISTANT PROFESSOR



New funding for NCARD

Firstly, by way of background: in 2006 NCARD was established as a national cooperative (an "institute without walls") by the Commonwealth through the National Health and Medical Research Council (NHMRC) to enable the best Australian scientists, clinicians and researchers in the field, using the best available modern technology, to work cooperatively to find a prevention and/or cure for asbestos cancers in the shortest realistic timeframe.

In mid 2010 the NHMRC decided to continue the funding of the national centre through the grant of a Centre for Research Excellence. The grant for five years was for \$2.5 million with a further \$2 million added for the national collaborative aspect. Funding began midway through 2011.

There are a further ten Associate Investigators from around Australia.

DR MATTHEW TILBROOK, NCARD BUSINESS MANAGER

The Chief Investigators are:

Prof. Bruce Robinson

School of Medicine
and Pharmacology, UWA

Prof. Jenette Creaney

School of Medicine
and Pharmacology, UWA

Prof. Anna Nowak

School of Medicine
and Pharmacology, UWA

Prof. Richard Lake

School of Medicine
and Pharmacology, UWA

Prof. Bill Musk

Dept of Respiratory
Medicine, Sir Charles
Gairdner Hospital

**Prof. Barbara Fazekas
de St Groth**

Centenary Institute,
University of Sydney

Prof. Lyle Palmer

Ontario Institute for Cancer
Research

Prof. Richard Simpson

La Trobe University Institute
of Molecular Science

Prof. Steve Skates

Harvard Medical School

Prof. Neil Watkins

Monash Institute of Medical
Research



WORLD CONFERENCE ON LUNG CANCER VENUE IN AMSTERDAM

14th World Conference on Lung Cancer

The 14th World Conference on Lung Cancer was held in Amsterdam from 3-7 July 2011. Asbestos-induced cancers were discussed in a number of sessions – a welcome change, as in previous conferences they have been largely neglected. This may have been due to the role of ADRI's Professor Nico van Zandwijk as a co-convenor.

The most intensely debated topic was the role of surgery in mesothelioma. The first stage of the MARS trial from the UK was presented. It was clear that the data were interesting but preliminary, however when the presenter tried to imply that the conclusion of the study was that there was no role for surgery, the audience reacted. That was not because they favoured surgery, but because they felt that any conclusion that has implications for altering treatment for this fatal disease should be based on solid, well controlled clinical trial data. That saga continues to be played out in the journals. No conclusion can be drawn at this stage.

Revision of the IMIG staging system was discussed, though this is really a surgical issue. A new IASLC-IMIG staging system will be available within the next two years.

There were other excellent papers. A number of studies are continuing with

immunotherapy for mesothelioma, eg. using dendritic cells along with cyclophosphamide to 'remove the brake' effected by regulatory T-cell, but no cure has yet been found using this approach.

New studies to discover biomarkers were discussed in the sessions and 'offline' and this remains a very intense area of study, as it could have major importance in terms of improving the speed of diagnosis, monitoring therapy and discovering mesotheliomas at early, potentially curable stages.

In terms of lung cancer (which can also be asbestos-induced), one paper (Richard Peto, UK) mentioned that although smoking consumption has halved in France since 1970, government revenue has doubled because of the increased price of cigarettes. He felt this was a message for current governments, including those in Asia – it represents a win-win for the



PROFESSOR NICO VAN ZANDWIJK,
CO-CONVENOR OF WCLC14

anti-cancer groups as well as governments which gain large tax incomes from cigarette taxes.

The next major meeting is the international Mesothelioma Interest Group (IMIG) meeting in Boston in September 2012.

PROFESSOR BRUCE ROBINSON,
NCARD DIRECTOR