

In this issue

- A Celebration of NCARD
- Half Year Highlights
- WA Cancer Council Awards
- Science For Dummies:
Immunohistochemistry



BRUCE ROBINSON WITH HIS "KILLER CELL".



ANNA NOWAK TALKS ABOUT WHAT MOTIVATES THE SCIENTISTS OF NCARD: PATIENT CARE, AND THE HOPE FOR NEW TREATMENTS.



A TALL STORY FROM THE ASBESTOS DISEASES SOCIETY'S DR GREG DELEUIL WITH DR SCOTT FISHER, PROFESSOR RICHARD LAKE AND DR JOOST LESTERHUIS FROM NCARD. (ROSE MARIE VOJAKOVIC FAR LEFT).

A Celebration of NCARD

An event was held on Thursday 28 June 2018 to acknowledge the outstanding contribution of Professor Bruce Robinson in both establishing NCARD, which was officially launched in 2006, and leading the Centre for more than a decade, as he steps down from the directorship and officially hands over to Professor Anna Nowak.

June is cold and flu season in Perth, and this accounted for a number of the guests who were unable to attend the function. And it was the imminent six winter recess of state parliament which inspired the unwelcome extension of debate and kept our honorary parliamentary guests, the Deputy Premier and Minister for Health the Hon Roger Cook MLA, and the Hon Kate Doust MLC from joining us.

Nonetheless Mr John Akehurst, who has been the Chair of the NCARD Board from its beginning, and has generously shared so much of his time and wisdom, took on the role of MC to introduce Bruce, who he described as "a friend since their first meeting".

Bruce described the inspiration of a meeting with stockbroker Tim Willoughby while he was a member of the board of the Western Australian Institute for Medical Research (WAIMR, now the Harry Perkins Institute), who put it to him to identify what would be needed to cure mesothelioma. Who would you need? How much would it take? This changed Bruce's thinking, and galvanised a process that eventually became NCARD. As a group for which the whole is greater than the sum of its parts, NCARD has been the highest research grant winner in Western Australia for some time, and is acknowledged as the world number one in this field.

continued on page 2



ANNE-LOUISE WILLOUGHBY MEETS THE RECIPIENTS OF THE WILLOUGHBY FOUNDATION TRAVEL GRANT. FROM LEFT: POSTDOCTORAL FELLOW DR SCOTT FISHER, PHD STUDENT RACHAEL ZEMEK, ANNE-LOUISE, PHD STUDENT WES WILSON.

Bruce, in true form, used a football analogy. The captain, he said, is not the best player in the team; he is simply given that job. For his part, Bruce said he will be "returning to the half forward flank".

He specifically acknowledged the other members of the leadership team, Professor Richard Lake, Professor Jenette Creaney, Dr Joost Lesterhuis, and Professor Anna Nowak; and the support of the WA State government, the Insurance Commission of Western Australia, the Asbestos Diseases Society of WA ("friends for over 30 years") the members of the NCARD Board, and the "exceptional EQ" of John Akehurst to help an "eccentric" group of scientists work together.



NCARD CHAIR MR JOHN AKEHURST WITH ROSE MARIE AND ROBERT VOJAKOVIC, ASBESTOS DISEASES SOCIETY.

Professor Anna Nowak shared the story of a medical oncologist who wanted to do a PhD – herself – 20 years ago, at a time when there were no oncologists in Perth with lab experience. She had some ideas that were being greeted as "wacky", and no one wanted to take a chance on a clinician with no lab experience, and no funding – except Bruce. Those ideas are now culminating in the DREAM Trial, which suggests that chemotherapy and immunotherapy work better together than could possibly have been imagined.

Anna has been having informal meetings with NCARD staff for some weeks, and has been struck by how motivated they are by patient care, by the possibility of allowing patients to see "more birthdays, more anniversaries, more grandchildren", through new treatments.



FROM PHD STUDENT AND SUPERVISOR, TO COLLEAGUES AND FRIENDS.

Thanks to Jeremy McGready, our current IT manager and former professional photographer, for capturing the evening.

NCARD HIGHLIGHTS

March

Joost tries to get his skates on

Dr Joost Lesterhuis was looking forward to a rare chance to ice skate again when he attended the Keystone Symposium Cancer Immunotherapies: Combinations Conference in Montreal in late March. Alas, although he did spot an ice rink near his hotel, it wasn't to be. Nonetheless Joost did enjoy a conference with a balance between academia and pharma/biotech and some "good science", and was grateful to the Cancer Council of WA Fellowship which made travelling to beautiful Montreal possible.



THE CAKE POPS ON THE LEFT MADE BY POSTDOCTORAL FELLOW DR ALISON MCDONNELL AND TIN OF GINGERBREAD FONDANT AT THE BACK MADE BY RESEARCH ASSISTANT DANIKA HOPE BOTH REPRESENT IMMUNE CELLS. THE COLOURFUL CAKES IN THE FOREGROUND MADE BY HONOURS STUDENT NICOLA PRINCIPE REPRESENT A T-CELL RECEPTOR, WHILE PHD STUDENT CAITLIN TILSED PRODUCED THE BLACK AND WHITE CAKES, WHICH (OBSVIOUSLY!) ARE BALB-C AND C57-BL 6T MICE.



JOOST WAS PLEASED TO MEET UP WITH HIS FORMER HONOURS STUDENT, DR ESDY ROZALI, NOW BASED AT THE NATIONAL CANCER CENTRE IN SINGAPORE.

April

Vancouver to Perth return

The Canada-Australia theme continued with a visit from former NCARD staffer Craig Rive, now based at the BC Cancer Agency in Vancouver for more than a year, working with our valued collaborator Professor Rob Holt. Craig presented a seminar which covered aspects of his research related to the engineering of immune cells to target tumour cells in an immunotherapy approach to cancer treatment. This work includes aspects of CART (Chimeric Antigen Receptor) and modified TCR (T cell receptor) research.

NCARD on You Tube

A video of just under two minutes has been added to You Tube which succinctly describes the work being done in collaboration

with New Zealand-based Douglas Pharmaceuticals, NCARD and the Telethon Kids Institute in the development of immunotherapy treatments for cancer. Interviewed are Dr Joost Lesterhuis from NCARD and Dr Anthony Bosco from TKI, and featured are Research Assistant Sarah Henn and PhD student Rachael Zemek.

New collaborations to improve treatments for cancer patients:
<https://www.youtube.com/watch?v=NX0DcGI44Yw>

Immunology Cakes

The International Day of Immunology, 29 April, was once again "observed" in a very NCARD kind of way, with baking, imagination and ingenuity.

May iMig in Ottawa

It turns out that there is no easy way to get from Perth to Ottawa! Western Australian researchers were, nonetheless, well represented at the

continued on page 4



SERIOUSLY TALENTED SCIENTISTS REPRESENTING WESTERN AUSTRALIA AT iMIG. FROM LEFT: RACHAEL ZEMEK, NCARD; PROFESSOR FRASER BRIMS, SCGH; WES WILSON, NCARD; SOPHIE GANIC (FORMERLY FROM NCARD, NOW BASED IN VANCOUVER); PROFESSOR JENETTE CREANEY, NCARD; PROFESSOR ROS FRANCIS, SCGH/UWA; DR SCOTT FISHER, NCARD; PROFESSOR ANNA NOWAK, NCARD; PROFESSOR STEVE MUTSAERS, INSTITUTE OF RESPIRATORY HEALTH.

International Mesothelioma Interest Group (iMig) Conference in early May, with Professor Anna Nowak an invited speaker, and Professor Jenette Creaney attending on behalf of Professor Bruce Robinson, Jenette garnering the Best Poster Award.

The Willoughby Travel Grant, provided by Anne-Louise Willoughby and the Willoughby Foundation in memory of the late Tim Willoughby – an inspiration and driving force behind the establishment of NCARD – enabled postdoctoral researcher Dr Scott Fisher and PhD student Wes Wilson to attend. It also meant that when PhD student Rachael Zemek made such a favourable impression with her presentation that she was invited

to attend the International NTNU Symposium on Clinical Biomarkers in June in Trondheim, Norway by renowned mesothelioma researcher Professor Oluf Dimitri Røe, she was able to accept.

May/June

To those of us who are not clinicians, the size of some of the major international cancer conferences is nothing short of mind boggling. One such conference is the American Society of Clinical Oncology (ASCO) Annual Meeting, which attracts around 30,000 delegates and was this year held in Chicago. As what is elsewhere considered a rare cancer, mesothelioma rarely gets a platform at

such an event. Thus it was particularly prestigious for Professor Anna Nowak to not only give a presentation of the interim results of the DREAM trial, but for this presentation to be included in a Highlights of the Day session, and to generate international oncology media interest.

Prestige aside, what is particularly exciting is that the interim results of the DREAM trial suggest that a combination of chemotherapy and immunotherapy in mesothelioma may be more effective than chemotherapy alone. The culmination of nearly 20 years of research by the NCARD team commencing with Anna Nowak's own PhD, Anna has said she is "excited and cautiously optimistic that we may be instrumental in a breakthrough in this disease". While the result of the final analysis of the initial 54 patients will be presented at another major conference (the World Lung Cancer Conference, in Toronto in September, with around 7000 delegates), funding for a larger confirmatory clinical trial is still being actively sought to provide the proof of benefit required before this could be adopted into standard therapy.

June

Visit from Evan Newell

NCARD hosted research collaborator Professor Evan Newell in mid-June for a brief but full visit, before Evan moves from the position of Senior Principal Investigator at the Singapore Immunology Network (SIgN) to Associate Member at the Fred Hutchinson Cancer Research Centre – known as The Hutch – in Seattle. Evan gave a seminar on T cells and T cell responses in infectious disease and cancer, a focus of his laboratory. High dimensional mass cytometry analysis and the rapidly evolving computational analysis tools are particular areas of his interest and expertise.

Apart from being a leading scientist, Evan has earned a good sport award by allowing us to use the only available photo of his visit, despite having his eyes half-open. Thank you Evan!



PROFESSOR ANNA NOWAK PRESENTS AT ASCO.



FROM LEFT: PROFESSOR BRUCE ROBINSON, PROFESSOR JENETTE CREANEY, PROFESSOR ANNA NOWAK, PROFESSOR EVAN NEWELL ENJOY A CASUAL DINNER DURING EVAN'S VISIT TO NCARD.

WA CANCER COUNCIL LUNCH AND AWARDS

The WA Cancer Council held its annual Cancer Research Awards lunch on Friday 13 April 2017, and NCARD was well represented. Recipients of recent grants Dr Joost Lesterhuis and Dr Alison McDonnell, and three Honours students – Nicola Principe, Andre Wang and Rasa Islam, each of whom had won a Cancer Council scholarship – attended the lunch, at which Anna Nowak was named WA Cancer Researcher of the Year. This award recognises an individual who has made the most outstanding contribution to cancer research over the past 3 years.

The WA Cancer Council noted:

Professor Nowak is a world-leading clinical researcher in mesothelioma. She combines detailed laboratory knowledge with outstanding clinical trials experience, collaborative spirit and multidisciplinary drive, to improve both cancer research and patient outcomes. Professor Nowak was one of the first to demonstrate that cancer chemotherapy exerts positive immunological effects, which can be exploited by combining chemotherapy with immunotherapy. She has initiated and led multiple clinical trials, allowing WA mesothelioma patients access to cutting-edge experimental treatments. Professor Nowak has a strong commitment to mentoring the next generation of cancer researchers and doctors and is dedicated to service and advocacy within the broader healthcare community.

The awards lunch is also an opportunity for researchers to meet invited supporters of the Cancer Council, talk about their research, and enjoy a menu which is specially prepared by the Parmelia Hilton chefs to promote healthy eating. A signature feature is that no alcohol is served.

Congratulations to all NCARD grant and scholarship recipients!



HONOURS STUDENTS ANDRE WANG AND NICOLA PRINCIPE



RASA ISLAM WITH HER NEW FRIEND CYNTHIA. IN RASA'S WORDS "CYNTHIA IS AN AMAZING LADY WHO HAS HAD MANY FRIENDS AND FAMILY LOST TO OR SURVIVING FROM CANCER. SHE IS A SUPPORTER OF THE CANCER COUNCIL AND WAS ALSO AWARDED AT THE LUNCH."



WA CANCER RESEARCHER OF THE YEAR PROFESSOR ANNA NOWAK WITH DR CHAN CHEAH, WA EARLY CAREER CANCER RESEARCHER OF THE YEAR 2018 (LEFT), AND PROFESSOR ROB NEWTON, CANCER RESEARCH CAREER ACHIEVEMENT AWARD 2018 (RIGHT).

Q and A with Anna:

Some of the most challenging aspects of cancer research are...

maintaining funding for a research program. With success rates for most grant funding schemes around 20% or less, there are good years and bad years. Sometimes we just don't have enough funding for researcher salaries and we lose experienced and valued cancer researchers to other areas of science – or they leave science altogether.

Some of the most rewarding are...

taking a concept all the way through from the laboratory to treating people with cancer, and seeing it improve people's lives. I have been fortunate to be able to do this with research that was part of my PhD. Now, almost 20 years later, I'm treating my patients with combinations of chemotherapy and immunotherapy that 20 years ago were thought to work against each other. To be able to show someone their scan and tell them that their cancer has shrunk by 90% on a research study is extraordinarily gratifying.

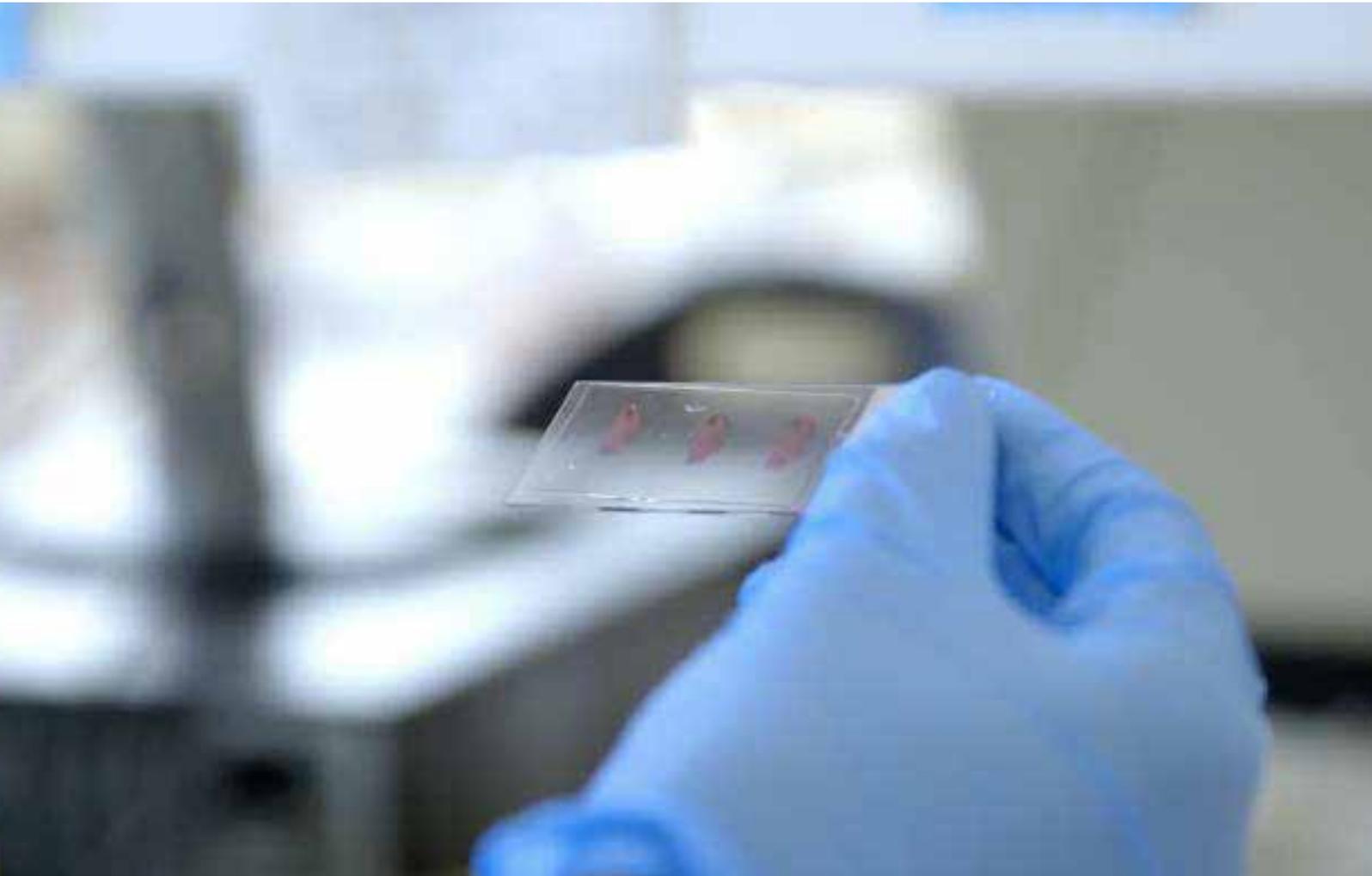
What is particular to cancer research in Western Australia is...

the spirit of collaboration. We have a relatively small cancer research community, but I have usually found that other researchers are happy to join forces, embrace new ideas, and apply their area of expertise to a different cancer type. With collaboration, the whole is more than the sum of the parts, and it's wonderful to see a new collaboration blossom.

I am feeling optimistic about...

new technologies in cancer research. It is only recently that we have been able to do single cell sequencing in WA, and had researchers who can apply the complex bioinformatics required to interpret this information. I'm excited about being able to apply this technology to samples from my clinical trials, although I can't get too excited until we have the funding to actually do this.

An interview with Anna can be viewed on YouTube: Top mesothelioma investigator named Cancer Researcher of the Year https://www.youtube.com/watch?v=N8ZxCpd_sps



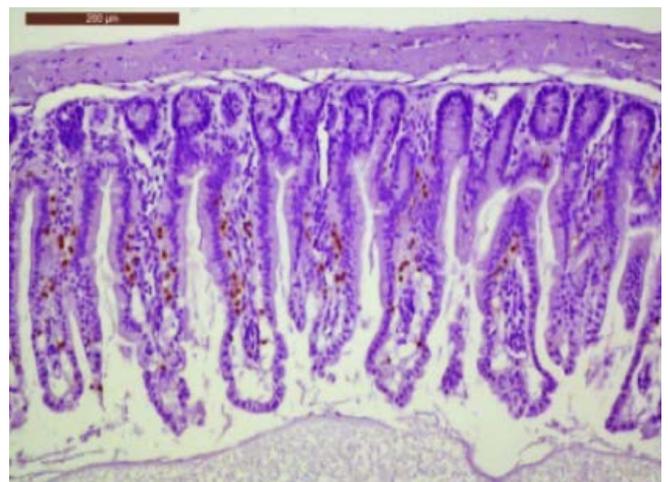
SCIENCE FOR DUMMIES: IMMUNOHISTOCHEMISTRY

SARAH HENN

What is immunohistochemistry, and why do we use it?

Immunohistochemistry (or IHC) involves the use of antibodies and biochemical reactions to detect specific antigens (proteins) in tissues and cells isolated from patients and experimental models. It is a technique commonly used in disease diagnosis, investigation and drug development. For example, IHC is often used by pathologists to determine if a patient's tumour expresses proteins that would make specific treatments more effective. Increased or decreased expression of a particular protein may also help in staging and grading of disease, and determining patient prognosis.

Although we use lots of different techniques in the laboratory to quantify protein expression, IHC has the added value of allowing us to keep the tissue in an almost perfect condition structurally. This allows us to not only quantify, but visualise where in the tissue our proteins of interest are found. For example, by staining for proteins found on blood vessels, we can see how well vascularised a tissue is, or by staining for immune cells we can see where in the tissue these cells are.



So, how does it actually work?

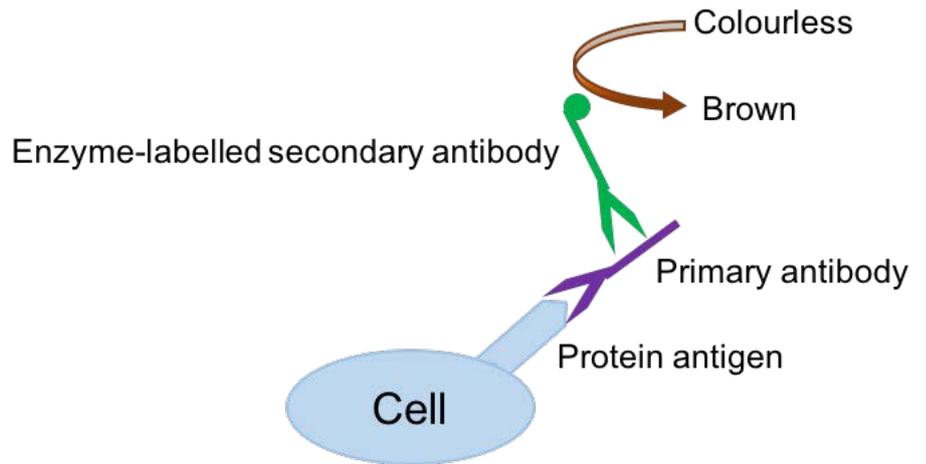
The first step of IHC is to take a piece of tissue, fix it and turn it into a wax block. This preserves the tissue and supports the structure long term. We do this slowly over time by draining the tissue of water with alcohol, and replacing all the water molecules with wax.

continued on page 7

Once we've made our block, we use a microtome, which works a bit like a butcher's meat slicer, to cut tiny thin sections of the tissue which we place on a slide. We cut the sections so that they are only one cell thick (about 5µm) so that when we look at the slides we can clearly visualise the tissue. After this, we put the sections of tissue back through changes of alcohol and water to rehydrate the tissue so that they're back in a more physiological state, but they're very fragile here so we have to keep them damp at all times.

The preserving process causes some changes to the structure of proteins, which can cause some difficulties when trying to identify these proteins with antibodies which bind to specific structures. So, next we do a thing called "antigen retrieval" which involves heating the tissue sections in a buffer to return their structures to normal. This can often be quite fiddly, as different protein antigens need to be incubated in different buffers for different lengths of time to return to their original state.

After adding some reagents to prevent unspecific binding and chemical reactions, we can start adding our



antibodies. The antibody specifically binds only to the protein of interest, but we can't see anything just yet. Instead, we add a second antibody that binds to the first, and has an enzyme tag at one end. To visualise where the antibody is bound, we add a solution that causes the enzyme to catalyse a biochemical reaction resulting in a colour change (from colourless to brown). Finally, to see everything else in the

tissue we counterstain in haematoxylin, which stains all cell nuclei purple. So, anywhere our antibodies have bound will be brown, while the rest of the tissue is stained purple. To keep the tissue sections stable for a long time and to better visualise with a microscope, we dehydrate them again and cover them with a small slip of glass. We can then have a look at the slides.



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