
ANNUAL REPORT
2019

Olivia
Newton-John
Cancer Research Institute

CONTENTS

# FOCUSED ON OUTSMARTING CANCER

## ONJCRI ANNUAL REPORT 2019



# MESSAGE FROM OLIVIA

## DAME OLIVIA NEWTON-JOHN DBE, AC
## OUR FOUNDING CHAMPION

In a world of uncertainty, hope has never been more important. The vital research being done by the dedicated team at the Olivia Newton-John Cancer Research Institute (ONJCRI) provides real hope to a global population – that we will one day live in a world beyond cancer.

Indeed, to find kinder and more effective treatments for cancer, we must keep asking questions and conducting research of the highest standard, to personalise care for those living with and beyond this disease.

I continue to be immensely proud of the work being done by the team at ONJCRI. I am inspired by their determination to never stop looking for answers, and it comforts me to know that these great minds are focused on this important issue that affects us all.

I believe in a holistic approach to cancer prevention, treatment and cure. Medical research has played an important role in my cancer experience, and I continue to watch with great anticipation as ONJCRI generates discoveries for global benefit.

This research is only possible thanks to ONJCRI's team of leaders, researchers, clinicians, professional services staff, students, volunteers, supporters and partners. I offer my heartfelt gratitude to all of them.

I would like to specifically thank the outgoing ONJCRI Board Chair, The Hon John Brumby AO, for his amazing leadership; ONJCRI was created and now thrives as a result of his dedication to research. I also offer thanks to my dear friend Prof Jonathan Cebon, the Institute's outgoing Medical Director, who helped bring my vision of a comprehensive cancer centre to reality.

I sincerely welcome the new Board Chair, The Hon Jenny Macklin, and I look forward to a productive partnership, to write the next great chapter of ONJCRI's extraordinary story.

I hope you find this report as inspiring as I do.

Thank you for your ongoing support of ONJCRI.

Love and Light,

Olivia xx

# OUTGOING CHAIR'S REPORT

## THE HON JOHN BRUMBY AO

One of the key priorities for the ONJCRI Board of Directors and leadership team continues to be a shared commitment to strengthening our translational cancer research efforts. This focus and determination is truly changing the way research is conducted across the Institute and it means that more discoveries will directly influence patient treatment and care.

In November, I stepped down from my role as Chair of the ONJCRI Board of Directors, a role I have been immensely proud to hold since the Institute launched in 2014. In this time, I have witnessed strong growth in leadership, research capability and research outcomes that have made a direct impact on the lives of patients.

I would sincerely like to thank my fellow Board members, the Executive, Institute staff, clinicians, students, volunteers, supporters and partners for their continuing support of the Institute. I thank Dame Olivia Newton-John DBE, AC for entrusting me to lead this dedicated team who wholeheartedly share her commitment to doing all that we can to win over cancer. I also wish the incoming Chair, The Hon Jenny Macklin, the Board, and the wider Institute team every success.

As I reflect on the Institute's many achievements during my tenure, I am struck by this team's tenacious approach to cancer research. Their unwavering focus on finding new cancer treatments ensures that all projects are firmly backed by a desire to translate research for better patient outcomes.

One of the projects that I have had the opportunity to see translate from concept development to clinical trial focuses on neutralising cachexia, a process that affects up to 80 per cent of people with advanced stages of cancer and involves weight loss and muscle wastage. Cachexia can limit a patient's response to treatment and the work of Prof Andrew Scott AM, his research team, and collaborators at La Trobe University and Austin Health paved the way for a clinical trial that commenced in mid-2019 with 18 pancreatic, lung and colorectal cancer patients. You can read more about this project on page 35.

I look forward to continuing my involvement with the Institute in my role as Chancellor of La Trobe University and our shared La Trobe University School of Cancer Medicine.

# INCOMING CHAIR'S REPORT

## THE HON JENNY MACKLIN

In 2019, I had the honour of joining the ONJCRI as Chair to lead the team who share the common goal of finding a cure for cancer. The belief and passion of our Board and staff to reach this goal is fuelled by the knowledge that research holds the answers to the treatment and recovery of patients living with cancer. This focus also continues to be driven by the ongoing work of our Founding Champion Dame Olivia Newton-John DBE, AC whose dedication to winning over cancer remains a great source of inspiration.

I would like to acknowledge the enormous contribution that The Hon John Brumby AO, the inaugural Chair of the ONJCRI has made over the last five years. Since ONJCRI's inception in 2014, John has been instrumental in guiding the direction of the Institute in its mission to conduct world-class cancer research and clinical translation underpinned by scientific excellence.

In December, our Medical Director, Prof Jonathan Cebon retired from his dual appointment at the Institute and the Austin Health Division of Cancer Services and Neurosciences. In these roles, Jonathan has provided exceptional patient care, led numerous highly successful research projects and clinical trials and cemented his position as a leader in shaping cancer care nationally. I recognise the great personal commitment Jonathan has demonstrated toward the establishment and ongoing success of the Olivia Newton-John Cancer Wellness and Research Centre.

I extend my congratulations to Prof Matthias Ernst who will take on the new leadership role of Institute Director from January 2020. I look forward to working with him to further strengthen our position as one of Australia's leading cancer research institutes. I also sincerely thank my fellow Board members who generously share their guidance and expertise.

Our ability to undertake such significant basic and translational research continues to be underpinned by the important relationships we hold with our key collaborators including Austin Health and La Trobe University. These important partnerships ensure that our research efforts remain innovative, relevant and patient focused. I also gratefully acknowledge the ongoing support of the Victorian Government.

In my former role as the Federal Member for Jagajaga, the ONJCRI is located around the corner from the electorate office. I have proudly watched the Institute grow in capability and size over the years. I now look forward to ensuring we continue to grow and tackle research questions that have life changing impact.

Some of the Institute's research achievements in 2019 include the repurposing of a drug used for osteoporosis in inhibiting the growth of gastrointestinal tumours and using barcodes to identify, track and analyse the genetic properties of aggressive breast cancer cells.

I trust you will enjoy reading about these achievements and more of our research in this report.

# DIRECTORS' REPORT

## PROF MATTHIAS ERNST
SCIENTIFIC DIRECTOR

The past year has been a period of renewed focus across the Institute to outsmart cancer. We will achieve this goal by concentrating our efforts on new research, new opportunities, new thinking and most importantly by renewed dedication and commitment of our staff.
Much of our success to date has been underpinned by the visionary leadership of our inaugural Chair of the Board, The Hon John Brumby AO and the Institute's Medical Director, Prof Jonathan Cebon. Both played critical roles in ensuring that within the five years since its inception, the Olivia Newton-John Cancer Research Institute (ONJCRI) has become a readily recognised name among national and international leaders in cancer research. Both John and Jonathan stepped down from their respective roles at the end of 2019 entrusting the leadership to a team ready to take the Institute forward into a new decade under the Board's new Chair, the Hon Jenny Macklin.

I would like to express my sincere gratitude to John and Jonathan. Their vision and tireless advocacy have been critical from the very outset in establishing the Olivia Newton-John Cancer Centre, in a purposefully-built building that combines world-class discovery, translational and clinical research as an integrated offering of a comprehensive cancer centre. I am delighted that John, in his new role as Chancellor of La Trobe University, will help to forge strategic synergies between the University and ONJCRI as its School of Cancer Medicine. Together with all my colleagues at the Institute, we are indebted to Jonathan for sharpening our focus on translational research and directing our research towards the clinical areas with the highest unmet needs. In his position as the Institute's Medical Director and the Medical Director of Austin Health's Division of Cancer Services and Neurosciences, Jonathan was the pivotal driver and enabler of the seamless integration of clinical oncologists into our laboratory-based activities. This partnership model has since been adopted by many of our colleagues across the country as the most effective way for bundling clinical expertise with research excellence to collectively achieve the greatest benefit for patients now and in the future.

There are many different ways of quantifying success by the ONJCRI team: meaningful engagement with our partners and stakeholders; collaborations with our clinicians and medical oncologists across Melbourne and beyond; the magnitude of our discoveries and their likelihood of being translated into the clinic; the recognition of our work by our peers and the granting agencies that award us with highly competitive public funding; the nurturing and fostering of new talent and emerging leaders. But most of all, it is the hope afforded by novel treatments that we can offer to cancer patients and their families which is the real measure of our success. The 2019 Annual Report provides you with a plethora of such stories that I would like to encourage you to explore in more detail with us at ONJCRI.

## PROF JONATHAN CEBON
MEDICAL DIRECTOR

Progress in cancer research requires brilliant discoveries and the ability to translate their potential into clinical practice.

Thanks to our successful relationship with Austin Health, this has been possible and our clinician scientists form a bridge between ONJCRI and the hospital.

Clinical translation is one of the Institute's core strengths and is exemplified in some of our clinical highlights of the year including: ongoing work targeting brain tumours with monoclonal antibodies from Prof Andrew Scott AM, Prof Hui Gan and colleagues; a pilot clinical trial for patients with rare upper gastrointestinal neuroendocrine and gynaecological cancers headed by Dr Oliver Klein, run collaboratively with Bristol Myers Squibb and Rare Cancers Australia; and work being developed in breast cancer by Drs Delphine Merino and Belinda Yeo thanks to the Love Your Sister partnership.

2019 was my last year as Medical Director of ONJCRI and Medical Director of Cancer Services at Austin Health. It has been a great privilege to work with so many wonderful people in both organisations and I look forward to an ongoing association with both the Institute and Austin Health in a part-time capacity.





# ABOUT THE OLIVIA NEWTON-JOHN CANCER RESEARCH INSTITUTE

We want to see a future where we better understand cancer so that we can make it a manageable disease.

To achieve this, our teams of laboratory-based researchers and patient-focused clinicians work together to discover and translate research breakthroughs to deliver better health outcomes for patients.

Our work is only possible because our teams, our research partners, our volunteers, and our supporters share our common belief that **together we will outsmart cancer.**

Our Institute is a leader in the development of experimental and breakthrough cancer treatments. Our research is primarily focused on investigating and developing treatments for cancers of the breast, bowel and gastrointestinal tract, lung, skin, prostate, liver and brain. We also undertake research in understudied rare cancers and proactively look for opportunities to extend our efforts to other cancers.

**Our vision** is to help people live better with cancer and defeat it.

**Our mission** is to discover and develop breakthrough cancer therapies to provide the best health outcomes for patients.

**Our values** drive everything we do. These values are:

- **brilliance in science**
- **respect**
- **optimism**
- **together**
- **making a difference**

We do this by discovering and developing new cancer therapies to provide real and life changing benefits for patients.

# TRANSLATING OUR RESEARCH

Our researchers are based just metres from where people are receiving treatment, which means that our scientific discoveries are rapidly translated into breakthrough clinical therapies.

In 2019, our researchers and clinician scientists led 157 clinical trials, giving patients access to potential new treatments including immunotherapies and personalised medicine.

We use observations from the clinic to create a continual cycle of learning and improvement between scientific research and patient care.

## JAN

**Prof Jonathan Cebon leads a pioneering clinical trial,** treating rare cancers using immunotherapy drugs.

**Olivia Newton-John OBE, receives a Companion of the Order (AC)** Australia Day honour for her eminent service to community health and as a songwriter and performer.

**104**
**STAFF**

## FEB

**Clinician Scientist, Dr Belinda Yeo is appointed** joint Victorian Comprehensive Cancer Centre (VCCC) Research and Education Lead – Breast Cancer.

**Dr Delphine Merino co-authors a paper publishes in *Nature Communications*** about using barcodes to identify, track and analyse the genetic properties of aggressive breast cancer cells that spread to other parts of the body or resist drug treatment.

Read more on page 32

## MAR

**ONJCRI partners with Love Your Sister** to commence a three-year study to focus on the future of personalised medicine.

Read more on page 30

**ONJCRI Board Chair The Hon John Brumby AO is installed into the role** of Chancellor of La Trobe University.

**157**
**CLINICAL TRIALS LED BY INSTITUTE INVESTIGATORS**

**258**
**RESEARCH COLLABORATIONS**

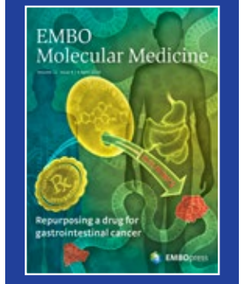
## APR

**53%**
**FEMALE STAFF**

## MAY

**Dr Ashwini Chand publishes a paper** through the *European Molecular Biology Organisation (EMBO)* about repurposing existing drugs to treat gastric cancers.

Read more on page 16




## JUN

**Dr Moritz Eissmann publishes a paper** in *Nature Communications* journal about a potential target for new cancer drugs for gastric cancer.

Read more in our feature story on page 15

**38**
**STUDENTS**





## JUL

## AUG

**ONJCRI celebrates Equality Day** knowing that in the last three years the Institute has more than doubled female representation in leadership roles.

**Olivia Newton-John OBE, AC and the ONJCRI Executive team head to Parliament House in Canberra** to discuss our research efforts and potential for new cancer treatments.

**$37.7**
**MILLION**
**SECURED EXTERNAL FUNDING**

**19%**
**PHD STUDENTS WITH MEDICAL TRAINING**

**121**
**ONJCRI SCIENTIFIC PAPERS PUBLISHED**

## SEP

## OCT

**More than five thousand people bring love, compassion and hope to the 2019 Wellness Walk and Research Run** at Alexandra Gardens, raising more than $1.1 million for the Olivia Newton-John Cancer Wellness and Research Centre.

**The ACRF Centre for Imaging the Tumour Environment** launches at ONJCRI, allowing researchers to expose the secret life of cancer.

Read more on page 42

**Prof Andrew Scott AM, and Prof Matthias Ernst and are awarded more than $4.5 million in funding by the NHMRC.**

**After five years as the inaugural Chair of the ONJCRI, The Hon John Brumby AO retires;** and the Hon Jenny Macklin is appointed as Chair.

## NOV

## DEC

**Prof John Mariadason publishes a paper** in *Nature Communications* about a research project focused on colon cancer but also resulting in a discovery that could lead to a new treatment for obesity.

Read more on page 25

**Olivia Newton-John AC receives a Damehood on the Queen's New Year Honours list** for her services to charity, cancer research and entertainment.

**Seven new Advocates are welcomed into our volunteer team** to work with our researchers to help ensure their projects continue to focus on the needs of the community and those impacted by cancer.

Read more about the role of our advocates on page 22

**42%**
**LEADERSHIP POSITIONS HELD BY WOMEN**

# OUR RESEARCH

Our researchers are committed to making scientific discoveries which will benefit patients living with cancer. Our research teams are investigating and developing novel treatments for a broad spectrum of cancer types.

ONJCRI is the research and discovery 'engine' of a comprehensive cancer centre where our laboratories are co-located with patient wards. This means we never lose sight of the impact of our research. Through our translational approach we can accelerate learning between the laboratory bench and the patients undergoing treatment at the Olivia Newton-John Cancer Centre.

## PROGRAM STAFF

### CANCER AND INFLAMMATION PROGRAM

**Cancer and Inflammation Laboratory**
Laboratory Head:
Prof Matthias Ernst

***Researchers:*** Mariah Alorro, David Baloyan, Christine Dijkstra, Moritz Eissmann, Matthias Ernst, Gangadhara Gangadhara, Anne Huber, Jennifer Huynh, Saumya Jacobs, Kim Le, Riley Morrow, Megan O'Brien, Lokman Pang, Ashleigh Poh, Jasmin Traichel

**Tumour Microenvironment and Cancer Signaling Group**
Group Head:
Dr Michael Buchert

***Researchers:*** Shoukat Afshar-Sterle, Michael Buchert, Annalisa Carli, Lena Elias, Daniela Gebert, Ryan O'Keefe, Janson Tse

**Cancer Therapeutics Development Group**
Group Head:
Dr Ashwini Chand

***Researchers:*** Ashwini Chand, Rhynelle Dmello, Belinda Duscio, Pathum Thilakasiri

### CANCER IMMUNOBIOLOGY PROGRAM

**Cancer Immunobiology Laboratory**
Laboratory Head:
Prof Jonathan Cebon

***Researchers:*** Miles Andrews, Surein Arulananda, Jonathan Cebon, Cyril Deceneux, Tom John, Mina Khalaji, Ensieh Poursani, Dani Tutuka

**Tumour Immunology Laboratory**
Laboratory Head:
Dr Andreas Behren

***Researchers:*** Joshua Adalin, Andreas Behren, Jessica Duarte, Simone Ostrouska, Luke Quigley, Elnaz Tavancheh

**Translational Genomics and Epigenomics Laboratory**
Laboratory Head:
A/Prof Alexander Dobrovic

***Researchers:*** Zi Qing Chai, Daniel Cox, Hongdo Do, Alexander Dobrovic, Basant Ebaid, Mohammadreza Eftakarijan, Tess McClure, Ashan Musafer, Tom Witkowski, Boris Wong, Lujia Yang

**Mucosal Immunity and Cancer Laboratory**
Laboratory Head:
Dr Lisa Mielke

***Researchers:*** Anita Kumari, Lisa Mielke, Dinesh Raghu, Kevin Schmid, Kelly Tran

### GASTRO-INTESTINAL CANCER PROGRAM

**Oncogenic Transcription Laboratory**
Laboratory:
Prof John Mariadason

***Researchers:*** Zakia Alam, Fiona Chionh, George Iatropoulos, Laura Jenkins, Stan Kaczmarczyk, Ian Luk, John Mariadason, Jennifer Mooi, Irvin Ng, Rebecca Nightingale, Camilla Reehorst, Kael Schoffer, Natalia Vukelic, Andrew Weickhardt, David Williams

**Cell Death and Survival Laboratory**
Laboratory Head:
A/Prof Doug Fairlie

***Researchers:*** Marco Evangelista, Doug Fairlie, Tiffany Harris, Jane Kishore, Erinna Lee, Nikita Steinohrt, Sharon Tran

### TRANSLATIONAL BREAST CANCER PROGRAM

**Metastasis Research Laboratory**
Laboratory Head:
Prof Robin Anderson

***Researchers:*** Robin Anderson, Nilofar Ansari, Stefan Bader, Caroline Bell, Allan Burrows, Leo Chi, Bedrich Eckhardt, Haiyan Liao, Kellie Mouchemore, Rick Redvers, Charlotte Roelofs, Suraya Roslan, Victoria Simovich, Belinda Yeo

**Matrix Microenvironment and Metastasis Laboratory**
Laboratory Head:
Dr Normand Pouliot

***Researchers:*** Delphine Denoyer, Lamia Farook, Miriam Fuentes, Melissa John, Harleen Kaur Singh, Aadya Nagpal, Ellen O'Brien, Normand Pouliot

**Tumour Progression and Heterogeneity Laboratory**
Laboratory Head:
Dr Delphine Merino

***Researchers:*** Simone Alexander, Jean Berthelet, Farrah El-Saafin, Sabrina Lewis, Michal Merdas, Delphine Merino, Antonin Serrano, Jacqueline Yap

**Cancer Single Cell Genomics Laboratory**
Laboratory Head:
Dr Bhupinder Pal

***Researchers:*** Paula Fuge-Larsen, Shalini Guleria, Maria Pia Iaci, Bhupiner Pal, Jordan Wilcox

### TUMOUR TARGETING PROGRAM

**Tumour Targeting Laboratory**
Laboratory Head:
Prof Andrew Scott AM

***Researchers:*** Laura Allan, Ingrid Burvenich, Diana Cao, Puey Ling Chia, Adriana Constantinou, Hui Gan, Benjamin Gloria, Nancy Guo, Umbreen Hafeez, Eliza Hawkes, Nhi Huynh, Cameron Johnstone, Zhanqi Liu, Alex McDonald, Siddharth Menon, Carmel Murone, Sagun Parakh, Adam Parslow, Angela Rigopoulos, Andrew Scott, Fiona Scott, Christian Wichmann

**Receptor Biology Laboratory**
Laboratory Head:
A/Prof Peter Janes

***Researchers:*** Stacey Allen, Frederick Durrant, Peter Janes, Mary Vail, Hengkang Yan

### CENTRE FOR RESEARCH EXCELLENCE IN BRAIN CANCER

Co-Directors:
Prof Andrew Scott AM and Prof Hui Gan

***Researchers:*** Hui Gan, Alex McDonald, Sagun Parakh, Andrew Scott, Fiona Scott, Kerryn Westcott

### CLINICIAN SCIENTISTS

Chun Fong
Hui Gan
Eliza Hawkes
Tom John
Andrew Weickhardt
David Williams
Belinda Yeo

### FACILITIES AND EQUIPMENT

Our research and discovery efforts are underpinned, enhanced and advanced by outstanding platform technologies, facilities, technical expertise and support services that operate within 5,500 square-metres of 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)
- Flow Cytometry Core Facility

# CANCER AND INFLAMMATION PROGRAM

PROGRAM HEAD:
**PROF MATTHIAS ERNST**

### Program goals

The research conducted in the Cancer and Inflammation Program focuses on a better molecular understanding of the interactions between cancer cells and their surrounding normal counterparts. Some of these interactions will provide critical 'achilles heels' to stop the cancers from growing, metastasising to distant organs and make cancer cells 'invisible' to the immune system. Over the years, the work from the Program has identified a few of the molecules and types of normal cells that are coerced and corrupted by the cancer cells to provide a cellular environment that enables unrestricted growth of the cancer.

### Achievements in 2019

In 2019, we built on our previous work on the transcription factor STAT3, which is not only expressed in cancer cells to fuel proliferation, but also in many normal cells of the tumour microenvironment to enable the growth of nutrient-supplying blood vessels, as well as to suppress an effective anti-tumour immune response.

The latter involves an immune cell type called myeloid cells and our discovery that the kinase molecule HCK acts as a molecular determinant to enforce an immune suppressed tumour microenvironment. The conditioning of the latter occurs at least in part by production of the soluble factor interleukin-11, which in turn stimulates STAT3.

Because many cancer cells prefer to grow in a framework of extracellular matrix, our Program is also investigating how specific cancers molecules, such as the kinase Dclk-1, lead to extracellular matrix production. We are therefore keen to discover the mechanisms that underpin cancer cell-specific dysregulation of Dclk-1 activity.

### 3 publication highlights

*Eissmann, M. F., C. Dijkstra, A. Jarnicki, T. Phesse, J. Brunnberg, A. R. Poh, N. Etemadi, E. Tsantikos, S. Thiem, N. D. Huntington, M. L. Hibbs, A. Boussioutas, M. A. Grimbaldeston, M. Buchert, R. J. J. O'Donoghue, F. Masson and M. Ernst. "IL-33-mediated mast cell activation promotes gastric cancer through macrophage mobilization." Nat Commun 10(1): 2735. (2019)*

*Thilakasiri, P., J. Huynh, A. R. Poh, C. W. Tan, T. L. Nero, K. Tran, A. C. Parslow, S. Afshar-Sterle, D. Baloyan, N. J. Hannan, M. Buchert, A. M. Scott, M. D. Griffin, F. Hollande, M. W. Parker, T. L. Putoczki, M. Ernst and A. L. Chand. "Repurposing the selective estrogen receptor modulator bazedoxifene to suppress gastrointestinal cancer growth." EMBO Mol Med 11(4). (2019)*

*Huynh, J., A. Chand, D. Gough and M. Ernst. "Therapeutically exploiting STAT3 activity in cancer - using tissue repair as a road map." Nat Rev Cancer 19(2): 82-96. (2019)*





## CANCER AND INFLAMMATION LABORATORY

### Laboratory Head: Prof Matthias Ernst

The goal of the Cancer and Inflammation Laboratory is to discover novel and druggable targets that enable therapeutic inhibition of mechanisms by which cancer cells corrupt their cellular environment and escape discovery by the immune system. Our efforts therefore aim to molecularly characterise such targets to rationally design novel therapeutic lead compounds and to build better preclinical models in which these leads can be tested.

#### 2019 highlights

One of the main focuses of our Laboratory was to identify two myeloid cell populations called mast cells and macrophages, which collectively promote the growth of gastric cancers through the soluble molecular mediator interleukin-33. Critical to this work was the development of a novel preclinical model that mimics the salient features of inflammation-associated gastric cancer in humans. In turn, this allowed us to use genetic and pharmacologic approaches to functionally validate our correlative observations that we had made in the human disease.

Simultaneously, we continued to focus our efforts on the kinase HCK and the transcription factor STAT3 alongside its important regulator interleukin-11 as major determinants of the activity of macrophages and myeloid-derived suppressor cells. Both these normal and non-mutated myeloid cell types are abundant within the tumour microenvironment and play a critical role in suppressing the capacity of immune cells to kill cancer cells.

## TUMOUR MICROENVIRONMENT AND CANCER SIGNALING GROUP

### Group Head: Dr Michael Buchert

The overall research goals of the Tumour Microenvironment and Cancer Signaling Group are to (i) identify the role of doublecortin-like kinase 1 (Dclk-1) in gastric cancer; (ii) identify the role of the tuft cell/type 2 innate lymphoid cells (ILC2) circuit in promoting gastric cancer; (iii) better understand tuft cell biology.

#### 2019 highlights

In 2019, we have continued to further characterise the mechanisms by which Dclk-1 promotes gastric cancer. We could establish that this happens through cell intrinsic and cell extrinsic mechanisms, and we have now started a whole proteome and phosphoproteome approach in order to pinpoint the Dclk-1 substrates and affected pathways.

We have established the functional importance of the tuft cell/ILC2 cell circuit not only during gastric cancer but also during the early stages of gastritis and metaplasia, potentially leading the way to enable early diagnosis of this disease.

We have initiated single cell transcriptomics of gastric epithelial cells and sorted tuft cell populations from various tissues in our effort to uncover new biological functions for tuft cells.

## CANCER THERAPEUTICS DEVELOPMENT GROUP

### Group Head: Dr Ashwini Chand

Research projects in the Cancer Therapeutics Development Group are focused on discovering new treatments for breast, gastric and colon cancers. In addition to novel drug discovery, we investigate the possibility of repurposing drugs, currently used as therapies for non-cancer related conditions, for use as cancer treatments.

#### 2019 highlights

In 2019, we discovered that drugs that are used to treat osteoporosis can reduce the growth of gastric and colon cancer. Our ongoing work is involved in identifying whether directed suppression of certain inflammation signals can prevent the spread of triple negative breast cancer to other parts of the body. By understanding how these pro-inflammatory cytokines facilitate cancer spread, we will be able to design new agents that have anti-cancer effects.

Highlights for 2019 include the publication of our findings in *EMBO Molecular Medicine*, with our research featured on the cover of the April 2019 issue. Our research was also featured by Channel 9 News and we were invited to submit two review articles in notable journals discussing drug repurposing as cancer treatments. We have developed new collaborations with groups at other institutes to increase the impact of our collective research efforts.



# A MASTER OF LEARNING AND DISCOVERY

Teaching's loss is medicine's gain as **Dr Moritz Eissmann** tackles some of cancer's most complex puzzles.

Growing up in Berlin, Moritz wanted to teach but his father, who was a teacher and knew about the commitment and challenges involved, warned him against it.

Instead, Moritz followed his passion for science and discovery, studying medical biotechnology in Berlin, bioengineering in South Korea and pharmacy in Frankfurt. "The idea of finding something that nobody else in the world had discovered was intriguing," he said. "Doing something that actually helps people got me going and keeps me interested."

"THE IDEA OF FINDING SOMETHING THAT NOBODY ELSE IN THE WORLD HAD DISCOVERED WAS INTRIGUING"

Fast forward to 2019, and now as a Postdoctoral Research Fellow in the Cancer and Inflammation Laboratory at ONJCRI, Moritz is helping to uncover some of cancer's deepest mysteries by investigating the complex relationships between cells. His focus recently turned to the mast cell, an immune cell that had largely escaped attention.

Discovered 100 years ago, mast cells play an important role in inflammation, both positive and negative. Mast cells can promote wound and infection healing, but have also been linked to allergies, autoimmune diseases and possibly tumours. Researchers who noticed large numbers of mast cells in gastric cancer patients with poor survival outcomes believed these cells may have stimulated the tumour growth.

This observation was not lost on Moritz, who had noticed the same association in preclinical models. The gastric tumour burden was lower in models lacking mast cells than in those which retained these cells. Curious about why the body's immune cells would promote tumour growth, Moritz set out to look for the culprit. He discovered it in the form of a signalling molecule called interleukin-33 or IL-33, which acts as the messenger between different cell types. Moritz's work showed that IL-33 provides an important trigger for mast cells to attract a second immune cell type called macrophages, which then promote the growth of gastric tumours.

Moritz's discovery provides one molecular mechanism to explain whether a mast cell attacks or stimulates a tumour depending upon the stimulus it receives, making IL-33 signalling a potential target for new cancer drugs.

Moritz's research was published in 2019 in the *Nature Communications* journal, and received an additional boost through a grant from Cancer Council Victoria to further define potential benefits of IL-33 singalling inhibitors for the treatment of cancer. This area has become his main research interest. "Year by year it became more important and took more of my time and focus," he said. "There's definitely potential to focus our attention on mast cells and IL-33 signalling as targets."

As for teaching, it is still a big part of Moritz's life. His wife, Yun Hee, whom he met while studying in South Korea, is a teacher. Their son, Max, 13, was born in Berlin and their daughter, Hanna, 6, was born in Australia.

Moritz also enjoys mentoring university students and talking in high schools. "In a way I'm teaching a little bit," he says. "I feel that it's nice to have a teaching component to some degree, to get a little bit of what is cutting edge science to the younger generation."

# REPURPOSING EXISTING DRUGS TO TREAT GASTRIC CANCERS

**Repurposed drugs could treat people with one of Australia's most common cancers.**

More than 17,000 Australians are diagnosed with colon cancer each year, and 100 die each week. New treatments can take years to be approved, but ONJCRI Cancer Therapeutics Development, Group Head, Dr Ashwini Chand (pictured) hopes to change this.

In 2019, Ashwini published a research article through the *European Molecular Biology Organisation (EMBO)* that highlighted how an existing drug could possibly be used for colon cancer in order to bypass the lengthy process. If Ashwini's team can find ways to repurpose drugs that have already passed the clinical trial stage for other conditions, then they could hopefully be prescribed to cancer patients sooner. Due to the approved status of such drugs, they may also be better tolerated, easily accessible and less expensive.

Her *EMBO* paper evaluated the effectiveness of bazedoxifene, a drug clinically approved to treat osteoporosis, to supress the growth of gastrointestinal tumours. Ashwini's work focused on a class of 'signalling molecules' called inflammatory cytokines, which regulate aspects of normal inflammatory responses, and can also contribute to the progression and treatment resistance of cancer.

Colon or bowel cancers frequently progress due to excessive signalling through a cytokine receptor called gp130. Ashwini's study found that bazedoxifene could mimic interactions between the gp130 receptor and its corresponding interleukin-6 (IL-6) family cytokine, thereby occupying gp130 so that the cytokine no longer can bind and activate the receptor. As a result, bazedoxifene can potentially suppress the growth of gastrointestinal tumours and their progression to advanced cancer.

Ashwini is excited about the findings because this is the first study to show that a small molecule drug can block the IL-6 signalling pathway. Her future work will try to better understand in which cancer patients a drug like bazedoxifene could offer the most benefit as a cancer therapy.

"It is great that preclinical models have discovered a treatment that could be implemented in the clinic for patients with gastrointestinal cancer."

"This is also exciting because therapeutic doses of bazedoxifene have already been established and that minimises any side-effects," she said. "The next step will be to work out the drug's efficacy in patients with gastrointestinal cancer."



# CANCER IMMUNOBIOLOGY PROGRAM

## PROGRAM AND LABORATORY HEAD: **PROF JONATHAN CEBON**

### Program goals

One of the most effective ways of treating cancer is to mobilise the immune system. Research over the last decade has resulted in dramatic clinical progress. As a result, there are now many different cancers that can be treated successfully for the first time. We pioneered immunotherapy for melanoma in Australia. Our continuing goals are to build on past successes by extending immunotherapy to patients with different cancer types and to develop treatments that are even more effective. This involves basic laboratory research to better understand the cellular and molecular mechanisms of immune cancer recognition and killing, as well as trials to enable translation into the clinic. We are better characterising the immune (biomarker) features of tumours that respond to immunotherapy. Because of these studies, we will be able to use biomarkers to personalise future immunotherapies and guide treatment decisions.

### Achievements in 2019

In collaboration with colleagues at the Peter Doherty Institute for Infection and Immunity and CSL Limited, Dr Andreas Behren and his team identified a molecule which plays a critical role in regulating specialised immune cells known as gamma delta T-lymphocytes. These cells are an important first line of defence for the recognition of cancer and bacterial infections. Dr Oliver Klein, together with colleagues at the Peter MacCallum Cancer Centre and Monash Health, and in partnership with community advocates at Rare Cancers Australia, pioneered immunotherapy in patients with rare cancers. They used a combination of two potent antibodies that have proven successful in melanoma and lung cancer, and demonstrated dramatic clinical benefit in rare gynaecological, upper gastro-intestinal and neuro-endocrine tumours. A/Prof Alex Dobrovic and his team have previously pioneered the use of ultra-sensitive DNA-based blood tests to monitor cancer patients. They have now extended these studies to assist monitoring transplant rejection after liver transplantation.

### 3 publication highlights

*Behren, A., E. W. Thompson, R. L. Anderson and P. T. Ferrao. "Editorial: Cancer Plasticity and the Microenvironment: Implications for Immunity and Therapy Response." Front Oncol 9: 276. (2019)*

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*Goh, S. K., H. Do, A. Testro, J. Pavlovic, A. Vago, J. Lokan, R. M. Jones, C. Christophi, A. Dobrovic and V. Muralidharan. "The Measurement of Donor-Specific Cell-Free DNA Identifies Recipients With Biopsy-Proven Acute Rejection Requiring Treatment After Liver Transplantation." Transplant Direct 5(7): e462. (2019)*

## TUMOUR IMMUNOLOGY LABORATORY

### Laboratory Head: Dr Andreas Behren

Our current research focus is understanding the extent of engagement between all parts of the immune system and a tumour. We are developing methods and tests to understand how the immune-tumour interaction can be qualified, quantified and influenced, with the ultimate goal of improving outcomes and quality of life for cancer patients.

**2019 highlights**

Our 2019 highlights included editing a research topic across two *Frontiers* journals that was subsequently voted as third best of more than 1000 topics, several publications and multiple successful grant applications (including a CASS Foundation Grant, a Tour de Cure Pioneering Cancer Research Grant, and a two-year PdCCRS Grant from Cancer Australia funded by Cure Cancer for our Postdoc Dr Jessica Duarte). We are especially happy that the importance of B cells and antibodies in the cancer setting, as tirelessly advocated by Jessica, slowly gains more acceptance and traction in the scientific community.

The most important outcome in 2019 was the exciting results from a clinical trial using combination immunotherapy in patients with rare cancers. Led by our clinical colleagues Prof Jonathan Cebon and Dr Oliver Klein, this trial is showing unprecedented response rates in these cancers. We are very fortunate to run the biomarker discovery research for this trial.

As an academic scientific achievement, the main highlight of the year was the outcome of a great collaboration with colleagues from the Peter Doherty Institute for Infection and Immunity and our longstanding industry partner CSL Limited. We were awarded a five-year National Health and Medical Research Council (NHMRC) Ideas Grant and our publication about the mechanism of gamma-delta T cell activation via phosphoantigens was also accepted for publication in *Science* in 2020.

## MUCOSAL IMMUNITY AND CANCER LABORATORY

### Laboratory Head: Dr Lisa Mielke

Our main goals over the past year have been to establish new funding and collaborations allowing us to expand our projects investigating immunity in the gastrointestinal tract. In particular we aim to expand our studies to investigate the cross talk that occurs between immune cells, the microbiome and epithelium, allowing us to better understand how immune cells control homeostasis in the gut, but also how they contribute to the development of bowel cancer.

**2019 highlights**

The Mucosal Immunity and Cancer Laboratory was established at ONJCRI in 2018. In this short-time we have established exciting new projects to investigate the role of novel immune cell populations in the intestine. We study these immune cells at steady state, investigating how they maintain a healthy gut environment, but we also ask questions about what happens in disease.

This work is important to discover the role of immune cells in the development of and defence against bowel cancer. These projects were established on the back of our recent publication in the *Journal of Experimental Medicine*, a leading journal in the field of immunology. The potential of our work has been recognised by prestigious funding agencies and we have recently received grants from the Victorian Cancer Agency and National Health and Medical Research Council (NHMRC). We hope that this work will deliver new candidates for the development of novel immunotherapy drugs to treat bowel cancer.





## TRANSLATIONAL GENOMICS AND EPIGENOMICS LABORATORY

### Laboratory Head: A/Prof Alex Dobrovic

The Translational Genomics and Epigenomics Laboratory undertakes genomics-based research. We aim to advance personalised medicine for cancer patients with a particular focus on our expertise in liquid biopsies. i.e. using blood rather than tissue for cancer diagnostics and monitoring.

When a patient has cancer, DNA from the cancer (called circulating tumour DNA) can be found in the blood. Circulating tumour DNA has the same genetic changes that are found in the cancer. Monitoring these genetic changes via liquid biopsies can measure the extent of the cancer and determine appropriate treatment. Liquid biopsies are minimally invasive compared to conventional tissue biopsies and thus enable more frequent monitoring of the success of therapy.

**2019 highlights**

In 2019, our work in the area of liquid biopsies was supported by grants from the National Breast Cancer Foundation and the National Health and Medical Research Council (NHMRC) to develop methodologies to monitor breast cancer and lung cancer respectively.

Research highlights were our continuing collaborations with Professor Clare Scott and the NHMRC Clinical Trials Centre in predicting the response to a class of drugs known as PARP inhibitors, which are used in breast and ovarian cancer.

Our team also collaborated with the Austin Health Department of Surgery in using circulating DNA to monitor the health of liver transplant patients. Our Laboratory relocated to this department in December 2019. We retain an honorary affiliation with the ONJCRI and will continue all the projects described above.

# AN INSPIRING LEADER AND COLLABORATOR

Ask **Prof Jonathan Cebon** what his proudest achievements have been during 27 years of leadership, and he directs attention to others.

Jonathan insists that teamwork and research collaborations, with a strong focus on patients, are just as important as individual initiatives.

"The best success results from collaborations," he said. "There have been many really great achievements from working together with all sorts of people in different fields. I think it's about passion and commitment and of course having the right connections."

Jonathan's vision, leadership and creativity have been an inspiration to many over the past 27 years. In 1992, he became Director of a new collaborative unit that linked oncology at what is now Austin Health with the Ludwig Institute for Cancer Research (ONJCRI's predecessor).

In 1993, Jonathan helped create the precursor of Cancer Trials Australia and later played a pivotal role in developing the vision and strategic direction for both ONJCRI and the Olivia Newton-John Cancer Wellness and Research Centre. Once ONJCRI became an independent medical research institute in 2015, he served as Medical Director for both ONJCRI and for the Austin Health Division of Cancer Services and Neurosciences until his retirement from both roles in December 2019.

Jonathan said ONJCRI's success incorporated exceptional clinical, laboratory and administrative expertise. "Lots of people have been involved," he said. "What has been created is really the result of a shared vision. What I'm most proud of is a great group of people who have all worked together to achieve such a fantastic outcome."

As Medical Director for both organisations, Jonathan led and shaped cancer care nationally. He helped establish the ONJCRI Clinician Scientist Fellowship Program, mentored medical oncologists and clinician scientists, established a cancer immunotherapy program, successfully lobbied for State and Federal funding and contributed to local and international cancer agencies.

*Prof Jonathan Cebon, Dame Olivia Newton-John DBE, AC and The Hon Dr Denis Napthine former Premier of Victoria at the official opening of ONJCRI on 8 September 2014.*

In his role as a medical oncologist, Jonathan was among those who pioneered immunotherapy and has followed clinical developments closely. He guided many new melanoma treatments into the clinic, published more than 200 papers and patented eight novel therapies. "It's been a very exciting time to be involved," he said. "The whole field has exploded."

## "THE BEST SUCCESS RESULTS FROM COLLABORATIONS"

Most recently, Jonathan oversaw a clinical trial which showed for the first time that immunotherapy can be highly effective for a variety of rare cancers. Together with the Head of ONJCRI's Tumour Immunology Laboratory, Dr Andreas Behren, and collaborators at the Peter Doherty Institute for Infection and Immunity and CSL Ltd, Jonathan also described a new mechanism by which immune cells detect infections and cancer. This breakthrough discovery will be published in the leading journal *Science* early in 2020.

Jonathan is also working with Dame Olivia Newton-John, DBE, AC, to develop clinical trials at the Olivia Newton-John Cancer Centre to assess the value of medicinal cannabis for cancer patients. For him, it has been an honour and a privilege to contribute to a world class cancer centre known internationally for its research and, perhaps most importantly, patient care and wellbeing.

Nothing is more important to him than knowing that patients appreciate what he and his colleagues do for them. "Patients, and their families, value what we have to offer enormously," he said. "All of the feedback that we get from patients and their families is positive. It's wonderful."

Jonathan's skills and experience have not been entirely lost. He will continue part-time to treat patients at the ONJ Cancer Centre and lead researchers as Cancer Immunobiology Program Head.

This will allow more time with husband Chris Cobbett and their daughter Eva, 13. Jonathan hopes to travel for pleasure – a trip to Italy is already planned – and possibly learn a musical instrument and a language. More reading is likely, although many years of poring over scientific papers took their toll. "Reading for pleasure is something I need to re-learn," he said.

# A PATIENT DRIVEN APPROACH TO RESEARCH

In 2011, **Dr Jessica Duarte** had just begun her PhD studies in Medical Biochemistry in South Africa and studied melanomas when she noticed a mole on her skin that looked suspiciously like the ones she was seeing in her research.

Jessica went to her GP, who also thought it was highly suspicious and removed the mole then and there. Jessica then had to wait a nerve-wracking week for her biopsy results.

"I got a glimpse of what tens of thousands of people go through when they have a suspicious growth and don't yet know whether it is benign or not. And I was lucky, because I was told that my mole was caught just in time," she says.

Three years later, Jessica supported her aunt as she struggled with the side effects of chemotherapy, which unfortunately did not slow down her colon cancer. She died a year later.

These experiences have inspired Jessica's patient-focused approach at ONJCRI, where she works with cancer advocates to ensure her research – which eventually will help doctors with diagnostics and treatment decisions – is tailored to patient needs.

Her research focuses on improving the application of a tool she developed during her PhD studies, which requires less than a drop of blood to potentially not only detect the early stages of a range of cancers, but also may help predict treatment effectiveness and side-effects, and monitor recurrence.

In 2018, Jessica turned her research attention to prostate cancer, but needed help understanding the key issues specific to this disease. "And there's nothing better than talking to a consumer," she says.

Enter James Doulis, a prostate cancer survivor and advocate for ONJCRI, who says: "I think one of the powerful things about cancer patient advocates is we bring a clean set of eyeballs to a project." He could share his insights with Jessica into the difficult process of living with the implication of having elevated levels of Prostate-Specific Antigen (PSA) cancer marker, undergoing invasive tests and not knowing whether prostate removal was necessary.

"Because of the notorious unreliability of tests like the one for PSA, it is clear that patients need better diagnostics, including more accurate ways of determining whether their cancer is aggressive. There are a lot of prostate patients having unnecessary, invasive tissue surgery," says Jessica.

*Dr Jessica Duarte and advocate James Doulis*



# GASTROINTESTINAL CANCER PROGRAM

PROGRAM HEAD:
**PROF JOHN MARIADASON**

**Program goals**

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 these tumours to survive and grow, and we are testing whether drugs which work in other cancers can be repurposed for the treatment of gastrointestinal cancers.

**Achievements in 2019**

In 2019, our team completed a major study in biliary tract cancer in which we identified a series of potential new treatment targets for these cancers, including FGFR, ERBB2, ERBB3 and IDH.

Our team also made the important discovery that patients with Stage 3 colorectal cancers who harbour mutations in the gene *TP53* derive less benefit to conventional chemotherapy, highlighting the need to identify additional treatments for these patients.

Finally, through detailed biochemical studies, the team led by A/Prof Doug Fairlie made an important discovery of how proteins essential for cell survival interact with each other under conditions of cell stress, which may ultimately increase our understanding of how tumour cells survive.

**3 publication highlights**

*Lau, D. K., D. Mouradov, W. Wasenang, I. Y. Luk, C. M. Scott, D. S. Williams, Y. H. Yeung, T. Limpaiboon, G. F. Iatropoulos, L. J. Jenkins, C. M. Reehorst, F. Chionh, M. Nikfarjam, D. Croagh, A. S. Dhillon, A. J. Weickhardt, T. Muramatsu, Y. Saito, N. C. Tebbutt, O. M. Sieber and J. M. Mariadason. "Genomic Profiling of Biliary Tract Cancer Cell Lines Reveals Molecular Subtypes and Actionable Drug Targets." iScience 21: 624-637. (2019)*

*Williams, D. S., D. Mouradov, C. Browne, M. Palmieri, M. J. Elliott, R. Nightingale, C. G. Fang, R. Li, J. M. Mariadason, I. Faragher, I. T. Jones, L. Churilov, N. C. Tebbutt, P. Gibbs and O. M. Sieber. "Overexpression of TP53 protein is associated with the lack of adjuvant chemotherapy benefit in patients with stage III colorectal cancer." Mod Pathol. (2019)*

*Lee, E. F., N. A. Smith, T. P. Soares da Costa, N. Meftahi, S. Yao, T. J. Harris, S. Tran, A. Pettikiriarachchi, M. A. Perugini, D. W. Keizer, M. Evangelista, B. J. Smith and W. D. Fairlie. "Structural insights into BCL2 pro-survival protein interactions with the key autophagy regulator BECN1 following phosphorylation by STK4/ MST1." Autophagy 15(5): 785-795. (2019)*

## ONCOGENIC TRANSCRIPTION LABORATORY

### Laboratory Head: Prof John Mariadason

The Oncogenic Transcription Laboratory is seeking to develop new treatments for cancers of the gastrointestinal tract, including cancers of the bowel and biliary tract. In particular, we are seeking to develop treatments which can prevent cancer cells from moving around the body by causing cancer cells to resemble and behave more like normal cells. We refer to this as 'differentiation therapy'.

**2019 highlights**

For several years our group has been studying the potential of blocking a family of proteins called histone deacetylases HDACs to achieve this. Drugs which block these proteins are currently used in the treatment of some forms of lymphoma, and our objective is to understand if these drugs can also be used to treat gastrointestinal cancers.

In 2019 we made the remarkable discovery that one member of this family, HDAC3, controls the rate at which normal intestinal cells metabolise lipids, a process essential for energy production. We are now utilising this knowledge to understand how energy metabolism changes in colon cancer cells, how this drives growth of the tumour, and whether targeting HDAC3 can reverse these changes.

We have also made the important discovery that combining HDAC inhibitors with a class of drugs known as MEK inhibitors, greatly increases their capacity to induce 'differentiation'. We are currently working with the Australasian Gastro-Intestinal Trials group (AGITG) to design a clinical trial which can test the safety and efficacy of this drug combination in patients with advanced colorectal cancer.

## CELL DEATH AND SURVIVAL LABORATORY

### Laboratory Head: A/Prof Doug Fairlie

The Cell Death and Survival Laboratory focuses on how cells determine their own fate. This is critical for our wellbeing. However, disruption of the underlying processes can also lead to cancer. Recently a new class of drugs has been developed that can activate the natural 'cell suicide' mechanisms to kill tumour cells.

**2019 highlights**

We published a large study on how a new class of drugs could potentially be used in melanoma. As part of this study, we identified critical 'survival factors' within melanoma cells and some potent drug combinations that triggered their death. Our aim now is to extend these studies into animal models. We also have projects applying the experimental pipeline established for melanoma studies to cancers such as mesothelioma, biliary tract cancer and breast cancer.

We also published a study on a different process which enables cells to survive under stress. We are particularly interested in one protein that is critical for triggering this process and has a direct, but not well understood, connection with cell death pathways. This study provided high-resolution structural information on how these pathways intersect at a molecular level.

We are now investigating this protein at the whole animal level and have shown its important role in the gastrointestinal system, which is now a key focus.



# CANCER STUDY REVEALS KNOCKOUT OBESITY GENE

**What started as a research project into colon cancer has resulted in a discovery that could lead to a new treatment for obesity.**

The study, which was published in *Nature Communications* in 2019, has found that disabling a gene called *HDAC3* specifically in the intestine could protect people from diet-induced obesity.

In 2014, a NHMRC grant allowed Prof John Mariadason, (pictured), Head of ONJCRI's Gastrointestinal Cancer Program, to begin a research study looking at the function of a specific set of proteins called histone deacetylases or HDACs in colon cancer. There are 10 HDAC genes within our bodies, and drugs targeting these proteins are currently used to treat blood cancers.

This pre-clinical study originally aimed to assess if these drugs could also be repurposed for treating colon cancer. As part of this study, John and his team inactivated the *HDAC3* gene in the intestine and colon of pre-clinical models to assess the impact of HDAC3 on colon cancer development. During these studies John's team made the remarkable finding that models lacking the *HDAC3* gene were protected against obesity.

The normal job of the intestine is to absorb nutrients including lipids or fats, and then move these into the liver. However, the team discovered that when intestinal cells lack the *HDAC3* gene, these cells start doing an additional job – they break down the lipids within the intestinal cells themselves. This results in less lipid being available for uptake into the body, and ultimately, over time, a reduction in weight gain of the entire animal.

Having made this surprising discovery, Prof Mariadason expanded the study with Dr Mercedes Dávalos-Salas, a post-doctoral fellow in his team; Prof Matthew Watt, Head of Department of Physiology, School of Biomedical Sciences at the University of Melbourne; and Prof Andrew Scott AM, Head, Tumour Targeting Program ONJCRI, Director, Department of Molecular Imaging and Therapy, Austin Health.

> "WE HAVE FOUND THAT THERE IS A NEW ROLE FOR THE *HDAC3* GENE IN THE BREAKDOWN OF FATS"

"We have found that there is a new role for the *HDAC3* gene in the breakdown of fats," said John.

"We know that obesity is linked to cancer and if we can block this particular gene then we could protect people from diet-induced obesity and a new obesity treatment could be delivered," he said.

The colon cancer study has also continued and findings are expected to be released in 2020.

# LEADING THE WAY IN THE FIGHT AGAINST CANCER

Leadership comes in many forms. For Dr Erinna Lee (pictured), it means improving our understanding of the rulebreaker in biology that leads to cancer. Erinna investigates molecular mechanisms that fuel cancers to obtain novel insights that will ultimately improve treatments for cancer patients. To do this, she studies pathways that regulate death and survival of cancer cells because deregulation of these processes play important roles in the development and progression of most cancers.

This precise and exact work is also rewarding. In 2019, Erinna became Cancer Theme Leader at the La Trobe Institute of Molecular Science (LIMS) where she is a laboratory head. She is also a Visiting Scientist at ONJCRI in the Cell Death and Survival Laboratory led by A/Prof Doug Fairlie, with whom she has collaborated with for more than 15 years.

The dual appointments make perfect sense given ONJCRI is the La Trobe University School of Cancer Medicine. They allow Erinna to bridge expertise between the University and ONJCRI to make an even bigger difference, with more scope to progress research into how cells decide to live or die, and how these processes change to cause diseases such as cancer. This has enabled her to establish a range of collaborations between leading researchers in both institutions and attract students.

Through her role as Cancer Theme Leader, Erinna helps to develop programs and opportunities for researchers at LIMS, ONJCRI and the wider La Trobe University community. “Once we fully understand all the ways in which cancer cells attain their ability to grow uncontrollably, we will be better equipped to develop drugs to destroy them,” she says. “Ultimately, the main goal is to draw on the collective strengths that we have at LIMS and ONJCRI to work towards better outcomes for cancer patients.”

Erinna now sits on the LIMS Research Committee and is the ONJCRI representative on the LIMS Honours Student Committee, mentoring students enrolled through LIMS but based at ONJCRI.

The role has opened Erinna’s eyes to the research potential offered across the two sites and she is excited that her colleagues from both organisations have approached her with excellent ideas to foster closer collaboration. “I hope that I will be able to encourage and facilitate further conversations between the two sites and enable researchers from LIMS and ONJCRI to work together effectively to achieve our common goal of outsmarting cancer,” she says.



# TRANSLATIONAL BREAST CANCER PROGRAM

## PROGRAM HEAD: **PROF ROBIN ANDERSON**

### Program goals

Metastasis is the major cause of death for those afflicted with breast cancer. While the majority of patients respond well to the initial therapy and are essentially cured, secondary disease develops up to two decades later in approximately 15% of these cases. When the cancer spreads to distant sites, we call it metastasis, from the Greek word meaning ‘removal’ or ‘change’.

Our Program is focused on understanding the cellular and molecular mechanisms that allow tumour cells to escape from the primary tumour in the breast and establish secondary tumours in vital organs such as the lungs, liver, bone and brain. We aim to provide benefit to these breast cancer patients, by helping to identify the most effective therapy if the cancer metastasises to other organs.

### Achievements in 2019

Dr Delphine Merino’s Laboratory is using preclinical models and an elegant DNA cell-tracking technique to follow the fate of individual cells as they grow in a primary tumour in the mammary gland and metastasise to other organs. She finds that only a few cells within the primary tumour have the capacity to metastasise to some organs such as the liver and brain. Her results were published in *Nature Communications* in 2019.

Dr Normand Pouliot’s Laboratory has developed a clinically relevant preclinical model of breast cancer that metastasises to the brain – a major issue in the management of patients with advanced disease. In a paper published in *Breast Cancer Research* in 2019, he describes how a new drug, currently in clinical trials, is effective in reducing the incidence of brain metastasis that is driven by the oncogene called *HER2*.

Dr Bhupinder Pal’s Laboratory has successfully established the single cell genomics platform, now widely used by other research groups at our Institute. This new technology allows investigators to study gene expression or DNA mutations in individual cells within a tumour, thus helping us to understand the genes that allow single cells in the primary tumour to form metastatic tumours. These genes are potential targets for therapy against metastatic disease.

Prof Robin Anderson’s Laboratory is investigating the mechanism by which several genes function to control metastasis, either though suppression or promotion of the process. A highlight of 2019 was the publication in *Nature Reviews Clinical Oncology* of a consensus report on the best way forward for accelerating the use of anti-metastatic drugs in the clinic.

This paper arose from a meeting of the Metastasis Working Group in London, UK, comprising representatives from not-for-profit, academic, government, industry and regulatory bodies focused on developing recommendations on how to tackle the challenges associated with treating metastatic disease. In the paper, Prof Anderson and colleagues proposed new approaches for discovery and development of anticancer agents designed specifically to prevent or delay the metastatic outgrowth of cancer.

### 3 publication highlights

*Merino, D., T. S. Weber, A. Serrano, F. Vaillant, K. Liu, B. Pal, L. Di Stefano, J. Schreuder, D. Lin, Y. Chen, M. L. Asselin- Labat, T. N. Schumacher, D. Cameron, G. K. Smyth, A. T. Papenfuss, G. J. Lindeman, J. E. Visvader and S. H. Naik. “Barcoding reveals complex clonal behavior in patient-derived xenografts of metastatic triple negative breast cancer." Nat Commun 10(1): 766. (2019)*

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*Anderson, R. L., T. Balasas, J. Callaghan, R. C. Coombes, J. Evans, J. A. Hall, S. Kinrade, D. Jones, P. S. Jones, R. Jones, J. F. Marshall, M. B. Panico, J. A. Shaw, P. S. Steeg, M. Sullivan, W. Tong, A. D. Westwell, J. W. A. Ritchie, U. K. Cancer Research and C. R. C. A. M. W. G. Cancer Therapeutics. "A framework for the development of effective anti-metastatic agents." Nat Rev Clin Oncol 16(3): 185- 204. (2019)*

## METASTASIS RESEARCH LABORATORY

### Laboratory Head: Prof Robin Anderson

The goal of our research is to develop improved therapies for metastatic breast cancer. To achieve this, we use preclinical models and samples from patients' cancers to identify genes that drive the spread of the cancer from the breast to other organs. Knowledge of the genes that drive metastasis will enable the development of therapies that target these genes.

#### 2019 highlights

We are assessing the function of two genes that we have shown to be able to reduce the extent of metastasis of breast cancer. A gene called *Caveolin-1* can suppress metastasis when it is present in the normal cells surrounding the tumour and we have shown that loss of the protein from breast cancers is associated with poor survival. In 2019 we secured new funding to investigate the mechanism by which this host protein can send signals that reduce the ability of the cancer cells to escape the primary tumour.

A second metastasis suppressor is called BMP4. In preclinical models, we have shown that when treated with this protein, or when the protein is highly expressed in the tumour cells, metastasis is suppressed. However, in some other types of cancer, BMP4 has been reported to have the opposite effect, promoting metastasis. Our current research is aimed at dissecting the signalling pathways triggered by BMP4 binding to tumour cells, to enable us to understand the different responses to BMP4 in different cancers.

Another major project aims to identify an immunotherapy approach that will be effective in blocking breast cancer progression. 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. We are developing a new type of immunotherapy that targets tumour-promoting neutrophils that can block the anti-tumour activities of cytotoxic T cells and natural killer cells. We have found that early application of this anti-neutrophil therapy reduces the number of tumour cells escaping from the primary tumour.

## MATRIX MICROENVIRONMENT AND METASTASIS LABORATORY

### Laboratory Head: Dr Normand Pouliot

Our research seeks to understand how breast cancer spreads to distant organs (metastasis) and why some cancers become resistant to therapy. Our long-term goal is to develop new methods to identify patients whose disease is more likely to recur and spread, and develop more effective therapies for incurable brain metastases.

#### 2019 highlights

in 2019 we have made promising advances towards improving treatment for two aggressive subtypes of breast cancer called HER2+ve and Triple Negative Breast Cancer (TNBC). Both subtypes are associated with rapid development of treatment-resistant brain metastases. Our work published in *Nucleic Acid Therapeutics* describes the development and validation of a promising new strategy using small molecules called 'aptamers' to deliver chemotherapy across the natural protective barrier of the brain and specifically target TNBC cells in the brain. A key benefit of aptamers as a drug delivery vehicle is that they could provide better control of cancer cell growth in the brain while minimising toxicity of chemotherapy to healthy tissues.

We have developed a new mouse model of HER2+ve breast cancer that aggressively spreads from the breast (mammary gland) to the brain and other organs in mice with an intact immune system. In this model, we have identified a new mechanism (termed ferroptosis) by which a drug called neratinib can kill HER2+ve breast cancer cells. Our work published in *Breast Cancer Research* showed that neratinib extends life significantly and is particularly effective at preventing the growth of HER2+ve brain metastases when treatment is initiated before surgical removal of the tumour in the breast. This work, presented at the Clinical Oncology Society of Australia annual scientific meeting, was awarded Best of the Best oral presentation.





## TUMOUR PROGRESSION AND HETEROGENEITY LABORATORY

### Laboratory Head: Dr Delphine Merino

Our Laboratory is focussing on metastatic breast cancer. Developing new technologies and using patient samples, we are trying to understand how cancer cells spread from the breast to different sites, how some cells escape current therapies, and what novel combinations of drugs can be used to treat recurrent disease.

#### 2019 highlights

Our team is using patient samples to molecularly dissect the journey of metastases at the genetic level. We recently discovered that a few cells, present in a patient's tumour at the time of diagnosis or surgery, can spread to different parts of the body and resist chemotherapy (Merino, Weber et al., *Nature Communications* 2019).

In order to better study the biology of these aggressive cells, we established innovative technologies including barcoded patient-derived xenograft models, single cell sequencing, 3D imaging and drug response predictions.

We recently found that the genetic makeup of cancer cells varied according to their tumour microenvironment. In collaboration with Dr Belinda Yeo, we are validating our results in samples taken at different times in patients with breast cancer. By identifying the genes that are deregulated during tumour progression, we will be able to identify new treatments for patients with metastatic breast cancer.

## CANCER SINGLE CELL GENOMICS LABORATORY

### Laboratory Head: Dr Bhupinder Pal

Our Laboratory's research vision is to:

- understand the role of cancer cell heterogeneity and tumour microenvironment
- identify molecular mechanisms responsible for treatment resistance in breast cancer patients
- validate the use of single-cell genomics in clinical settings to help design effective personalised treatment for cancer patients
- identify critical molecular drivers of the mammary epithelial differentiation program.

#### 2019 highlights

During 2019, we successfully established a fully functional in-house genomics work station accessible to ONJCRI researchers and collaborators. As a result, we are now able to provide training to ONJCRI students in Next Generation Sequencing (NGS) based work flow and innovative single cell multi-omics techniques including transcriptome, epigenome and protein profiling at single cell level. Having access to such novel techniques has helped ONJCRI researchers generate novel molecular insight into cancer progression and response to treatment.

# FOCUSING ON THE FUTURE OF PERSONALISED MEDICINE

*ONJCRI Research Assistant Caroline Bell with Love Your Sister's Samuel Johnson OAM*

**While we often hear in the media that the survival rate of people diagnosed with breast cancer is increasing, unfortunately the survival rate for those with secondary breast cancer or metastatic breast cancer paints a very different picture.**

The *Love Your Sister* charity and ONJCRI are now working together to try and change this statistic. Thanks to a new three-year grant from *Love Your Sister*, dedicated Research Assistant Caroline Bell is playing a critical role in a new translational breast cancer research project that sees her working with our researchers, Drs Belinda Yeo and Delphine Merino.

Belinda is a clinician scientist who treats breast cancer patients, while Delphine runs a breast cancer research laboratory that specifically studies the cancer cells responsible for forming metastatic cancers. And while they make a great team, Caroline is bridging a gap to help achieve the ultimate goal of guiding clinicians to the most effective treatment option for individual patients with metastatic breast cancer.

"WE HOPE THAT THIS RESEARCH COULD LEAD TO A NEW TREATMENT APPROACH, WHICH IS A VERY EXCITING POSSIBILITY"

Caroline works closely with Belinda to obtain necessary consent from the many patients who are happy to donate a sample of their tumour to research. She then works with the patient's surgical teams and pathologists and transports these precious samples to Delphine's Tumour Progression and Heterogeneity Laboratory. Delphine and her team, which are all part of the ONJCRI Translational Breast Cancer Program led by renowned breast cancer researcher Prof Robin Anderson, then examine the genetic makeup of the cells present in each sample and start screening how these cells respond to a large number of drugs that are currently used in the clinic.

Once this screening is conducted across many different tumour samples with many different drugs, the team will be able to use Artificial Intelligence to better predict the most effective treatment for an individual patient. Integral to this screening approach is Caroline's expertise to grow 'mini organ-like' structures from these patients' samples. Because these organoids better reflect how the cancer cells behave in a patient's body, organoids can often predict more accurately how cancer cells respond to treatment than when they are grown as a layer of cell in a tissue culture dish.

Caroline explains, "We ultimately want to get to a point where the findings from this research can be used to guide decisions by oncologists to a personalised treatment plan, based on results predicted and tested by scientists".

"Thanks to the tremendous support of *Love Your Sister* and their village of supporters, we hope that this research could lead to a new treatment approach, which is a very exciting possibility".

# BARCODING CELLS TO STOP BREAST CANCER

A technique used at supermarket checkouts is helping to fight breast cancer. Dr Delphine Merino (pictured), Head of the Tumour Progression and Heterogeneity Laboratory, and her team are using barcodes to identify, track and analyse the genetic properties of aggressive breast cancer cells that spread through the body, or resist drug treatment.

This work follows a paper Delphine co-authored in the prestigious journal *Nature Communications* in March 2019. Barcodes were introduced in the 1970s to identify and track millions of unique products. In recent years, medical research has adopted the same technique to categorise and track millions of individual cells.

"THERE IS HOPE FOR NEW TREATMENTS BY BETTER UNDERSTANDING HOW TUMOUR CELLS SPREAD"

Genetic barcoding labels individual cells with a unique nucleic acid sequence – or barcode – which allows the cells to be tracked as they move around the body. Delphine is leading the way in using an optical version of barcodes to identify drugs that may prevent cancer cells from spreading or resisting standard treatment.

"Metastasis – the spread of cancer cells beyond their primary site – is the major cause of death of breast cancer patients," Delphine explained.

"Spreading cells are often biologically different than the cells at the primary tumour site. By labelling individual cells in a tumour we can then see how each tumour cell responds in the presence of a particular drug treatment."

Delphine's *Nature Communications* paper reported a study that she conducted together with her colleagues, Dr Shalin Naik, and Professors Jane Visvader and Geoffrey Lindeman at the Walter and Eliza Hall Institute of Medical Research. The work not only showed the different parts of the body to which individual barcoded breast cancer cells spread, but also that only a few cells were responsible for the 'seeding' of a new metastasis.

The research is an important step in understanding how breast cancer cells spread to other organs. Delphine said the cellular barcode research was part of a broader mission and she and her team were now analysing the genetic makeup of the 'seed' cells.

"There is hope for new treatments by better understanding how tumour cells spread," she said.

"Barcoding is helping us understand which cells we need to target, so that we can improve the diagnosis and treatment of this terrible disease."

# TUMOUR TARGETING PROGRAM

## PROGRAM HEAD:
## PROF ANDREW SCOTT AM

### Program goals

The Tumour Targeting Program, which includes the Tumour Targeting Laboratory, Receptor Biology Laboratory, and Centre for Research Excellence in Brain Cancer, focuses on the targeting, molecular imaging and treatment of tumours, as well as defining receptor-based signalling pathways responsible for cancer cell growth and unravelling mechanisms that result in resistance to targeted therapies. We have identified novel targets for cancer drug development which are suited for antibody-based and engineered protein therapy.

Our goal is to develop novel diagnostic and therapeutic approaches to a range of cancers and extend these into clinical studies in cancer patients. The Program has strong collaborative links to Austin Health's Department of Molecular Imaging and Therapy, directed by Prof Andrew Scott AM, and Cancer Clinical Trials Centre, directed by Prof Hui Gan, enabling the iterative research cycle from laboratory to the clinic and back.

### Achievements in 2019

During 2019 our Program developed novel approaches to imaging and therapeutically exploiting targets in the tumour cells and in the tumour microenvironment. Preclinically, utilising the institute's ACRF Centre for Translational Cancer Therapeutics and Imaging, we also continued to assess the anti-tumour efficacy of our targeted therapies, and to investigate the molecular imaging of tumours to evaluate tumour response, to aid in selecting patients most likely to benefit from a particular drug therapy. In the clinic we continued to lead Phase I/II clinical trials with tumour targeting antibodies developed by the Program, and are pursuing novel molecular imaging probes in cancer patient trials.

### 3 publication highlights


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## TUMOUR TARGETING LABORATORY

### Laboratory Head: Prof Andrew Scott AM

Over the past 12 months we have continued to pursue novel targets for cancer drug development and explore novel therapeutic approaches. Novel antibodies developed in our Laboratory against receptors expressed in the tumour microenvironment and on cancer cells have been explored in model systems as signalling inhibitors, as a mechanism for targeted payload delivery to tumours through antibody-drug conjugates (ADCs) or antibody-radioisotope conjugates, and for enhancement of immune response.

**2019 highlights**

Our research into new therapies for glioblastoma (GBM) has shown highly promising results in patients from studies with depatuxizumab mafodotin (depatux-m, ABT-414) a tumour-selective anti-EGFR ADC comprised of mAb806 and the monomethyl auristatin F (MMAF) warhead (Lassman et al *Neuro-oncology* 2019), and we continue to investigate third generation mAb806-based-ADCs and combinations with chemotherapy.

To translate our novel antibodies to the clinic, we have developed techniques for generation and humanisation of antibodies. During 2019 we pursued the humanisation of new, novel therapeutic antibodies that target key molecules in breast, lung, prostate and colon cancer. With collaborators at La Trobe University, we are also working on the development of a novel treatment approach for cancer cachexia and exploration of an imaging surrogate marker or serum biomarker for cachexia (NCT04127981).

Our Laboratory is developing novel imaging probes through sophisticated chemistry techniques to identify patients suited to treatment with hormone therapies or anti-cachexia agents, inhibitors of certain key oncogenic signalling pathways, and immunotherapy. NHMRC supported preclinical investigations with targeted alpha-particle therapy are being successfully pursued using novel chelates developed in collaboration with chemists at the University of Melbourne. We are also conducting grant supported bioimaging clinical trials with $^{89}$Zr labelled antibodies aimed at validating targets, identifying optimal dose and patient selection for therapy in patients with glioma and lymphoma (NCT03374943; NCT03610061).

## RECEPTOR BIOLOGY LABORATORY

### Laboratory Head: A/Prof Peter Janes

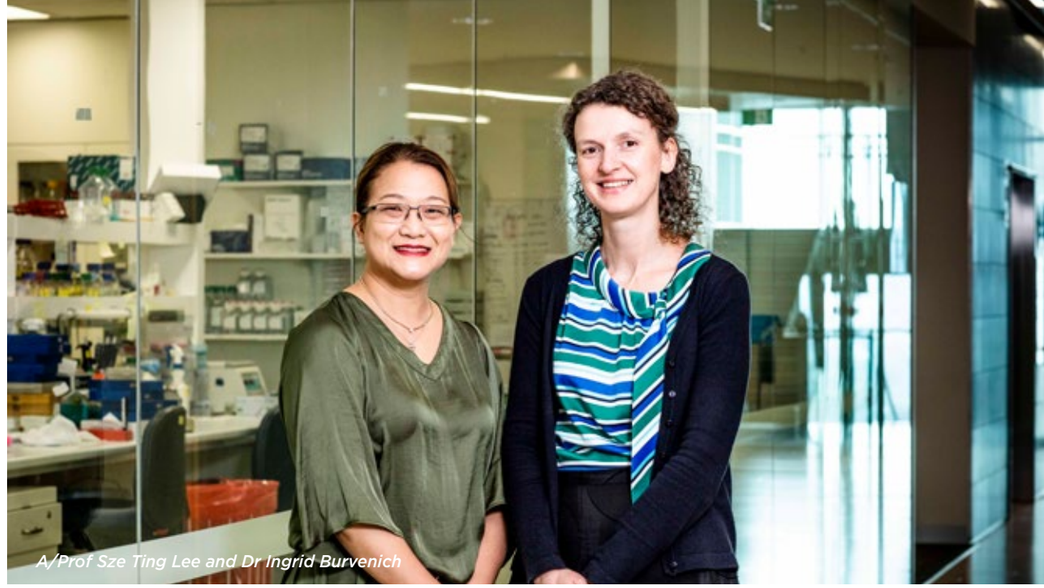
The Receptor Biology Laboratory focuses on the investigation of cell surface proteins particularly abundant or active in tumours and/or the tumour microenvironment (TME), as potential targets for new therapies. In particular, we investigate two families of cell surface proteins which have important roles in tumour cell interactions with the TME: Eph receptors, which control cell-cell communication and cell migration; and ADAM proteases, which shed other proteins from the cell surface and control tumour growth, drug resistance and invasion. We are developing novel antibody-based drugs to inhibit these activities.

**2019 highlights**

In 2019, we continued to investigate the role of EphA3 in promoting tumour development, using novel mouse strains in which we can reduce EphA3 levels specifically in the TME. We showed that reducing EphA3 expression on 'host' cells in the TME is able to inhibit tumour growth in these mice, by inhibiting new blood vessel formation and improving anti-tumour immune responses. Similarly, we investigated the function of ADAM10, by deleting it from glioma (brain cancer) cells, which markedly inhibits tumour growth in mice, and converts the tumour cells to a more differentiated, benign form.

We also expanded our testing of antibodies (proteins made by the immune system) that bind EphA3 and ADAM10 as a way to specifically target cytotoxic drugs to the tumour/TME. Our anti-EphA3 antibody has been previously licensed to Humanigen (San Francisco), while our ADAM10 antibody is the subject of license negotiations. We have presented our work at local and international meetings, and published two papers in respected international journals.





*A/Prof Sze Ting Lee and Dr Ingrid Burvenich*

# GIVING STRENGTH TO THOSE WITH CANCER-RELATED WEIGHT LOSS

Many people with advanced stages of cancer experience weight loss and muscle wastage, which can limit their ability to respond to treatment. This process, known as cachexia, affects up to 80 per cent of late stage cancer patients and disrupts their metabolism, causing fatigue, and fat and muscle loss.

ONJCRI and La Trobe University researchers hope to produce the first targeted treatment following the 2015 discovery by La Trobe University's Emeritus Prof Nick Hoogenraad and his team that Fn14, a receptor often present on the membrane of cancer cells, can cause cachexia. They developed an antibody drug (mAb002) that targets Fn14 and is able to neutralize or prevent cancer cachexia in pre-clinical models.

"WE AIM TO SEE WHETHER THE PET SCANS CAN DETECT SPECIFIC METABOLIC CHANGES IN CACHECTIC PATIENTS"

ONJCRI's Tumour Targeting Laboratory, led by Prof Andrew Scott AM, is collaborating with La Trobe University researchers to develop 'humanised' mAb002 antibody versions to be able to test the new drug in clinical trials. In 2019, the first of these 'humanised' mAb002 antibodies performed well in preclinical models, paving the way for human trials.

The teams are also working together on blood tests and imaging probes to identify those patients who may respond to mAb002 treatment. A first human trial began in mid-2019, with 18 pancreatic, lung and colorectal cancer patients undergoing FDG-PET scans.

Tumour Targeting Laboratory Senior Clinician Researcher and Austin Health Nuclear Medicine Physician A/Prof Sze Ting Lee is running the trial with Profs Andrew Scott and Hui Gan. "We aim to see whether the PET scans can detect specific metabolic changes in cachectic patients," she said.

The research team presented their exciting findings at the 2019 Australia and New Zealand Society of Nuclear Medicine (ANZSNM) annual meeting in Adelaide and the 12th International Conference on Cachexia, Sarcopenia & Muscle Wasting in Berlin. Their ANZSNM oral presentation was shortlisted for the Shimadzu Award.

Tumour Targeting Laboratory Senior Postdoctoral Researcher Dr Ingrid Burvenich is undertaking nuclear imaging work for the project. "If successful, the use of a non-invasive imaging technique to monitor disease and response to our therapy will increase the success of subsequent clinical trial studies with the anti-Fn14 antibody, as well as other anti-cachectic drugs under development world-wide," she said.

*Prof Andrew Scott AM (left) and Prof Hui Gan*

# AN AGGRESSIVE BRAIN CANCER MAY HAVE MET ITS MATCH

**A new way to attack tumours, developed and tested in Melbourne, could provide benefit to patients with one of the most aggressive forms of brain cancer.**

The first human trial of the novel antibody drug on people with recurrent glioblastoma (GBM), which causes aggressive tumours and has a low survival rate, found it could potentially halt their growth.

A team led by ONJCRI scientists and involving colleagues from Monash University and QIMR Berghofer Medical Research Institute developed the drug ifabotuzumab which is now licensed to Humanigen.

Ifabotuzumab is a monoclonal antibody that targets the EphA3 protein, which is associated with several cancers and often found in the tumour's microenvironment. The microenvironment includes the supporting tissue, immune cells and blood vessels that facilitate tumour growth.

Data from this trial was presented to the American Association for Cancer Research in April 2019 and the American Society for Neuro-Oncology in November 2019. So far it has shown that ifabotuzumab is well tolerated, penetrates the brain cancer in high concentrations and alters its blood supply.

Led by Profs Andrew Scott AM and Hui Gan and supported by a *Cure Brain Cancer Foundation* grant, the trial has achieved two thirds of its planned recruitment across Austin Health and the Royal Brisbane and Women's Hospital. Prof Scott, who heads ONJCRI's Tumour Targeting Laboratory and is Director of the Austin Health Department of Molecular Imaging and Therapy, is excited by the results.

"We're very encouraged," he said. "We have not only shown that the antibody specifically targets GBM, but we also have been able to observe high concentrations of antibodies at the site of the tumour. It is also targeting the tumour microenvironment, which is the supporting structure surrounding the cancer cells. This is a very new concept."

"IFABOTUZUMAB REPRESENTS A NEW WAY OF ATTACKING GBM"

The team is now investigating the use of ifabotuzumab to deliver other drugs and radiation treatment. It may also have the potential to treat other cancers with high levels of *EphA3* in their microenvironment, such as colon, lung, kidney, bladder and melanoma.

Prof Gan, who is Co-Director of the ONJCRI Centre for Research Excellence in Brain Cancer, is also optimistic. "Ifabotuzumab represents a new way of attacking GBM. The drug appears to be well tolerated and has the potential to be used both alone and in combination with other treatments."



# DARRYN'S STORY

**"Cancer research gives people like me and my family hope," says 56 year old Darryn Hooper.**

Darryn first felt symptoms in August 2017, he thought he may have had a stroke. He started to mix his words and was looking and feeling very vague. Darryn was sent for a brain CT scan and within a few hours he had a call from his GP.

Darryn was diagnosed with Glioblastoma or GBM – the most common type of primary brain cancer that impacts Australians.

Darryn had surgery two weeks after his diagnosis and also started standard treatment of radiotherapy and chemotherapy. Tests on the tumour revealed Darryn was also eligible for a global phase 3 clinical trial that was testing a potential new therapy for glioblastoma patients.

"THESE ARE SPECIAL PEOPLE AND THERE'S A LOT OF HARD YAKKA THAT GOES INTO TRYING TO FIND AN ANSWER"

This trial aimed to study the effects of the drug Depatuxizumab mafodotin (depatux-m, ABT-414) when combined with chemotherapy. The Tumour Targeting Program at ONJCRI, led by Prof Andrew Scott AM, made a major contribution to the early development of this drug. Prof Hui Gan, Senior Clinical Research Fellow in the Tumour Targeting Program at ONJCRI and Medical Director of Cancer Clinical Trials at Austin Health, locally led the clinical trial.

Darryn's wife Cheryl says that "when it came down to the treatment options, chemo and radiation were a given. But knowing that his doctors also felt that this clinical trial was the best fit for Darryn, we felt comforted to start on the trial straight away".

Darryn and Cheryl both felt incredibly supported by everyone in the treatment team when making a decision about starting on the trial and during treatment.

Darryn started on the ABT-414 trial in October 2017 and he continued on this through to April 2019. Darryn is now participating in another early phase clinical trial through the Olivia Newton-John Cancer Centre.

"These are special people and there's a lot of hard yakka that goes into trying to find an answer," Darryn says.

"Knowing someone is doing this research gives you hope that an answer might actually be found".

# CENTRE FOR RESEARCH EXCELLENCE IN BRAIN CANCER

CENTRE DIRECTORS:
**PROF ANDREW SCOTT AM AND PROF HUI GAN**

**About the Centre**
The Centre for Research Excellence in Brain Cancer commenced in mid-2019 at the ONJCRI. Supported by The Victorian Cancer Agency of the Victorian Government, the Centre builds on the unique strengths of the existing ONJCRI activities and established national and international collaborative programs in brain cancer research. The Centre focuses on the development of imaging techniques and chemistry, molecular assays and novel therapeutics. The Centre's program extends from primary brain cancer to metastatic disease, and links in with new targets for molecular imaging and therapy, biomarkers aiding in the selection of patients to specific treatments and prognosis, as well as the development of novel techniques for optimising drug delivery to brain cancer.

**2019 highlights**
Since the commencement of the Centre for Research Excellence in Brain Cancer and in collaboration with the University of Sydney, we have been successful in obtaining $500,000 in funding for the first year of the Low & Intermediate Grade Glioma Umbrella Study of Molecular Guided TherapieS (LUMOS) clinical study through the Australian Brain Cancer Mission Innovative Clinical Trials Grant Scheme. The multi-centre study will commence in early 2020 and, working with Cooperative Trials Group for Neuro-Oncology (COGNO), we aim to obtain additional funding to allow this study to achieve the full patient cohort recruitment.

In support of our investigations into biomarkers in 2019, we have created a Research Electronic Data Capture (REDCap)-based database for the collection of brain cancer patient information including demographics, clinical details and treatment details. This secure REDCap database will also record information on samples being collected with the patient's written informed consent for research purposes.

**Feature publications**


*Lassman, A. B., L. A. Roberts-Rapp,I. Sokolova, M. Song, E. Pestova, R. Kular,C. Mullen, Z. Zha, X. Lu, E. Gomez, A.Bhathena, D. Maag, P. Kumthekar, H.K. Gan, A. M. Scott, M. Guseva, K. D.Holen, P. Ansell and M. J. van den Bent."Comparison of Biomarker Assays forEGFR: Implications for Precision Medicinein Patients with Glioblastoma." ClinCancer Res. 25(11): 3259-3265 (2019)*

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# UNITED APPROACH TO IMPROVE BRAIN CANCER RESEARCH

The Centre for Research Excellence in Brain Cancer is the first such centre in Australia. It aims to improve patient outcomes by having a single centre which unites both clinicians and scientists to tackle this terrible disease. Opened in September 2019 following a $2 million grant from the Victorian Cancer Agency, the Centre is closely aligned with the ONJCRI Tumour Targeting Program. Local and international researcher collaborators can better inform their vital brain cancer research at this new Centre through innovative discovery research, and translational research involving brain cancer patients.

Scientific Project Officer Kerryn Westcott (pictured) is one of the members of this exciting new Centre. She works closely with the doctors in the brain cancer neuro-oncology team and manages the collection of brain cancer tissue and blood samples obtained from consenting patients for local and global projects. Kerryn ensures that the de-identified samples provided to scientists remain annotated with all of the relevant treatment details, including the particularly valuable series of samples that are collected throughout a patient's cancer journey.

Kerryn works closely with Centre Directors Prof Andrew Scott AM, who is ONJCRI Tumour Targeting Program Head and Austin Health Department of Molecular Imaging and Therapy Director, and Prof Hui Gan, who is Co-Director of the ONJCRI Centre of Research Excellence and Austin Health Cancer Clinical Trials Centre Director.

"Although I'm the first port of call, it's a real group effort," Kerryn said. "The Centre's aim is to make a difference to treatments available to patients with brain cancer and facilitate research studies that are finding new treatments that are more effective. We have to be better at what we're doing and that only really comes through working together."

One program already benefitting from the Centre's activity is the Low & Intermediate Grade Glioma Umbrella Study of Molecular Guided TherapieS (LUMOS) trial, a study involving patients with low and intermediate grade brain tumours, who otherwise have little if any access to clinical trials. Kerryn oversees the collection of tissue samples from this study so that they can undergo state-of-the-art molecular testing and to help identify better treatments for these patients.

Prof Scott said the Centre would make a big difference. "We're bringing on board leading experts in laboratory science, chemistry and clinical care to identify and evaluate new imaging and therapy approaches," he said. "We aim to identify and develop new therapeutics and imaging approaches that will ultimately aim to improve the outcomes of patients with brain cancer."

# PARTNERSHIPS AND COLLABORATIONS

We proactively find opportunities for collaboration and the exchange of knowledge and expertise. This ensures we can strengthen our ability to translate breakthrough cancer research into treatments that save lives.

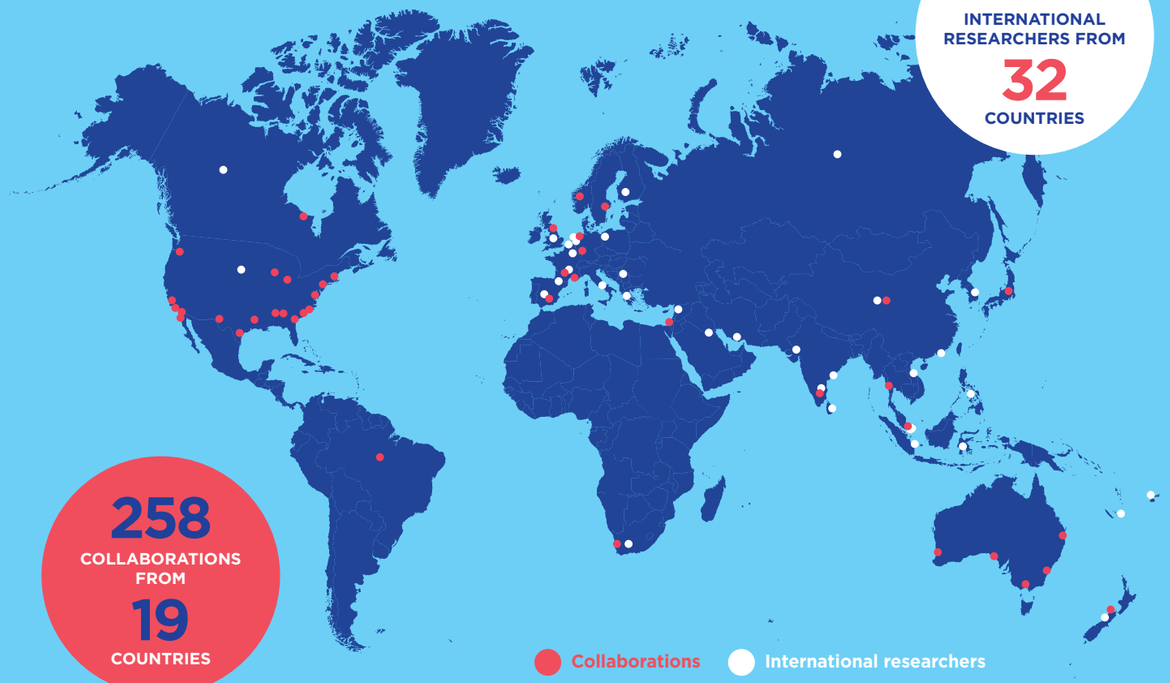
Our independent Institute is located in the Olivia Newton-John Cancer Centre, which is operated by Austin Health, a major provider of tertiary health services, research and health professional education in Victoria.

The Institute occupies three floors of dedicated research space in a purpose-built comprehensive cancer centre, where we integrate clinical medicine with laboratory and clinical research.

ONJCRI also collaborates with a wide range of national and international researchers, clinicians, industries and academia, including our partnership with La Trobe University, to enhance the depth and impact of our discoveries.

## OUR GLOBAL NETWORK

Our collaborative network with national and international organisations, leading clinicians and influential researchers enables us to deliver high-impact translational research.






## LA TROBE UNIVERSITY SCHOOL OF CANCER MEDICINE

ONJCRI is proud to be La Trobe University's School of Cancer Medicine and our Institute's Scientific Director, Prof Matthias Ernst is the inaugural Head of School.

The close relationship between ONJCRI's Faculty and their colleagues at the La Trobe University Institute of Molecular Sciences (LIMS) has provided unprecedented opportunities for collaborations and the exchange of knowledge and expertise. This enables both organisations to cross-fertilise basic research into cancer biology and to retain the pivotal interdependence that fosters creativity and underpins academic curiosity.

As La Trobe University's School of Cancer Medicine, ONJCRI attracts the university's best and brightest science graduates for their Honours degrees, which involve laboratory-based research projects. Upon completion of their Honours degrees, many students then commit themselves to a three to four-year PhD project with one of the group leaders at ONJCRI.

LA TROBE UNIVERSITY

### OUR FIRST LTU SCHOOL OF CANCER MEDICINE PHD GRADUATES

In 2019, we celebrated our first two PhD graduates from the La Trobe University School of Cancer Medicine. Both of which are already oncologists in their own right.

Congratulations to Dr David Lau who was awarded his PhD following his research on molecular targets in upper gastrointestinal cancers.

Congratulations to Dr Sagun Parakh who was awarded his PhD following his research on novel anti-ErbB antibodies in the treatment of cancer.

Sagun was also awarded the Nancy Miller Medal for outstanding PhD candidates for the exceptionally high quality of his thesis.

*Dr Mary Vail uses the confocal microscope in the ACRF Centre for Imaging the Tumour Environment*

# EXPOSING THE SECRET LIFE OF CANCER CELLS

Researchers could develop new personalised treatments by studying cancer cells in greater detail at a new imaging centre at ONJCRI.

AUSTRALIAN CANCER RESEARCH FOUNDATION

Our scientists now have the latest equipment to examine how cancer cells interact with others in their immediate cellular surrounding.

The October 2019 opening of the *ACRF Centre for Imaging the Tumour Environment* follows a $2 million Australian Cancer Research Foundation (ACRF) grant awarded to ONJCRI's Prof Matthias Ernst and his colleagues at the Institute and the La Trobe University Institute of Molecular Science (LIMS). The Centre houses state-of-the-art equipment including multiphoton and confocal microscopes, and a Nanostring molecular barcoding scanner.

With the *ACRF Centre for Imaging the Tumour Environment*, ONJCRI researchers, alongside their colleagues from many other institutions across Melbourne, will study a variety of tumour samples to investigate how tumour cells interact with their normal counterparts to better understand which drugs impact specific tumour types.

These insights will be used to improve immunotherapy and help to better match a particular treatment to a particular patient. This process, referred to as personalised cancer treatments, could eventually help clinicians to devise more precise treatment plans based on the predicted response of a patient's unique tumour and cell interactions.

ONJCRI Scientific Director Prof Matthias Ernst said the Centre would for the first time enable ONJCRI and LIMS researchers to observe how cancer cells are embedded and grow between normal cells. He said it would literally 'shine a light' on the immediate environment around a tumour, providing the information needed to develop more effective, targeted anti-cancer therapies.

"We know that tumour cells coerce and corrupt their environment to their advantage," he said. "If we understand the interactions and mechanisms they use to do this, we will better understand how to disrupt these processes that fuel the growth of tumours."



# DONORS AND SUPPORTERS

**The Olivia Newton-John Cancer Research Institute is grateful to the individuals and organisations who supported our research in 2019.**

## Individuals and Organisations

Australian Lebanon Chamber of Commerce and Industry (Vic)
Beanie Charity Golf Tournament
Blue Illusion
Freemasons Lord Northcote Lodge
Freemasons Foundation Victoria
Hector Davis
Macedonian Senior Citizens Group of Doncaster and Templestowe
Max, Sally and Sian Thomas
Moreland Primary School
Pam Stanley
Parents' and Friends' Association for Scotch College
Rightside Legal
Riverview Ladies Golf Club
Stacey Baker
Star Search 4 A Cause
State Trustees Australia Foundation
The Green Button
Thomas Atkinson
Virginia Prusa
Wellness Walk and Research Run
Anonymous Gifts (9)

## Trusts, Foundations, Industry Grants and Government Funding

American Association for Cancer Research
Australian Research Council
Austin Health
Austin Medical Research Foundation
Australasian Gastro-Intestinal Trials Group
Avner Pancreatic Cancer Foundation
Cancer Australia
Cancer Council Victoria
Department of Health and Human Services
Department of Industry, Innovation and Science
Harold Mitchell Foundation
La Trobe University
Love Your Sister Foundation
Ludwig Cancer Research
Lung Foundation Australia
Medical Research Future Fund
National Breast Cancer Foundation
National Health and Medical Research Council
Perpetual Trustee
Susan G Komen Foundation
The CASS Foundation Limited
The Ian Potter Foundation
The Jack Brockhoff Foundation
The Movember Group
The Kids Cancer Project
Tour de Cure
Victorian Cancer Agency
Victorian Comprehensive Cancer Centre
Victorian Government Operational Infrastructure and Support Program

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

Ken Stanley
Helen Edgar
Dale Bottrell
Gayle Burgess
Ladislav (Bob) Prusa

*Participants at the 2019 'The Beanie' charity golf tournament*

# 'THE BEANIE' CHARITY GOLF TOURNAMENT

There is not a golf course in the world that **Peter and Heather Wood** do not know something about.

Passionate golfers Peter and Heather have generously applied their knowledge and love of the sport to help raise funds for breast cancer research for close to 16 years.

During this time, they have organised approximately 12 charity golf tournaments, raising more than $150,000.

In 2019, their charity golf tournament – affectionately known as 'The Beanie' – raised more than $17,000 for the Translational Breast Cancer Program at ONJCRI.

Program Head, Prof Robin Anderson, has seen Peter and Heather's drive and enthusiasm to fundraise for her Program in action across many years.

Around 80 people attend the charity golf tournament, which has previously taken place at golf courses around Australia, including Port Douglas in Queensland, Barnbougle and King Island in Tasmania and most recently at the Bonville Golf Resort in northern NSW.

Robin says it is an exciting event, as like-minded golf enthusiasts come together to make a difference to cancer research.

The gratitude expressed by Robin and her team for this commitment to the Translational Breast Cancer Program cannot be overestimated.

"Their support is enormously valuable and this pledge to help cancer research at ONJCRI is admirable," she says.

"RECEIVING THESE EXTRA FUNDS GIVES US THE OPPORTUNITY TO ACQUIRE EQUIPMENT THAT WE WOULD NOT OTHERWISE BE ABLE TO PURCHASE."

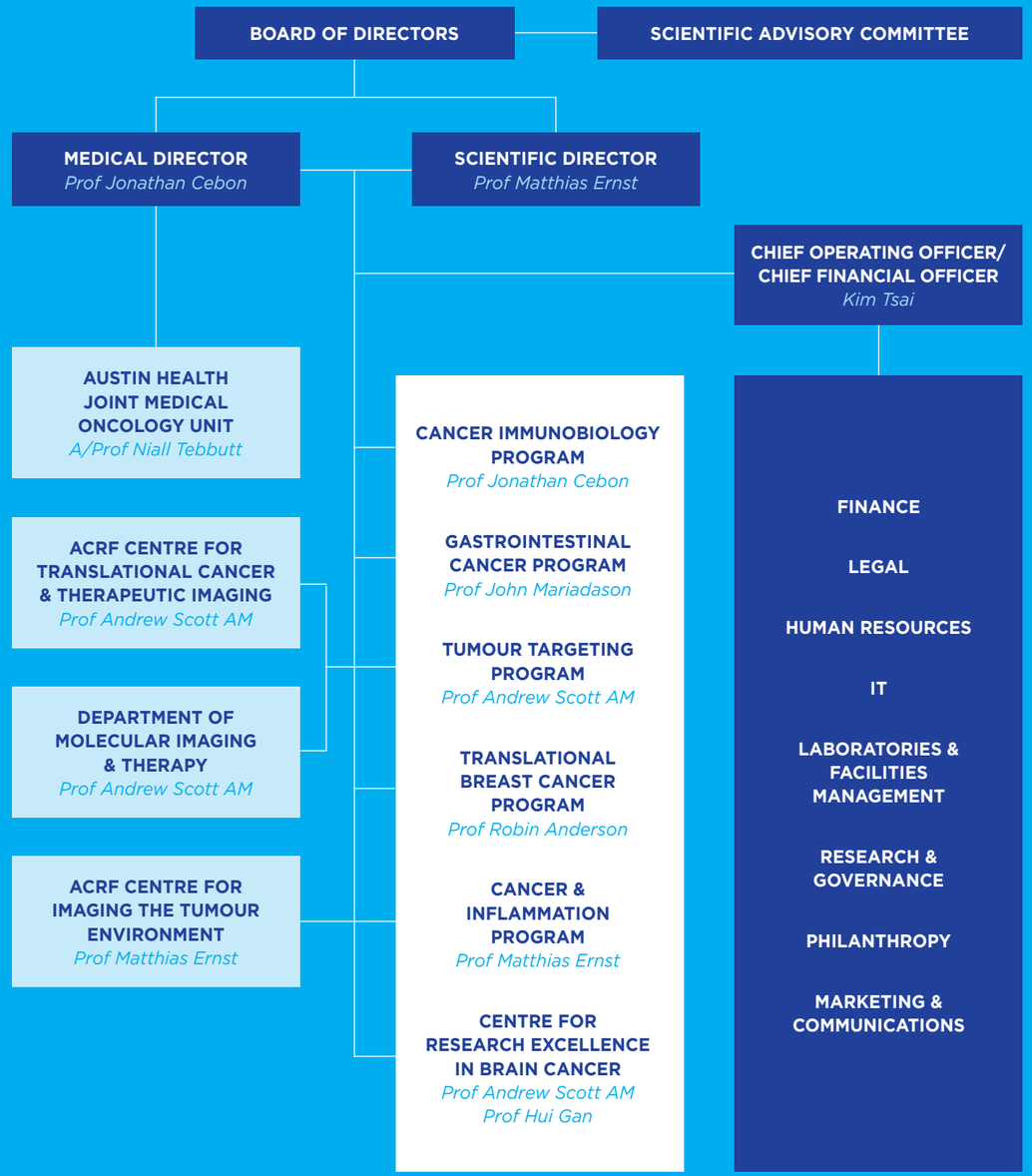
Over the years, funds raised have helped support the salaries of post-doctoral fellows and to purchase equipment, including a stereo microscope and a 10X Genomics Chromium Controller for single cell analysis that allows a more detailed examination of tumour cells than previously possible.

"We are at the forefront of discovering new molecular targets that will allow the development of improved drugs to treat breast cancer," says Robin.

"Through the generosity of people who join 'The Beanie' golf tournament, our dedicated researchers can continue their research that strives to understand the molecular mechanisms that drive breast cancer progression."



# ORGANISATIONAL CHART



# BOARD OF DIRECTORS

The **Olivia Newton-John Cancer Research Institute** is an independent organisation. Our Board of Directors governs the activities of our organisation, manages policies and provides strategic direction.

**The Hon Jenny Macklin, Chair** (joined the Board in November 2019)

Jenny Macklin is a Vice-Chancellor's Fellow at the University of Melbourne, in the School of Government. She is also the Chair of Odyssey House Victoria and a Member of the RAND Australia Advisory Board. In late 2019, Jenny was appointed by the Victorian Minister for Training and Higher Education to conduct a review of skills needed in the Victorian economy. Jenny retired from federal politics in 2019, after serving 23 years as the Federal Member for Jagajaga, the electorate in which the ONJCRI is located. Jenny was the longest serving woman in the House of Representatives and was the first woman to become the Deputy Leader of a major Australian political party. Jenny served as the Minister for Families, Housing, Community Services and Indigenous Affairs and the Minister for Disability Reform in the Rudd and Gillard Labor Governments.

**The Hon John Brumby AO, Outgoing Chair** (retired from the position of Chair in November 2019)

John Brumby is the Chancellor of La Trobe University and was previously the Treasurer and then Premier of Victoria. Since retiring from Parliament in 2010 he has become the Chair of MTAA Super, Citywide Solutions Pty Ltd, BioCurate Pty Ltd and the Melbourne Convention and Exhibition Trust. John is an Enterprise Professor at the University of Melbourne. He is active in a range of community and not-for-profit organisations including as the Chairman of the Fred Hollows Foundation and Trustee of the Como Trust.

**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 is a Director of Nelson Alexander and a Trustee of the Mary Jane Lewis Scholarship Foundation. She was also the first female director of the Collingwood Football Club. During 2019 Sally was the recipient of the McKinnon Emerging Political Leader of the Year and was awarded with the RMIT Honorary Doctorate of Law Honoris Causa.

**Richard Balderstone**

Richard Balderstone has worked in the financial and investment markets for 40 years. He is a Director of JCP Investment Partners, as well as a Trustee Director of several charitable organisations including the Baker Foundation and the Surf Life Saving Foundation. Richard was previously a Director of ABN AMRO (and BZW), a Trustee Director of the Commonwealth Public Service Superannuation Schemes (CSS/PSS) and a Director of the Australian Rail Track Corporation.

**Prof John Dewar AO**

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.

**Prof Ashley Dunn**

Prof Ashley Dunn became Head of the Molecular Biology Program at the Ludwig Institute for Cancer Research in 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.

**Dr Katherine Woodthorpe AO**

Dr Katherine Woodthorpe is currently Chair of the Bushfire and Natural Hazards CRC, Chair of the National Climate Science Advisory Group and Chair of Fishburners, Australia's largest technology startup co-working space. She is also 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.

**Dr Max Alexander** (joined the Board in December 2019)

Dr Max Alexander joined Austin Health as Interim CEO in December 2019. Max's prior hospital sector experience includes a five year stint as a CEO in the NSW public health system and Executive appointments to major health services in Victoria as Director Clinical Operations and Executive Medical Director. He has worked in the Australian public hospital sector for approximately 15 years. He is an experienced Board Director, including a number of appointments to Audit and Risk committees. He has had several years in consultant practice (including with Nous). Assignments included six months as acting CEO of Goulburn Valley Health for DHHS. Early training and experience was in General Practice, including doing a related fellowship in health services research. He also had around ten years in a health communications IT start-up.

**Sue Shilbury** (retired from the Board in December 2019)

Sue Shilbury held the position of CEO at Austin Health from early 2017 to the end of 2019. Sue's roles have included General Manager of North Shore Ryde Health Service, in which she oversaw the delivery of New South Wales Health's largest capital works program, the $1.3 billion redevelopment of Royal North Shore Hospital. Sue has also held roles as General Manager of the Central Hospital Network (South Eastern Sydney and Illawarra Health District); Director of the Division of Critical Care and Surgery at St George Hospital; and Director of Clinical Services at the Royal Hospital for Women. Sue is now the Director Children, Youth and Families at Uniting.

## SCIENTIFIC ADVISORY COMMITTEE

Our Scientific Advisory Committee regularly provides guidance and expertise to the Institute's Directors about the strategic direction of the Institute. The Committee's 2019 review helped inform and shape ONJCRI's Strategic Plan for the next 5 years.

We greatly appreciate our committee members:

**Prof David Bowtell**

**Prof Ashley Dunn, Chairman**

**Prof Michelle Haber AM**

**Prof Andy Hill**

**Prof Nick Hoogenraad AO**

**Dr Eugene Maraskovsky**

**Dr George Morstyn**

# CHIEF OPERATING OFFICER'S REPORT

**KIM TSAI**
CHIEF OPERATING AND FINANCIAL OFFICER

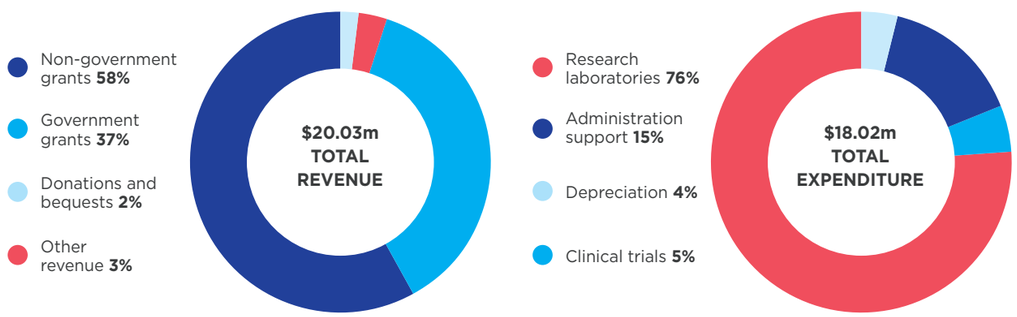
Everything we do at ONJCRI is focused on finding and developing new or better cancer treatments. As a team, we share a passion for creating real change and the strength of this team is because of the people who are involved, including researchers, research support staff, professional services staff, volunteers, partners, collaborators, donors and supporters. Thank you for your continued commitment in 2019, supporting our work, and helping us to focus our efforts on translational research that can transform cancer treatments.

We are incredibly proud to be recognised as one of Australia's leading research institutes. We know that we only get to hold this position because we combine our research with likeminded collaborators and partners, onsite and across the globe.

During 2019, we renewed our partnership with La Trobe University as the School of Cancer Medicine. We are immensely proud of the many opportunities that this partnership brings, including our role in nurturing future research leaders. We also continued our important relationships with key stakeholders including the Federal Government, Victorian Government and Austin Health. I specifically acknowledge the generosity of the Victorian Cancer Agency of the Victorian Government, who have boosted support for our researchers by investing $8m in funding over the next four years.

A large number of our researchers and their teams were awarded access to innovative grant funding which will allow them to continue their important and life-changing work. We remain ever vigilant to ensure all government, collaboration and philanthropic funding that we receive is used to maximum effect.

I want to express my heartfelt thanks to our outgoing Board Chair, The Hon John Brumby AO and our outgoing Medical Director, Prof Jonathan Cebon who both stepped down from their roles at the end of 2019. Both have been inspiring leaders who played a crucial role since the establishment of ONJCRI. Their vision and guidance over the last five years have helped to position our Institute among some of the best in country. I also welcome our incoming Board Chair, The Hon Jenny Macklin and I look forward to working with Jenny to ensure our research efforts continue to have the greatest possible impact for people living with cancer.








## Statement of Profit or Loss and Other Comprehensive Income For the Year ended 31 December 2019

| REVENUE | 2019 | 2018 |
|---|---|---|
| Grants | 18,947,611 | 15,704,485 |
| Donations and fundraising | 531,963 | 595,132 |
| Investment and other revenue | 560,246 | 468,921 |
| **Total Revenue** | **20,039,820** | **16,768,537** |
| **EXPENDITURE** | | |
| Research Laboratories | 12,839,044 | 11,297,752 |
| Clinical Trials | 874,980 | 819,781 |
| Administration Support | 3,544,907 | 3,030,594 |
| Depreciation | 767,994 | 456,542 |
| **Total Expenditure** | **18,026,925** | **15,604,669** |
| **Total Comprehensive Income** | **2,012,895** | **1,163,868** |

## Statement of Financial Position as at 31 December 2019

| ASSETS | 2019 | 2018 |
|---|---|---|
| Current assets | 10,547,575 | 11,737,762 |
| Non-current assets | 17,383,699 | 13,222,708 |
| **Total Assets** | **27,931,274** | **24,960,470** |
| **LIABILITIES** | | |
| Current liabilities | 21,239,793 | 20,343,316 |
| Non-current liabilities | 278,491 | 217,063 |
| **Total Liabilities** | **21,518,284** | **20,560,379** |
| **Net Assets** | **6,412,990** | **4,400,091** |
| **EQUITY** | | |
| **Total Equity** | **6,412,990** | **4,400,091** |

*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

**Dr Jessica Da Gama Duarte**
Tumour Immunobiology Laboratory

International Congress of Immunology, Beijing, China. *Circulating antibodies as novel cancer biomarkers.*

**A/Prof Alex Dobrovic**
Translational Genomics and Epigenomics Laboratory

Circulating Cell-free DNA Symposium, Molecular Medicine TriConference, San Francisco. *Clinical applications of droplet digital PCR for liquid biopsies.*

AACR Annual Meeting 2019, Atlanta. *A case-control study of constitutional BRCA1 methylation in a mammographically screened cohort.*

4th Asian Pacific droplet digital PCR Symposium. Hong Kong. *Expanding the ddPCR toolbox.*

**Prof Matthias Ernst**
Cancer and Inflammation Laboratory

Innate and Non-Classical Immune Cells in Cancer Immunotherapy, Keystone, Colorado, USA. *Targeting the myeloid-cell specific kinase HCK improves anti-tumor immunity.*

Cell Plasticity in Colorectal Carcinogenesis Symposium, Frankfurt, Germany. *Limiting GI – cancer growth beyond interference with oncogenic driver mutations.*

**A/Prof Peter Janes**
Receptor Biology Laboratory

Keystone Myeloid Cells conference, Santa Fe, New Mexico, USA. *A role for the cell guidance receptor EphA3 on myeloid-derived cells in the tumour microenvironment.*

Proteases in TiME, Prato, Italy. Seminar: *Targeting the ADAM10 metalloprotease in tumours and the TME.*

**Dr Sze Ting Lee**
Tumour Targeting Laboratory

Society of Nuclear Medicine and Molecular Imaging Annual Meeting, Anaheim, USA. *PET/CT in Staging and Restaging of Metastatic Melanoma.*

14th International Conference on Radionuclide Therapy, Nanjing, China. *Molecular Imaging of Hypoxia in Malignant Diseases.*

**Dr Delphine Merino**
Tumour Progression and Heterogeneity Laboratory

European Network of Breast Development and Cancer, Weggis, Switzerland. *Genetic and optical barcoding to follow tumour & metastasis heterogeneity.*

**Dr Bhupinder Pal**
Cancer Single Cell Genomics Laboratory

11th European Network of Breast Development and Cancer Laboratories (ENBDC) Workshop, Switzerland. *Understanding epithelial lineage relationships in breast tissue microenvironment.*

**Dr Ashleigh Poh**
Cancer and Inflammation Laboratory

3rd International Conference on Cytokine Signalling in Cancer, Rhodes Island, Greece. *Targeting HCK to enhance anti-tumour responses to immunotherapy.*

**Dr Normand Pouliot**
Matrix Microenvironment and Metastasis Laboratory

University of Munster, Muenster, Germany. *Investigating mechanisms of resistance to tyrosine kinase inhibitors to enhance their efficacy against brain-metastatic HER2 breast cancer.*

Centre de Recherches en Cancérologie de Toulouse (CRCT), Toulouse, France. *Tyrosine kinase inhibitors for the treatment of HER2+ve breast cancer brain metastasis.*

**Prof Andrew Scott AM**
Tumour Targeting Laboratory

Society of Nuclear Medicine and Molecular Imaging Annual Meeting, Anaheim, USA. Plenary: *Oncology and Therapy Highlights lecture.*

Memorial Sloan-Kettering Cancer Center, New York, USA. *Molecular imaging and therapy in brain cancer.*

Columbia University Medical Center, New York, USA. *Novel approaches for the imaging and therapy of brain tumours.*

Korean Society of Nuclear Medicine 58th Annual Meeting, Seoul, Korea. Plenary: *Health Technology Assessments for Nuclear Medicine – Challenges and Opportunities.*

Hwansun Molecular Imaging Conference, Gwanju, Korea. Henry Bom Lecture: *Molecular Imaging in Drug Discovery and Development.*

Cyprus Society of Nuclear Medicine conference, Limassol, Cyprus. Plenary: *Tumour Markers Imaging.*





# OUR PUBLICATIONS


**1.** Anderson, N. J., J. E. Jackson, M. Wada, M. Schneider, M. Poulsen, M. Rolfo, M. Fahandej, H. Gan and V. Khoo. "The changing landscape of head and neck cancer radiotherapy patients: is high-risk, prolonged feeding tube use indicative of on-treatment weight loss?" J Med Radiat Sci. (2019)

**2.** Anderson, R. L., T. Balasas, J. Callaghan, R. C. Coombes, J. Evans, J. A. Hall, S. Kinrade, D. Jones, P. S. Jones, R. Jones, J. F. Marshall, M. B. Panico, J. A. Shaw, P. S. Steeg, M. Sullivan, W. Tong, A. D. Westwell, J. W. A. Ritchie, U. K. Cancer Research and C. R. C. A. M. W. G. Cancer Therapeutics. "A framework for the development of effective anti-metastatic agents." Nat Rev Clin Oncol 16(3): 185-204. (2019)

**3.** Arnaud-Coffin, P., D. Maillet, H. K. Gan, J. J. Stelmes, B. You, S. Dalle and J. Peron. "A systematic review of adverse events in randomized trials assessing immune checkpoint inhibitors." Int J Cancer. (2019)

**4.** Arulananda, S., H. Do, G. Rivalland, Z. Loh, A. Musafer, E. Lau, P. Mitchell, A. Dobrovic and T. John. "Standard dose osimertinib for erlotinib refractory T790M-negative EGFR-mutant non-small cell lung cancer with leptomeningeal disease." J Thorac Dis 11(5): 1756-1764. (2019)

**5.** Arulananda, S., P. Mitchell and T. John. "DDR Alterations as a Surrogate Marker for TMB in SCLC - Use it or Lose it?" J Thorac Oncol 14(9): 1498-1500. (2019)

**6.** Baladakis, J., M. Perera, D. Bolton, N. Lawrentschuk and A. Adam. "Is There an Optimal Curative Option in HIV-Positive Men with Localized Prostate Cancer? A Systematic Review." Curr Urol 12(4): 169-176. (2019)

**7.** Barthel, F. P., K. C. Johnson, F. S. Varn, A. D. Moskalik, G. Tanner, E. Kocakavuk, K. J. Anderson, O. Abiola, K. Aldape, K. D. Alfaro, D. Alpar, S. B. Amin, D. M. Ashley, P. Bandopadhayay, J. S. Barnholtz-Sloan, R. Beroukhim, C. Bock, P. K. Brastianos, D. J. Brat, A. R. Brodbelt, A. F. Bruns, K. R. Bulsara, A. Chakrabarty, A. Chakravarti, J. H. Chuang, E. B. Claus, E. J. Cochran, J. Connelly, J. F. Costello, G. Finocchiaro, M. N. Fletcher, P. J. French, H. K. Gan, M. R. Gilbert, P. V. Gould, M. R. Grimmer, A. Iavarone, A. Ismail, M. D. Jenkinson, M. Khasraw, H. Kim, M. C. M. Kouwenhoven, P. S. LaViolette, M. Li, P. Lichter, K. L. Ligon, A. K. Lowman, T. M. Malta, T. Mazor, K. L. McDonald, A. M. Molinaro, D. H. Nam, N. Nayyar, H. K. Ng, C. Y. Ngan, S. P. Niclou, J. M. Niers, H. Noushmehr, J. Noorbakhsh, D. R. Ormond, C. K. Park, L. M. Poisson, R. Rabadan, B. Radlwimmer, G. Rao, G. Reifenberger, J. K. Sa, M. Schuster, B. L. Shaw, S. C. Short, P. A. S. Smitt, A. E. Sloan, M. Smits, H. Suzuki, G. Tabatabai, E. G. Van Meir, C. Watts, M. Weller, P. Wesseling, B. A. Westerman, G. Widhalm, A. Woehrer, W. K. A. Yung, G. Zadeh, J. T. Huse, J. F. De Groot, L. F. Stead, R. G. W. Verhaak and G. Consortium. "Longitudinal molecular trajectories of diffuse glioma in adults." Nature 576(7785): 112-120. (2019)

**8.** Behren, A., E. W. Thompson, R. L. Anderson and P. T. Ferrao. "Editorial: Cancer Plasticity and the Microenvironment: Implications for Immunity and Therapy Response." Front Oncol 9: 276. (2019)

**9.** Berghen, C., M. Albersen, P. Blanchard, A. Bossi, A. Briganti, C. Cozzarini, K. Decaestecker, V. Fonteyne, K. Haustermans, S. Joniau, D. Lim Joon, V. Khoo, P. L. Nguyen, P. Ost, G. Villeirs, C. Vulsteke, A. Zietman and G. De Meerleer. "Readressing the rationale of irradiation in stage I seminoma guidelines: a critical essay." BJU Int 124(1): 35-39. (2019)

**10.** Bodei, L., A. Chiti, I. M. Modlin, A. M. Scott and H. Schoder. "The Path to the Future: Education of Nuclear Medicine Therapeutic Specialists as Responsible Physicians." J Nucl Med 60(12): 1663-1664. (2019)

**11.** Bolton, D. and M. Frydenberg (2019). "From indecision to precision: advances in imaging in metastatic prostate cancer." World J Urol 37(7): 1237. (2019)

**12.** Brown, H., J. Vansteenkiste, K. Nakagawa, M. Cobo, T. John, C. Barker, A. Kohlmann, A. Todd, M. Saggese, J. Chmielecki, A. Markovets, M. Scott and S. S. Ramalingam. "Brief Report: Programmed Cell Death Ligand 1 Expression in Untreated EGFR Mutated Advanced Non-Small Cell Lung Cancer and Response to Osimertinib versus Comparator in FLAURA." J Thorac Oncol. (2019)

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**14.** Chang Lee, R. and N. Tebbutt. "Systemic treatment of advanced hepatocellular cancer: new hope on the horizon." Expert Rev Anticancer Ther 19(4): 343-353. (2019)

**15.** Chapman, J., A. Naweed, C. Wilson and J. Dorrian. "Investigating the relationship between work day sleep, days off sleep, and cardiovascular risk in Australian train drivers." Ind Health 57(6): 691-700. (2019)

**16.** Cheung, Y. M., S. K. Ramchand, B. Yeo and M. Grossmann. "Cardiometabolic Effects of Endocrine Treatment of Estrogen Receptor-Positive Early Breast Cancer." J Endocr Soc 3(7): 1283-1301. (2019)

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**18.** Chia, P. L., A. M. Scott and T. John. "Epidermal growth factor receptor (EGFR)-targeted therapies in Mesothelioma." Expert Opin Drug Deliv. (2019)

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**23.** David, S., J. Tan, P. Savas, M. Bressel, D. Kelly, F. Foroudi, S. Loi and S. Siva. "Stereotactic ablative body radiotherapy (SABR) for bone only oligometastatic breast cancer: A prospective clinical trial." Breast 49: 55-62. (2020)

**24.** Doebele, R. C., A. Drilon, L. Paz-Ares, S. Siena, A. T. Shaw, A. F. Farago, C. M. Blakely, T. Seto, B. C. Cho, D. Tosi, B. Besse, S. P. Chawla, L. Bazhenova, J. C. Krauss, Y. K. Chae, M. Barve, I. Garrido-Laguna, S. V. Liu, P. Conkling, T. John, M. Fakih, D. Sigal, H. H. Loong, G. L. Buchschacher, Jr., P. Garrido, J. Nieva, C. Steuer, T. R. Overbeck, D. W. Bowles, E. Fox, T. Riehl, E. Chow-Maneval, B. Simmons, N. Cui, A. Johnson, S. Eng, T. R. Wilson, G. D. Demetri and i. trial. "Entrectinib in patients with advanced or metastatic NTRK fusion-positive solid tumours: integrated analysis of three phase 1-2 trials." Lancet Oncol 21(2): 271-282.(2020)

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**27.** Dufton, P. H., A. Drosdowsky, M. F. Gerdtz and M. Krishnasamy. "Socio-demographic and disease related characteristics associated with unplanned emergency department visits by cancer patients: a retrospective cohort study." BMC Health Serv Res 19(1): 647. (2019)

**28.** Duncan, C., D. L. Joon, N. Lawrentschuk, T. Jenkins, M. Schneider, V. Khoo, M. Chao, M. Lawlor, R. O'Meara, C. Berry, A. Viotto, K. Brown, M. Wada, F. Foroudi and S. Sengupta. "Fiducial markers: can the urologist do better?" World J Urol 37(7): 1281-1287. (2019)

**29.** Eissmann, M. F., C. Dijkstra, A. Jarnicki, T. Phesse, J. Brunnberg, A. R. Poh, N. Etemadi, E. Tsantikos, S. Thiem, N. D. Huntington, M. L. Hibbs, A. Boussioutas, M. A. Grimbaldeston, M. Buchert, R. J. J. O'Donoghue, F. Masson and M. Ernst. "IL-33-mediated mast cell activation promotes gastric cancer through macrophage mobilization." Nat Commun 10(1): 2735. (2019)

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**111.** Thilakasiri, P. S., R. S. Dmello, T. L. Nero, M. W. Parker, M. Ernst and A. L. Chand. "Repurposing of drugs as *STAT3* inhibitors for cancer therapy." Semin Cancer Biol. (2019)

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**117.** Williams, D. S., D. Mouradov, C. Browne, M. Palmieri, M. J. Elliott, R. Nightingale, C. G. Fang, R. Li, J. M. Mariadason, I. Faragher, I. T. Jones, L. Churilov, N. C. Tebbutt, P. Gibbs and O. M. Sieber. "Overexpression of TP53 protein is associated with the lack of adjuvant chemotherapy benefit in patients with stage III colorectal cancer." Mod Pathol. (2019)

**118.** Yap, M. L., J. D. McFadyen, X. Wang, M. Ziegler, Y. C. Chen, A. Willcox, C. J. Nowell, A. M. Scott, E. K. Sloan, P. M. Hogarth, G. A. Pietersz and K. Peter. "Activated platelets in the tumor microenvironment for targeting of antibody-drug conjugates to tumors and metastases." Theranostics 9(4): 1154-1169. (2019)

**119.** Yoshino, O., V. Muralidharan, A. Dobrovic and S. K. Goh. "Letter to the editor: Elevated Plasma Levels of Cell-Free DNA During Liver Transplantation Are Associated With Activation of Coagulation." Liver Transpl. (2019)

**120.** Young, A. R., J. D. G. Duarte, R. Coulson, M. O'Brien, S. Deb, A. Lopata, A. Behren, S. Mathivanan, E. Lim and E. Meeusen. "Immunoprofiling of Breast Cancer Antigens Using Antibodies Derived from Local Lymph Nodes." Cancers (Basel) 11(5). (2019)

**121.** Zhang, X., J. Z. Tang, I. A. Vergara, Y. Zhang, P. Szeto, L. Yang, C. Mintoff, A. Colebatch, L. McIntosh, K. A. Mitchell, E. Shaw, H. Rizos, G. V. Long, N. Hayward, G. A. McArthur, A. T. Papenfuss, K. F. Harvey and M. Shackleton. "Somatic hypermutation of the YAP oncogene in a human cutaneous melanoma." Mol Cancer Res. (2019)


EXTERNAL AND INTERNATIONAL

# LECTURES AT ONJCRI*

*does not include speakers from ONJCRI or Austin Health

**A/Prof Jyotsna Batra**
Queensland University of Technology, Brisbane
*Dissecting the genetic complexity of prostate cancer.*

**Dr Steve Baylin**
Johns Hopkins, Baltimore USA
*A key role for abnormalities of DNA methylation in initiation of, and risk for, colon cancer.*

**Prof Jonathan Blackburn**
University of Cape Town, South Africa
*Discovery of proteomic and autoantibody-based cancer biomarkers for precision medicine.*

**Dr Philippe Bouillet**
The Walter and Eliza Hall Institute of Medical Research
*Impaired post-transcriptional regulation of TNF causes developmental defects and inflammatory diseases.*

**Prof Carole Bourquin**
University of Geneva, Switzerland
*New targets to enhance the anti-tumour immune response.*

**Prof David Bowtell**
Peter MacCallum Cancer Centre
*Going to extremes: Studies on ovarian cancer exceptional responders.*

**Dr Margs Brennan**
The Walter and Eliza Hall Institute of Medical Research
*Developing the humanised MCL-1 mouse model for evaluating MCL-1 as a drug target for cancer therapy.*

**Dr Christine Chaffer**
Garvan Institute of Medical Research
*Modulating cancer cell plasticity to inhibit metastasis.*

**Prof Arlene Chan**
Curtin University, Perth
*CNS disease in breast cancer: Clinical burden and systemic options.*

**Prof Weisan Chen**
La Trobe Institute for Molecular Science
*Host CD8a+ and CD103+ DCs prime transplant antigen-specific CD8+ T cells via MHC-peptide cross-dressing.*

**A/Prof Simon Conn**
Flinders University, Adelaide
*Going in circles: Formation and function of circular RNAs.*

**Dr Thomas Cox**
Garvan Institute of Medical Research
*The dynamic ECM landscape in cancer progression and metastasis.*

**Prof Sarah-Jane Dawson**
Peter MacCallum Cancer Centre
*Blood worth bottling: Circulating tumour DNA in cancer.*

**Prof Paul Donnelly**
University of Melbourne
*Diagnosis and therapy with radio-labelled peptides and antibodies: Copper and zirconium theranostic radiopharmaceuticals.*

**Dr Lisa Ebert**
University of South Australia, Adelaide
*CAR-T cell therapy for glioblastoma.*

**Dr Caroline Ford**
UNSW, Sydney
*Hear the ROR! The role of ROR1 and ROR2 in ovarian and endometrial cancer.*

**Dr David Gallego-Ortega**
Garvan Institute of Medical Research
*Understanding the contribution of the tumour microenvironment to breast cancer metastasis and therapy resistance at single cell resolution.*

**Prof Dale Godfrey**
The Peter Doherty Institute for Infection and Immunity
*Development and diversity of MR1-restricted T cells.*

**Dr Goknur Giner**
The Walter and Eliza Hall Institute of Medical Research
*Statistical methods to develop more precise strategies for cancer research.*

**Dr Joanna Groome**
The Walter and Eliza Hall Institute of Medical Research
*Multiple paths of T follicular helper cell differentiation: Dissecting mechanisms of Immune diversity.*

**Dr Fernando Guimares**
The Walter and Eliza Hall Institute of Medical Research
*The emergence of natural killer cells as a major target in immunotherapy.*

**Prof Nikolas Haass**
The University of Queensland, Brisbane
*The role of the extracellular matrix architecture in melanoma proliferation and invasion.*

**Dr Anis Hamid**
University of Melbourne
*In pursuit of genomic determinants of aggressive prostate cancer.*

**Prof Phil Hansbro**
University of Newcastle, NSW
*Understanding pathogenesis to develop new treatments for chronic respiratory diseases and lung cancer.*

**Dr Kate Lawlor**
Hudson Institute of Medical Research
*Cell death-induced pathways to inflammasome activation.*

**Dr Kyren Lazarus**
University of Cambridge, UK
*BCL11A: A tale of two cancers.*

**Prof Peter Leedman**
The University of Western Australia, Perth
*RNA therapeutics for cancer – dawn of a new era.*

**A/Prof Laura Mackay**
The Peter Doherty Institute for Infection and Immunity
*Local immunity by tissue-resident lymphocytes.*

**Dr Ian Majewski**
The Walter and Eliza Hall Institute of Medical Research
*Bad blood: Tracing the origins of leukaemia.*

**Dr Yu (Rebecca) Miao**
Stanford University, USA
*Neutralizing PD-L1 and PD-L2 for enhancing the efficacy of immune checkpoint therapies.*

**Dr Samantha Oakes**
Garvan Institute of Medical Research
*Flicking the switch off; targeting MCL-1 in cancer.*

**Prof Chris Ormandy**
Garvan Institute of Medical Research
*ELF5 and resistance to hormone therapy of breast cancer.*

**Dr Alexander Pinto**
Baker Heart and Diabetes Institute
*Mapping the cardiac cellular landscape in health and disease.*

**Prof Anthony Purcell**
Monash University
*Insights into the antigenic landscape of melanoma.*

**Prof Gail Risbridger**
Monash University
*Prostate cancer stem cells: Research discoveries that inform changes to treatment.*

**Dr Charis Teh**
The Walter and Eliza Hall Institute of Medical Research
*Capturing the cellular gymnastics of survival and killer proteins in blood cancers by mass cytometry (CyTOF).*

**Dr James Whittle**
Peter MacCallum Cancer Centre
*Cell survival pathways and mechanisms of response in breast cancer.*

**Dr Dan Worthley**
SAHMRI, Adelaide
*The origin and contribution of stromal factors in colorectal cancer.*

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