



CHANGING
THE FUTURE
OF **CANCER**

ANNUAL REPORT
2018



Olivia
Newton-John
Cancer Research Institute

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CHANGING THE FUTURE OF CANCER

ONJCRI ANNUAL REPORT 2018

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INSTITUTE
CELL
CANCER
EXCELLENCE
PUBLICATIONS
BRAIN
NOW
TUMOUR
METASTATIC
BIOLOGY
COLLABORATION
RESEARCH
PARTNERSHIPS
PERSONALISED
COMMUNITY
CLINICIAN
SCIENTIST
IMMUNOBIOLOGY
SUPPORTERS
PATIENTS
GRADUATES
DNA
TRANSLATIONAL
FUTURE LEADERS
MENTOR
MARKERS
SCIENTISTS
GASTROINTESTINAL
INFLAMMATION
INNOVATION LAB
BREAST



A MESSAGE FROM OLIVIA

OLIVIA NEWTON-JOHN AC, OBE **OUR FOUNDING CHAMPION**

During 2018 I personally gained unique insight into the very real impact of the incredible work being performed at the Olivia Newton-John Cancer Research Institute each and every day.

While I was receiving treatment at the ONJ Cancer Wellness and Research Centre, it was oddly comforting and humbling to know that cancer research was being undertaken in the Institute's laboratories mere metres down the hallway from my hospital bed.

Patients, just like me, are benefitting from the research of this passionate and dedicated team.

Several of these team members have shared their personal stories with me, and their motivations for working at the Institute.

Whether they have been touched by cancer in their families, or have been inspired by cancer researchers before them, their passion is the same – they want to see a future where we can win over cancer.

I share this passion and I am honoured to lead this dedicated team at the Research Institute.

A strong team of staff, partners, collaborators, supporters and advocates who share a vision for a future where cancer is both a manageable and curable disease.

I am incredibly proud of our ONJCRI supporters and excited to see the progress made for patients today and in the future.

Thank you to each and every person who makes the ONJCRI what it is today.

Love and light

Olivia



CHAIRMAN'S REPORT

THE HON JOHN BRUMBY AO
CHAIRMAN OF THE BOARD

2018 was a successful year for ONJCRI and one that I am very proud of as Chairman of the Board.

Throughout the year, we secured some of our largest funding to date which has allowed us to continue in our research endeavours including leadership roles in national clinical trials for rare cancers and brain cancer (see p22 and p40 for more details).

We recruited new leaders to expand our research and in turn fulfil our commitment to expanding treatment options available to patients. We strengthened and developed our collaborations and partnerships with national and international bodies who share our vision for a future where cancer is better understood. This has all happened while continuing to successfully undertake world leading research to identify breakthroughs for patients impacted by cancer today and in the future.

For such a young Institute these milestones are a testament to the success, drive and dedication of our entire Institute team. I thank the ONJCRI executive team, researchers, clinicians, students, professional services team and volunteers who work tirelessly to fulfil our promise of research discoveries and development. When combined with the generosity of our donors, supporters and key stakeholders the Institute is in a strong position to achieve our mission for better outcomes for patients with cancer.

I also extend my sincere thanks to my fellow Board of Directors members as well as those on our Scientific Advisory Committee. You all freely give your time to offer leadership and insight to ensure the Institute is positioned for the greatest success and you each make a very real and lasting impact.

I hope you enjoy reading in this Report the many different ways we are working together to fulfil our shared passion to win over cancer.

The Hon John Brumby AO



DIRECTORS' REPORT

PROF JONATHAN CEBON
MEDICAL DIRECTOR

PROF MATTHIAS ERNST
SCIENTIFIC DIRECTOR

2018 was an exciting time to be involved in cancer research.

The year provided Institute scientists with many new opportunities to discover and celebrate the way cancer is viewed and how it is treated. It was also a year of milestones and achievements.

As the La Trobe University School of Cancer Medicine, the Institute attracts the brightest and most dedicated students and early career researchers, who we cherish as future leaders. One such researcher is Dr Ashleigh Poh who is featured on the cover of this Report (full story on p14). Like many of our researchers, her passion is driven by her own family's cancer story. And although individual discoveries made by Ashleigh and our other colleagues may not always hit the headlines, their impact is cumulative and so can make a huge difference that many patients experience directly through clinical trials.

The ONJCRI team currently includes seven clinical scientists who create a bridge between our laboratory science and cancer care. On one hand, this bridge creates new opportunities for patient care and on the other, it provides clinical insights that inform our laboratory scientists' perspectives and helps to shape the direction of their research. This year alone, these clinicians have led more than 120 clinical trials, which have provided hundreds of patients with new treatment opportunities (find out more about our rare cancer trial on p22 and the national brain cancer study on p40).

The quality of work undertaken by our researchers continues to stand out and attract substantial support from various funding agencies at State and Commonwealth level, even though overall funding remains highly competitive. One reason for this success is ONJCRI's privilege to be co-located within Austin Health, one of Melbourne's largest public health services. This link provides seamless interactions between our researchers, clinician scientists, hospital care teams and cancer patients.

We are grateful for the united commitment of all of our staff and the wider Institute team including our Board of Directors, our Scientific Advisory Committee, our partnerships with La Trobe University and the Austin Health community, and our financial supporters including philanthropic donors and funding bodies.

Cancer care is rapidly changing and we are delighted to lead a generation of researchers and clinicians who are helping shape the future and transform the options available for treating patients with cancer.

Prof Jonathan Cebon/Prof Matthias Ernst

**ABOUT
THE OLIVIA
NEWTON-
JOHN
CANCER
RESEARCH
INSTITUTE**

The Olivia Newton-John Cancer Research Institute is a leader in the development of experimental and breakthrough cancer treatments. We investigate and develop treatments for cancers of the breast, lung, melanoma, prostate, liver, gastrointestinal tract and brain. This year our researchers and clinicians are running more than 120 clinical trials, giving patients access to potential new treatments including immunotherapies and personalised medicine.

ON
JC
RI

YEAR AT A GLANCE

JAN

FEB

MAR

APR

MAY

JUN

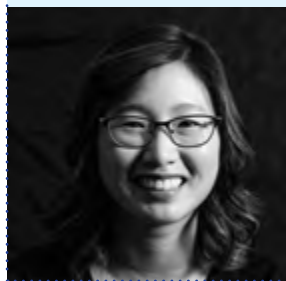
Dr Andreas Behren is one of the beneficiaries of a \$7m research boost from the Victorian Cancer Agency to further his research into predicting the risk for melanoma relapse.

[Find out more about Andreas' Laboratory on p19](#)

92
STAFF

Dr Ashleigh Poh is the first international recipient of the American Association for Cancer Research (AACR) Gastric Cancer Research Fellowship.

[Read more in our feature story on p14](#)



Dr Belinda Yeo, ONJCRI Clinician Scientist is involved in one of the largest studies in the world for patients with early stage breast cancer. This trial may result in genetic testing to determine which patients could be spared from undergoing chemotherapy.

\$1.5m in funding is announced by the Medical Research Future Fund (MRFF) for brain cancer research including high-grade glioma or glioblastoma (GBM).

[Find out more on p40](#)

53%

FEMALE
STAFF

A Greek dinner dance fundraiser is held in tribute of Melbourne musical legend, the late Steven Kirkopoulos to fund an ONJCRI Brain Cancer Research Fellowship for Dr Diana Cao.

Olivia Newton-John receives an honorary doctorate from La Trobe University, where she thanked students for allowing her to share their graduation, receiving her honorary doctors of letters honoris causa.

"You are the next generation of practitioners, and I'm really excited about the potential you have to impact the course of health care in Australia".



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CLINICAL TRIALS
LED BY INSTITUTE
INVESTIGATORS

The Victorian Government announces a \$10m funding boost to ONJCRI including for the establishment of the Centre for Research Excellence in Brain Cancer.

[Read more on p44](#)



27%

NHMRC GRANT
SUCCESS RATE

237

RESEARCH
COLLABORATIONS

A GLANCE

JUL

AUG

SEP

OCT

NOV

DEC

The Olivia Newton-John Cancer Wellness and Research Centre (ONJ Centre) is ranked among the Top 30 'Most Technologically Advanced Cancer Centres in the World'; and is listed 11th on the 'Top Master's in Healthcare Administration' List.

ONJCRI receives Federal funding to extend its Rare Cancer Trial that uses immunotherapy to treat patients with uncommon forms of gastrointestinal, neuroendocrine and gynaecological cancers.

[Read more on p22](#)

The Ian Potter Foundation with funding support from La Trobe University and ONJCRI enables the purchase of histology equipment to boost sample analysis at ONJCRI and the wider Melbourne cancer research community.

[Read more on p21](#)

23%

PHD STUDENTS WITH MEDICAL TRAINING

Thousands of supporters formed a community of hope and love at the 2018 Wellness Walk and Research Run at the beautiful La Trobe University Bundoora campus.



140

ONJCRI SCIENTIFIC PAPERS PUBLISHED

PhD Student Mariah Alorro is a finalist in the La Trobe University 'Three Minute Thesis' Competition. Mariah's presentation explains her research into STAT3, a protein found in stomach cancer.

The 'Girls Night Out' Fundraiser secured \$37k to purchase a 'Cryostat' which aids researchers such as Dr Normand Pouliot with his breast cancer research to look at freshly collected cancer biopsies.


[Read more on p35](#)

\$28.7 MILLION

SECURED EXTERNAL FUNDING

36 STUDENTS

Dr Surein Arulananda is awarded \$10k from the Lung Foundation Australia to continue his research into new treatments for mesothelioma - lung cancer caused by asbestos.



OUR PROGRAMS

Our researchers are investigating and developing treatments for a broad spectrum of cancer types. We are committed to making scientific discoveries that benefit patients living with cancer.

PROGRAM OVERVIEW

CANCER AND INFLAMMATION PROGRAM

Program Head:
Prof Matthias Ernst

Cancer and Inflammation Laboratory

Lab Head:
Prof Matthias Ernst

Researchers: Shoukat Afshar-Sterle, Mariah Alorro, David Baloyan, Nicola Boffinger, Michael Buchert, Ashwini Chand, Christine Dijkstra, Belinda Duscio, Moritz Eissmann, Matthias Ernst, Nima Etemadi, Jennifer Huynh, Saumya Jacob, Cameron Johnstone, Kim Le, Riley Morrow, Megan O'Brien, Robert O'Donoghue, Ashleigh Poh, Ursula Porage Dona, Pathum Thilakasiri, Janson Tse, Merridee Wouters

Tumour Microenvironment and Cancer Signaling Group

Group Head:
Dr Michael Buchert

Researchers: Shoukat Afshar-Sterle, Alex Azimpour, Michael Buchert, Annalisa Carli, Nima Etemadi, Ryan O'Keefe, Janson Tse

Cancer Therapeutics Development Group

Group Head:
Dr Ashwini Chand

Researchers: Ashwini Chand, Lokman Pang, Ursula Porage Dona, Pathum Thilakasiri, Kelly Tran

CANCER IMMUNOBIOLOGY PROGRAM

Program Head:
Prof Jonathan Cebon

Cancer Immunobiology Laboratory

Lab Head:
Prof Jonathan Cebon

Researchers: Surein Arulananda, Jonathan Cebon, Tom John, Oliver Klein, Candani Tutuka, Marzena Walkiewicz

Tumour Immunology Laboratory

Lab Head:
Dr Andreas Behren

Researchers: Andreas Behren, Cyril Deceneux, Jessica Da Gama Duarte, Sean MacDonald, William Murray-Brown, Simone Ostrowska, Simon Tsao

Translational Genomics and Epigenomics Laboratory

Lab Head:
A/Prof Alex Dobrovic

Researchers: Hongdo Do, Alexander Dobrovic, Basant Ebaid, Su Kah Goh, Nicholas Low, Ramyar Molania, Ashan Musafer, Marcin Szaumkessel, Thomas Witkowski, Boris Wong

Mucosal Immunity and Cancer Laboratory

Lab Head:
Dr Lisa Mielke

Researchers: Anita Kumari, Lisa Mielke, Dinesh Raghu

GASTRO-INTESTINAL CANCER PROGRAM

Program Head:
Prof John Mariadason

Oncogenic Transcription Laboratory

Lab Head: Prof John Mariadason

Researchers: Zakia Alam, Mercedes Davalos-Salas, Amardeep Dhillon, George Iatropoulos, Laura Jenkins, Stan Kaczmarczyk, David Lau, Analia Lesmana, Ian Luk, John Mariadason, Jennifer Mooi, Irvin Ng, Rebecca Nightingale, Camilla Reehorst, Cameron Scott, Niall Tebbutt, Wiphawan Wasenang, Andrew Weickhardt, David Williams

Cell Death and Survival Laboratory

Lab Head:
Dr Doug Fairlie

Researchers: Surein Arulananda, Marco Evangelista, Doug Fairlie, Tiffany Harris, Erinna Lee, Sharon Tran

TRANSLATIONAL BREAST CANCER PROGRAM

Program Head:
Prof Robin Anderson

Metastasis Research Laboratory

Lab Head:
Prof Robin Anderson

Researchers: Robin Anderson, Stefan Bader, Caroline Bell, Allan Burrows, Laphing Chi, Catherine Fang, Haiyan Liao, Kellie Mouchemore, Richard Redvers, Charlotte Roelofs, Victoria Simovich, Bill Tang, Kathryn Visser, Belinda Yeo

Matrix Microenvironment and Metastasis Laboratory

Lab Head:
Dr Normand Pouliot

Researchers: Delphine Denoyer, Miriam Fuentes, Aadya Nagpal, Normand Pouliot, Elnaz Tavancher

Tumour Progression and Heterogeneity Laboratory

Lab Head:
Dr Delphine Merino

Researchers: Simone Alexander, Jean Berthelet, Michal Merdas, Delphine Merino, Antonin Serrano,

Single Cell Cancer Genomics Laboratory

Lab Head:
Dr Bhupinder Pal

Researchers: Michal Merdas, Bhupinder Pal

TUMOUR TARGETING PROGRAM

Program Head:
Prof Andrew Scott

Tumour Targeting Laboratory

Lab Head:
Prof Andrew Scott

Researchers: Uwe Ackermann, Laura Allan, Ingrid Burvenich, Diana Cao, Puey Ling Chia, Adriana Constantinou, Hui Gan, Benjamin Gloria, Nancy Guo, Umbreen Hafeez, Eliza Hawkes, Sze Ting Lee, Daryl Liu, Alex McDonald, Mike McKay, Carmel Murone, Sagun Parakh, Adam Parslow, Evangelia Rigopoulos, Andrew Scott, Fiona Scott, Christian Wichmann

Receptor Biology Laboratory

Lab Head:
A/Prof Peter Janes

Researchers: Stacey Allen, Peter Janes, Mary Vail, Hengkan Yan

CENTRE FOR RESEARCH EXCELLENCE IN BRAIN CANCER

Co-Leads:
Prof Andrew Scott and A/Prof Hui Gan

CLINICIAN SCIENTISTS

Dr Chun Yew Fong
A/Prof Hui Gan
Dr Eliza Hawkes
A/Prof Tom John
A/Prof Andrew Weickhardt
A/Prof David Williams
Dr Belinda Yeo

FACILITIES AND EQUIPMENT

Our research and translational development are underpinned, enhanced and advanced by outstanding platform technologies, facilities, technical expertise and support services that operate within 5,500 square-metre state-of-the-art laboratories.

This includes:

- ACRF Centre for Translational Cancer Therapeutics and Imaging
- ACRF Centre for Imaging the Tumour Environment



- Vectra Multi-Spectral Imaging Platform
- Mammalian Protein Expression, Production and Purification Facility (MPEF)
- Molecular Diagnostics
- Flow Cytometry Core Facility

CANCER AND INFLAMMATION PROGRAM

PROGRAM LEAD: PROF MATTHIAS ERNST

Tumours are made up of cancer cells as well as many different types of normal cells that have been recruited into the tumour in order to help cancer cells to grow. Many of the molecular processes by which cancer and normal cells interact with each other are ancient mechanisms that are important during wound-healing. Cancer cells have hijacked some of these mechanisms to help them survive, grow, obtain a steady stream of nutrients, become stealth to the immune system and develop resistance against treatment.

The Cancer and Inflammation Program aims to understand some of the mechanisms by which cancer cells and certain types of normal cells communicate with each other within the tumour. Disrupting these lines of communication will make cancer cells more vulnerable as they become less supported by the normal cells in their vicinity. Importantly, this strategy may also help make tumour cells become more visible to the immune cells and therefore more vulnerable to treatment with contemporary immune-based therapies.

While the activities of our Program focus primarily on cancers of the bowel, stomach and breast, many of these molecular communication mechanisms are also found in other solid tumours. Therefore, the insights gained from our research could ultimately be translated into many different solid malignancies.

PUBLICATION HIGHLIGHTS:

Eissmann, M. et al. Interleukin 33 signaling restrains sporadic colon cancer in an interferon-gamma-dependent manner. Cancer Immunology Research 6: 409-421. (2018)

Poh, A.R. et al. Targeting macrophages in cancer: From Bench to Bedside. Front Oncol 8: 49. (2018)

Ziegler, P.K. et al. Mitophagy in Intestinal Epithelial Cells Triggers Adaptive Immunity during Tumorigenesis. Cell 174: 1-14. (2018)

CANCER AND INFLAMMATION LAB

Lab Head: Prof Matthias Ernst

The Cancer and Inflammation Laboratory focuses on three different strategies to interfere with the communication between cancer and normal cells within a tumour. All strategies are aimed at myeloid cells, a type of white blood cell that plays a central role during the wound healing process and thus during most aspects of tumour growth progression and metastasis.

We aim to suppress signals generated by cancer cells to attract myeloid cells into the tumour environment. Of particular interest is an alarmin molecule called interleukin-33, which is produced by cancer cells of the stomach and which helps to orchestrate the recruitment and activation of myeloid cells. In preclinical models, we showed that ablation of the receptor of interleukin-33 suppressed the accumulation of myeloid cells within the tumour environment which in turn reduced the tumour growth.

Our goal is to disrupt the communication between normal cells and cancer cells by targeting the signal generated by interleukin-11 and transmitted through the gp130 receptor and its associated intracellular signaling molecule Stat3. Interleukin-11 is produced by both cancer cells and certain normal cells, and in turn can engage the gp130/Stat3 signaling axis in cancer cells to promote their survival and proliferation. Meanwhile, gp130/Stat3 signaling in immune cells reduces their capacity to kill cancer cells. Therapeutic interference with the interleukin-11/gp130/Stat3 signaling axis therefore provides an Achilles heel that could suppress the growth of

cancer cells and simultaneously unleash a more effective anti-tumour immune response.

We aim to convert the tumour promoting and immune suppressing attributes of myeloid cells within the tumour into tumour suppressing and immune promoting characteristics. To achieve this, we have identified the myeloid cell-specific tyrosine kinase HCK to work as a intracellular molecular switch between these cellular properties. Accordingly, inhibition of HCK not only reduces the growth of primary and metastatic tumours in preclinical models, but importantly allows effector T-cells to enter into the tumour and to become more active in killing tumour cells.

TUMOUR MICROENVIRONMENT AND CANCER SIGNALING GROUP

Group Head: Dr Michael Buchert

The Tumour Microenvironment and Cancer Signaling Group (TMCS) seek to understand the intricate interactions between cancer cells and their surroundings to ultimately deliver better treatments and therapies for patients.

In 2018 we welcomed two new PhD students in Annalisa Carli and Ryan O'Keefe. Annalisa's project investigates the role of doublecortin-like kinase 1 (DCLK1) in gastric cancer. DCLK1 is a microtubule-associated protein with a functional kinase domain. DCLK1 has a proposed role as a cancer stem cell marker and potential driver of gastric tumorigenesis. A meta-analysis demonstrated positive correlations between DCLK1 expression levels, advanced malignancy and reduced overall survival.

Ryan's PhD project aims to increase our understanding of the role of a rare chemosensory cell population of the intestinal epithelium, called tuft cells, during initiation, development and progression of gastric tumours. In particular, we propose that the tuft cell population present throughout the gastrointestinal system together with the type 2 innate lymphoid cells (ILC2), a recently discovered immune cell population located at mucosal surfaces, contribute significantly to the development of gastric cancer.

Additional highlights of the TMCS included a detailed analysis of the oncogenic mechanisms by which miR21 contributes to gastric cancer, and the spectacular rescue of a mutant embryonic phenotype using an experimental Wnt pathway inhibitor. Both studies were spearheaded by postdoctoral researcher Dr Janson Tse. Finally, Dr Shoukat Sterle initiated an in-depth study to investigate the impact of DCLK1 expression on the cell's microtubular network using state-of-the art high-resolution confocal microscopy.

CANCER THERAPEUTICS DEVELOPMENT GROUP

Group Head: Dr Ashwini Chand

Research projects in the Cancer Therapeutics Development Group are focussed on discovering new treatments for breast, gastric and colon cancers. Our group has been working on how repurposing of existing drugs could be beneficial for cancer treatments, as well as our new drug development projects.

In 2018, we discovered that drugs that are used to treat post-menopausal osteoporosis in women could serve as novel treatment for gastric and colon cancers. Recent evidence points to the importance of understanding the interactions of the gut microbiome with human health. We are now beginning to develop projects targeted towards understanding how inflammation damages the intestinal barrier to alter host-microbiome interactions and how this contributes to cancer development or affects effectiveness of cancer treatments.

As our studies are directed at suppressing mediators of inflammation called cytokines, our recent work demonstrates the importance of such inflammatory cytokines in promoting triple negative breast cancer cells into becoming more prone to growth and spreading to other parts of the body. By understanding how pro-inflammatory cytokines facilitate these cellular effects, we have been able to identify molecular targets, for which we are now developing targeted treatments.



A PASSION FOR **CHANGE**

Her career has only just begun but ONJCRI researcher, **Dr Ashleigh Poh**, is already off to a flying start.

2018 has been an action-packed year for Ashleigh: making significant discoveries, securing prestigious grants, and presenting her findings to an international audience of experts on the other side of the world.

But through it all, she has never lost sight of why she got into the field of cancer research in the first instance. It was then, and remains now, the people touched by cancer who drive a deep passion for her work.

“My aunt was diagnosed with colon cancer when I was in high school, and passed away shortly after. It was devastating. A cancer diagnosis doesn’t only affect the person with cancer, but also friends and family,” she said.

Ashleigh’s aunt was one of four family members that she has lost to cancer and Ashleigh has witnessed first-hand the devastating toll cancer can take on individual people and their families.

“These experiences reinforced my belief that we need better ways of managing and treating the cancer and to discover new targets for therapy,” she said.

“I’m frequently asked if scientists are going to find a cure. This has always been a hard question to answer, because cancer is a complex disease and there is no ‘one-size-fits-all’ treatment and cure. The goal of our research is to better understand how cancer cells can hide from our immune system, which allows them to grow and spread from their initial site. By gaining insight on these important processes, we will be able to develop new and more effective therapies that will make cancer cells more ‘visible’ for detection and destruction.”

Ashleigh completed her PhD studies in 2017 in ONJCRI’s “Cancer and Inflammation Program” (see p12), but as an early career researcher since then has already racked up an impressive list of achievements.

In 2018, she was one of the five finalists for the Premier’s Award for Health and Medical Research and subsequently became the first international recipient of a fellowship for gastric cancer awarded by the prestigious American Association for Cancer Research.

Ashleigh conducted her ground-breaking work on a protein called Haematopoietic Cell Kinase (HCK). HCK is found in a type of immune cell known as a macrophage, which are a major component of solid cancers and often help tumours to become less visible to the immune system.

Macrophages can play two major, but mutually exclusive roles – they can act as “garbage collectors” to remove unwanted debris or damaged cells, or as “nurses” to facilitate regenerative processes at sites of injury.

Ashleigh’s research has shown that the more HCK activity a macrophage has, the more it is able to help tumours grow. Rather than acting as garbage collectors that clean up cancer cells, these macrophages ‘nurse’ the growth of tumour cells and hide them from being detected and destroyed. Ashleigh’s discoveries show that treatment with a drug that reduces HCK in macrophages slows the growth of over 6 tumour types, including stomach, bowel/colon and breast cancer.

“I am currently extending my discoveries to pancreatic and other types of solid tumours to find out whether targeting of HCK will improve the survival rate of these aggressive cancers. Our ultimate goal is to translate our current findings from the laboratory to the bedside to deliver better treatment outcomes for patients” she said.

**“IT IS THE PEOPLE TOUCHED BY
CANCER WHO DRIVE A DEEP
PASSION FOR MY WORK”**

One of the highlights of Ashleigh’s year was travelling to Florida to attend the fundraising gala in memory of Candace Netzer, and to meet Candace’s family who funded Ashleigh’s fellowship in memory of their loved wife, who passed away the previous year.

“I have had the opportunity to connect with survivors, patients and their families. Their positivity and resilience are a major driving force behind my passion for cancer research, and my goal to contribute to a better understanding how we can win over cancer. As scientists, these experiences are reminders of the people we do it for, and draws it all back into focus. It’s this aspect of my work that I love the most.” she said.



THE REWARDS OF BEING A SCIENTIST

“If you can’t accept failure, this probably isn’t the job for you.”

Dr Michael Buchert’s advice to aspiring scientists is informed by a long and successful career in medical research that has been as challenging as it has been fulfilling.

“It’s not a nine to five job where you go home at night and don’t think about work. It is constant, and intellectually challenging, and that can be stressful but it’s also very rewarding,” he said.

“There are a lot of setbacks - an experiment might not work or the hypothesis might be wrong - so you always have to go back to the drawing board and try to think, ‘What did I miss?’ But I’m not discouraged by failure - you have to go through a lot of failure before you reach success - that’s part of being a scientist.”

As Head of the Tumour Microenvironment and Cancer Signaling Group, Michael’s research focus is cancers of the stomach and colon - two of the main causes of cancer-related deaths worldwide. In 2018, he secured funding from the National Health and Medical Research Council (NHMRC), which allowed him to hire and train two scientists - a PhD student and a postdoctoral fellow - to accelerate his research.

“The funding was for studying how an immune defence mechanism used by the body to deal with parasite infections is hijacked by cancers to promote their own growth,” he said.

“In particular, we’re investigating how cancer cells change their immediate environment to their advantage, for example evading detection by the immune system to survive anti-cancer treatments and to disperse to distant sites.”

For Michael, being at the forefront where biomedical knowledge is gained and potentially improving outcomes for cancer patients are powerful motivators for his work, and he is excited about future breakthroughs in the cancer research, particularly in immunotherapy.

**“WE ARE INVESTIGATING HOW
CANCER CELLS MANIPULATE
THEIR ENVIRONMENT TO
THEIR ADVANTAGE”**

“We know immunotherapy works very well in some cancers but in others it hasn’t been working well at all, so there’s a lot of research needing to be done to understand how we can make those tumours adaptable to that way of treatment, but I have great hope that we will win the fight against this disease eventually.”



NURTURING THE NEXT GENERATION OF RESEARCHERS

In the fight against cancer, nurturing the next generation of cancer researchers is critical.

ONJCRI has a proud record of mentoring students with thriving projects that produce incredible results.

Dr Ashwini Chand, Head of the Cancer Therapeutics Development Group, relishes her role as a mentor and says it is one of the most rewarding experiences in her role.

"I really like the vitality and enthusiasm students bring to the Institute and to my team. Their curiosity really makes us better teachers, particularly if students bring new perspectives into their projects" she said.

**"THE QUESTIONS OUR STUDENTS
ASK REALLY MAKE US MORE
CONSIDERATE TEACHERS"**

"For me personally, the journey and progression of a student in terms of acquiring skills and knowledge during their candidature, sharing their exciting results and seeing them developing their own research story is just so rewarding. There are many pressures that students face and I have seen students undergoing immense personal hardship and showing resilience to achieve their goals – that makes me proud."

Both Honours students and PhD candidates at the Institute enjoy an environment where research and clinical work is interlinked and they can achieve translational outcomes on their projects.

At ONJCRI, students are paired with senior researchers in one-on-one mentorship programs. They are also part of mentorship panels themselves, together with other young graduates undertaking world leading research at ONJCRI.

"There is no better way for me to expose the Institute's students to the talent of visiting established scientists than to also act as ONJCRI's seminar convenor" Ashwini says, adding that "creating an excellent seminar program with speakers from all over Australia to report on the latest insights in cancer research is my most important contribution to creating a vibrant environment at ONJCRI."

"Our strong training program enables young scientists to go on to have bright careers and to make major contributions to cancer research. But the benefits flow both ways, with mentors getting as much from this relationship as the students they supervise."

CANCER IMMUNOBIOLOGY PROGRAM

PROGRAM LEAD: PROF JONATHAN CEBON

The research undertaken within the Cancer Immunobiology Program seeks to understand how cancer and the immune system affect each other. From this, we can then harness the power of the immune system to treat cancer by performing clinical trials with drugs that stimulate immune responses. In parallel, we are developing diagnostic tests based on our clinical experience to better select patients for immunotherapy and predict and manage auto-immune side effects.

Recent successes in a clinical trial for patients with rare cancers provides a powerful illustration of this (see full story on page 22). These cancers represent an important area of unmet need and the trial is showing life-saving benefit for a mixture of cancer types for which there are currently no effective treatments. These include rare cancers of the upper gastrointestinal tract such as the liver and bile ducts; cancer that develops from neuro-endocrine cells; and rare cancers of the female genital tract.

Both cancer and the immune system change with time – indeed they can shape each other. As immunity attacks, the cancer can adapt and escape immune recognition. Moreover, the cancer can also interfere with cells of the immune system in a variety of ways. We are particularly interested in understanding the targets that the immune system recognises, understanding how both cancer and immunity co-evolve to enable us to discover new therapeutic targets.

PUBLICATION HIGHLIGHTS:

Cebon, J. Perspective: cancer vaccines in the era of immune checkpoint blockade. *Mamm Genome* 29: 703-713. (2018)

Tsao, S.C. et al. Characterising the phenotypic evolution of circulating tumour cells during treatment. *Nat Commun* 9: 1482. (2018)

Da Gama Duarte, J. et al. Autoantibodies May Predict Immune-Related Toxicity: Results from a Phase I Study of Intravesical Bacillus Calmette-Guerin followed by Ipilimumab in Patients with Advanced Metastatic Melanoma. *Front Immunol* 9: 411. (2018)

Halse, H. et al. Multiplex immunohistochemistry accurately defines the immune context of metastatic melanoma. *Sci Rep* 8: 11158. (2018)

CANCER IMMUNOBIOLOGY LAB

Lab Head: Prof Jonathan Cebon

Our clinical trial in Rare Cancers has demonstrated that various cancers that were not known to respond to immunotherapy can indeed respond. During 2018, 60 patients were treated on our Rare Cancers protocol. We also obtained additional funding from the Medical Research Future Fund, which will enable us to treat an additional 60 patients during 2019. Using patient materials from this trial has enabled us to design laboratory studies that will identify biomarkers which will be able to predict benefits to patients.

These above laboratory studies are performed under the supervision of Dr Andreas Behren in the Tumour Immunology Laboratory. Dr Behren is an emerging leader who helped organise the highly successful Winter Retreat of the Melbourne Immunotherapy Network. He secured a prestigious fellowship from the Victorian Cancer Agency and has played an instrumental role in securing state-of-the-art equipment for imaging immune cells in the cancer tissue of trial patients at ONJCRI. The clinical biomarker team also includes Dr Jessica Duarte who has been studying the blood of trial patients to measure antibodies that naturally arise when the immune system is stimulated either to react against tumours or normal tissues, which can be an unwanted auto-immune consequence of immunotherapy.

Dr Lisa Mielke joined ONJCRI in 2018 as an expert in intestinal immune cell biology, following completion of her PhD in 2009 at the National Institute of Health, USA, followed by postdoctoral training at Trinity College Dublin, Ireland and the Walter and Eliza Hall Institute of Medical Research. She has led numerous studies revealing new and exciting cross-talk between our diet and transcriptional regulation of intestinal innate lymphoid cells (ILC) and so-called γ/δ T cell populations. These studies are opening an exciting new frontier of research in the field of mucosal immunology. Shortly after joining the ONJCRI, Dr Mielke was awarded a prestigious fellowship from the Victorian Cancer Agency that will fund research investigating the role of intestinal immune cell populations in gastrointestinal cancers.

TUMOUR IMMUNOLOGY LAB

Lab Head: Dr Andreas Behren

The Tumour Immunology Laboratory was launched in May 2018 as an independent laboratory embedded in the Cancer Immunobiology Program.

Our laboratory focuses on the interaction between the immune system and cancer, and on understanding how a successful anti-cancer immune response is orchestrated.

To ensure that our work has relevance for patients, we are working closely with Prof Jonathan Cebon and other clinicians across Melbourne to gain access to patient samples to re-evaluate findings and ideas from the laboratory in “real-life” samples. We firmly believe that collaboration across research institutes and pharmaceutical industry will lead to the best outcomes for patients. The laboratory has therefore established a network of collaborations with a strong clinical trial and industry-supported research component.

Our Winter Symposium for the Melbourne Immunotherapy Network (MIN) brought together more than 80 like-minded researchers from across Melbourne to exchange ideas and research.

Our research has led to multiple important discoveries that were published in 2018: in a collaboration with researchers in Queensland, our PhD student Simon Tsao found an easy and sensitive method to measure how tumour cells that are travelling in the blood of patients react to different therapies. In the future, this discovery could allow clinicians to detect very early if a patient will develop resistance to a therapy and how to tackle resistance.

Other exciting research is based on the use of protein arrays that can measure the presence of tumour antibodies in the blood of cancer patients. Dr Jessica Duarte, our postdoctoral research fellow, championed these studies and proposes that such arrays could be used to guide treatments. Indeed, Dr Duarte was successful in securing funding from the Cure Cancer Australia Foundation to further pursue this approach.

TRANSLATIONAL GENOMICS AND EPIGENOMICS LAB

Lab Head: A/Prof Alex Dobrovic

The Translational Genomics and Epigenomics Laboratory undertakes gene-based and genomics-based research in cancer with a focus on collaborative studies that optimise treatment of cancer patients. Because our laboratory is active in both research and diagnostics, it creates a synergy that benefits both areas.

We aim to advance personalised medicine for cancer patients with a particular focus on our expertise in the frontier area of liquid biopsies. When a patient has cancer, some of the tumour's DNA can be found in the blood. This DNA, referred to as circulating tumour DNA, can not only be detected, but it also carries the same genetic changes that are found in the cancer. Monitoring these specific changes via liquid biopsies can measure the extent of the cancer and guide towards appropriate treatment. Liquid biopsies are a rapidly growing area of research, because they are minimally invasive compared to conventional tissue biopsies and thus enable more frequent monitoring of the success of therapy.

In 2018, we were successful in obtaining a new grant from the National Breast Cancer Foundation to monitor breast cancer with liquid biopsies; this complements similar work we are conducting in lung cancer, which is funded through an existing grant from the National Health and Medical Research Council. Our team is also collaborating with the Austin Hospital Department of Surgery in using circulating DNA to monitor the health of liver transplant patients.

A research highlight was being part of a continuing collaboration with Prof Clare Scott at the Walter and Eliza Hall Institute and subsequent publication in Nature Communications. We showed that the precise measurement of DNA methylation of the BRCA1 gene was able to predict the response to a class of drugs known as a PARP inhibitors which are used to treat breast and ovarian cancer patients.

MUCOSAL IMMUNITY AND CANCER LAB

Lab Head: Dr Lisa Mielke

The body's mucosal surfaces include the lungs and gastrointestinal tract. There are specialised immune cells at these sites that play a critical role in maintaining these surfaces of the body to help protect you from the external environment. Because these surfaces are constantly under stress from the environment, including the air we breathe, the food we eat, the sun, and infectious organisms, these surfaces are also more prone to the development of cancer.

The Mucosal Immunity and Cancer Laboratory investigates how some of these specialised immune cells develop, how they function to maintain homeostatic renewal of the epithelial surfaces, and the role these immune cells play in development of and defence against cancer. Our Lab has been working closely with the Tumour Immunology Laboratory, Cancer and Inflammation Program, and Gastrointestinal Cancer Program at ONJCRI to uncover how some of these specialised immune cell populations of the intestine contribute to the development of bowel cancer.

Modulation of immune cells has revolutionised the treatment of some cancer types and it is now evident that manipulating the immune system is a powerful technique to treat and potentially support cancer prevention. Understanding the unique functions of immune cells in the intestine, and the role they play in tumourigenesis, will pave the way for discovery of new immunotherapies to harness the power of our own immune cells to eradicate tumours.



THE VITAL ROLE OF TECHNOLOGY

An intellectual curiosity into the complex nature of cell biology drove Dr Andreas Behren to pursue a career in cancer research.

He was intrigued by how a body's cells could lose partial control of their fate, and start to divide to the point that they could potentially kill a person. Curiously, such cells still remained highly organised and in constant communication with non-cancerous cells within their immediate "neighbourhood".

A need to better understand these processes and to ultimately help to develop new cancer treatments has motivated Andreas ever since he started his career in Germany and moved to Australia in 2008. As the Head of the Tumour Immunology Laboratory, Andreas has predominantly focused on understanding and slowing down the complex processes that govern the development of melanoma - one of the deadliest cancers if not detected early.

Andreas led two successful campaigns to obtain funding from the Ian Potter Foundation in 2015 and 2018 for the purchase of state-of-the-art imaging equipment, which allows better microscopic insights into the complex architecture of tumours. When purchased in 2015, the Vectra system provided the first multi-slide capacity in Australia, and allowed Andreas and his team to easily describe the spatial distribution within a tumour of the various cancer cell-killing immune cells that surround a tumour. This has now become a widely used technique and has revealed crucial information to better understand the interactions between the immune system and tumour cells. In his second bid, Andreas secured a \$100,000 grant from the Ian Potter Foundation, to match funding from the Institute and La Trobe University, to acquire an automated tissue stainer that enables streamlined preparation of histology slides.

"The Vectra system is a type of microscope with a specialised camera and software that allows you to simultaneously visualise various markers on cells and therefore different cell types within the tumour microenvironment" Andreas explains. "For the first time we can now see where and how the normal cells - like fibroblasts or immune cells - sit among the cancer cells within a patient's tumour."

Prior to using the Vectra system, the multitude of staining was a labour and time-intensive process and could never be done on the same tissue slide. By combining the multi stainer with the Vectra system, the work flow has become much more streamlined and time efficient not only for Andreas' group, but also for many researchers from around Melbourne and Australia who have access to this equipment. An important additional benefit from using these state-of-the-art pieces of equipment is that now all results can be directly compared between different researchers and institutes, as these machines reduce the unavoidable variability that comes with manual processing.

Andreas says in an era of immunotherapy, where patients are given targeted drugs to enhance their immune reaction to cancer, the technology plays a vital role. "The Vectra technology will help us to better understand why immunotherapy is working in some patients and why it isn't working in others, and how cells of the immune system interplay with tumour cells."

A man with short brown hair and glasses, wearing a white shirt and a grey patterned blazer, is standing in front of a large window with vertical blinds. He is looking out the window with a slight smile. The background is a bright, slightly blurred view of the outdoors.

PIONEERING RARE CANCER CLINICAL TRIAL

One of ONJCRI's greatest achievements in 2018 was the emerging success of a clinical trial to help patients living with rare cancers.

A \$1 million funding boost to the Institute from the Federal Government enabled 60 additional patients living in regional and rural areas to access immune-stimulating anti-cancer drugs. These patients all suffer from various rare types of cancers that affect fewer than six people in every 100,000. Access to immunotherapy drugs for these rare cancers are usually not subsidised by the Pharmaceutical Benefits Scheme, and therefore treatment can be cost-prohibitive for many rare cancer patients.

ONJCRI Medical Director, Prof Jonathan Cebon, said the funding will benefit a group of patients with rare gastrointestinal, neuroendocrine and gynaecological cancers for whom there are few effective drugs.

"Australians with rare cancers have limited access to effective treatments due to the lack of understanding of how their cancers will respond to treatment and

they are often excluded from large clinical trials," he said. "This generous funding from the Australian Government will not only result in more rare cancer patients being treated in the existing metropolitan sites, but will also enable us to take our trial to regional patients."

Working in partnership with Rare Cancers Australia and the Pharmaceutical company Bristol-Myers Squibb, clinicians have already treated 50 patients at three metropolitan centres with a combination immunotherapy, to activate the patients' immune system to seek out and kill cancer cells.

Prof Cebon said the early responses have been very promising, however not everyone benefits. "A suite of laboratory tests are also under development in our laboratories which will help guide clinicians to identify those who are most likely responding to treatment, and more importantly, those who will not. This means valuable time will not be lost for patients by pursuing ineffective treatments."



ANNA'S STORY

Anna Anderson is grateful to be alive. When she was diagnosed with stage four gallbladder cancer her surgeon told her she had just months to live.

That was in October 2017.

The cancer was rare and aggressive and had metastasised to her liver.

With the outlook bleak, the mother-of-three was encouraged to get her affairs in order.

In January 2018 Anna was enrolled in the rare cancer immunotherapy trial under the supervision of Dr Oliver Klein at the the Olivia Newton-John Cancer Research Institute. Almost immediately things started to improve.

Following less than a year on the trial, scans revealed Anna's tumours had reduced to five per cent of their original size.

**ANNA'S TUMOURS HAD
REDUCED TO FIVE PER CENT
OF THEIR ORIGINAL SIZE**

"The doctors are calling it a miracle," she said. "It's marvellous. I wouldn't be here if not for the clinical trial".

"I am incredibly grateful to the ONJCRI Team for the life changing work that they do. I hope that trials such as this will make it possible for others to benefit from the most up to date treatments modern medicine has to offer."



USING SCIENCE FOR BETTER PATIENT CARE

The ONJCRI had 26 PhD students involved in projects during 2018, but for Dr Su Kah Goh, completing his final PhD year at the Institute was something quite special.

Su Kah's project gave him the opportunity to investigate and repurpose a technique that was originally developed for cancer detection into another medical specialty – specifically liver transplantation, where 30-40% of patients develop organ rejection in the first 12 months after transplantation. However, the current means of diagnosing organ rejection is rather invasive. It involves the insertion of a large needle through the skin and into the liver under local anaesthetic in order to obtain a small sample of liver tissue.

Under supervision from both the ONJCRI Translational Genomics and Epigenomics Lab and the University of Melbourne Department of Surgery, Su Kah developed a blood test that can monitor organ health after liver transplantation. The test borrows techniques used in oncology to detect tumour cell DNA in the blood stream. Adjusting these liquid biopsy techniques to detect the earliest signs of organ rejection proved a great chance for Su Kah to exploit modern molecular technologies and genetics to improve diagnosis after liver transplantation.

"DNA between individuals is subtly different," said Su Kah and explains, "If I, the donor, were to put my liver inside of you, the recipient,

a small amount of my DNA would be shed into your bloodstream. The blood test that we have developed allows us to count the number of 'donor' DNA molecules that are in the recipient's blood. On that basis we have developed a blood test, in which the detection of elevated amounts of 'donor' DNA in the recipient can be used to diagnose organ rejection."

The hope is that perhaps one day this test may help clinicians reduce, or even better, replace liver biopsies. "More than 25% of liver transplantations performed at the Austin Health are for early stage liver cancers and often in these patients, surveillance for cancer recurrence is difficult," said Su Kah. The clinical acceptance of tests based on liquid biopsies will increase and it is through collaborations like that of Su Kah's, that we can start developing applications for liquid biopsies outside of oncology.

"Although I worked in a cancer-focused institute, my project is a good example of how sharing knowledge and expertise across disciplines can have great benefits for our patients."



AN EARLY INTEREST IN GENETICS IGNITES PASSION FOR SCIENCE

Dr Lisa Mielke found her inspiration for a career in research in her own family.

Her older brother has Down Syndrome, and as a child, she was curious about what made him different.

She began to explore the root causes of the condition, eagerly attending events and devouring books on genetics.

“As a young kid, it was extremely intriguing wanting to understand why my brother had a disability; and learning about our genes and how they can, to a large degree, define who we are,” she said.

Her early interest in genetics and biology ignited a burning passion for science that ultimately led her to her current role as Head of ONJCRI's Mucosal Immunity and Cancer Laboratory.

As one of several women heading up laboratories at the Institute, Lisa believes having more female scientists in senior roles is vital if we are to encourage girls to follow similar career paths.

“I believe that young girls have always been fascinated by science and technology, the difference is today there are more mentoring programs available to help them pursue a career in those fields,” she said.

“We still have a long way to reach gender equality in the STEM areas (Science, Technology, Engineering & Mathematics), especially in the areas of engineering and maths.”

“This is an important priority for me because I grew up in Gippsland and I understand the disadvantages faced by young people in regional Victoria, especially young women, in a non-metropolitan setting who traditionally have little access to STEM and related mentoring programs.”

Lisa says one of the greatest challenges for women forging a career in science is balancing starting a family with the competing demands of research projects, building their professional networks and accessing leadership programs.

**“IN THE LAST THREE YEARS
ONJCRI HAVE MORE THAN DOUBLED
FEMALE REPRESENTATION AT THE
FACULTY LEVEL”**

At ONJCRI, she feels she has found a supportive workplace that champions diversity and has made gender equity a priority.

“It is very much a family-friendly environment and our directors have done an amazing job in the last few years of hiring and promoting women to leadership positions within the Institute,” she said.

“In the last three years we've more than doubled our female representation at faculty level and we have gender neutral policies for parental leave.”

The ONJCRI is proud to offer our team an environment where we actively encourage, embrace, and promote gender equity and diversity.

GASTROINTESTINAL CANCER PROGRAM

PROGRAM LEAD: PROF JOHN MARIADASON

The Gastrointestinal Cancer Program is seeking to understand the biological causes of cancers of the colon (bowel), biliary tract and stomach in order for new treatments to be developed for patients affected by these diseases. In particular, we are seeking to identify and target the major proteins, which enable tumour cells to survive in the body, and we are testing whether drugs which work in other cancers can be repurposed for the treatment of gastrointestinal cancers.

In 2018, our team completed a phase II clinical trial with the drug everolimus in patients with advanced biliary tract cancer. Although a relatively rare cancer, approximately 700 patients die of biliary tract cancer each year in Australia, and there are currently few effective treatments for this disease. In a trial led by A/Prof Niall Tebbutt and PhD student and Medical Oncologist Dr David Lau, we found that some patients with biliary tract cancer gain benefits from treatment with everolimus, a drug that is currently used in the treatment of kidney cancer. Our program is now seeking to develop further treatment strategies for this disease, and in developing ways to tailor the best treatment for individual patients based on the genetic makeup of each patient's tumour.

PUBLICATION HIGHLIGHTS:

Mooij, J.K. et al. The prognostic impact of consensus molecular subtypes (CMS) and its predictive effects for bevacizumab benefit in metastatic colorectal cancer: molecular analysis of the AGITG MAX clinical trial. Ann Oncol 29: 2240-2246. (2018)

Lau, D.K. et al. Phase II study of everolimus (RAD001) monotherapy as first-line treatment in advanced biliary tract cancer with biomarker exploration: the RADiChol Study. Br J Cancer 118: 966-971. (2018)

Hockings, C. et al. Mcl-1 and Bcl-xL sequestration of Bak confers differential resistance to BH3-only proteins. Cell Death Differ 25: 719-732. (2018)

ONCOGENIC TRANSCRIPTION LAB

Lab Head:
Prof John Mariadason

During 2018, team members Ian Luk, Camilla Reehorst and Rebecca Nightingale made the significant discovery that loss of a gene known as EHF plays a previously unappreciated role in the development of colon cancer. With research support provided by a three-year grant from the Victorian Cancer Council, this discovery is now enabling us to investigate potential new treatments for this disease based on re-activating the EHF gene.

With support provided by a grant from Tour de Cure, the team also continued its pre-clinical research into a new drug combination for treating colon cancer. In work led by PhD student Laura Jenkins we have found that combining drugs which inhibit proteins called “HDACs” and “MEK” in colon cancer cells can induce a high rate of killing of tumour cells. We are now ideally positioned to undertake a clinical trial of this drug combination in patients with colon cancer.

Finally, our team discovered a new way of predicting whether a patient is likely to benefit from treatment with the colon cancer drug bevacizumab. In work led by A/Prof Niall Tebbutt and PhD student and Medical Oncologist Dr Jennifer Mooi, we identified a set of genes which, if active in a patient’s tumour, can improve the likelihood of a patient responding to this drug. Although ideally this finding needs to be confirmed by other researchers, it could provide a means for sparing patients unlikely to benefit from this treatment from unnecessary costs and side effects.

CELL DEATH AND SURVIVAL LAB

Lab Head:
Dr Doug Fairlie

The Cell Death and Survival Laboratory is interested in the fundamental processes that enable cancer cells to survive. In the last decade, there has been significant progress in the development of drugs to target one of these processes and induce death in the tumour cells through a process called apoptosis. While one of these drugs is now approved for use in patients with blood cancers, several others similar drugs are also under development.

In 2017, our lab started working with a range of these drugs in melanoma and showed remarkable improvement in their ability to kill tumour cells when used in specific combinations. That study was completed in 2018 and the manuscript describing the work is currently under review for publication. Building on the success of this observation, we have now extended this approach to other cancers, especially mesothelioma, where we have observed similar effects. This work is a close collaboration between our Lab and Dr Surein Arulananda and A/Prof Tom John, and the project is supported by a grant from the National Health and Medical Research Council to confirm our exciting preliminary findings. Other work in the laboratory in 2018 involved collaboration with Australian pharmaceutical company PharmAust. Here, we have provided important new insights into how a novel drug (monepantel) confers anti-cancer effects in a range of cancers.

Our Lab has a strong interest in a second important process, known as autophagy, which is required to keep cells alive. We are now investigating how this process contributes to the health of the gastrointestinal system and potentially prevents inflammatory bowel disease. Because autophagy and apoptosis are two fundamental mechanisms to keep organisms healthy, we recently published a study looking at the “cross-talk” between these two processes.

BEING AN ONJCRI STUDENT



Our Institute is a highly coveted seat of learning, with opportunities to be mentored by some of the sharpest scientific brains working at the forefront of cancer research.

There are opportunities for students to obtain higher degrees as Honours, PhD and Doctorate of Medical Science. We chatted to two students from the Oncogenic Transcription Lab on what drew them to ONJCRI.

CAMILLA REEHORST

Why did you choose ONJCRI?

It's a growing institution with great opportunities to translate findings from the laboratory bench to benefit patients, and it allows researchers to directly interact with patients. The Institute also promotes collaborations with other national and international research teams, which often helps delivering high quality research outcomes.

What research were you involved in during 2018?

My research focus has been to determine the impact of in-vivo deletion of a transcription factor called Ehf, and in 2018 I mainly focused on characterising the role of Ehf during murine mammary gland development.

I have also contributed to research into the role of Hdac3, another transcriptional regulator, which we have linked to diet-induced obesity.

What is it like being a student at ONJCRI?

It's challenging, but ONJCRI has encouraged and facilitated the foundation of a student society that helps support and empower our student community. I also believe that being away from the 'ivory tower' of a university campus better prepares students for what it actually means to conduct research as a career in the 'real world' after your studies finish.

DAVID LAU

Why did you choose ONJCRI?

I completed my medical oncology training at Austin Hospital in 2013 and I was a clinical fellow when the ONJCRI was known under the name of its predecessor Ludwig Institute for Cancer Research. Working mainly on melanoma, I was exposed to the marvellous and highly stimulating world of medical research. The integration of clinical research all the way from basic laboratory research, translational activities and culminating in clinical trials excited me.

What is it like being a student at ONJCRI?

As a medical oncologist, I was able to continue my practice and be actively involved in patient care. It is a privilege to be able to augment my clinical practice with medical research. As a clinician, I am all too familiar with the need to improve cancer treatments. Research brings a sense of optimism that patient care and outcomes can be improved.

What research were you involved in during 2018 and your time at ONJCRI?

My PhD focused on exploring novel molecular targets for the treatment of upper gastrointestinal cancers, specifically stomach and biliary tract cancers. In particular, I have been investigating the mechanisms of action of a new drug called regorafenib in stomach cancer and how patients can be better selected for that treatment with molecular biomarkers. In biliary tract cancers, I investigated the clinical use of the drug everolimus and investigated biochemical markers that correlate with clinical benefits.

What is your research focus and what is the potential impact for patients?

In 2018, my research focus has been on using next-generation sequencing to investigate new targets in biliary tract cancer such as the IDH1 and FGFRs genes. The results from my studies will assist researchers worldwide to develop new therapies in this disease.

At the end of 2018, David was successful in obtaining the Australasian Gastrointestinal Trials Group (AGITG) Clinical Research fellowship that enabled him to take on a position in the UK where he is currently furthering his research career at the Royal Marsden Hospital in London.



ACCELERATING RESEARCH THROUGH LA TROBE UNIVERSITY PARTNERSHIP

Through ONJCRI's role as the La Trobe University School of Cancer Medicine, scientists, students and patients are benefiting from a strong partnership with La Trobe University (LTU).

Together with the university, ONJCRI undertakes collaborative research, joint training of medical researchers and translates research into clinical practice, ultimately improving health outcomes for patients with cancer.

For Dr Doug Fairlie, Head of the Cell Death and Survival Laboratory with a joint appointment at LTU, the collaboration has allowed him to tap into the expertise of many of the university's world-leading scientists with expertise in fields complementary to those currently represented at the Institute.

"A primary interest of our Lab is to try to understand why cancer cells survive better and how we can use that information to try to kill them. There are a number of proteins in the cell that are essential to those processes, and for certain aspects of our studies, it is critical to understand what those proteins look like at an atomic level. These structural details are particularly important in terms of thinking about how we develop cancer drugs," he said.

"The partnership with La Trobe University enables us to work with their team of structural biologists who specialise in this type of atomic level analysis. Our Lab has been working in the field of cell death research for many years and this collaboration has been so important for the success of the projects we are pursuing."

Being able to recruit the best and brightest students from LTU for Honours, Masters and PhD students is also a benefit of the partnership, as is access to specialised equipment and facilities not currently available at the Institute.

"In a broader sense, we're also thinking about the idea of developing our own cancer drugs. Our LTU partnership will allow us to work with their team of specialised chemists to identify and progress opportunities for drug development."

"THE PARTNERSHIP ALLOWS US BOTH TO PERFORM CRITICAL EXPERIMENTS AND ACCELERATE RESEARCH OUTCOMES"

Overall, Doug believes that ONJCRI's partnership with LTU provides reciprocal benefit to both institutions to perform critical experiments and accelerate research outcomes.

TRANSLATIONAL BREAST CANCER PROGRAM

PROGRAM LEAD: PROF ROBIN ANDERSON

In 2018, over 18,000 Australian women and about 150 men were diagnosed with breast cancer and over 3,200 died, largely due to the spread of their cancer to other vital organs such as liver, lung and brain. The Translational Breast Cancer Program aims to provide benefits to these breast cancer patients, both by helping to identify the most effective initial therapy after diagnosis as well as the subsequent therapies that are effective if the cancer has spread to other organs through a process called metastasis.

Our Program comprises four research groups led by Drs Normand Pouliot, Delphine Merino, Bhupinder Pal and Prof Robin Anderson.

Dr Bhupinder Pal joined our Program in 2018 and provides complementary skills in analysis of patients' tumours at the level of individual cells within the tumour with the ultimate aim of being able to identify those genes that drive the growth of the cancer (read more on p37). He is working closely with other faculty members in the Program, including Dr Delphine Merino and our breast medical oncologist, Dr Belinda Yeo, to analyse tumours before and

after the patients have undergone therapy. This project aims to understand why some tumours respond to the therapy whilst others do not, and to predict the best therapy for individual patients (read more on p36).

Curative treatments for breast cancer that has spread to the brain are not yet available. One goal for our Program is to identify more effective therapies for these patients. A highlight of 2018 was the publication of our study, led by Dr Normand Pouliot, of a preclinical model of brain metastasis and possible therapies that could be trialled in the clinic.

Finally, in a study led by Prof Robin Anderson, we have shown that a protein called nephronectin, that we have demonstrated previously to promote breast cancer spread in our preclinical models, is also associated with poor prognosis in breast cancer patients.

PUBLICATION HIGHLIGHTS:

Steigedal T.S. et al. Nephronectin is correlated with poor prognosis in breast cancer and promotes metastasis via its integrin-binding motifs. *Neoplasia* 20: 387-400. (2018)

Kim S-H. et al. Identification of brain metastasis genes and therapeutic evaluation of histone deacetylase inhibitors in a clinically relevant model of breast cancer brain metastasis. *Disease Models & Mechanisms* 11: doi:10.1242/dmm.034850. (2018)

Merino D. et al. BH3-Mimetic Drugs: Blazing the Trail for New Cancer Medicines. *Cancer Cell* 34: 879-891. (2018)

Buus R. et al. Novel 18-gene signature for predicting relapse in ER-positive, HER2-negative breast cancer. *Breast Cancer Res* 20: 103. (2018)

METASTASIS RESEARCH LAB

Lab Head:
Prof Robin Anderson

The goal of the Metastasis Research Laboratory is to identify the genes that control metastasis, and to test or develop drugs that target these genes. We aim to provide more effective therapies for breast cancer patients with advanced disease. To achieve this, we have developed preclinical models of advanced breast cancer that allow us to identify metastasis related genes and test novel therapies. During 2018, we reported on the development of two new preclinical models of metastasis that we use extensively in our research.

Our Lab team have tested the function of several genes that we have identified as regulators of metastasis. The most advanced study is of a protein called BMP4 that is very effective in preventing metastasis. During 2018, we identified some compounds that possibly mimic the actions of BMP4 and we are actively testing these compounds in breast cancer cells. We also tested potential biomarkers in tumours from breast cancer patients to identify those patients for whom this therapy could be appropriate in the future.

In the era of immunotherapy, breast cancer, unlike some other types of cancer, has typically not been amenable to therapies that help the patient's immune system to fight the cancer. Indeed, immunotherapy has been shown to be effective only in a small proportion of breast cancer patients. We have tested an alternative approach to immunotherapy, targeting a different type of immune cell called the neutrophil. We have shown that early treatment with an antibody that prevents the neutrophils from leaving the bone marrow, can effectively prevent metastasis. Our focus is now on understanding how neutrophils promote metastasis and to identify the patients who will be most likely responsive to this therapy.

MATRIX MICROENVIRONMENT AND METASTASIS LAB

Lab Head:
Dr Normand Pouliot

The overarching goal of the Matrix Microenvironment and Metastasis Laboratory is to develop more effective treatments for patients with breast cancer metastasis. Ongoing research in our Lab focuses on identifying genes and proteins that can predict the spread of aggressive breast cancer and to test new therapies that prevent breast cancer from reaching and growing in the brain.

During 2018, we developed unique pre-clinical models of breast cancer brain metastasis that closely mimic the human disease and the associated clinical scenarios in patients. In these models, we have evaluated the efficacy of several new drugs either alone, or in combination with standard therapies. Our work published in the journal *Disease Models and Mechanisms* describes one such new model, called 4T1Br4, in which we demonstrated the efficacy of novel drugs called histone deacetylase inhibitors against brain metastasis. In collaboration with Australian and international researchers we are also testing novel combination therapies that block resistance to anti-cancer agents routinely used in the clinic. Finally, we also explore whether so called aptamers could improve drug delivery into the brain and minimise side effects of standard chemotherapy.

TUMOUR PROGRESSION AND HETEROGENEITY LAB

Lab Head: Dr Delphine Merino

There is a real need to understand the mechanisms by which cancer cells metastasize before the time of diagnosis, and how they escape current therapies.

During 2018, the Tumour Progression and Heterogeneity Laboratory in collaboration with breast cancer oncologist Dr Belinda Yeo and genetic expert Dr Bhupinder Pal, studied the genetic make-up of metastases from nine patients. Some of these patients had been treated with multiple therapies, and some had not yet received therapy. In both cases, we found that each tumour consisted of a mix of highly diverse cancer cell populations with each population having its own unique genetic profiles.

In order to better understand which of these subpopulations of cancer cells are responsible for the spread of the tumour to distant organs and also for developing resistance to therapy, we are using a new technology called 'cellular barcoding'. This technology allows us to "tag" each cancer cell from a patient tumour with unique DNA or optical mark to enable us to track each cancer cell individually and study its behaviour over time and in response to a particular therapy. We then can identify the most aggressive cells in a patient sample, and study its individual response when exposed to different drugs in the laboratory, including chemotherapy and those novel therapies that have entered the clinic for the treatment of other malignancies. The 'cellular barcoding' technology also enabled

us to identify those subpopulations of breast cancer cells that are resistant to chemotherapy, and to study their biology so that we can design better treatments for metastatic breast cancer.

SINGLE CELL CANCER GENOMICS LAB

Lab Head: Dr Bhupinder Pal

In 2018, we launched the newly formed Single Cell Cancer Genomics Laboratory. The goal of our Lab is to address key issues related to the failure of cancer treatments and to predict the risk of disease relapse in breast cancer patients. We believe that the subtle differences in RNA, DNA and protein composition of individual cancer cells collectively dictate how well and for how long a tumour will respond to a treatment. However, such cellular complexities cannot be detected using conventional diagnostic tests, because they generate an average genetic profile of all cancer cells in a tumour, thus masking clinically relevant information of individual cells.

Our research team specialises in the use of innovative single cell techniques that can reveal the genetic blue print of individual cancer cells as well as monitor the surrounding cell types residing within a tumour site. This approach can identify those few rare cells that ultimately will lead to treatment resistance and therefore inform us on how to develop more effective drugs and how to "personalise" treatment plans for cancer patients. Although, we are primarily focussed on analysing cancer cells from breast cancer patients undergoing treatment at the Olivia Newton-John Cancer Centre, we are also studying other cancer streams currently being investigated at the Institute (i.e. colon, lung, skin).



KEEPING IN TOUCH WITH THE REAL WORLD

Prof Robin Anderson's 'lightbulb' moment came at a breast cancer conference in the United States in the mid-1990s.

Cancer survivors were co-chairing lecturing sessions with scientists and clinicians, and telling their patient stories. At the time, it was such an unusual but innovative way to run a conference; Robin was inspired.

"You could sit down at lunch and instead of talking to a scientist you would find you were talking to a person with cancer. It was a real eye opener to me," she said.

"When I returned back to the world of science in my own laboratory, I realised that discussions with women with breast cancer have the potential to change the direction of my research.

**"IT REALLY IS SO VALUABLE TO
HAVE THAT SENSE OF WHAT A
PATIENT IS DEALING WITH"**

Since then, consumer advocates – patients who use their experience of living with or experiencing the burden of cancer – have become far more important contributors to cancer research. They play a critical role in Robin's work as Head of the Translational Breast Cancer Program and her Metastasis Research Laboratory.

She is currently working with five women who have had or are living with breast cancer, meeting over coffee or talking on the phone to discuss her research and obtain their input into research proposals submitted to granting agencies.

"These consumer advocates will tell us whether our research plans make sense to them, whether they feel our proposals are important and whether they think it might help the next person who has cancer," she said.

"It really is so valuable to have that sense of what a patient is dealing with and what research looks like from their point of view."

Keeping the patient experience at the forefront of her research is a priority for Robin and the students she mentors, and over the years she has developed strong bonds with some of these consumer advocates.

"There is one lady I've been working with since about 2010 and I regard her as a friend now. I call her up and have chats and a coffee. You do become quite close and that is lovely."



MEREDITH'S STORY

Meredith with her partner Alli and their son Augie.

Patients make critical contributions to the success of medical research, and helping to progress the development of new treatments for the benefit of many.

For Meredith Cowley, her involvement with cancer research began after she had undergone gene testing when first diagnosed with Stage 4 Metastatic Breast Cancer in October 2017 at the age of 38. As part of her gene testing, Meredith was given the option of donating her blood sample for further genetic research. Since this time, she has donated additional blood samples to research in consultation with her oncologist and ONJCRI Clinician Scientist Dr Belinda Yeo. In Meredith's words - *"This is about getting real results for cancer treatment."*

In talking with Belinda, Meredith shares her thoughts about why being involved in cancer research is so important...

"Having worked as a social worker in front line child protection for nearly 20 years, I understand the importance and value of different disciplines working together."

I really like that researchers and clinicians at the Olivia Newton-John Cancer Centre work as multidisciplinary teams. They are all part of the same big picture. It is the passion for the grass roots work of people like Belinda and her colleagues that really makes a difference.

I strongly believe that if you are truly wanting to make a difference, being involved in research is what you need to do.

I am benefitting from the people who have been involved in clinical trials and donated to cancer research in the past. Unfortunately, some of these people may not have been able to benefit from this but thanks to them - I can.

The success of cancer research might keep me alive, but if it is not me it might be the next person. And I certainly want to be able to give for future generations in the same way.

I feel like I've got a lot of life to live and being involved in cancer research is one way to contribute."



COMMUNITY SUPPORT ESSENTIAL FOR RESEARCH

**They say from little things
big things grow.**

And that is exactly what happened when three women who work at Scotch College came together with ONJCRI Fundraising Co-ordinator Helen Hovrell to raise funds in memory of loved ones lost to cancer.

The \$37,000 they raised at their Girls Night Out event was donated to ONJCRI and used to buy vital equipment to help in the fight against cancer.

This substantial donation allowed the Institute to purchase a cryostat - a versatile instrument, essential for any research involving biomarker studies.

Dr Normand Pouliot, Head of the Institute's Matrix Microenvironment and Metastasis Laboratory, said the cryostat is primarily used to freeze and cut thin slices of tissue samples.

This equipment is critical to progress his work to identify biomarkers such as proteins, DNA and RNA that help predict patients who are likely to see the disease recur or those who would benefit from a particular treatment.

"The presence of these biomarkers is commonly validated in 'archival' tumour tissues preserved in wax. However, tissues that are preserved in wax for long-term storage require treatment with harsh chemicals that affect the integrity of protein, DNA and RNA," he said.

"This often makes detection of these molecules very difficult and unreliable. The cryostat overcomes these limitations because it allows us to prepare slices of freshly frozen tissues without the use of these harsh chemicals and therefore enables to detect biomarkers easier and more reliably."

The Girls Night Out event was MC'ed by Lord Mayor of Melbourne, Sally Capp - a member of the ONJCRI Board and herself a past Scotch College mum - and featured a live auction and talks from ONJCRI Clinician Scientist and Austin Health's Director of Clinical Trials, A/Prof Hui Gan alongside survivors of brain and breast cancer.

The event was such a success that the organising team plan to work with ONJCRI and hold the event every two years.

Having the capacity to purchase urgently needed equipment like the cryostat through fundraising efforts not only transforms Normand's research, but also provides a huge boost to the research of many of his colleagues at ONJCRI.

"As research becomes more and more dependent on expensive technologies and equipment every institute struggles to find funds to satisfy the demands to perform cutting-edge research," he said.

"Without the engagement of the community to become involved with fundraising, we could not perform leading edge research, so these fundraising efforts are really essential to our work. We really can't thank our donors enough."

COLLABORATION BUILDS STRENGTH FOR BETTER PATIENT OUTCOMES

After seven years working together, Drs Delphine Merino and Bhupinder Pal share more than just a passion for science.

They have been 'partners in crime' on their rollercoaster ride of triumph and failure that comes with medical research.

At ONJCRI the pair continues to collaborate on a number of projects in the area of metastatic breast cancer.

While Delphine focuses on the biology of cancer samples at the cell or tissue level, Bhupinder brings his expertise in DNA and genetics.

Their shared passion is to develop and test new drugs for the treatment of the most aggressive cells present in a patient's cancer, and collaboration is the key to that research.

Dr Delphine Merino

In the movies, science is often depicted as a lonely pursuit – a solo researcher hunched over a microscope in a deserted lab.

But for the modern scientist, teamwork is key to success.

For Dr Delphine Merino, collaboration is the cornerstone of her work in translational breast cancer.

"The technologies are extremely complex these days and when we're trying to answer big questions, we rely on highly skilled people bringing together unique expertise, complementing research approaches, and specialised cutting-edge technologies," she said.

As the Head of the Tumour Progression and Heterogeneity Lab, Delphine collaborates with a variety of colleagues including clinicians, researchers, professional services and patient advocates.

"One of the really positive things about working at ONJCRI is that we are located in a hospital so we work closely with oncologists and we can follow the progress of the patients. This provides ongoing dialogues and conceptual inputs from colleagues with complementing knowledge; this is a real strength for all research teams at ONJCRI."

Engaging with experts in multiple fields has been a career highlight for Delphine, who says there has never been a more exciting time to be a scientist in translational cancer research.



WE ARE INVESTIGATING HOW SPECIFIC DIFFERENCES IN INDIVIDUAL CANCER CELLS CAN RESULT IN RESISTANCE TO TREATMENT

- DR BHUPINDER PAL

"We are now able to apply the latest technologies in cellular imaging, DNA sequencing and drug screening on patient samples. Thanks to the collaborative efforts between clinicians, geneticists, mathematicians, chemists, biologists, microscopists and computational scientists, we are now for the first time able to understand the progression of cancer in greater depth," she said.

Dr Bhupinder Pal

Dr Bhupinder Pal joined ONJCRI in June 2018 to set up a new laboratory in the Translational Breast Cancer Program.

As the Single Cell Cancer Genomics Laboratory Head, he is building a team committed to translating research findings into novel diagnostic tools that will help to better match specific treatment with specific patients. This is referred to as personalised cancer treatments.

"My research focusses on understanding how specific differences in individual cancer cells residing within a tumour can influence the treatment outcome, including disease relapse and spread to other locations in the body," he said.

Collaboration is a pivotal part of Bhupinder's research and he works closely with many research groups within ONJCRI as well as teams from other research institutes.

"If we want to maximise the insights into how cancers work we need a multi-disciplinary approach and for that we need to bring together experts from all the areas that are relevant for a particular project."

"Together with my colleagues Drs Belinda Yeo and Delphine Merino, we are trying to understand how we can effectively monitor breast cancer treatment and prevent spread of the disease to other vital organs."

Bhupinder comes to the Institute having completed his postdoctoral training at the prestigious Walter and Eliza Hall Institute in Melbourne and is thriving at ONJCRI on the opportunity to work closely with clinicians and to lead a team at one of the forefronts of cancer research.

"ONJCRI is young and growing and as an institute, it provides a lot of support to new Lab heads like me; this environment will certainly help me as I progress my career as a researcher."



TUMOUR TARGETING PROGRAM

PROGRAM LEAD: PROF ANDREW SCOTT

The Tumour Targeting Program focuses on the targeting, molecular imaging and treatment of tumours, as well as defining receptor-based signaling pathways responsible for cancer cell growth, and to uncover mechanisms that result in resistance to targeted therapies.

The Program has strong collaborative links to Austin Health's Department of Molecular Imaging and Therapy, directed by Prof Andrew Scott and Cancer Clinical Trials Centre, directed by A/Prof Hui Gan, enabling the iterative research cycle from laboratory to the clinic and back.

During 2018, we continued to develop new drugs to inhibit some of the most important cancer pathways, in order to improve patient survival and quality of life. We also continued to investigate the molecular imaging of tumours to evaluate tumour response and aiding in selecting the most suitable patient for a particular drug. Accordingly, we commenced Phase I/II clinical trials with tumour targeting antibodies developed by the Program.

PUBLICATION HIGHLIGHTS:

Roswall P. et al. Microenvironmental control of breast cancer subtype elicited by paracrine platelet derived growth factor-CC signalling. *Nature Med* 24: 463-473. (2018)

Gan H. K. et al. Safety, Pharmacokinetics and Antitumor Response of Depatuxizumab Mafodotin as Monotherapy or in Combination with Temozolomide in Patients with Glioblastoma. *Neuro-Oncology* 20: 838-847. (2018)

Burvenich I. J. G. et al. Molecular Imaging of T Cell Co-regulator Factor B7-H3 with 89Zr-DS-5573a. *Theranostics* 8: 4199-4209. (2018)

TUMOUR TARGETING LAB

Lab Head: Prof Andrew Scott

During 2018, the Tumour Targeting Lab continued to identify novel targets for cancer drug development and explored different therapeutic approaches. Novel antibodies developed in our Lab against receptors expressed in the tumour microenvironment and on cancer cells have been explored in model systems to inhibit signalling, to work for antibody-drug conjugates (ADCs), and for enhancement of patients' anti-tumour immune responses.

Our research into new therapies for glioblastoma patients has shown highly promising results from studies with a drug called Depatuxizumab mafodotin (depatux-m, ABT-414), a tumour-selective anti-epidermal growth factor receptor ADC comprised of our monoclonal antibody (mAb) 806 and the monomethyl auristatin F "warhead" to kill cancer cells. We were also continuing to investigate next generation mAb806-based ADCs and their combinations with chemotherapy.

We are also developing therapeutics that target key molecules in breast, lung, prostate and colon cancer, and with collaborators at La Trobe University are developing a novel treatment approach for cancer cachexia.

In order to explain the biological and pathological role(s) of signalling from a molecule called PDGF-CC, we collaborated with colleagues from the Karolinska Institute in Sweden to engineer high affinity neutralising mAbs that recognise the human PDGF-CC and that have therapeutic effectiveness in cancer and stroke

models. Remarkably, we showed that mAb-based intervention of PDGF-CC activity converted basal-like breast cancers into a hormone receptor-positive state, and enhanced sensitivity to endocrine therapy in preclinical models. Meanwhile, in a model of stroke, the intraperitoneal administration of the chimeric anti-PDGF-CC mAb ch6B3 reduced PDGF-CC-induced disruption of the blood-retinal barrier.

Our Lab is developing novel imaging probes through sophisticated chemistry techniques to identify patients suited to treatment with hormone therapies or anti-cachexia agents, specific oncogenic signalling pathways, and immunotherapy. Grant funding supported commencement of our clinical bioimaging trial with 89Zr labelled mAbs to validate therapeutic targets as well as to identify optimal dose and patient selection for therapy (NCT03374943; NCT03610061).

RECEPTOR BIOLOGY LAB

Lab Head: Dr Peter Janes

Following a move from Monash University, the Receptor Biology Lab joined the Tumour Targeting Program at the end of 2018.

The Lab investigates those cell surface proteins that are particularly abundant or active in tumours and/or the surrounding microenvironment, as potential targets for new therapies. In particular, we study two families of cell surface proteins, namely the Eph receptors, which guide cell migration, and the ADAM proteases, which shed proteins from the cell surface and thereby control cancer cell growth, drug resistance, and invasion and spreading to other tissues (see full story on p42).

In 2018, we continued to investigate the role of EphA3 in the tumour microenvironment, because we previously found that EphA3 is most commonly present in non-tumour cells that travel to the tumour and can aid its growth. By reducing EphA3 levels, we found that tumour growth depends on 'host' cells which are recruited to the tumour and promote the formation of new blood vessels and suppress anti-tumour immune responses.

Similarly, we investigated the function of ADAM10, which is highly active in certain tumour cells, by blocking the production of this protease in order to inhibit the growth of tumours in models for colon cancer and glioma. In collaboration with the Tumour Targeting Laboratory, we have developed and tested monoclonal antibodies (mAbs) which bind to either EphA3 or ADAM10 as a way to specifically target and inhibit tumour growth. Our ADAM10 mAb, which specifically binds to an active form of ADAM10 that is highly abundant in tumours, was recently licensed to Carina Biotech for the development of a new immune cell-based anti-cancer therapy. We also tested the effects of our mAbs linked to cytotoxic drugs to build antibody-drug conjugates to specifically kill tumour cells.



IMPROVING PATIENT OUTCOMES THROUGH NATIONAL BRAIN CANCER STUDY

Glioblastoma, or GBM, is one of the most aggressive types of brain cancer. Patient symptoms are often non-specific, the tumours grow and spread quickly, and survival rates are low.

Treatment for GBM traditionally involves chemotherapy and radiotherapy, often alongside invasive surgery. Now, thanks to \$1.52m in funding from the Medical Research Future Fund (MRFF) and \$200k in funding from the Cure Brain Cancer Foundation, Prof Andrew Scott, Head of the Tumour Targeting Lab, is leading a national brain cancer study investigating novel treatments for patients with GBM. The MRFF funding was announced by Federal Health Minister Greg Hunt MP in February 2018, and will be received over five years. This allows Prof Andrew Scott to conduct a multi-centre study that will bring together 19 investigators from major hospitals and universities across Australia.

“Currently only 25 percent of patients with GBM are still alive two years after diagnosis and just 10 percent live for 5 years despite receiving treatment,” says Andrew. “New imaging techniques that incorporate prognostic information are required to improve patient outcomes because they allow us to better tailor care to individual patients.” The study

investigates the benefits of incorporating FET-PET imaging technology into the treatment of GBM patients.

Fluoroethyl-tyrosine (FET) is an amino acid metabolism tracer agent that measures cell proliferation. It is regarded as one of the best markers for positron emission technology (PET) imaging of common primary brain tumours, as it allows researchers to view the patient’s tumour at an illuminated focal point, rather than being obscured by normal brain tissue. For patients with particularly aggressive forms of brain cancer, such as GBM, it is important to precisely determine the extent of disease prior to initiating the treatment, which this study will evaluate. The ability of FET-PET to more accurately evaluate response to treatment will also be evaluated, as current imaging techniques cannot always distinguish between treatment response and progression of disease, which is crucial information in determining the best treatment approach for patients.

“This trial will determine how we can use the FET-PET technology to provide optimal treatment to GBM patients, and hopefully improve survival rates,” Andrew says.

A total of 210 patients are planned to be enrolled in the study, and it will be conducted at 10 sites around Australia.

BEING PART OF THE QUESTIONS AND THE ANSWERS

As a Clinician Scientist, Dr Eliza Hawkes believes she has the best of both worlds.

She gets to combine her passion for medical research with the reward of helping patients in face-to-face cancer care.

"I enjoy being part of the questions and the answers - seeing patients with problems we can't yet solve, then going to the research laboratory and trying to find that answer, rather than hoping that someone else is working on it," she said.

As an oncologist and the Head of the Lymphoma Service for the Olivia Newton-John Cancer Centre, Eliza provides the front-line of treatment for patients living with cancer, and this often helps to inform her research in the laboratory.

"Marrying our understanding of the biology of cancer and how it behaves in patients closes the research loop from which both the advancements in the laboratory and the patients can benefit simultaneously.

"I enjoy helping patients on an individual level in their cancer experience, but then also contributing to the global effort to improve outcomes."

Teamwork plays a big role in her job and Eliza works with a range of staff including medical, scientific, nursing, allied health and administrative, in a way that she says is a "constant learning process."

**"I GET TO COMBINE MY
PASSION FOR MEDICAL
RESEARCH WITH THE
REWARD OF HELPING
PATIENTS"**

"I really enjoy the variety of being in the clinic treating patients and working with clinical nurse specialists, other consultants and the junior doctors; particularly mentoring and teaching them, then shifting gear and heading into the research space," she said.

"Working with a lot of different people who have different backgrounds - patients, nurses, allied health and the ancillary staff in the clinics and on the ward; all the way through to the lab scientists - I am learning from them all constantly and it helps me improve across the board."

Her research focuses on immunotherapy drugs and other novel therapies in lymphoma and how these drugs can be combined with standard treatments, as well as investigating blood, tissue and imaging markers to predict which patients are likely to benefit from these treatments.



DEVELOPING NEW ANTI- CANCER DRUGS

**Dr Peter Janes is one of
ONJCRI's newest recruits,
joining the Institute in 2018.**

As Head of the Receptor Biology Laboratory, he is fascinated by the way our bodies function on a cellular level, and how normal developmental processes can become hijacked by tumours.

Peter is particularly interested in developing antibodies that can bind and block proteins that are more abundant in cancerous tissue and aid tumour growth.

It is this focus that informs his collaborative work with the Tumour Targeting Lab as he investigates the function of key cell surface proteins and develops monoclonal antibodies as potential new anti-cancer drugs.

Peter's research in 2018 focused on two families of cell surface proteins: The EphA3 receptor, which guide cell migration, and ADAM proteases, which clip certain proteins from the cell surface thereby stimulating tumour growth and drug resistance.

"We're investigating these proteins because they're more abundant or more active in tumour cells, or in the microenvironment that supports the tumour. We want to target these proteins with novel cancer therapies," he said.

"Our research focuses on the biological roles these proteins play in cancer and how inhibiting

these proteins with antibodies may reduce the capacity of tumours to grow and therefore result in novel therapies."

The role the EphA3 receptor plays in the tumour microenvironment is a key focus of Peter's team, and the insights from their recent research provides promising cues.

"Cell migration is a key to the spreading of cancers to distant organs. Cancer cells can "coerce" normal cells to migrate towards the tumour to help the tumour grow, and also to hide cancer cells from being detected by the immune system. We believe that the EphA3 receptor plays a critical role in guiding this cell migration", he said.

"Ideally we'd be able to block this migratory activity so that we can stop those normal cells from helping the cancer grow."

**"IDEALLY WE WOULD BE ABLE TO
INHIBIT MIGRATION OF NORMAL
CELLS TOWARDS THE TUMOURS
SO THAT THEY NO LONGER
SUPPORT THE CANCER TO GROW"**

A complementary strategy is to exploit antibodies that recognise proteins that are highly abundant on cancer cells. Coupling such antibodies with cytotoxic drugs enables the selective killing of tumour cells to avoid many of the side effects associated with standard chemotherapies.

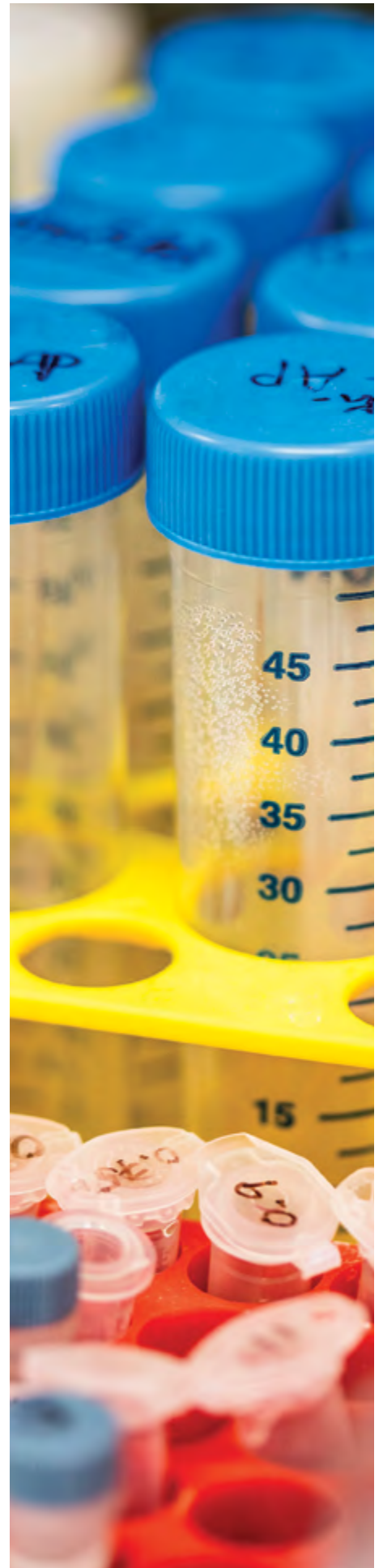
"Our initial work suggests these new cytotoxic antibody-drug conjugates can inhibit the growth of cancer cells in the lab, and we are now very keen to find out whether these experimental approaches can be developed for use in patients in the long term."

CENTRE FOR RESEARCH EXCELLENCE IN BRAIN CANCER

CO-LEADS:
**PROF ANDREW SCOTT
AND A/PROF HUI GAN**

In 2018, the Victorian Government announced funding for the establishment of a Centre for Research Excellence in Brain Cancer at the ONJCRI (see full story on p44). This was based on the achievements and reputation of key researchers at the ONJCRI in developing new and innovative strategies for imaging and treating brain cancer, and the ongoing commitment of the Victorian Government to support further research in this area.

The structure of the Centre for Research Excellence in Brain Cancer builds on the unique strengths of the existing ONJCRI activities in brain cancer research. The Centre will focus on the development of imaging techniques and chemistry, molecular assays and novel therapeutics. The Centre's program will extend from primary brain cancer to metastatic disease, and link in with new targets for molecular imaging and therapy, biomarkers aiding in the selection of patients to specific treatments and prognosis, as well as developing novel techniques for optimising drug delivery to brain cancer.



AN INSIGHT INTO OUR NEW CENTRE FOR RESEARCH EXCELLENCE

In May 2018, the Victorian Government announced a \$10million funding boost to the Olivia Newton-John Cancer Research Institute.

Part of this funding will allow the establishment of a Centre for Research Excellence with a focus on brain cancer. Centre co-Directors A/Prof Hui Gan and Prof Andrew Scott, explain what this Centre for Research Excellence (CRE) means for our researchers and patients.

What will be your role at the new Centre for Research Excellence?

A/Prof Gan is a medical oncologist and recipient of a ONJCRI Clinician Scientist Fellowship, specialising in the management of brain tumour patients, as well as head and neck cancer and Phase 1 studies. He is also the Director of Cancer Clinical Trials at Austin Health.

Prof Scott is a clinician scientist with extensive experience in molecular imaging of cancer, and discovering and translating new therapeutic approaches for cancer therapy. He is Head of the Tumour Targeting Program in the ONJCRI, and Director of the Department of Molecular Imaging and Therapy at Austin Health.

What is a Centre for Research Excellence?

A Centre for Research Excellence is a multi-disciplinary collaborative consortium that has come together to undertake research in a specific area. The CRE in Brain Cancer at ONJCRI will bring together national and International clinicians, scientists and other researchers in brain tumours to accelerate the development of treatments, diagnostic modalities and biomarkers. Collectively, this will improve survival in this very poor prognosis cancer.

What will be some of the main areas of focus for the Centre team?

1. New imaging probes: to assist with initial diagnosis, evaluate prognosis, guide treatment, and assess response to treatment more accurately than current techniques.
2. Developing new molecular assays: for characterisation of brain cancers, leading to improved decision making and selecting the most appropriate treatment for patients.
3. Developing new drugs and approaches to treatment: that will result in improved responses and survival in brain cancer patients.

What are the next steps for the Centre and what are the long-term goals?

The CRE in Brain Cancer will formally commence operation in 2019. Our goals are to improve patient survival through the development of novel imaging probes and molecular assays, coupled with new drug discoveries that are translated into clinical trials.

How will patients benefit from this Centre?

Our group has a proven track record in rapid translation of its discoveries into the early phase clinical trials, as shown by our success in bringing two novel therapeutics (ABT-414 and KB004) into clinical trials in GBM patients. New discoveries from the CRE in Brain Cancer will also be extended into clinical trials, aiming to improve access to new and more effective treatments for brain cancer patients.

What will the Centre offer to our researchers?

The CRE in Brain Cancer will comprise a truly collaborative group of researchers with world-class expertise to undertake novel research that is focused on the needs of patients, and the development of novel treatments to improve survival.

What does it mean for you both to be involved in such an important milestone?

To be involved in the CRE in Brain Cancer is very gratifying. It builds on the research and work we have done to date, and represents an opportunity to accelerate our research and create new programs of discovery that will lead to clinical trials aimed at improving outcomes for brain cancer patients.



COMBINING SCIENCE AND LAW

As a self-confessed “science nerd”, lawyer Gabrielle Hirsch has found her ideal job as the legal counsel for the Olivia Newton-John Cancer Research Institute.

“I always loved science but got into law because I inadvertently sat in on a biotechnology law lecture and thought it was really fascinating, so I decided to study both science and law at university as a way to combine the two fields” she said.

“It’s been a really great way to harness those different aspects of my personality and approach to problem solving – combining scientific curiosity and an analytical approach with the critical thinking and strategic approach associated with legal thinking. Of course, using language effectively is also a really important part of being a lawyer and having a good understanding of both legal and scientific terminology and concepts allows me to communicate more effectively with diverse audiences and help find common ground.”

“WORKING AS LEGAL COUNSEL IN THE MEDICAL RESEARCH SECTOR ALLOWS A RARE COMBINATION OF MY TWO VERY DIFFERENT INTERESTS – SCIENCE AND LAW”

Gabrielle is responsible for managing all of the Institute’s legal affairs and the intellectual property it generates. As the sole legal counsel, it is a huge job but one that allows her to enjoy enormous variety in her work.

“One morning I might be reviewing a clinical trial agreement or a material transfer agreement. At noon, I might be negotiating a software licence or providing corporate governance advice, and in the afternoon, I’ll be meeting with researchers to discuss a potential collaboration or finalising a grant agreement to ensure our researchers have the funding support to progress their research.”

In 2018, Gabrielle was among the first cohort of women to be accepted into the Victorian Women in Leadership Development program, which provides mentoring for female leaders in the areas of science, technology, engineering and mathematics. She was also named a finalist in the Healthcare, Pharmaceuticals and Biotech Lawyer of the Year and Not-for-Profit Lawyer of the Year categories of the Lawyers Weekly Corporate Counsel Awards, a national award which recognises high achieving lawyers across Australia.

She feels very fortunate to work in a field that is interesting, challenging and impactful. “Being a lawyer in the medical research sector gives me the opportunity to combine my two very different intellectual interests – science and law – to try to make a difference in the lives of people today and tomorrow.” she said. “Cancer touches the lives of every one of us in different ways and our Institute is filled with people who are dedicated to a shared mission of winning over cancer and they work tirelessly to improve the lives of people with cancer. It’s amazing to be part of it.”

Ben Service with his wife Jess and their two young children Darwin and Henry at the Centre for Excellence in Brain Cancer funding announcement at Parliament House, Victoria.



BEN'S STORY

Cancer survivor Ben Service, 32, says he has advances in cancer research to thank for being alive.

"Research means I was able to see my little girl's first day at school. Without research I simply wouldn't be here," the Warrigal man says.

Ben was diagnosed with malignant melanoma in 2016. Shortly after diagnosis his cancer spread to his bones, liver and brain. Under normal circumstances this would have been rapidly fatal, however he was able to receive life-saving immunotherapy treatment.

He was also able to receive highly-targeted radiotherapy to control the tumours in his brain.

"To imagine, in December 2016, I thought it was my last Christmas and New Year with my family," he says.

**"WITHOUT RESEARCH
I WOULDN'T BE HERE"**

Ben's wife Jess describes the results as "out of this world".

"I thought I was going to lose him so many times. I am so grateful; from the bottom of my heart," she says.

PARTNERSHIPS AND COLLABORATIONS

ONJCRI is an independent Medical Research Institute. It is embedded in the Olivia Newton-John Cancer Wellness and Research Centre, which is operated by Austin Health, a major provider of tertiary health services, research, and health professional education in Victoria. ONJCRI occupies three floors of dedicated research space in a purpose-built comprehensive cancer centre building, where we integrate clinical medicine with laboratory and clinical research.

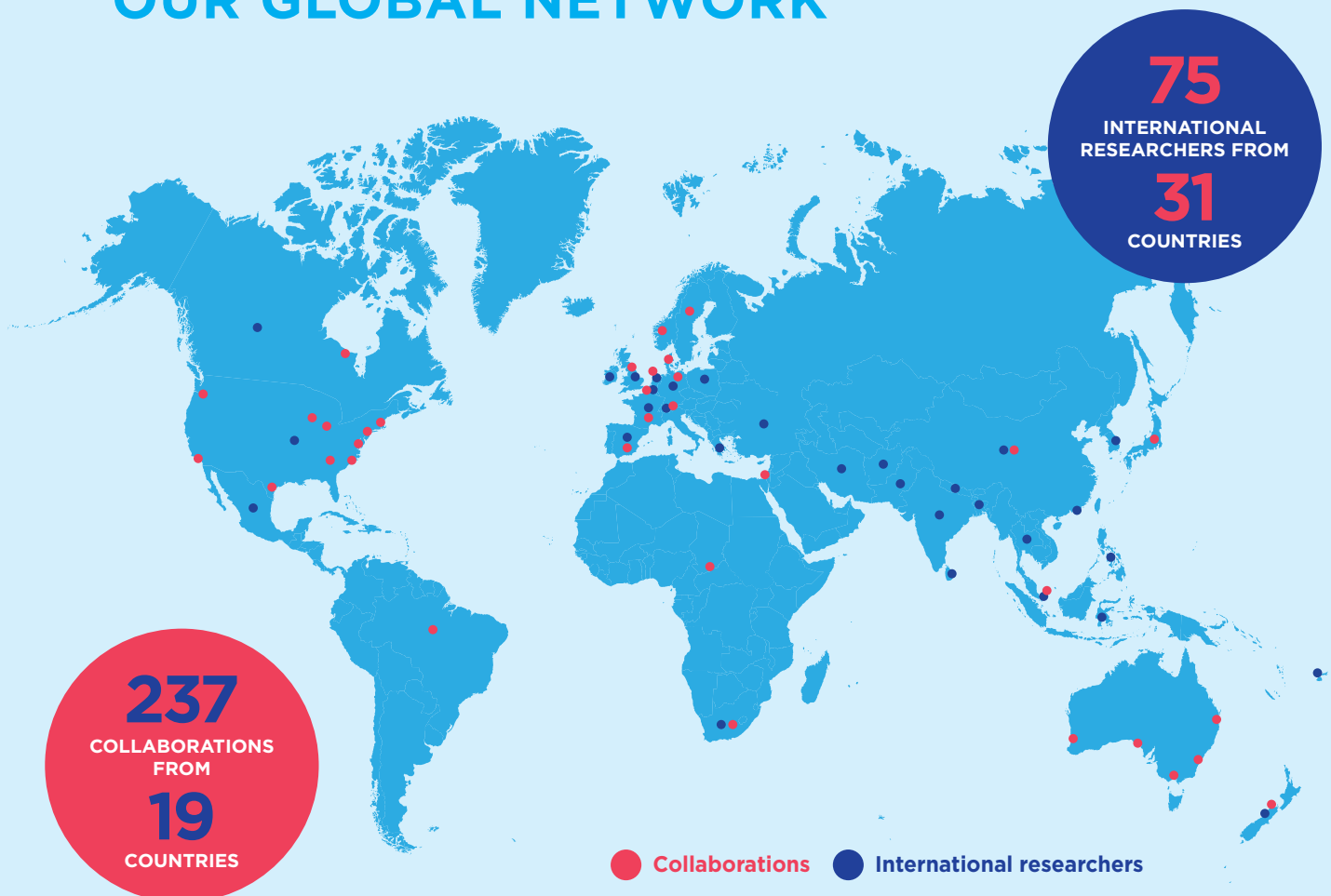
The researchers and clinicians at ONJCRI proactively find opportunities for collaboration and the exchange of

knowledge and expertise to ensure we can strengthen our ability to translate breakthrough cancer research into treatments that save lives. Our collaborations include a wide range of colleagues and span all the way from academic researchers and clinicians to universities and pharmaceutical industries to enhance the depth and impact of our research.

ONJCRI is proud to be part of La Trobe University where it is its School of Cancer Medicine. This is led by our Scientific Director, Prof Matthias Ernst, as the Head of School.

Together we share knowledge, skills and training to turn our research into more effective clinical practice and improved patient outcomes.

OUR GLOBAL NETWORK



Prof Ashley Dunn

Prof Ashley Dunn became Head of the Molecular Biology Program at the Ludwig Institute for Cancer Research (Melbourne) in 1982. Two years later he and colleagues molecularly cloned GM-CSF, a cytokine used to aid recovery of bone marrow in cancer patients following chemotherapy treatment. He served as Associate Director of the Institute until 2004, is currently a Professorial Fellow of the Department of Surgery at the University of Melbourne and serves on several scientific advisory boards.

Prof John Dewar (not pictured)

Prof John Dewar is the Vice-Chancellor and President of La Trobe University. An internationally-known family law specialist and researcher, he has held senior leadership positions at Griffith University and the University of Melbourne as Provost, and has served on a number of higher education and legal bodies, groups and committees, including for the State and Federal Governments. He is a director of Universities Australia and Adjunct Professor in both the Melbourne and La Trobe Law Schools.

The Hon John Brumby AO, Chairman

The former Premier of Victoria John Brumby served for more than seven years as State Treasurer, six years as Leader of the Victorian Opposition and seven as Federal MHR for Bendigo. Since retiring from politics, he has become the Chair of MTAA Super, Citywide Solutions Pty Ltd, BioCurate Pty Ltd and the Melbourne Convention and Exhibition Trust. John is the Chancellor of La Trobe University and an Enterprise Professor at the University of Melbourne. He is active in a range of community and not-for-profit organisations as the Chairman of Trustees of the Joe Welch Bursary Trust, the Como Trust and the Fred Hollows Foundation.

Sue Shilbury

Sue Shilbury has been the CEO of Austin Health since 2017 and currently holds various non-executive positions across the Victorian healthcare landscape. She has previously held numerous Executive positions in the NSW Public Health Sector, including General Manager of North Shore Ryde Health Service and the Central Hospital Network as well as Director of the Division of Critical Care and Surgery at St George Hospital and Director of Clinical Services at the Royal Hospital for Women.

Richard Balderstone

Richard Balderstone has worked in the financial & investment markets for over 35 years. He is a Director of JCP Investment Partners, as well as a Trustee Director of several charitable organisations including the Baker Foundation, Cormack Foundation, Surf Life Saving Foundation and the



BOARD OF DIRECTORS

ONJCRI is an independent medical research institute governed by a Board of Directors including representatives from stakeholders Austin Health and La Trobe University.

SecondBite Future Trust. Richard was previously a Director of ABN AMRO (and BZW) for over 10 years, a Director of the Australian Rail Track Corporation and a Trustee Director of the Commonwealth Public Service Superannuation Schemes (CSS/PSS).

Sally Capp

The Right Honourable, The Lord Mayor of Melbourne Sally Capp has extensive experience in executive leadership roles including at the Property Council of Australia, the Victorian Chamber of Commerce, KPMG and ANZ Bank, and represented the Victorian Government as Agent General across Europe and Israel. She has acted on a number of boards including for private and public companies, not-for-profit organisations and was the first female director of the Collingwood Football Club.

Dr Katherine Woodthorpe AO

Dr Katherine Woodthorpe is currently Chair of the Bushfire and Natural Hazards CRC as well as Chairing the Antarctic Climate and Ecosystems CRC and the HEARING CRC. She is Chair of the National Climate Science Advisory Committee and Chair of Fishburners, Australia's largest technology startup co-working space. She is also Chair of TIP Group Ltd and a Director of Bioplatforms Australia, a member of the NSW Council of the AICD and the Industry Member of the National Health and Medical Research Council, NHMRC.

Linda Bardo Nicholls AO

(not pictured – retired from the board in May 2018)

Linda Bardo Nicholls is a corporate advisor and non-executive director of a number of leading Australian companies and organisations. She is Chairman of Japara Healthcare and

a Director at Ingham's Enterprises and Medibank Private. Linda has a B.A (economics) from Cornell University, an MBA from Harvard Business School and more than 30 years of experience as a senior executive and director in banking, insurance and funds management in Australia, New Zealand and the United States. Linda retired from the ONJCRI board in May 2018.

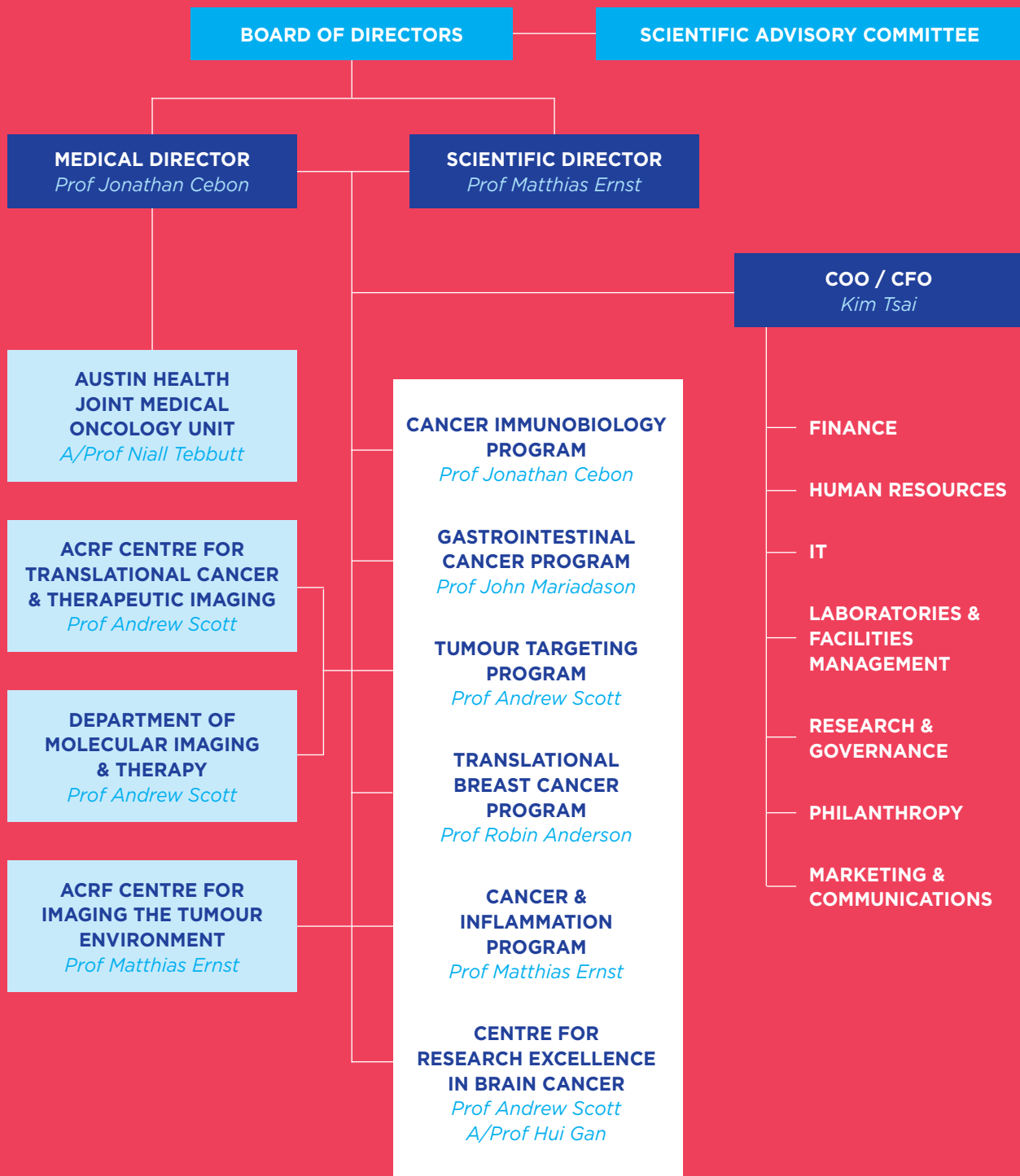
Morry Schwartz AM

(not pictured – retired from the board in May 2018)

Morry Schwartz is a publisher of Australian books, journals and periodicals and an Adjunct Professor of Journalism at RMIT. In a career spanning 40 years, his company Schwartz Media publishes the Saturday Paper, The Monthly, Quarterly Essay and Australian Foreign Affairs. After 15 years of involvement with the Ludwig Institute and ONJCRI, Morry retired from the ONJCRI Board in May 2018.



ORGANISATIONAL CHART



DONORS AND SUPPORTERS

The Olivia Newton-John Cancer Research Institute is grateful to the individuals and organisations who supported our research in 2018.

Individuals and Organisations

Ashton-Nixon Bequest	Freemasons Peninsula Preceptory No 19	Rightside Legal
Associazione Padovani Nel Mondo	Girls Night Out BB Fundraiser	Riverview Ladies Golf Club
ATF Paul Krongold Investment Trust	George Kirkopoulos	Rotary Club of Williamstown Friends R-4
Bev Beacham	KSU Design	Kaye Stacey
Blue Illusion	Simon Lay	Pam Stanley
The Hon John Brumby AO	Lovegelico Collection	Star Search 4 A Cause
Micaela, Mark & Pippa Byers	Macedonian Senior Citizens Group of Doncaster and Templestowe	Stephen Kirkopoulos Brain Cancer Research Fundraiser
Cancer Research Advocate Bikers	Yvonne Moon OAM	Peter Sullivan
Collingwood Football Club Foundation	ONJCRI Ladies Golf Day	Union of Christians from Constantinople
Hector Davis	Pacific Pension & Investment Institute	Anonymous Gifts (6)
Stephen Eastgate	John and Barbara Ralph	
Eltham Weight Loss Club		

Trusts, Foundations, Industry Grants and Government Funding

American Association for Cancer Research	Cure Brain Cancer Foundation	National Breast Cancer Foundation
Austin Medical Research Foundation	Glaxo Smith Kline Biologicals S.A.	National Health and Medical Research Council
Australian Cancer Research Foundation	Harold Mitchell Foundation	The CASS Foundation
Australian Government - Department of Industry, Innovation and Science	Ian Potter Foundation	The Collie Foundation
Bristol-Myers Squibb	Ivan Maurice Jones Endowment (Perpetual Trustees)	The Ian Potter Foundation
BUPA Australia Foundation	John T Reid Charitable Trusts	The Myee Dodrington Medical Foundation (Perpetual Trustees)
Cancer Australia	La Trobe University	Tour de Cure Australia
Cancer Council Victoria	Lodge Amicus - Freemasons Victoria	Victorian Cancer Agency
Carrie's Beanies 4 Brain Cancer	Ludwig Cancer Research	Victorian State Government Operational Infrastructure Support Program
	Lung Foundation Australia	

Our special thanks to family and friends who made generous gifts in memory of:

Bev Byers	Jim McMeckan	Sheryl Sullivan
Peter John Davies	Bob Schway	
Helen Edgar	Ken Stanley	



COO'S REPORT

KIM TSAI
CHIEF OPERATING AND
FINANCIAL OFFICER

When ONJCRI started in 2014 we made a commitment to bring together people who have a real desire to win over cancer. As I reflect on all that has been achieved in 2018, I am incredibly humbled to know that four years on we have a team of dedicated staff, clinicians, students and volunteers who are working each and every day to fulfil our original commitment.

But this team has not come together by accident. We have built an Institute where each and every staff member is valued and encouraged to think outside the square. I truly believe cancer research needs this type of thinking. We have established a diverse, supportive, and family friendly work environment and we are incredibly proud of the culture we can offer our team.

Through careful stewardship from the Executive team and Board of Directors, we have seen steady and strategic growth across the Institute during the past year and we have continued to ensure our business model is the most efficient and effective possible. This guarantees that we can continue to dedicate maximum resources to perform life changing cancer research.

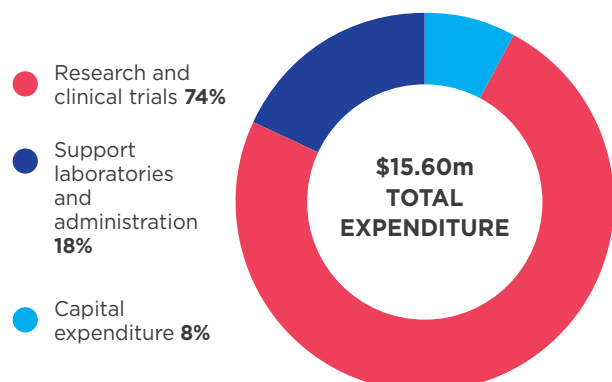
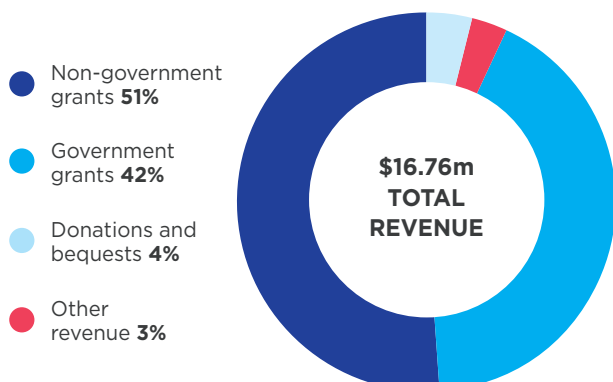
We have also continued to build our strong Institute infrastructure that supports our researchers in all that they do. This includes state of the art laboratory facilities and equipment; an engaged team of research support staff and a dedicated professional services team.

During 2018, we were very fortunate to access a range of innovative funding opportunities that allow us to continuously diversify the types of research we undertake so that we can achieve our goal of finding answers and new treatments for patients with cancer.

I extend my thanks to our great supporters and donors who continue to take this journey with us and our key stakeholders including the Australian Government, Victorian Government, La Trobe University and Austin Health.

Our commitment to cancer research is not just for the short term. While we do and should take time to celebrate our wins during the last year, we also know that the road ahead in cancer research is a long one. But as a team we are committed to seeking even more opportunities for growth and working hard as we know so many people are counting on us.

Kim Tsai



FINANCIAL SNAPSHOT

Statement of Profit or Loss and Other Comprehensive Income For the Year ended 31 December 2018

REVENUE	2018	2017
Grants	15,704,484	13,521,984
Donations and fundraising	595,132	846,547
Investment and other revenue	468,921	330,299
Total Revenue	16,768,537	14,698,830
EXPENDITURE		
Research Laboratories	11,754,294	11,507,171
Clinical Trials	819,781	298,405
Administration Support	3,030,594	2,780,331
Total Expenditure	15,604,669	14,585,907
Total Comprehensive Income	1,163,868	112,923

Statement of Financial Position as at 31 December 2018

ASSETS	2018	2017
Current assets	11,737,762	12,367,563
Non-current assets	13,222,708	6,900,714
Total Assets	24,960,470	19,268,277
LIABILITIES		
Current liabilities	20,343,316	15,888,565
Non-current liabilities	217,063	143,489
Total Liabilities	20,560,379	16,032,054
Net Assets	4,400,091	3,236,223
EQUITY		
Total Equity	4,400,091	3,236,223

The summary financial information provided above have been extracted from the audited general purpose financial statements of Olivia Newton-John Cancer Research Institute (ACN 167 192 752). The extract does not include all the information and notes normally included in a statutory financial report. The audited general purpose financial report can be obtained upon request to the Chief Financial Officer.

The statutory financial report (from which the summary financial information has been extracted) has been prepared in accordance with the requirements of the Corporation Act 2001, Australian Charities and Not-for-profits Commission Act 2012 and Regulations 2013, Australian Accounting Standards and other authoritative pronouncements of the Australian Accounting Standards Board.

SELECTION OF INTERNATIONAL PRESENTATIONS

Prof Robin Anderson

Metastasis Research Laboratory
17th Biennial Congress of the Metastasis Research Society, Princeton, USA
BMP4 is a bonafide breast cancer metastasis suppressor.

International Symposium Korea University
College of medicine BK21 Plus Graduate Program, South Korea
Regulation of breast cancer metastasis by two growth factors, BMP4 and G-CSF.

Dr Ashwini Chand

Cancer Therapeutics Development Group
100th Annual Meeting of the Endocrine Society – ENDO 2018, Chicago, USA
Repurposing of Angiotensin Receptor Blockers as treatments for Breast Cancer.

Repurposing the Selective Estrogen Receptor Modulator Bazedoxifene to suppress colon cancer growth.

A/Prof Alexander Dobrovic

Translational Genomics and Epigenomics Laboratory
3rd Asian Pacific ddPCR Symposium, Shanghai
Moving forward with clinical applications of droplet digital PCR.

Association for Molecular Pathology Annual Meeting, San Antonio, USA
Expanding the use of droplet digital PCR for clinical applications.

27th International Congress, The Transplantation Society, Madrid, Spain
Donor-specific cell-free DNA as an emerging biomarker of organ rejection after liver transplantation.

Prof Matthias Ernst

Cancer and Inflammation Laboratory
ISREC-SCC Symposium, Lausanne, Switzerland
Drugging the myeloid-cell kinase HCK improves anti-tumour immunity.

European Wnt Meeting 2018, Heidelberg, Germany
A physiological in vivo assay to test efficacy of putative Wnt/ β -catenin inhibitors.

A/Prof Hui Gan

Tumour Targeting Laboratory
77th Annual Meeting of the Japanese Cancer Association, Osaka, Japan
Novel Antibody Drug Conjugates for High Grade Gliomas and Other EGFR Expressing Tumours.

A/Prof Peter Janes

Receptor Biology Laboratory
Eph/ephrin congress, Parma, Italy
Inducible knock-down of endogenous EphA3 in mice reveals novel roles for EphA3 in the inflammatory tumour microenvironment.

A/Prof Tom John

Cancer Immunobiology Laboratory
ESMO Asia, Singapore
Efficacy and Safety of Entrectinib in patients with NTRK fusion positive tumours.

Dr Erinna Lee

Cell Death and Survival Laboratory
Asia-Pacific Protein Association Workshop, Niigata, Japan
What's the John Dory?...building understanding and collaboration Down Under.

Dr Sze Ting Lee

Tumour Targeting Laboratory
South African Society of Nuclear Medicine, Johannesburg, Durban and Cape Town, South Africa
Latest Innovations in PET/CT Imaging in Oncology; Radionuclide Therapy in Neuroendocrine Tumour and Prostate Cancer.

Dr Lisa Mielke

Mucosal Immunity and Cancer Laboratory
Singapore Society of Immunology meeting, Singapore
TCF-1 limits the formation of Tc17 cells via repression of the MAF-ROR γ t Axis.

Innate Immunity and Infectious Diseases, Immunology Teaching Course, Institut Pasteur International Network and Institut Pasteur du Cambodge, Phnom Penh, Cambodia
The Microbiome and Immunity.

Mucosal Innate Immunity.

Dr Normand Pouliot

Matrix Microenvironment and Metastasis Laboratory
17th Biennial Congress of the Metastasis Research Society, Princeton, USA
Evaluation of Neratinib efficacy and mechanisms of resistance in a new syngeneic model of spontaneous breast cancer brain metastasis.

Prof Andrew Scott

Tumour Targeting Laboratory
Mind and Brain conference, Hamamatsu, Japan
Innovation in Biology Research and Therapeutics Development.

Memorial Sloan-Kettering Cancer Centre, New York, USA
Molecular Targets for Imaging and Therapy of Cancer.

SNMMI conference, Philadelphia, USA
SNMMI Oncology and Therapy Highlights.

IAEA meeting on Global Nuclear Medicine Strategic Directions, Vienna, Austria
Molecular Imaging and Therapy: Asia-Oceania.

Arab Society of Nuclear Medicine conference, Amman, Jordan
Theranostics for Immune Based Therapies in Cancer; Global Trends in Nuclear Medicine.

International Symposium on Radiopharmaceutical Therapy, Helsinki, Finland
PSMA Targeting and Therapy Trials in Australia; and Global Trends in Nuclear Medicine.

IAEA Conference on Theranostics, Singapore
PET in Dementia Diagnosis and Management.

Dr Belinda Yeo

Metastasis Research Laboratory
SABCS, San Antonio, USA
The importance of the metastatic biopsy: Clinical and translational relevance in a real world series of patients with metastatic breast cancer.

MEA Breast Cancer Leaders Summit, Cairo, Egypt
1st-line Therapy for HR+ve, HER2-ve Advanced Breast Cancer.

Experience from clinical practice on the use of CDK4/6 inhibitors in Advanced Breast Cancer.

OUR PUBLICATIONS

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ONJCRI SEMINARS*

*does not include speakers from ONJCRI or Austin Health

Dr Gabriela Brumatti

Walter and Eliza Hall Institute of Medical Research
RIPping leukaemia apart - Exploring the regulation of cell death pathways in the development and treatment of leukaemias.

A/Prof Daniel Buchanan

University of Melbourne Centre for Cancer Research
Genomic Approaches that Improve the Identification and Clinical Actionability of Hereditary Colorectal Cancer and Polyposis syndromes.

A/Prof Irina Caminichi

Monash University
Hierarchical immunogenicity of tumour derived neo-antigens.

Dr Andrew Cox

Peter MacCallum Cancer Centre
Metabolic reprogramming in zebrafish models of cancer.

Dr Andrew Deans

St Vincent's Institute
Biochemical reconstitution of DNA repair pathways that predispose to cancer.

Prof Mark Febbraio

Garvan Institute of Medical Research
Novel insights and therapies for the treatment of obesity driven liver cancer.

A/Prof Thomas Gebhardt

The Peter Doherty Institute for Infection and Immunity
Tissue-resident memory T cells drive melanoma-immune equilibrium in skin.

Prof Jenny Graves

La Trobe University
Animal sex determination by genes, chromosomes and the environment.

Dr Philip Gregory

Centre for Cancer Biology, SA Pathology and UniSA
MicroRNAs - master regulators of gene expression and splicing during cancer progression.

A/Prof Natasha Harvey

Centre for Cancer Biology, SA Pathology and UniSA
Lymphatic vessels: origin, development and how things go wrong in human disease.

A/Prof Nick Huntington

The Walter and Eliza Hall Institute of Medical Research
Targeting NK cells in cancer immunotherapy.

A/Prof Louis Irving

The Royal Melbourne Hospital
Recent insights into the biology and management of malignant pleural effusions.

Dr Misty Jenkins

The Walter and Eliza Hall Institute of Medical Research
Killer T cell immunotherapy and brain cancer.

Dr Lev Kats

Peter MacCallum Cancer Centre
Understanding and Targeting Aberrant Epigenetic Regulators in Acute Myeloid Leukaemia.

Dr Conor Kearney

Peter MacCallum Cancer Centre
The role of Tumor Necrosis Factor (TNF) in anti-tumor immunity.

A/Prof Paul Macklin

Indiana University, Bloomington IN, USA
An open source virtual laboratory for high-throughput 3-D studies of cancer.

Dr Andreas Möller

QIMR Berghofer Medical Research Institute
Extracellular vesicles in cancer progression and metastasis.

Prof John Moses

La Trobe Institute for Molecular Science
Click Chemistry in Drug Discovery and Target Identification — What Can It Do For You?

Prof Stuart Pitson

Centre for Cancer Biology, SA Pathology and UniSA
Targeting sphingolipid metabolism in cancer.

Dr Gretchen Pootinga

Peter MacCallum Cancer Centre
Targeting ribosomal DNA transcription and nucleolar chromatin in cancer.

Dr Jodi Sanus

Centre for Clinical Research, University of Queensland
Biomarkers of prognosis, treatment response and distant relapse in breast cancer.

Prof Mark Shackleton

Alfred Health
Studies in melanoma heterogeneity.

Dr Sarah Shigdar

Deakin University
Aptamers as novel theranostic agents.

Dr Clare Slaney

Peter MacCallum Cancer Centre
Using Chimeric Antigen Receptor (CAR) T cell immunotherapy against solid cancers.

A/Prof Erica Sloan

Monash Institute of Pharmaceutical Sciences
Neural signalling regulates tumour cell mechanotype: Defining mechanisms to optimally target new anti-metastasis drugs.

Dr Kortnye Smith

Peter MacCallum Cancer Centre
The use of genomic sequencing in the clinical management of patients with solid tumours.

Prof Tony Tiganis

Monash Biomedicine Discovery Institute
Obesity, NAFLD and liver cancer.

Dr Ajithkumar Vasanthakumar

University of Melbourne
Harnessing adipose tissue adaptation mechanisms of regulatory T cells to treat metabolic diseases.

Prof Raymund Wellinger

Université de Sherbrooke, Québec, Canada
The telomere - telomerase connection: all is well that ends well.

A/Prof Adrian Wiegman

QIMR Berghofer Medical Research Institute
Novel mechanisms of chemoresistance mediated by Prion protein: guiding clinical choices.

OUR VISION FOR THE FUTURE



The one overarching goal that drives all activities at the Olivia Newton-John Cancer Research Institute is our ambition to not only understand how cancer works, but also to convert it into a manageable disease.

To achieve this, our researchers and clinicians continuously work together on discoveries and research breakthroughs to ultimately deliver better health outcomes for today's and tomorrow's cancer patients.

Our work is only possible because of the team of staff, clinicians, partners, supporters and advocates who share our belief that together – we can win over cancer. Thank you for being a part of this journey with us.

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