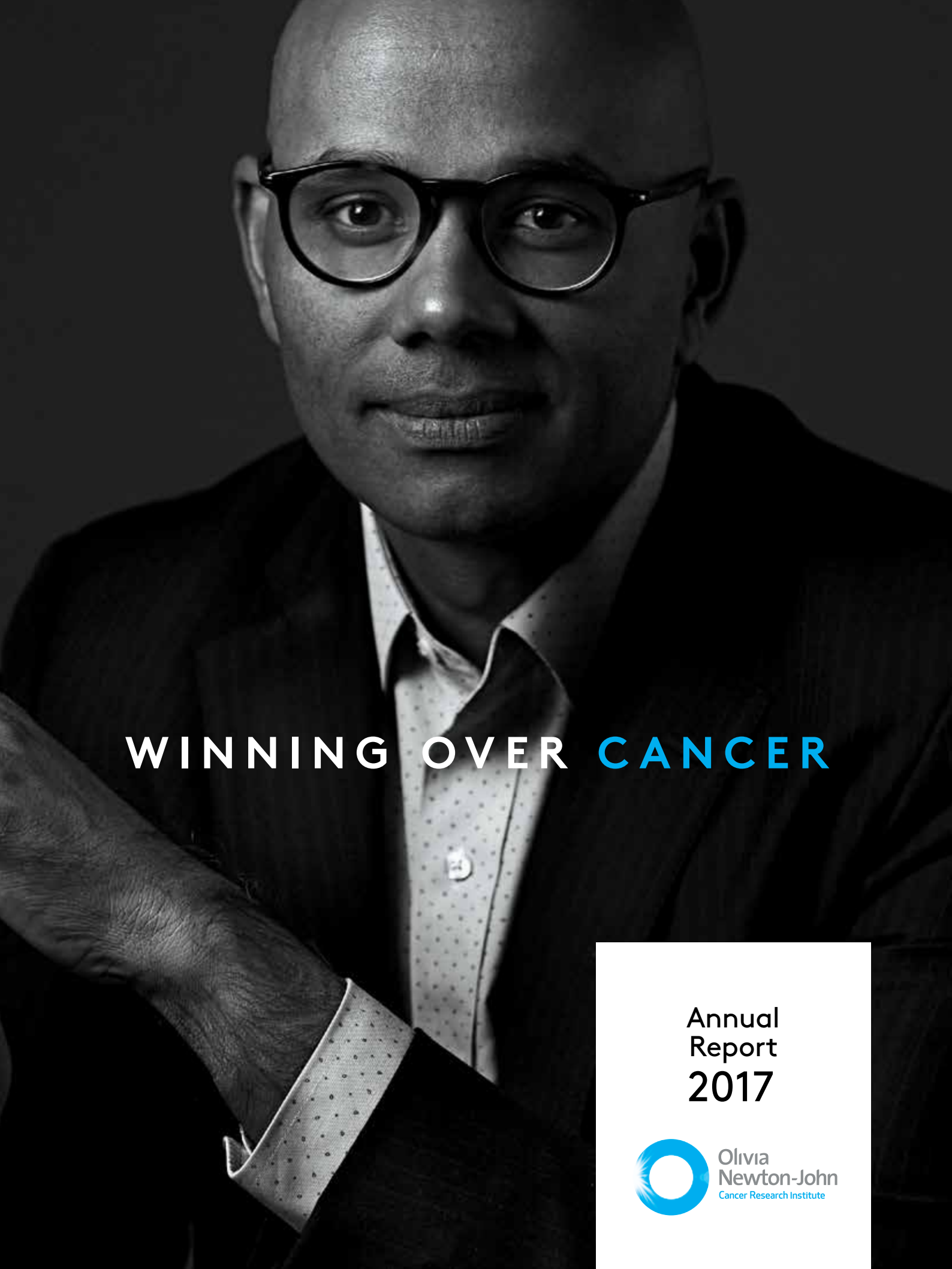


# WINNING OVER CANCER

Annual Report 2017

Olivia Newton-John Cancer Research Institute

CONTENTS



*Front cover image: Dr Tom John is tackling the biggest cancer killer with translational research that combines laboratory work and clinical practice to find new hope for patients (full story on page 10).*



# Message from our founding champion, Olivia Newton-John AO, OBE

During the last year, I have been overwhelmed by the outpouring of love and support that followed the news that my cancer had returned.

Of course, it has been a personal challenge but I feel privileged to be able to give hope to others who are going through cancer. It's a challenging and amazing journey that I have been through before and I am winning over again!

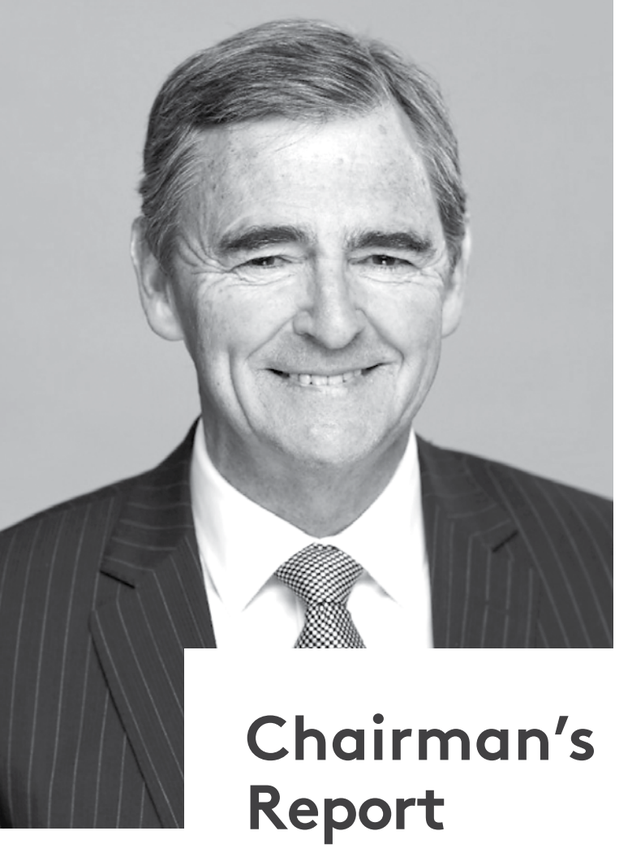
I am grateful for and incredibly proud of the important work being done at the Olivia Newton-John Cancer Institute. It is hugely reassuring to know that scientists, doctors, volunteers and other healthcare practitioners are working around the clock to win over cancer and that they are helping so many people who come to the Centre for support.

The ONJCRI holds a special place in my heart in this regard. Medical research and scientific endeavour run through my veins - and although I chose a musical path, I am proud to come from a family of scientists, doctors and artists. Creativity is the magic that links science and the arts, and it's wonderful to know that so many smart, creative young women and men are devoting their lives to find a cure, or to make cancer a manageable disease.

Thank you to all the scientists and staff at ONJCRI who are making such an important contribution to the progress in this global endeavour. And thank you to our many friends and supporters whose generosity is helping the ground-breaking research at the Institute.

## LOVE AND LIGHT

Olivia



# Chairman's Report

## THE HON JOHN BRUMBY AO

CHAIRMAN OF THE BOARD

As each year passes, I continue to be inspired by the people, passion and perseverance at ONJCRI, and I am truly privileged to be Chair of the Board.

Our scientists and clinicians work tirelessly at the coalface of cancer care and at the cutting edge of research, clinical trials and technology. This makes the Institute a leader in the development of experimental and breakthrough treatments for cancer of the brain, breast, bowel and lung, as well as lymphoma and melanoma.

In 2017 the Institute continued to punch above its weight with a unique formula that achieves results.

Our clinicians and researchers work closely together to combine their laboratory work and patient care, and we have established clinician scientist fellowships to further enable this model. The integration of laboratory bench and bedside helps refine our research, make new discoveries and create more targeted treatments for patients.

Our researchers and clinicians were also involved in a wide variety of clinical cancer trials, with Institute investigators leading 128 trials in 2017.

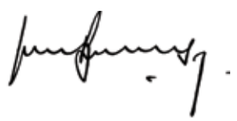
These trials give patients access to potential new treatments, such as immunotherapies and targeted therapies. They are an integral part of our journey in finding more effective treatments. You can read the personal stories of two patients and their trial experiences in this report.

ONJCRI's collaborative power is backed by our partnerships, and we continued to build these relationships through the establishment of a new ACRF Tumour Imaging Centre and the deepening of our ties with La Trobe University.

Most importantly, we have spent the year giving hope to patients; there are people who will be with us tomorrow as a result of our efforts.

I thank the members of the ONJCRI Board, who freely donate their time and expertise to guide the Institute, and the Executive Officers who oversee the day-to-day business of the Institute.

And, lastly, I want to express my gratitude to the donors and supporters who bolster our quest to win over cancer. I trust that you will enjoy reading about our work in this report.



THE HON JOHN BRUMBY AO



## YEAR AT A GLANCE

**89** Staff

**51%** Female staff

**25** PhD & Honours students

**29%** PhD students with medical training

**13%** Clinician scientists (% of research staff)

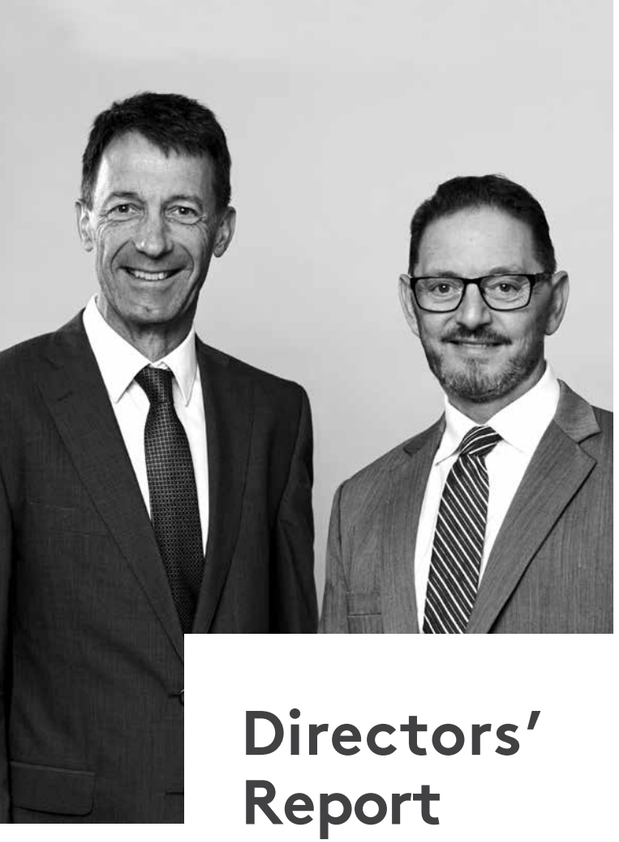
**128** Clinical trials led by Institute investigators

**170** Research collaborations

**$26.9M** Secured external funding

**25%** NHRMC grant success rate

**130** ONJCRI scientific papers published



# Directors' Report

**PROF JONATHAN CEBON**
MEDICAL DIRECTOR

**PROF MATTHIAS ERNST**
SCIENTIFIC DIRECTOR

We were recently asked to describe what makes ONJCRI an exceptional medical research institute. Our response? Aside from excellence, creativity and effectiveness, it is our passion for clinical translation – a process of turning great scientific discoveries from the laboratory into clinical practice, and taking observations from our patients back to the laboratory to understand the underlying biology.

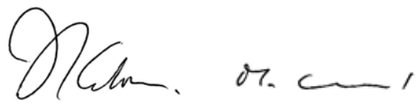
There are many great medical research institutes that study fundamental questions about cancer and excellent hospitals that offer wonderful care. But very few have managed to achieve the critical mix where scientists, doctors, patients and families collaborate to make an impact on cancer care. This ability to partner and collaborate is what motivates us and drives the excellence showcased in this year's annual report.

During 2017 ONJCRI increased the strength and breadth of our science by recruiting new laboratory teams such as the Tumour Progression & Heterogeneity Laboratory. We received wide acclaim for our clinician scientists who developed better brain cancer treatments, and the very sad news of Olivia's returned breast cancer put our breast cancer dormancy research into sharp focus. Meanwhile, our ongoing work in lung, colon and other gastrointestinal cancers, lymphoma and melanoma remained strong areas of focus and achievement, both in the laboratory and at the bedside.

Within our laboratory programs, we continued to develop new non-invasive blood tests to improve diagnosis and better monitor a patient's response to cancer treatments. Our disease-based research was complemented by our pursuit to better understand cell death and the interplay between cancer, inflammation and immunity as processes important for many types of cancers.

The Institute could not succeed without the diligent support of a dedicated Board of Directors and Scientific Advisory Committee, our partnership with La Trobe University and the broader Austin Health campus, and most importantly the financial support of various granting bodies and philanthropic donations.

We trust you will enjoy reading about our work in this report, and we invite friends and supporters to visit us and learn more about our work, how you can support the Institute's continuous growth and how, as Olivia puts it, we can "win over cancer".



PROF JONATHAN CEBON / PROF MATTHIAS ERNST





# FLICKING THE SWITCH ON COLON CANCER'S OWN KILLER

Extending the life expectancy for colon cancer patients and improving their quality of life has driven Prof John Mariadason for the last two decades.

"When I started in the field, the life expectancy was about 12 months for a patient with advanced colon cancer. I've seen that improve to about 30 months now," says John, who leads the Oncogenic Transcription Laboratory.

"I've also seen progress in the treatment of other cancers that have been historically very very difficult to manage. That has given me and my colleagues around the globe the conviction that we can and will achieve major breakthroughs for colon cancer."

John's team is one step closer to that breakthrough with its latest research findings, which are part of a PhD being done by Janson Tse. Last year the team revealed that a class of drugs commonly used to halt the growth of leukemias and lymphomas could be used to potentially target and kill colon cancer cells.

The class of drugs, known as HDAC inhibitors, block proteins that drive the growth of cancer cells in leukemia, lymphoma, breast cancer and lung cancer. The secret of how these HDAC inhibitors work in cancer cells? John's team discovered that these drugs activate a gene called ATF3.

"We discovered that turning ATF3 on is required for killing cancer cells. So ATF3 is not just a marker, it is actually functionally important," John says.

The implications of these findings are likely to be significant. "We now have a potential test we can apply to a patient. All we need to do is treat a sample of a patient's tumour cells with HDAC inhibitors in the lab, and within a matter of hours we know if this gene is turned on and whether a tumour is likely to respond to this treatment," he says.

John estimates this diagnostic test could lead to the development of a tailored treatment for up to one in five patients with colon cancer, and that would be significant progress given the limited treatment options for these patients.

"There are probably five or six treatments that are approved at the moment for colon cancer and often patients will be given all of those and yet their cancers will still keep growing," he says. "Our exciting finding needs to be tested in the clinic, but we have a way forward to safely test a new treatment for patients with colon and other solid tumours, which is urgently needed."

# REDUCING THE COSTS OF LUNG CANCER MISDIAGNOSIS

Misdiagnosis of lung cancer comes at a significant personal and public cost. When lung cancer patients relapse, the T790M mutation in the EGFR gene is frequently the culprit and a new, expensive 'super' drug offers considerable hope of survival.

However, administration of the drug is based on a test that often gives a so-called false positive reading, meaning that it indicates the presence of the EGFR T790M mutation, although this mutation is absent.

"Imagine a patient is falsely diagnosed for having a lung cancer with the EGFR T790M mutation," says Associate Prof Alex Dobrovic, the leader of the Translational Genomics & Epigenomics Laboratory. "There is a drug that costs tens of thousands of dollars a year, and you pay for that and then you say, 'Oh, actually we have found out that the mutation in the tumour was wrongly diagnosed.' A lot of money is going to be wasted and patients won't see any benefits."

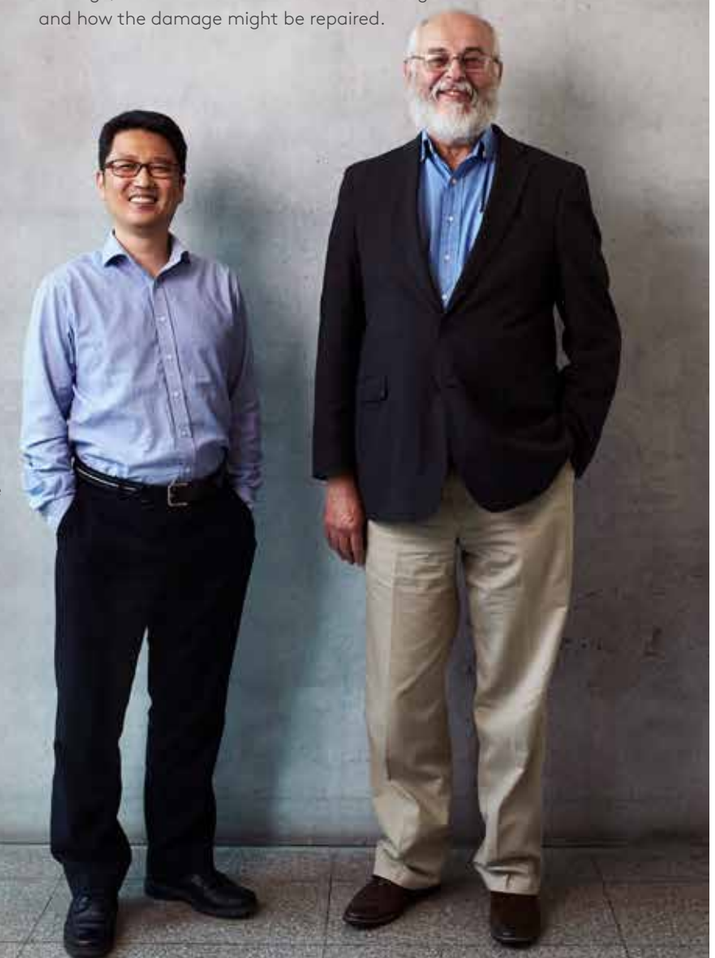
Really it's a wake-up call for many of us.

Alex's team has found a simple way to reduce false positive test outcomes of this lung cancer mutation by identifying DNA damage in formalin-preserved tumour tissue and pre-treating it with an enzyme called thymine-DNA glycosylase. Best of all, the benefits of this finding can be rolled out almost immediately to clinicians and patients.

"The more scientists know about our discovery, the more they will recognise potential problems with the accuracy of genetic tests and they will start to modify their tests," says Alex. "Really it's a wake-up call for many of us: this is a mutation that we should be very careful in calling, especially if it seems to be present in low levels."

The research, published in the journal *Clinical Chemistry*, was led by Dr Hongdo Do, a postdoctoral research fellow in Alex's team and regarded by Alex as "perhaps the best scientist working in this space in Australia".

Hongdo says there is still much to learn about EGFR T790M and how damaged DNA in test samples can affect the accuracy of genetic tests. Future research needs to identify other forms of DNA damage, understand what causes the damage and how the damage might be repaired.



# SUPPRESSING CANCER CELL CORRUPTION

The Cancer & Inflammation Laboratory hit the headlines last year when it halted the growth of bowel cancer by preventing a type of immune cell from 'nursing' cancer cells.

Prof Matthias Ernst and his team identified a 'molecular switch' in macrophages that cancer cells corrupt to stop these white blood cells from doing an essential immune-system role. This switch is a protein called Haemopoietic Cell Kinase (HCK), which the team successfully targeted with a drug-like molecule to inhibit the growth of bowel cancer.

Macrophages play a dual role in the immune system – they can act as 'garbage collectors' that gobble up dead and unwanted cells, or as 'nurses' that promote wound healing after an injury or infection.

"What we have discovered is a protein that acts as a switch between the gobbling role and the wound-healing role," says Matthias, who worked with Dr Robert O'Donoghue and Dr Ashleigh Poh.

"It turns out that the cancer cells corrupt macrophages so that their HCK protein remains active and forces macrophages to retain their wound-healing characteristics."

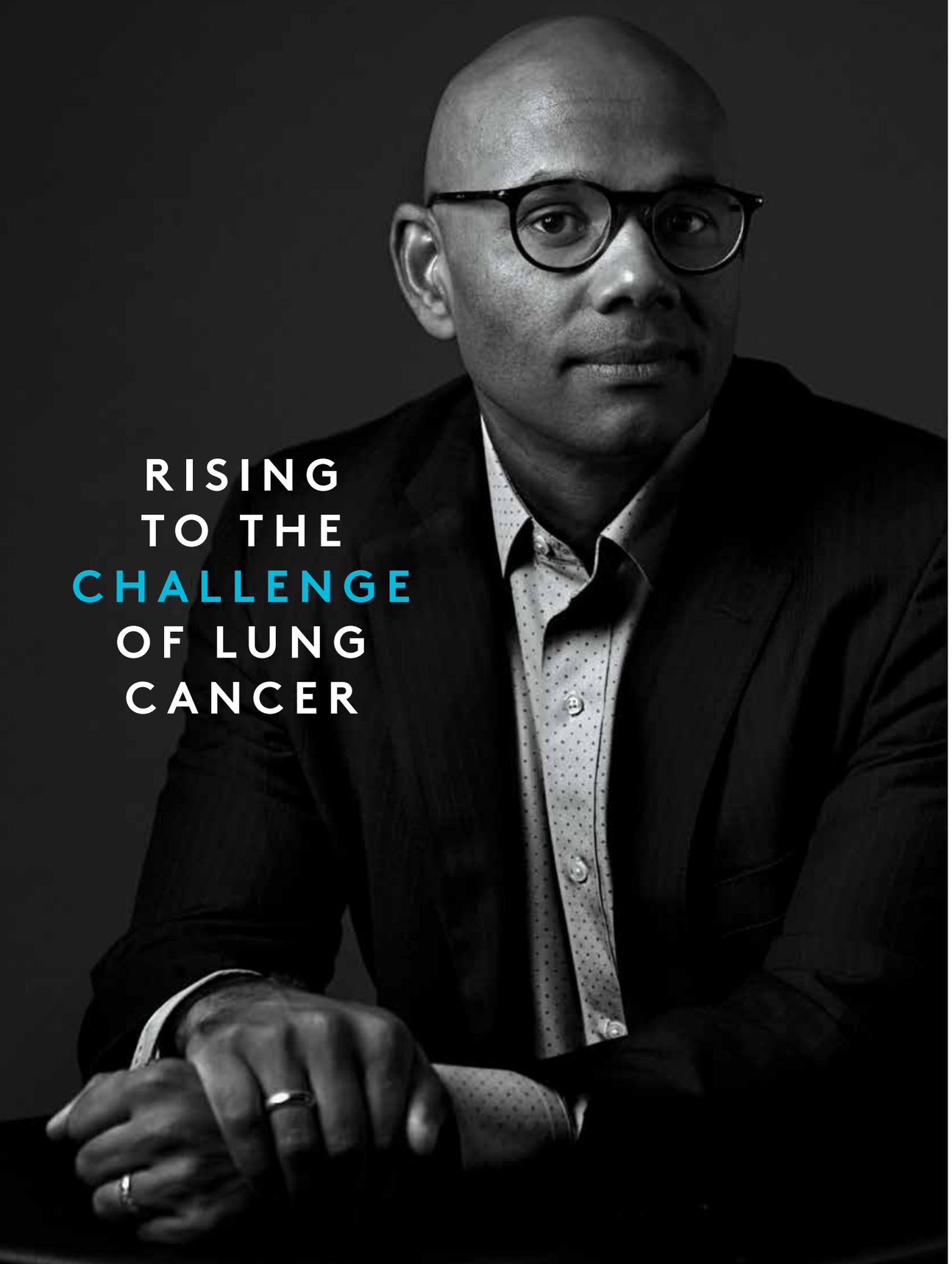
These findings not only attracted significant interest within the academic community following its publication in the journal *Cancer Cell*, but prompted a collaboration between ONJCRI and the Cancer Therapeutics Cooperative Research Centre, CTx. Together with the Institute, CTx is now investing in the development of a drug that can target HCK.

"The CTx takes on perhaps a maximum of one new project a year," Matthias enthuses. "This shows our discovery is not only striking biology but has real potential to lead to a therapeutic outcome."

Matthias says it may take at least three to five years to develop a drug ready for clinical trials and to assess whether the success of anti-HCK therapy in preclinical models will deliver its promise to cancer patients.

"Then we are probably talking about five or six years of extensive clinical trialing before a drug would get approval by the Therapeutic Goods Authority," Matthias says.

Such time frames, he says, underline the importance of long-sighted funding that invests in translating exciting laboratory findings to novel treatments that benefit cancer patients.



# RISING TO THE CHALLENGE OF LUNG CANCER



Dr Tom John has picked up the gauntlet of the world's biggest and most stigmatised cancer killer, and his patients are reaping the benefits.

When Lisa Briggs was given the opportunity to join one of Tom's lung cancer clinical trials, her first thoughts were: 'lab rats'.

It was a perspective that that would quickly change.

Three years later, the 36-year-old Stage 4 lung cancer patient is not only still here, but she has also become a passionate advocate for clinical trials and the work of Tom and his colleagues at the Olivia Newton-John Cancer Research Institute.

"I was concerned that a clinical trial was like being a lab rat that gets pricked and prodded all the time. In fact, it's quite the opposite," says Lisa.

"I had access to the best quality drugs available at that time, I had a really dynamic team of clinicians and researchers who were investing their time into this trial and therefore investing their time into me, and the relationship I've since developed with Tom has been second to none."

For Tom, 46, these relationships and successes motivate him to achieve more with his translational research, which turns lab findings and clinical trials into more effective treatments for lung cancer and mesothelioma patients. He is also motivated by the challenge of the diseases themselves.

Lung cancer is the biggest cancer killer globally, with patients facing only a 5 per cent chance of living to five years. The prognosis for mesothelioma is grimmer still. This rare and aggressive cancer develops in the lining of the lungs, abdomen or heart, and "almost universally kills everyone".

"I became interested in lung cancer mainly because it was a real challenge, and because there was the development of some new drugs during my training," Tom says. "You also see these glimpses of success where patients do extraordinarily well, and you know that in time it's going to improve across the board."

He's particularly excited about the possibilities of harnessing the body's own immune system and using targeted therapies.

"You hit the right biological marker and the right target, you can have a massive impact," Tom says. "We've discovered that some of those tumors have particular mutations that respond very well to targeted therapies. Fifteen years ago, those patients would have all been dead within a few months, but they are now living well past five years. So that's a pretty dramatic improvement."

He says Lisa's story highlights these improvements in lung cancer treatments and outcomes. It also flags the possibility of a cure in the future.

---

In 2014 Lisa was pregnant with her second child when she started wheezing. A doctor prescribed Ventolin, reassuring her that the symptoms would stop after the birth, and an initial chest x-ray revealed nothing unusual. But four months after giving birth, Lisa still struggled to breathe – and then she coughed up blood.

"I couldn't lay down flat, I needed to be propped up, and when I went in the swimming pool at my cousin's birthday, I was in a lot of pain. I was sitting at home, looking after my newborn and my toddler, and I just thought, 'Something's not right.' I was actually on the way to the doctor when I coughed up blood," says Lisa.

He is one of the most approachable, genuine and knowledgeable doctors that I know.

Taken by ambulance to a nearby hospital, Lisa was told that she had bronchitis and sent home with a script. Thankfully, she ignored it and went back to her GP, who sent her for a CT scan.

After the scan showed a suspected mass on her lung, Lisa headed straight to the Austin Hospital. There they diagnosed her with Stage 4 lung cancer, which had spread to her liver, lymph nodes, adrenal glands, pelvic bone and gluteal tissue.

Further tests revealed that she had the ALK gene mutation, which is linked to a subset of lung cancer patients. Six weeks later she started the clinical trial led by Tom, which used a second-generation inhibitor drug to block a lung cancer survival pathway.

"I now view clinical trials as cutting-edge technology that gives patients the best opportunity to live," says Lisa.

Tom devotes a lot of time to clinical trials, both at the Austin Hospital and as part of the Australian Lung Trials Group, where he is on the scientific advisory committee.

He is also currently the Global Principal Investigator and part of the International Steering Committee for a Phase I trial of a drug developed by AstraZeneca. ONJCRI's Cancer Immunobiology Laboratory will also provide bioanalysis for the trial, which is testing a drug that targets the EGFR mutation in non-small cell lung cancers.

The pharmaceutical company approached Tom after he ran clinical trials for Osimertinib, another AstraZeneca drug that the FDA has recently approved as the front-line treatment for non-small cell lung cancer.

"That's one of the advantages of being a translational researcher. Companies and people approach you to do studies that you can't just do in any centre," says Tom, who offers access to cutting-edge facilities and bioanalysis expertise at our Institute.

Tom is also collaborating with our Cancer Immunobiology Laboratory (p 16) to conduct a Phase 1 trial of an engineered virus, which is designed to stimulate T-cells to seek, enter and destroy lung cancer cells.

Meanwhile, his preclinical research on mesothelioma includes working with the Tumour Targeting Laboratory (p 20) to explore antibody drug conjugates, and collaborating with the Cell Death & Survival Laboratory (p 24) to investigate drugs that block a tumour survival pathway.

He says working in the lab and at the bedside of patients is a powerful conduit for potential cancer breakthroughs.

"It's the ideal way to do research: having the initial signal and being able to work with it in the lab and figure out the things that might predict which tumors are more likely to respond to a particular agent and then to test your hypothesis in the clinic. You can then make an observation in the clinic and take it back to the lab where you test and refine your hypotheses," he says.

But stigma and lack of funding remain challenges to his research.

"Lung cancer is quite a tough disease to research," says Tom. "The majority of people who are diagnosed with lung cancer are smokers and people just think, 'well, you deserved it'. So it doesn't receive a lot of press, and it doesn't receive a lot of funding dollars despite it being a massive killer."

It's a dynamic that motivates Lisa to talk to policymakers, researchers, schools and patients to boost funding for research. She also spends her time linking patients to any possible clinical trials.

"Patients are screaming out for these clinical trials," she says. "We need to have access to these drugs here in Australia, and the only way we can do that is through generating the data through clinical trials."

She says Tom's work not only provides opportunities for people to live, but he empowers patients to make choices about how they want to do it.

"Tom puts in an enormous amount of time and effort into making sure he is providing patients with the right types of clinical trials and really meeting the needs of his patients," says Lisa. "He is one of the most approachable, genuine and knowledgeable doctors that I know."



# LABORATORIES

Our nine laboratories are the driving force behind our cutting-edge research to identify breakthrough treatments for breast cancer, lung cancer, bowel cancer, lymphoma, melanoma and brain cancer.

# Cancer & Inflammation Laboratory

## TARGETING ‘BAD NEIGHBOUR’ INFLUENCE

**PROF MATTHIAS ERNST**
Scientific Director and Laboratory Head
Head of School of Cancer Medicine, La Trobe University

**In 2017 the Cancer & Inflammation** Laboratory (CIL) focused on disrupting the communication between normal cells and their ‘bad neighbour’ cancer cells.

These bad neighbours embed themselves amongst communities of normal cells, where they often exploit the normal cells for their own ends. For example, the cancers may coerce normal cells to form new blood vessels for them.

Understanding and targeting the interactions between cancer cells and normal cells holds great promise for developing new drugs to treat cancer patients.

To do this, CIL is deconstructing cancers of the bowel and stomach to better understand the types of normal cells that support cancer cells, and the mechanisms that cancer cells use to corrupt and exploit normal cells.

In 2017 we established a novel preclinical model that can switch on or off a ‘communication hub’ protein, either in the cancer cells or in the normal cells of the tumour environment.

We focused on the protein STAT3, which acts as a communication hub in both cancer and normal cells. This molecule relays information from the surface of the cells to the nucleus where it regulates the synthesis of proteins that help cancer cells to survive and grow.

Our model will enable us to better understand how future anti-STAT3 drugs may act in cancer patients and to assess their effectiveness.

These ‘bad neighbours’ embed themselves amongst communities of normal cells.

We are also focusing on other communication methods between cancer cells and normal cells, such as cytokines and other soluble mediators. We are seeking to better understand which of these cytokines act on cancer cells, how they operate and how we can stop this with novel drugs.

Many of these cytokines also support a variety of important roles during the day-to-day functioning of our bodies, so CIL is focusing on interleukin-11. Many cancer cells depend on interleukin-11, but most normal cells are much less reliant on it.

In addition to targeting cell communication hubs or soluble mediators, we can also direct novel therapies to the cells that produce the cytokines in the tumour environment.

Macrophages are large white blood cells that can act as cytokine factories when corrupted by cancer cells. In 2017 CIL identified a ‘molecular switch’ in macrophages, which promotes the growth of tumours. This molecular switch is a protein called HCK, which can be inhibited by drug-like molecules (see highlight, p9).

### RESEARCH TEAM

*Shoukat Afshar-Sterle, Mariah Alorro, David Baloyan, Michael Buchert, Annalisa Carli, Ashwini Chand, Christine Dijkstra, Belinda Duscio, Moritz Eissmann, Matthias Ernst, Nima Etemadi, Emilie Garside, Jennifer Huynh, Saumya Jacob, Cameron Johnstone, Riley Morrow, Megan O’Brien, Robert O’Donoghue, Lokman Pang, Ashleigh Poh, Rebecca Rau, Pathum Thilakasiri, Merridee Wouters*

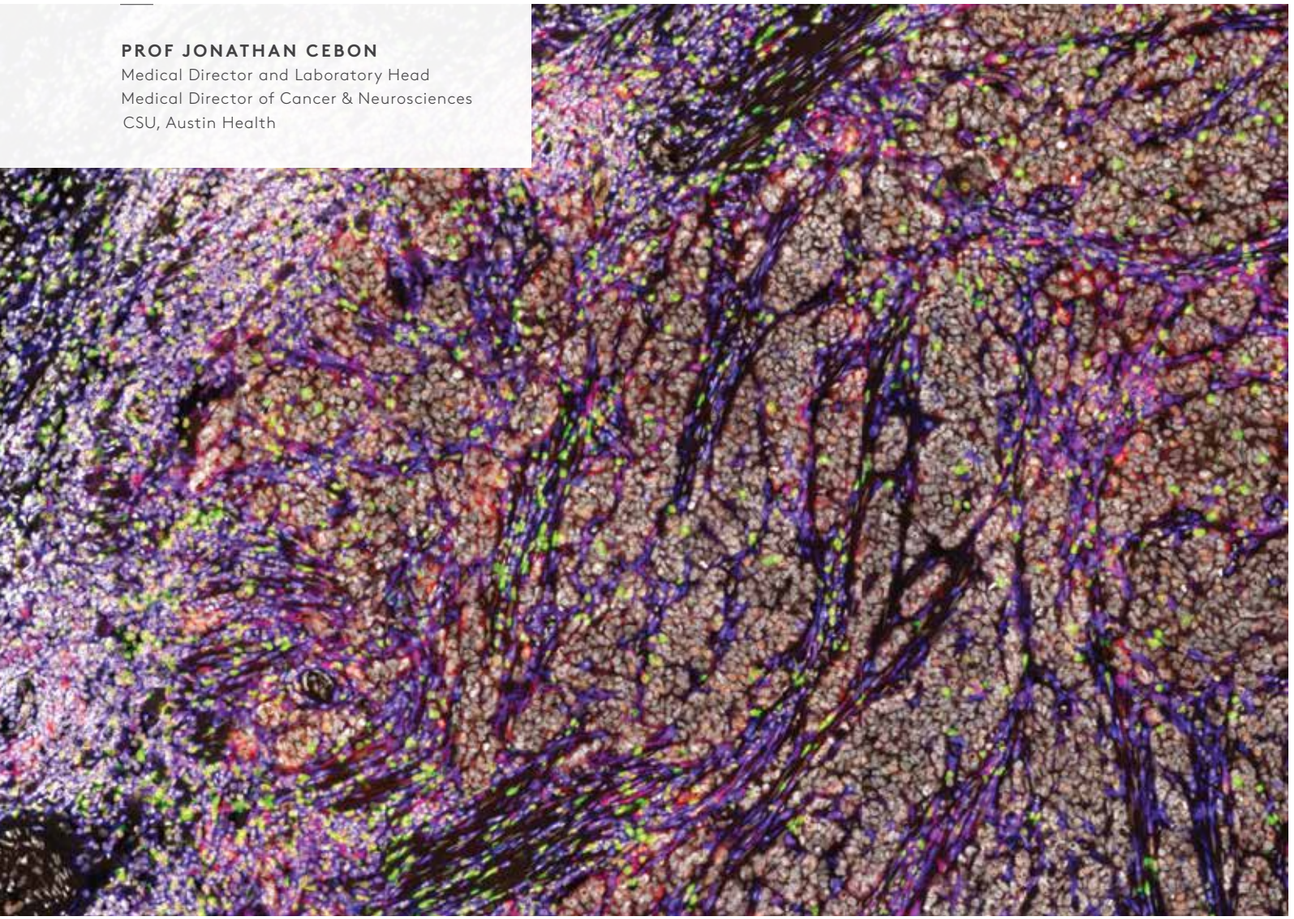
### PUBLICATION HIGHLIGHTS


- *Poh, A. et al. Inhibition of hematopoietic cell kinase activity suppresses myeloid cell-mediated colon cancer progression. Cancer Cell 31: 563-575 e565. (2017)*
- *Alorro, M. et al. Generation of an inducible mouse model to reversibly silence Stat3. Genesis 55: e23023. (2017)*
- *Huynh, J. et al. The JAK/STAT3 axis: a comprehensive drug target for solid malignancies. Seminars Cancer Biol 45: 13-22. (2017)*

# Cancer Immunobiology Laboratory

## HARNESSING IMMUNE-SYSTEM POTENCY

**PROF JONATHAN CEBON**
Medical Director and Laboratory Head
Medical Director of Cancer & Neurosciences
CSU, Austin Health



**Last year the Cancer Immunobiology** Laboratory (CIBL) stimulated T killer cells with an engineered virus and identified a potential new way to overcome drug resistance. We also revealed how to avoid the nasty side effects of a common melanoma drug, and we dug deeper into the relationship between melanomas and anti-tumour responses by the immune system.

Boosting immunity to treat cancer has rapidly become the most exciting area of clinical cancer research, and there has been enormous progress for a large variety of cancer types. CIBL continues to build on its past successes with treatments for malignant melanomas and with more effective treatment approaches that use potent drug combinations to harness the immune system's power.

In 2017 we injected an engineered virus into malignant melanomas to stimulate the entry of killer T lymphocytes, and we assessed the combination of highly effective therapies, such as the anti-CTLA4 antibody Yervoy with the anti-PD1/PD-L1 drugs Opdivo and Keytruda.

In particular, we looked at how these treatments might eradicate cancer in parts of the body that have previously been considered out-of-bounds for immunotherapy, such as secondary tumours in the brain.

Our lab also focused on proteins in melanoma cells that promote cancer growth and that can confer resistance to anti-cancer drugs. For instance, drugs that inhibit BRAF are highly effective in melanoma cells, but often stimulate colon cancer and other non-melanoma cancer cells. We identified a molecular mechanism by which a new class of second-generation BRAF inhibitors can avoid this side effect.

We also identified a new mechanism by which cancer cells become resistant to BRAF inhibitors. This involves cells passing on a protein to their neighbouring cells via microscopic vesicles known as exosomes.

Our discovery provides a better understanding of how drug-resistance can occur at multiple secondary tumour sites and a potential way to overcome drug resistance by blocking this process.

In collaboration with Australian melanoma experts at the University of Queensland, we assessed the genomics of major melanoma subtypes. Together with Dr Marian Burr and her colleagues at the Peter MacCallum Cancer Centre, we found that melanoma cells affect anti-tumour immune responses through a mechanism that controls the expression of the immune checkpoint molecule PD-L1.

> CIBL continues to build on its past successes with treatments for malignant melanomas.

### RESEARCH TEAM

*Surein Arulunanda, Andreas Behren, Jonathan Cebon, Jessica Duarte, Thomas John, Oliver Klein, Andrew Lim, Sean Macdonald, Anupama Pasam, Bibhusal Thapa, Candani Tutuka, Marzena Walkiewicz, Katherine Woods*

### PUBLICATION HIGHLIGHTS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- *Vella, L. et al. Intercellular resistance to BRAF inhibition can be mediated by extracellular vesicle-associated PDGFRbeta. Neoplasia 19: 932–940. (2017)*


# Translational Genomics & Epigenomics Laboratory

## MAKING LIQUID BIOPSIES MATTER

**A/PROF ALEXANDER DOBROVIC**
Group Leader

**In 2017 the Translational Genomics** & Epigenomics (TGEG) Laboratory collaborated with the Victorian Comprehensive Cancer Centre to develop an individualised liquid biopsy test that can detect circulating tumour DNA in patients with early-stage operable lung cancer.

The National Health and Medical Research Council is funding the project, which will enable better cancer management and more customised medical treatment by giving clinicians an efficient tool to monitor the success of therapies and to detect any relapse.

When a patient has cancer, some of the tumour's DNA can be found in the blood. This is called circulating tumour DNA, and it carries the mutations that are found in the cancer. Monitoring these specific mutations via liquid biopsies can measure the extent of the cancer and determine appropriate treatment.

Liquid biopsies are a rapidly growing area of research because they are considered minimally invasive procedures compared to conventional tissue biopsies, which require highly invasive surgical procedures and have a risk of complications.

In addition to identifying circulating DNA in early-stage lung cancer patients, our team is also collaborating with the Austin Hospital Department of Surgery to monitor donor-derived circulating DNA. We are using liquid biopsies to help detect organ rejection in transplantation patients.

> This project will enable better cancer management and more customised medical treatment.

Last year our laboratory became the first Australian laboratory to gain accreditation for droplet digital PCR testing of liquid biopsies from cancer patients, DNA methylation analysis of tumours, and next-generation sequencing testing for targetable lung cancer chromosome rearrangements. This was granted by the National Association of Testing Authorities/Royal College of Pathologists Laboratory Accreditation Program.

Medical oncologists are increasingly seeking out our tests to support their patient treatment plans, and the development and use of different analysis approaches will enable the fuller implementation of personalised medicine via innovative and cutting-edge technologies.

The TGEG Laboratory undertakes gene-based and genomics-based research into cancer diagnostics with a focus on collaborative studies that optimise treatment of cancer patients. Our laboratory is active in both research and diagnostics, which creates a dynamic synergy that benefits both areas.

### RESEARCH TEAM

*Ida Candiloro, Andrew Colebatch, Hongdo Do, Alexander Dobrovic, Basant Ebaid, Su Kah Goh, Anh Le, Thomas Mikeska, Ramyar Molania, Ashan Musafer, Eloise Shaw, Marcin Szaumkessel, Matthew Wallis, Thomas Witkowski, Giada Zapparoli*

### PUBLICATION HIGHLIGHTS

- *Do, H. et al. Reducing artifactual EGFR T790M mutations in DNA from formalin-fixed paraffin-embedded tissue by tissue of thymine-DNA glycosylase. Clin Chem 63: 1506–1514, doi:10.1373/clinchem.2017.271932. (2017)*
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# Tumour Targeting Laboratory

## DEVELOPING BRAIN TUMOUR THERAPIES

**PROF ANDREW SCOTT**
Laboratory Head
Director, Department of Molecular Imaging and Therapy, Austin Health

**In 2017 the Tumour Targeting (TT)** Laboratory collaborated with Abbvie, a major pharmaceutical company, to develop and test a novel antibody therapy for glioblastomas, which are showing promising results.

We also collaborated with Monash University and the Queensland Institute of Medical Research (QIMR) to develop, licence and successfully test a novel antibody on leukemia patients.

Glioblastomas are high-grade brain tumours with a poor prognosis and few therapeutic options available to patients and clinicians. This lack of effective treatments has been explained by tumour heterogeneity, poor penetration of therapeutic agents through the blood–brain barrier and, above all, the lack of suitable targets.

Together with Abbvie, we tested a tumour-selective antibody drug conjugate on patients with first-line and recurrent glioblastomas. The antibody drug conjugate, ABT-414, contained a toxin attached to the mAb806 antibody that was previously developed by our laboratory. This antibody binds to a tumour-specific form of the Epidermal Growth Factor Receptor (EGFR) expressed on cancer cells.

ABT-414 showed highly promising results in those glioblastomas that have amplified expression of EGFR, highlighting the need to now develop other therapies against tumors where expression of EGFR is not amplified.

So our collaboration with Abbvie also explored the new antibody drug conjugate ABBV-221 to evaluate if the antibody's increased affinity for EGFR may have broader utility against tumours with only modest EGFR overexpression.

Our preclinical studies showed that ABBV-221 displays improved anti-tumour activity against a range of EGFR-expressing xenografts. Based on these results, ABBV-221 has progressed to an international Phase I clinical trial in patients with advanced solid tumours.

In collaboration with Monash University and QIMR, we developed a novel antibody called KB004, which targets the EphA3 receptor, and licensed it to the biotech company Humanigen. We conducted initial clinical trials with KB004 on leukemia patients and demonstrated the safety and therapeutic potential of this antibody.

We also developed molecular probes to visualise tumours and to identify patients suited to treatments that are based on either hormones, oncogenic signalling pathways or immunotherapy.

These included assessing Positron Emission Tomography (PET) probes that can identify osteosarcoma lesions, or signatures in prostate cancer that predict a patient response to anti-androgen therapy.

We developed other probes to evaluate hypoxia in tumours and to image response to drugs that target various signaling pathways. Finally, we commenced preclinical trials with 89Zr-labelled antibodies to help select the patients most likely to respond to these antibodies.

We co-developed a novel antibody and licensed it to Humanigen.

### RESEARCH TEAM

*Uwe Ackermann, Laura Allan, Ingrid Burvenich, Diana Cao, Puey Ling Chia, Hui Gan, Benjamin Gloria, Rachel Goh, Nancy Guo, Eliza Hawkes, Dylan King, Nathan Lawrentschuk, Sze Ting Lee, Fook Thean Lee, Zhanqi Liu, Michael McKay, Carmel Murone, Sagun Parakh, Adam Parslow, Angela Rigopoulos, Andrew Scott*

### PUBLICATION HIGHLIGHTS


- *Reardon, D. et al. Efficacy and safety results of ABT-414 in combination with radiation & temozolomide in newly diagnosed patients with glioblastoma. Nuero Oncol 19: 965–975. (2017)*
- *Gan, H. et al. Antibody–drug therapeutics in glioblastoma: the right drugs to the right cells. Nature Rev Clin Oncol 14: 695–707. (2017)*


# Oncogenic Transcription Laboratory

## DISCOVERING NEW TREATMENTS

**PROF JOHN MARIADASON**
Laboratory Head

**The Oncogenic Transcription** Laboratory (OTL) has identified a potential new drug treatment for patients with biliary tract cancer, and developed a series of tests that identify the patients most likely to respond to this drug.

The new treatment is not curative, but it provides a new treatment option for patients with biliary tract cancer. Cancers of the biliary tract occur in the bile duct that drains bile out of the liver and into the gallbladder, and patients currently have very few options for effective treatments.

A Phase II clinical trial, led by Associate Prof Niall Tebbutt and conducted largely at Austin Health, found that approximately half of the patients with biliary tract cancer who received the drug Everolimus gained some clinical benefit.

Everolimus blocks a protein called mTOR, which is required for the growth of cancer cells. The drug is also used to treat advanced kidney cancer.

Lead study author Dr David Lau, a medical oncologist and PhD student at the Institute, analysed tumour samples from the trial patients and found that those with simultaneous cancers in the gallbladder were less likely to respond to Everolimus treatment.

It provides a new treatment option for patients with biliary tract cancer.

In a supporting study, we also undertook a series of laboratory experiments that shed light on why the cancers of some patients respond better to this drug than others.

We discovered that cancers with mutations in a gene called KRAS did not respond as well to Everolimus as cancers without KRAS mutations. Similarly, we found that biliary tract cancers that have high levels of the active form of a protein called AKT respond well to this drug.

A better understanding of how Everolimus works in cancer cells enabled the OTL team to identify drug combinations that can improve the anti-cancer activity of Everolimus. We can now test the activity of these drug combinations in further clinical trials in selected patients with biliary tract cancer.

### RESEARCH TEAM

*Latham Caselli, Fiona Chionh, Mercedes Davalos-Salas, Amardeep Dhillon, Laura Jenkins, Emily Jong, Stan Kaczmarczyk, David Lau, Analia Lesmana, Ian Luk, John Mariadason, Jennifer Mooi, Eka Moseshvili, Irvin Ng, Rebecca Potter, Dunya Rabah, Camilla Reehorst, Cameron Scott, Lars Togel, Janson Tse, Wiphawan Wasenang, Andrew Weickhardt*

### PUBLICATION HIGHLIGHTS


- *Chueh, A. et al. ATF3 repression of BCL-XL determines apoptotic sensitivity to HDAC inhibitors across tumour types. Clin Cancer Res 23, 5573-5558. (2017)*
- *Yeung, Y. et al. K-Ras mutation and amplification status is predictive of resistance and high basal pAKT is predictive of sensitivity to everolimus in biliary tract cancer cell lines. Mol Oncol 11, 1130-1142. (2017)*
- *Chionh, F. et al. Oral versus intravenous fluoropyrimidines for colorectal cancer. Cochrane Database Syst Rev 7, CD008398. (2017)*

# Cell Death & Survival Laboratory

## LISTENING TO CELLULAR CROSS-TALK

**DR DOUG FAIRLIE**
Laboratory Head

**Last year the Cell Death & Survival** (CDS) Laboratory and The Walter and Eliza Hall Institute (WEHI) discovered a way to dramatically enhance the power of existing drugs to activate the cell death machinery of melanoma cells.

We also completed a key study about the molecular interactions between cell death and cell survival processes, and kicked off a collaboration with a biotechnology company to dual target molecules involved in cell death.

All cells in the body possess the ability to kill themselves if they are no longer needed or pose a threat to our well-being. Similarly, there is a mechanism that promotes cell survival when a cell is stressed by environmental factors or by infectious agents.

When either process is disrupted, this can help develop cancer and impair the ability of cancer drugs to effectively treat patients.

The CDS Laboratory is interested in cell death and cell survival processes as there is growing evidence these processes can 'talk' to each other at a molecular level, and this cross-talk could have significant implications for cancer development.

Our long-term collaboration with WEHI showed that drugs that target different 'pro-survival factors' within melanoma cells provide very little benefit on their own. However, the activity of such drugs is dramatically enhanced when they are combined, providing potential new avenues to treat cancers.

There is growing evidence these processes can 'talk' to each other at a molecular level.

We have also been developing our own drug-like molecules that can kill melanoma cells. These are only research tools at this stage, but they provide important clues for ultimately developing drugs to treat patients. Our study is near completion and has been funded by Worldwide Cancer Research (UK).

In addition to our key study on molecular interactions between cell death and cell survival processes, we have developed novel preclinical models that will provide further insight into this cross-talk. Such models have been lacking in the field to date, and the Australian Research Council is supporting this work.

In 2017 the CDS Laboratory started a research collaboration with the Australian biotechnology company Phylogica, which is funded by the National Health and Medical Research Council.

Our initial studies showed that novel reagents developed at Phylogica and ONJCRI could have significant potential in dual targeting key molecules that control cell death. They could also target a critical cell growth factor that is often excessively activated in cancer cells.

### RESEARCH TEAM

*Marco Evangelista, Doug Fairlie, Chethana Galketiya, Tiffany Harris, Chloe Hobbs, Erinna Lee, Luke McCaloon, Sharon Tran*

### PUBLICATION HIGHLIGHTS


- *Chueh, A. et al. ATF3 repression of BCL-XL determines apoptotic sensitivity to HDAC inhibitors across tumour types. Clin Cancer Res 23, 5573-5558. (2017)*
- *Brouwer, J. et al. Conversion of Bim-BH3 from activator to inhibitor of Bak through structure-based design. Mol Cell 68: 659-672 e659 (2017).*

# Metastasis Research Laboratory

## REVEALING A METASTASIS MECHANISM

**PROF ROBIN ANDERSON**
Head of Translational Breast Cancer Program and Laboratory Head

**In 2017 the Metastasis Research** (MR) Laboratory revealed how a protein reduces the spread of advanced breast cancer to other vital organs and discovered how cancer cells can corrupt normal cells to help these cancer cells form metastases.

In preclinical models, the MR Laboratory discovered how Bone Morphogenetic Protein BMP4 reduces metastasis. We found that BMP4 targets cancer cells as they escape from the primary tumour, making them more susceptible to dying, and that BMP4 activates the immune system to attack the tumour.

This led us to investigate how BMP4 acts on macrophages and neutrophils – immune cells that normally protect the body from infections. We discovered that cancer cells corrupt normal cells to produce less BMP4, which unleashes the tumour-promoting activities of macrophages and neutrophils, and helps the tumour cells to metastasise at distant locations.

We are now testing therapies that block the activity of these cancer-promoting macrophages and neutrophils.

We also continued our work identifying genes that create drug resistance for patients with HER2 positive breast cancer. There are now very good therapies for patients with this type of breast cancer; however, some develop resistance to these improved therapies. Our gene screening research will allow us to identify targets for new therapies.

Access to samples of breast cancers is vital for our research, so we established a program call BROCADE that helps us obtain a collection of metastatic, secondary tumours. Primary tumours in the breast are usually available, but secondary tumours are often not removed by surgery.

> We found that BMP4 targets cancer cells as they escape from the primary tumour.

The BROCADE program liaises with patients and families to facilitate written consent for an autopsy after death to remove these tumour tissues for research purposes. To provide maximum benefit to the research community, the collected tissues are available to all Australian breast cancer researchers. The National Breast Cancer Foundation supports this program.

Every year over 17,000 Australians are diagnosed with breast cancer and around 3,000 people die from this disease. Death in nearly all cases is caused by spread of the cancer to other vital organs such as lung, liver and brain.

Treatments for early breast cancer have improved the survival rates impressively over the past five decades, but survival prospects are not good for those whose disease spreads. Often, the therapy that was effective initially is no longer active against a recurrent tumour or a secondary tumour in a distant organ.

### RESEARCH TEAM

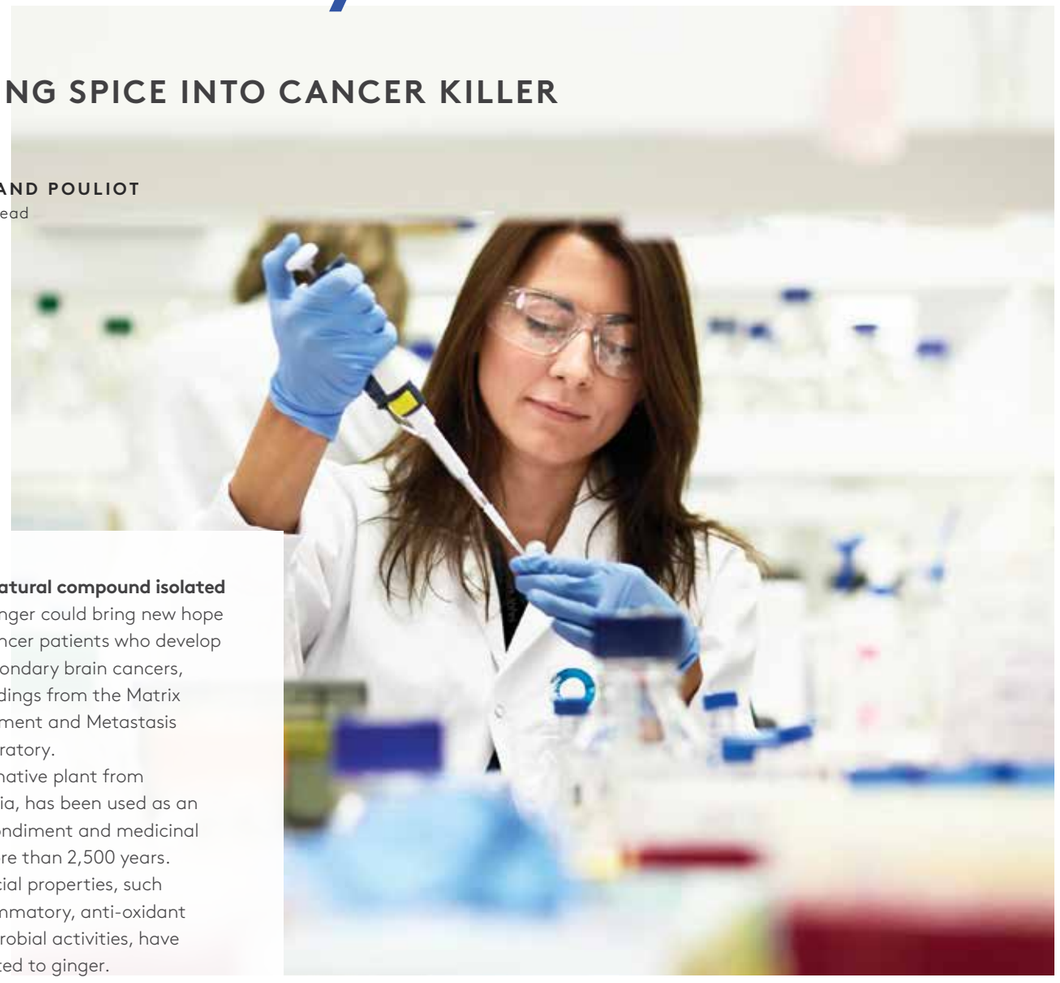
*Robin Anderson, Stefan Bader, Caroline Bell, Allan Burrows, Laphing Chi, Genevieve Dall, Catherine Fang, Kathryn Gurner, Jing Hao, Kellie Mouchemore, Richard Redvers, Charlotte Roelofs, Bill Tang, Kathryn Visser, Belinda Yeo*

### PUBLICATION HIGHLIGHTS


- *Lee, M. et al. G-CSF receptor blockade ameliorates pain and disease. J Immunol 198: 3565-3575. (2017)*
- *Dall, G. et al. Sca-1 labels a subset of estrogen responsive biopotential repopulating cells within the CD24+ CD49fhi mammary stem cell-enriched compartment. Stem Cell Reports 8: 417-431. (2017)*

# Matrix Microenvironment & Metastasis Laboratory

## TURNING SPICE INTO CANCER KILLER



**DR NORMAND POULIOT**
Laboratory Head

**A safe and natural compound isolated** from fresh ginger could bring new hope for breast cancer patients who develop incurable secondary brain cancers, thanks to findings from the Matrix Microenvironment and Metastasis (MMM) Laboratory.

Ginger, a native plant from Southeast Asia, has been used as an important condiment and medicinal agent for more than 2,500 years. Many beneficial properties, such as anti-inflammatory, anti-oxidant and anti-microbial activities, have been attributed to ginger.

In 2017 our team found that one compound in ginger, called [10]-gingerol, could block and kill 'triple negative' breast cancer (TNBC) cells grown in petri dishes.

We then collaborated with the University of São Carlos in Brazil to use [10]-gingerol to reduce the development of secondary TNBC in multiple organs of preclinical models. In particular, [10]-gingerol significantly reduced the incidence of cancers spreading to the brain and did not induce observable side effects. This research was published in the high-profile journal *Oncotarget*.

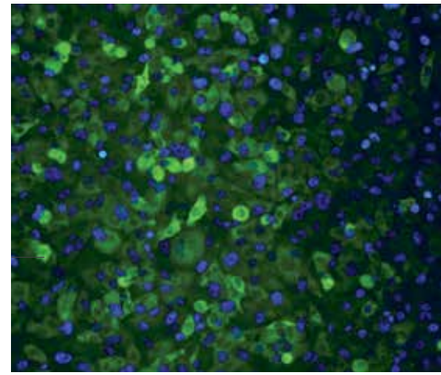
Each year more than 17,000 Australian women are diagnosed with breast cancer and approximately 3,000 of them die due to the spread of the disease to distant organs (metastasis).

Patients with the aggressive TNBC have a higher probability of developing brain metastasis; however, it is hard to predict which patient will develop these secondary brain cancers and it is difficult to deliver anti-cancer drugs to the brain.

While our [10]-gingerol results are extremely encouraging, we believe that this compound alone is unlikely to completely eradicate brain metastases from TNBC.

Therefore, our team will now investigate whether [10]-gingerol could increase the benefits of chemotherapy and radiotherapy and reduce the side effects of these standard-of-care treatments.

[10]-gingerol significantly reduced the incidence of cancers spreading to the brain.



### RESEARCH TEAM

*Miriam Fuentes, Katie McIntyre, Effie Mouhtouris, Aadya Nagpal, Normand Pouliot, Elnaz Tavancheh*

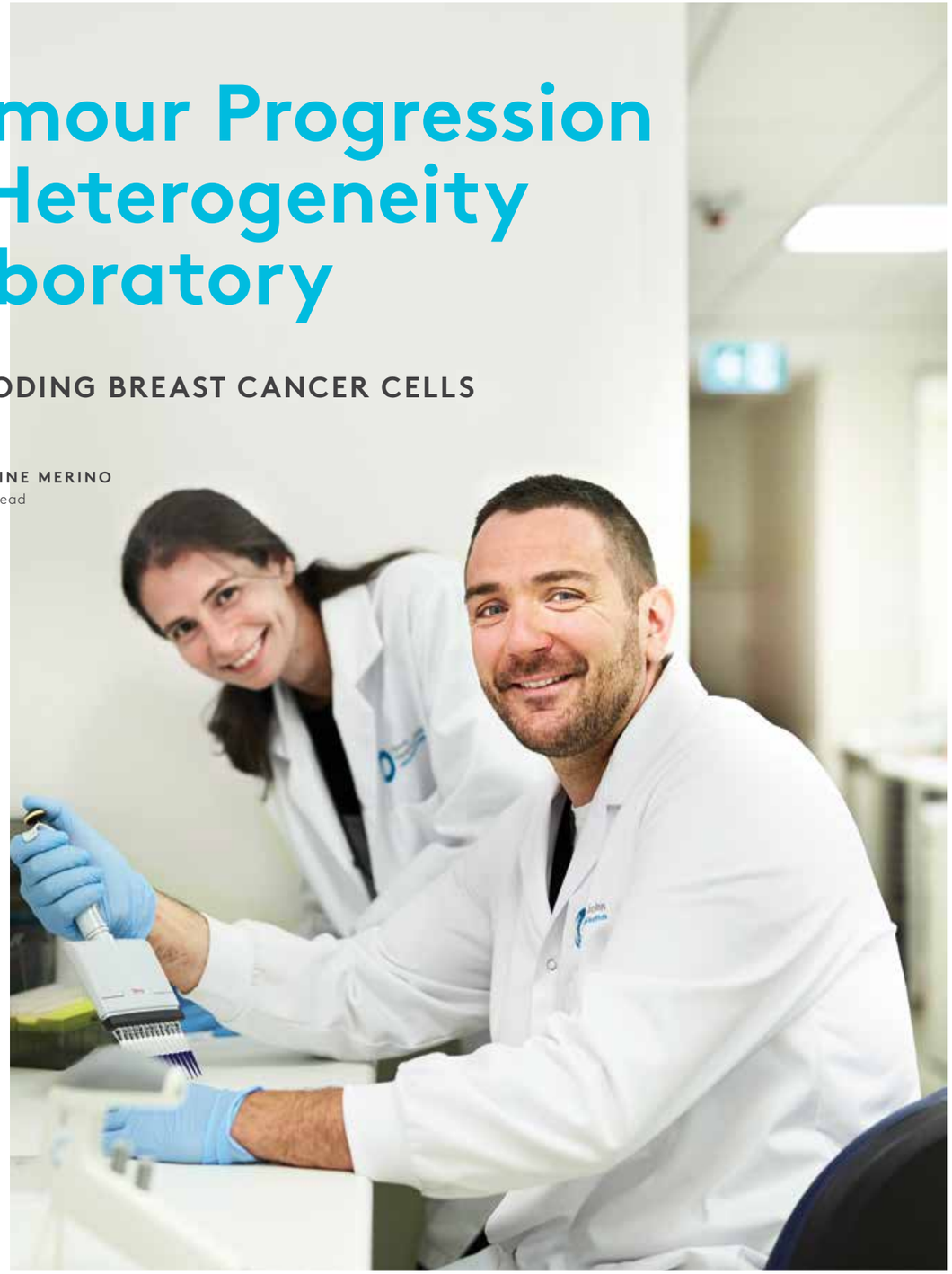
### PUBLICATION HIGHLIGHTS


- *Martin, A. et al. [10]-gingerol induces apoptosis and inhibits metastatic dissemination of triple negative breast cancer in vivo. Oncotarget 8: 72260-72271. (2017)*

# Tumour Progression & Heterogeneity Laboratory

## BARCODING BREAST CANCER CELLS

**DR DELPHINE MERINO**
Laboratory Head



**The Tumour Progression &** Heterogeneity (TPH) Laboratory is using 'barcodes' to identify the genetic properties of aggressive breast cancer cells that spread to other parts of the body or become resistant to drug treatment. This research will help us identify drugs to prevent these cells from spreading or becoming resistant to current therapies.

Metastasis, the spread of cancer cells beyond their primary site, is the primary cause of mortality of breast cancer patients. Spreading cells are often biologically different from most of the cells in the original tumour. Therefore, many metastatic, secondary tumours are often resistant to therapies used for the primary cancer.

The TPH Laboratory is focusing on triple negative breast cancer (TNBC), the most aggressive type of breast cancer, which is associated with poor prognosis. Our team's objective is to understand the genetic properties of the most aggressive cells in the tumour at the time of diagnosis and to identify and target the 'seeds' of metastasis.

To do this, we labelled individual cancer cells with optical tags and used these 'barcoded' cancer cells to establish several pre-clinical models of TNBC. This allowed us to study the ability of individual tumour cells to survive, proliferate or die in the presence of various drugs.

We discovered that cells within a given tumour are very diverse in terms of their proliferation, metastatic potential and resistance to standard therapy.

As part of our research, the TPH Laboratory collected cancer cells from patients, who gave their consent for tissue to be used for research purposes. This enables us to relate our findings to the clinical history of each patient, and can ultimately help direct patients to the most suited clinical trials.

We are also developing models of advanced disease from tumours that have never seen treatment – so called 'drug-naive' tumours – to predict which drugs can prevent breast cancer recurrence. We will use these models to improve the diagnosis, prevention and treatment of metastatic disease.

Drugs that boost immunity are having unprecedented impact as new anti-cancer treatments.

**RESEARCH TEAM**

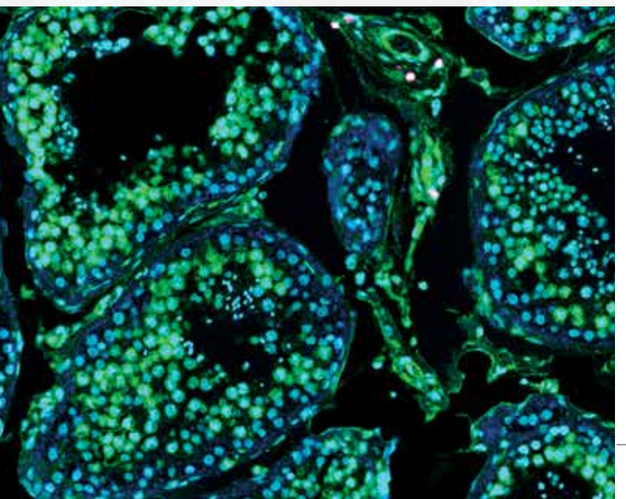
*Amarachi Amah, Jean Berthelet, Delphine Merino, Antonin Serrano*

**PUBLICATION HIGHLIGHTS**

- *Merino, D. et al. Synergistic action of the MCL-1 inhibitor S63845 with current therapies in preclinical models of triple-negative and HER2-amplified breast cancer. Sci Transl Med 9:eaam7049. (2017)*

# EQUIPMENT, FACILITIES AND SERVICES

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



### ACRF CENTRE FOR TRANSLATIONAL CANCER THERAPEUTICS AND IMAGING

The ACRF Centre was established for medical research and preclinical investigations through a grant from the Australian Cancer Research Foundation. The Centre enables PET MRI Imaging, SPECT CT Imaging and IVIS Spectrum Bioluminescent and Fluorescence Imaging. Supported by radiochemistry and medical physics expertise, these sophisticated molecular imaging capabilities facilitate our research into novel cancer therapies and mechanisms of cancer, including exploring the immune response and processes of metastasis.

### VECTRA MULTI-SPECTRAL IMAGING PLATFORM

The first of its kind in Australia, the Vectra Imaging platform was established in 2016 through a grant from the Ian Potter Foundation. This automated, high-throughput quantitative pathology imaging system allows researchers to gain a deeper level of understanding of cancer mechanisms through insight into the role of immune cells within solid tumours and the tumour microenvironment. It utilises seven-colour multiplexing and visualisation capabilities enabling the accurate detection and measurement of weakly expressing and overlapping biomarkers within a single tissue section.

### MAMMALIAN PROTEIN EXPRESSION, PRODUCTION AND PURIFICATION FACILITY (MPEF)

The MPEF is a dedicated facility that can produce small to large amounts of high-quality recombinant proteins and antibodies for use in medical research. The MPEF specialises in cell line development, biologics production, protein purification, protein analysis and protein characterisation. These products include novel cancer targeting monoclonal antibodies that our researchers have generated and are characterising through preclinical cancer models for clinical translation.

### MOLECULAR DIAGNOSTICS

The Translational Genomics & Epigenomics Laboratory is the first lab in Australia to have a NATA-accredited test using tumour DNA to detect tumour growth.
This innovative blood test makes it possible to diagnose and monitor a patient's cancer treatment progress without invasive tests and worryingly lengthy waiting times to get results. The testing services include:

- Plasma BRAF V600E/K mutation melanoma testing using droplet digital PCR (melanoma)
- Plasma EGFR T790M mutation testing using droplet digital PCR (lung and colorectal cancer)
- MGMT methylation testing (brain cancers)
- MLH1 methylation testing (colorectal and endometrial cancers)
- BRCA1 methylation testing (breast and ovarian cancers).

### FLOW CYTOMETRY CORE FACILITY

Flow cytometry is a powerful laser-based technology used to rapidly analyse the properties of single cells. This facility provides analytical cytometry and high-speed cell sorting services to the research community of ONJCRI, affiliates and external users. Flow cytometry can also be applied to prepared cellular components in basic cancer cell biology, preclinical or translational analyses such as examining patient blood cell populations and immune cell changes with therapy.

## ACRF Centre for Imaging the Tumour Environment

In 2017 the Australian Cancer Research Foundation (ACRF) awarded a **$2,000,000 grant** to ONJCRI and La Trobe University Institute of Molecular Sciences (LIMS) to establish the ACRF Centre for Imaging the Tumour Environment.

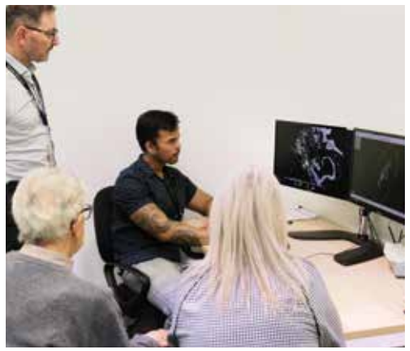
This new centre will be housed in a dedicated, purpose-built section of the laboratories at ONJCRI, and will contain high-end microscopy equipment for subcellular analysis of cancers and their adjacent normal tissues and cells. This will include a confocal microscope to enable three-dimensional insights into cultured cells and a multiphoton microscope to 'see' through several layers of cells in living normal and cancer tissues.

The vision was to seamlessly connect the new centre to ONJCRI's existing ACRF Centre for Translational Cancer Therapeutics and Imaging. Strategically linking the two centres allows the Institute to expand its imaging capacity from a macro level of looking at individual organs to a micro level of studying cellular and subcellular distributions of molecules and drugs.

In the spirit of ACRF's generous support for the two centres, both facilities are available for researchers throughout the Austin Health Campus in Heidelberg, as well as to our colleagues at LIMS in Bundoora.

# T MARKS THE SPOT

Sometimes the distance between breakthrough and saved lives is as close as your own back fence



**In December 2017 Jennifer Hall received the news** that all Stage 4 melanoma patients hope for: the secondary tumours in her right lung, abdominal wall and hip had disappeared after taking part in an international clinical trial at ONJCRI.

The ongoing trial used a combination of potent immune-stimulating drugs to boost T-cells in the blood, which then seek, enter and kill secondary tumours.

Jennifer was stunned at the success, but she was even more amazed to discover that she shared a back fence with the man who paved the way to saving her life, 57 years ago.

Her neighbour? The softly spoken Jacques Miller, a French-born scientist who identified the immune-system roles of the thymus, T-cells and B-cells in the 1960s, laying the foundations of immunotherapy science and the incredible advances we are now seeing in cancer treatments.

"It was really special to meet Jacques. He's so clever, kind and just interested in people — and he loves all this stuff too. We chat quite a lot now, and we have built a really nice friendship," says Jennifer, who has unknowingly lived next to Jacques for 24 years.





"We went off to dinner a few weeks ago with his friends from the Walter and Eliza Hall Institute, and he took me as 'living proof' to show that all their research had worked."

For Jacques, Jennifer is not only a friend and professional legacy incarnate, but she also personifies his reasons for taking up medical research in 1958: to understand diseases and make a difference to patients.

"I did medicine first and then I did two years in hospital as an intern, but I still wanted to do medical research because I thought, 'I'm so curious about what's happening.' In hospitals, you see patients, but you don't understand why they have got this disease," says Jacques.

And this drive to make a difference continued to sustain him, even when his research was challenged.

In 1961 his PhD research revealed that the thymus was not a vestigial organ, but instead played a vital role in developing the immune system – an idea initially dismissed by many leading lights of immunology.

"Peter Medawar, who got a Nobel Prize for Immunology, said 'we shall come to regard the presence of lymphocytes in the thymus as an evolutionary accident of no very great significance'. That was after one of my talks when I was a PhD student," remembers Jacques. "When a great man says that, I thought I must be wrong, but it urged me to do more."

In 1966 Jacques identified two types of white blood cells, T-cells and B-cells. T-cells mature in the thymus and have a variety of immune system roles, including killing foreign invaders, while B-cells develop in the bone marrow and produce antibodies.

These landmark findings have become central tenets of immunology, and they heralded the emergence and growth of the cancer immunotherapy field and treatments like the one undertaken by Jennifer.

"To me it's extremely exciting that immunotherapy is coming of age," says Jacques, now 87 years old.

This coming of age means that Stage 4 melanoma patients like Jennifer may no longer face the death sentence they faced five years ago.

It also means that our institute will continue to lead the way in developing new cancer immunotherapy treatments and achieving better results for patients through our synergistic combination of laboratory work and bedside practice, and through more clinical trials.

"We provide access to treatments that wouldn't be otherwise available – they are not standard out in the community but they are standard for us," says ONJCRI Medical Director Jonathan Cebon, who leads the team taking care of Jennifer.

Jennifer will continue to take the clinical trial drugs for the next two years, but she says she's feeling pretty good. "From start to finish, it's been fabulous and the guidance from the doctors and trial nurses has been fantastic. It's a great team to work with."

To me it's extremely exciting that **immunotherapy** is coming of age.

# THE SYNERGY OF CIRCLES

Dr George Morstyn has come full circle with his donation to our clinician scientist fellowship, and he sees the integration of clinician and researcher as closing an important loop too.

By taking research from the lab to the bedside and back to lab again, clinician scientists can study, apply and continually refine their research to create more effective and tailored treatments for their patients.

"In the last 20 years, it's just incredible the number of advances that have been made in the areas of cancer because of this integration between the lab and the clinic," he says.

To ensure that our institute keeps making such advances, **George has donated $100,000** to fund a clinician scientist for two years so they can spend essential research time in the laboratory.

George is also keen to support ONJCRI as the successor of the Melbourne-Austin Ludwig Institute for Cancer Research and the Joint Austin Ludwig Oncology Program, where he became Director in 1990.

The collaboration between the Austin Hospital and the Ludwig Institute, an international organisation headquartered in New York, married the best of academic research with clinical care, much like we do today.

This philosophy helped inform the career trajectory of George, who had previously been the Head of Oncology at the Austin Hospital, Head of Clinical Trials for the Ludwig Institute, and responsible for the first clinical trials of blood growth factors.

"My work at the Ludwig showed me that clinical trials and the development of new drugs required scientists in laboratories to work very closely with the clinicians who were treating patients," he says.

In 1991 he applied this translational research approach to his new job with US biotechnology company Amgen, which was struggling to recruit senior clinicians.

"I decided to move to Amgen, where I became the Chief Medical Officer, and instead of being responsible for patients one by one, I was responsible for hundreds of thousands of patients," says George.

## These clinicians can also learn from a terrific team.

Now Director of Symbio, the Co-operative Research Centre for Cancer Therapeutics and Actinogen, George says clinician scientists and the ONJCRI fellowship have essential roles to play in cancer research and much-needed clinical trials.

"Having trained clinicians who can participate in the clinical trial process allows us to get more effective therapies out into the community more quickly," he says.

"These clinicians can also learn from a terrific team at ONJCRI, which includes Jonathan Cebon, Matthias Ernst, Andrew Scott and others."





# Clinician scientist fellowship to support future leaders

ONJCRI is delighted to announce the inauguration of a program to support clinician scientists to perform translational research.

Seven outstanding young clinicians have been awarded these fellowships to build their research careers. Their work will involve clinical translation through collaboration with laboratory teams, thereby bringing together the best of laboratory science and clinical medicine.

Additionally, they will take lessons and experiences from their clinical practice into the laboratory to assist with the development of potentially life-saving scientific discoveries.

The Institute is proud to follow the precedent established by the Ludwig Institute for Cancer Research in creating a career path for clinician scientists. We believe that the future best lies in the hands of young women and men who can forge a union between the discoveries of laboratory and best practice in the clinic.

We are confident that in the hands of these young clinicians, the future of translational cancer research is ensured.

# GLOBAL NETWORK

Our network of international collaborative organisations, clinicians and researchers enables us to deliver high-impact translational research.


# THE POWER OF PARTNERSHIPS

By working with others, we strengthen our ability to translate breakthrough cancer research into treatments that save lives.

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

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.

As successor to the Australian operations of the Ludwig Institute for Cancer Research (LICR), our founding laboratory heads continue to collaborate with the global LICR community.

ONJCRI also collaborates with a wide range of national and international researchers, clinicians and industries to enhance the depth and impact of our research.

This includes our partnership with La Trobe University, which shares knowledge, skills and training to turn our research into more effective clinical practice and improved patient outcomes.





# Our collaboration with La Trobe University

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

The ongoing partnership between ONJCRI and La Trobe University remains a critical pillar to the future success of the Institute at many different levels. It builds on the anticipated synergies outlined in the five-year Research Collaboration Agreement, which was signed in 2014.

In particular, 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 independence 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 facilitates this by generously allocating PhD scholarships to ONJCRI and awarding additional scholarships to recipients of prestigious research grants from the National Health and Medical Research Council (NHMRC) and Australian Research Council.

The partnership between ONJCRI and La Trobe University provides exciting opportunities to form strategic research collaborations, and to commercialise and clinically develop discoveries from the laboratory bench. One such discovery, an antibody that may prevent muscle wasting associated with advanced stage cancer, will now be further developed with funding from the Victorian Cancer Agency and NHMRC as a joint effort between LIMS' Prof Nick Hoogenraad and ONJCRI's Prof Andrew Scott.

# The next generation

The talent and enthusiasm of our young scientists is boosting the work of the Institute's laboratories and benefiting cancer research globally.

## MARIAH ALORRO

Mariah is two years into her PhD investigating whether inhibiting a protein called STAT3 lowers tumour growth in gastrointestinal cancer.

"Stomach and colon cancers are often diagnosed late, when they're hard to treat. We need to find new treatments to use with chemotherapy and immunotherapy so we can prolong people's lives," she says.

Last year Mariah was a finalist in La Trobe University's three-minute thesis competition in which she had just three minutes to explain her research without scientific jargon.

"The competition really helped me improve how I explain my research to people. It's so important for scientists to communicate effectively to find collaborators," she says.

Mariah appreciates the supportive student community at the Institute and the mentorship of highly experienced researchers. "Doing my PhD in a hospital, working closely with oncologists, I'm always looking for how my research can make a difference for patients."

## DR SAGUN PARAKH

Sagun won the Institute's Student Medal in 2017, and completed his PhD in just three years while also working as an oncologist. During that time, Sagun mastered scientific research techniques, generated an impressive amount of data and published 10 papers in peer-reviewed journals.

For his PhD, Sagun developed antibodies to target proteins called the ErbB family, which help cancer cells survive and grow.

"Antibodies are naturally produced by the body to fight viruses, bacterial infections or cancer. I'm studying how these new antibodies we've developed in the lab could be used to treat cancer," he says.

Sagun treats patients with brain and lung cancer, and is involved in clinical trials. "Working as a doctor gives me the privileged opportunity to help people when they're most vulnerable. My aim is to one day provide them with a new, more effective treatment with fewer side effects, which gives people a better quality of life," Sagun says.





The Olivia Newton-John Cancer Research Institute is grateful to the individuals and organisations who supported our research in 2017.

## INDIVIDUALS AND ORGANISATIONS

Richard Balderstone and Sophie Holt
John and Meredith Baldwin
Banyule Primary School
Campania Sports and Social Club Inc (in liquidation)
The Beanie Golf Tournament
Bell Charitable Fund
The Hon John Brumby AO
Cancer Research Advocate Bikers
City of Melbourne
Hector Davis
Prof John Dewar
Prof Ashley Dunn
Mary Hill
Inner Wheel A61
Rae Johnston
KPMG
Macedonian Senior Citizens Group
Susan McCarthy and Tina Karrer
Monash University Mathematics Education Team
Dr George and Rosa Morstyn
Nelson Alexander - Foundation Day
Linda Bardo Nicholls AO
Point Cook Soccer Club
John and Barbara Ralph
Retired Tramways Employees Association
Rotary Club of Williamstown Friends R-4
Sally Capp
Ken Stanley and his family and friends
Dr Katherine Woodthorpe AO
Peter and Heather Wood AO
Anonymous (5)

## TRUSTS, FOUNDATIONS, INDUSTRY GRANTS AND GOVERNMENT FUNDING

Austin Medical Research Foundation
Australian & New Zealand Urogenital and Prostate Cancer Trials Group (ANZUPCTG)
Australian Government - Department of Industry, Innovation and Science
Australasian Gastro-Intestinal Trials Group (AGITG)
Harold and Cora Brennan Benevolent Trust (Equity Trustees)
Bayer Pharmaceuticals
Brian Smith Endowment (Equity Trustees)
Bristol Myers Squibb
Cancer Australia
Cancer Council Victoria
Carrie's Beanies 4 Brain Cancer
Cure Brain Cancer Foundation
Glaxo Smith Kline Biologicals S.A.
Harold Mitchell Foundation
Ian Potter Foundation
Ivan Maurice Jones Endowment (Perpetual Trustees)
John T Reid Charitable Trusts
La Trobe University
Lodge Amicus – Freemasons Victoria
Ludwig Cancer Research
Movember Foundation
The Myee Dodrington Medical Foundation (Perpetual Trustees)
National Breast Cancer Foundation
National Health and Medical Research Council
The Royal Australian and New Zealand College of Radiologists
The CASS Foundation
The Collie Foundation
Tour de Cure
Victorian Cancer Agency
Victorian State Government Operational Infrastructure Support Program
Wellcome Trust
Worldwide Cancer Research

## OUR SPECIAL THANKS TO FAMILY AND FRIENDS WHO MADE GENEROUS GIFTS IN MEMORY OF:

George Artemiou
David Brown
Ronnie Goldberg OAM
Margaret Macdonald
Anthony Middleton
Sheryl Sullivan
Armando Tolo
Mary Tomazic
Pauline Venn
Vittoria Zaffina

## GIFTS IN WILLS

Estate of At Gehrig Darrer Muir Flei

# SHARING OUR WINS WITH GOVERNMENT

The Olivia Newton-John Cancer Research Institute may include a household celebrity name, but governments are often unaware of the great work we do, says Neil Pharaoh, our government relations adviser.

"The ONJCRI story is a really exciting one, and I think it's one where there are lots of opportunities, but the Institute is not the best at shouting its stories from the rooftops like some other centres," says Neil. "People also assume the Institute has lots and lots of money."

So over the past year, we have taken every opportunity to make politicians more aware of our breakthroughs and the value of supporting our world-class research. We have also focused on a "top-down" and "bottom-up" approach of high-level engagement and grassroots communication.

Olivia Newton-John's recent visit to Canberra is a prime example of this successful top-down approach.

In September 2017 Olivia met Prime Minister Malcolm Turnbull, Opposition Leader Bill Shorten and other senior ministers and their shadow ministers to talk about the Institute's work.

"That was critical to raise our profile with government, get a seat at the policy table, as well as to secure future opportunities for funding," Neil says.

Among the outcomes was a federal Opposition pledge of $20 million to the Institute for breast and brain cancer research. The following month, the Federal Minister for Health Greg Hunt visited the Institute to meet brain cancer researchers and brain cancer survivor Tom Scrivens.

He also announced $50 million in government funding for the Australian Brain Cancer Mission, whose strategic advisory group will include Prof Andrew Scott, the Head of the Institute's Tumour Targeting Laboratory.

No less important is the bottom-up approach, which makes local members aware of how the Institute's breakthrough science reaches into their constituencies and saves the lives of patients like Tom.





# Amazing gift leaves a lasting legacy for cancer research

When Preston's Campania Sport and Social Club dissolved in 2016, the members decided to donate the money from the sale of their clubhouse to four Melbourne charities, including the Olivia Newton-John Cancer Research Institute.

The Campania Club's **generous gift of $212,000** has enabled the Institute to create two clinician scientist fellowships, and to purchase a bench-top centrifuge machine, which helps researchers to analyse blood samples at a cellular level.

Most importantly, the donation will fund life-saving cancer research and have a lasting positive impact on patients, both now and into the future.

The Olivia Newton-John Cancer Research Institute extends a sincere thank you to all the members of the Campania Sport and Social Club for this generous legacy.

The Campania Club was formed in 1975 by a group of men from the Campania region in Italy. Members met each week to enjoy social activities, to remember their homeland and to pass on their culture and traditions to their children. The Club members have been fundraising on behalf of local community organisations for decades.

The clinician scientist fellowships were awarded to Associate Prof Andrew Weickhardt and Dr Chun Fong.

Andrew is a medical oncologist at the Austin Hospital and a senior researcher at the Institute, who is investigating new treatments for aggressive bladder cancer. He has designed a clinical trial to test an immunotherapy drug that he hopes will boost the effectiveness of radiation and chemotherapy in shrinking tumours.

Chun is a haematologist at the Austin Hospital and a clinician scientist at the Institute, who is focusing on developing new targeted anti-cancer drugs to treat acute leukemia.

Joe De Amicis and Andrew Weickhardt.

## HELP FIND A CURE FOR CANCER

With your support, our researchers and clinicians can continue to work together to help people live better with cancer and defeat it.

For further information or to make your gift today, please call **+61 3 9496 5726** or contact **philanthropy@onjcri.org.au**

# Board of Directors

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

### THE HON JOHN BRUMBY AO, CHAIRMAN

The former Premier of Victoria, Mr Brumby served for more than seven years as State Treasurer, six years as Leader of the Victorian Opposition and seven as Federal MHR for Bendigo. Since retiring from politics, he has accepted a number of board positions, an appointment as an Enterprise Professor at the University of Melbourne, and is active in a range of community and not-for-profit organisations.

### RICHARD BALDERSTONE

Richard Balderstone has worked in the financial and investment markets for over 35 years. He is Chairman of JCP Investment Partners, a specialist investment management organisation with over $5 billion in funds under management, having been a founding partner when the business was established in 1999. Richard is a Trustee Director of several charitable organisations including the Baker Foundation, Surf Life Saving Foundation and the SecondBite Future Trust.

### SALLY CAPP

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

### PROF JOHN DEWAR

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

### LINDA BARDO NICHOLLS AO

Linda Bardo Nicholls is a corporate advisor and director of a number of leading Australian companies and organisations, including Fairfax Media, Inghams Enterprises, and Medibank Private, and is Japara Healthcare's Chairman. Previously, she was a director of Pacific Brands and Sigma Pharmaceuticals, and of the Walter and Eliza Hall Institute of Medical Research, Chairman of Australia Post, and a trustee and Vice President of the Harvard Business School Alumni Board. Her executive career was in banking and financial services.

### MORRY SCHWARTZ AM

Morry Schwartz is a publisher of Australian books, journals and periodicals. His company Schwartz Publishing operates Black Inc. books and La Trobe University Press. It also publishes the journals *Quarterly Essay* and *Australian Foreign Affairs*. Its sister company, Schwartz Media, publishes *The Monthly Magazine* and *The Saturday Paper*. For many years Morry operated the property company Pan Urban, which developed a wide range of major projects in Melbourne. He is Adjunct Professor of Journalism at RMIT.

### SUE SHILBURY

Sue Shilbury joined Austin Health as CEO in early 2017, following a three-decade career in the New South Wales public health sector. Previously a General Manager of North Shore Ryde Health Service and the Central Hospital Network, Sue has been a Director of the Division of Critical Care and Surgery at St George Hospital and Director of Clinical Services at the Royal Hospital for Women.

### DR KATHERINE WOODTHORPE AO

Dr Woodthorpe is currently Chair of the Antarctic Climate and Ecosystems CRC, Chair of The HEARing CRC, the National Climate Science Advisory Committee, and of Fishburners, a not-for-profit charity dedicated to assisting Australian technology startups. She is also non-Executive Director of Sirtex Medical Ltd, an ASX 200 company, Bioplatforms Australia, ARENA, the renewable energy agency and a member of the NSW Council of the AICD.

# ORGANISATIONAL CHART

**BOARD OF DIRECTORS**

**SCIENTIFIC ADVISORY COMMITTEE**

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*Prof Jonathan Cebon*

**SCIENTIFIC DIRECTOR**
*Prof Matthias Ernst*

**CHIEF FINANCIAL/ OPERATING OFFICER**
*Kim Tsai*

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- **Human Resources**
- **Information Technology & Bioinformatics**
- **Laboratory & Facilities Management**
- **Marketing & Communications**
- **Philanthropy**
- **Research Management & Governance**

**Austin Health Joint Medical Oncology Unit**
*A/Prof Niall Tebbutt*

**ACRF Centre for Translational Cancer Therapeutics & Imaging**
*Prof Andrew Scott*

**Department of Molecular Imaging & Therapy**
*Prof Andrew Scott*

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  *Prof Matthias Ernst*
- **Cancer Immunobiology Laboratory**
  *Prof Jonathan Cebon*
- **Cell Death & Survival Laboratory**
  *Dr Doug Fairlie*
- **Oncogenic Transcription Laboratory**
  *Prof John Mariadason*
- **Tumour Targeting Laboratory**
  *Prof Andrew Scott*
- **Translational Genomics & Epigenomics Laboratory**
  *A/Prof Alex Dobrovic*
- **Translational Breast Cancer Program**
  *Prof Robin Anderson*
  - **Metastasis Research Laboratory**
    *Prof Robin Anderson*
  - **Matrix Microenvironment & Metastasis Laboratory**
    *Dr Normand Pouliot*
  - **Tumour Progression & Heterogeneity Laboratory**
    *Dr Delphine Merino*



# COO's Report

**KIM TSAI**
CHIEF OPERATING AND FINANCIAL OFFICER

Over the last few years, we have focused on laying the foundations of our financial and administration systems so our scientists can concentrate on achieving research breakthroughs, develop innovative treatments and provide the best patient outcomes.

Such systems not only enable our operations to run seamlessly, but they also support our scientists and clinicians so they can spend more time at the laboratory bench and patient bedside instead of doing administration.

More importantly, our donors are essential to increasing and improving this bench-bedside time, and we are grateful to the individual donors and philanthropic institutions that helped make that happen this year. We couldn't do it without you.

The journey from laboratory to new cancer treatment can be a long one, and government research grants can only take us so far. Exciting projects can potentially flounder when this funding runs out, but private and philanthropic donations pick up the baton and help these projects reach the critical finishing line.

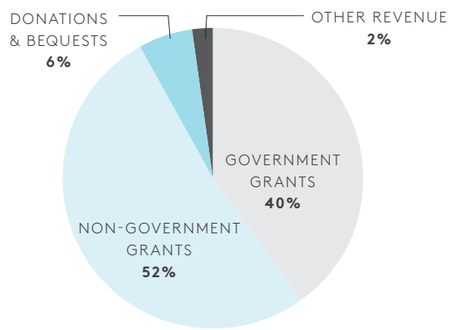
This annual report highlights a range of exciting projects and amazing scientists who all face this long game of cancer breakthroughs. We hope that you consider supporting them on this journey.

To those who have joined us on the journey so far, I give my heartfelt thanks. The researchers, support staff and I are grateful to receive the support of our donors and key stakeholders including the Australian Government (Department of Health), Victorian Government (Department of Health and Human Services), La Trobe University and Austin Health.

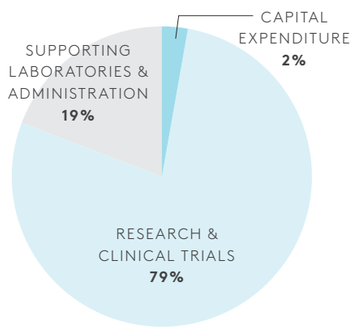
I would also like to take the opportunity to thank our small team of highly skilled and dedicated administration and research support staff, who help keep us all on track so we can keep our sights on the journey ahead.

KIM TSAI

**TOTAL REVENUE**




**TOTAL EXPENDITURE**



# Statement of profit or loss and other comprehensive income for the year ended 31 December 2017

| REVENUE | 2017 | 2016 |
|---|---|---|
| Grants | 13,521,984 | 12,868,143 |
| Donations and fundraising | 846,547 | 352,303 |
| Investment and other revenue | 303,299 | 344,747 |
| **Total Revenue** | **14,698,830** | **13,565,193** |
| **EXPENDITURE** | | |
| Research laboratories | 11,507,171 | 10,814,067 |
| Clinical trials | 298,405 | 34,166 |
| Administration support | 2,780,331 | 2,606,618 |
| **Total Expenditure** | **14,585,907** | **13,454,851** |
| **TOTAL COMPREHENSIVE INCOME** | **112,923** | **110,342** |

# Statement of financial position as at 31 December 2017

| ASSETS | 2017 | 2016 |
|---|---|---|
| Current assets | 12,367,563 | 15,133,488 |
| Non-current assets | 6,900,714 | 1,592,258 |
| **Total Assets** | **19,268,277** | **16,725,746** |
| **LIABILITIES** | | |
| Current liabilities | 15,888,565 | 13,508,360 |
| Non-current liabilities | 143,489 | 94,086 |
| **Total Liabilities** | **16,032,054** | **13,602,446** |
| **NET ASSETS** | **3,236,223** | **3,123,300** |
| **EQUITY** | | |
| **Total Equity** | **3,236,223** | **3,123,300** |

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.



# INVITED INTERNATIONAL PRESENTATIONS

**Dr Andreas Behren**
2nd International Conference on Cytokine Signaling in Cancer, Heraklion, Greece
*Inflammation mediates profound changes to the immunopeptidome of melanoma and alters tumour recognition by T cells.*

**Dr Michael Buchert**
Keystone Symposia on Cell plasticity within Tumor Microenvironment, Big Sky, USA
*Elucidating the role of Tuft cells in gastric cancer.*

Locksley Lab, Department of Medicine, USCF, San Francisco, USA
*Investigating the role of DCLK1 and Tuft cells in gastric cancer.*

**Prof Jonathan Cebon**
Current Trends in Immuno-Oncology, Tokyo, Japan
*Immune checkpoint inhibitors and new aspects of immuno-oncology in cancer.*

European Society for Medical Oncology (ESMO) Asia 2017 Congress, Singapore
*New vaccines.*

**Dr Hongdo Do**
Second Asia-Pacific Droplet Digital PCR Symposium, Seoul, South Korea
*Use of cell-free DNA for the management of lung cancer patients and liver transplant recipients.*

**A/Prof Alexander Dobrovic**
Chinese University of Hong Kong
*It's in the blood: a tale of 3 cities.*

AstraZeneca Symposium "New Technology of Liquid Biopsy", Shanghai, China
*Droplet digital PCR for detection of EGFR mutations in circulating tumour DNA.*

Circulating Cell-Free DNA Symposium: Overcoming Technical Challenges to Provide Clinical Solution, 24th International Molecular Medicine Tri-Conference, San Francisco, USA
*Clinical Implementation of Digital PCR for Cancer Diagnostics and Monitoring.*

**Dr Moritz Eissmann**
2nd International Conference on Cytokine Signaling in Cancer, Heraklion, Greece
*IL-33 promotes gastric tumour growth in a mast cell dependent manner.*

Ludwig Maximilian University Munich, Germany
*The tumor microenvironment in gastric cancer mouse models.*

University Clinic Frankfurt, Frankfurt, Germany
*IL-33-signalling and its role in gastric cancer.*

University of Ulsan, Ulsan, South Korea
*IL-33 signaling in gastro-intestinal cancer.*

Ajou University Medical Center, Suwon, South Korea
*Cytokine signalling in gastric cancer and novel models for gastric cancer.*

24th Asia Pacific Cancer Conference, Seoul, South Korea
*IL-33 promotes gastric tumour growth in a mast cell dependent manner.*

**Prof Matthias Ernst**
Roche Pharmaceuticals, Penzberg, Germany
*Targeting the myeloid compartment to suppress tumorigenesis in preclinical models.*

International Conference on Tumor-Host interactions, Monte Verità, Switzerland
*Excessive HCK kinase activity in the tumor stroma polarizes macrophages and promotes solid malignancies.*

2nd International Conference on Cytokine Signaling in Cancer, Heraklion, Greece
*Gp130/Stat3 signaling in cancer – a plethora of therapeutic opportunities.*

Inflammation-driven cancers Keystone Symposium, Keystone, USA
*IL33-mediated mast cell activation promotes gastric cancer through macrophage mobilization.*

**A/Prof Hui Gan**
AACR Annual Meeting, Washington DC, USA
*AACR clinical trials mini-symposium – novel agent and intervention trials.*

World Federation of Neuro-Oncology conference, Zurich, Switzerland
*Re-thinking EGFR.*

**Dr Su Kah Goh**
10th international symposium on circulating nucleic acids in plasma and serum, Montpellier, France
*Donor-specific cell-free DNA as a non-invasive marker of organ rejection after liver transplantation: a pilot study.*

**Dr Eliza Hawkes**
International Conference on Malignant Lymphoma, Lugarno, Italy
*Phase II study of single-agent copanlisib in patients with relapsed or refractory diffuse large B-cell lymphoma.*

European Hematology Association Conference, Madrid, Spain
*CHOP versus GEM-P in the first-line treatment of T-cell lymphoma: initial results of the UK NCRI phase II randomised chemo-t trial.*

American Society of Hematology conference, San Diego, USA
*Urine cultures at the onset of febrile neutropenia (FN) rarely impact antibiotic management in asymptomatic patients.*
*A multicenter retrospective review of outcomes of diffuse large B cell lymphoma (DLBCL) in the elderly treated with RCHOP in Australia.*
*An international multicenter retrospective comparison of induction.*

**Dr Erinna Lee**
5th Asia Pacific Protein Association Conference and 12th International Symposium of the Protein Society of Thailand, Bangsaen, Thailand
*Disarming the critical drivers of cancer.*

**Dr Delphine Merino**
Gordon Mammary Gland Biology Conference, Stowe, USA
*Tracking and targeting aggressive clones in triple negative breast cancer.*

Institut Paoli-Calmettes, Marseille, France
*Triple negative breast cancer, track and treat.*

**Dr Jennifer Mooi**
European Society of Medical Oncology (ESMO) Congress, Barcelona, Spain
*Consensus Molecular Subtypes (CMS) as predictors of benefit from bevacizumab in first line treatment of metastatic colorectal cancer: retrospective analysis of the MAX clinical trial.*

**Prof Andrew Scott**
International Atomic Energy Agency (IAEA) technical conference, Vienna, Austria
*Molecular imaging pathways in Australia and New Zealand.*

Asian Nuclear Medicine Academic Forum conference, Shanghai, China
*Global strategies for nuclear medicine.*

Vanderbilt University, Nashville, USA
*Novel therapeutics for targeting the epidermal growth factor receptor in epithelial cancers.*

Singapore Society of Nuclear Medicine Conference, Singapore
*Nuclear medicine and global initiative in radiopharmaceuticals.*
*iMolecular imaging and therapy of the tumour microenvironment.*

Antibody Therapeutics and Technology Conference, Prato, Italy
*Antibody drug conjugates for cancer therapy.*

International Atomic Energy Agency (IAEA) General Conference, Vienna, Austria
*Global burden of neuropsychiatric disorders.*

Asia Oceania Congress of Nuclear Medicine and Biology, Yokohama, Japan
*Nuclear medicine in Asia-Oceania.*

*Strategies for the future nuclear medicine.*

European Association of Nuclear Medicine conference, Vienna, Australia
*Health technology assessment for PET.*

**Dr Jian Zhong (Bill) Tang**
New Zealand Breast Cancer Symposium, Auckland, New Zealand
*Discovery of new therapy targets in HER2-enhanced breast cancer using a transposon mutagenesis screen.*

# PUBLICATIONS


**1.** Abou-Alfa, G. K., Blanc, J. F., Miles, S., Ganten, T., Trojan, J., Cebon, J., Liem, A. K., Lipton, L., Gupta, C., Wu, B., Bass, M., Hollywood, E., Ma, J., Bradley, M., Litten, J. and Saltz, L. B. "Phase II Study of First-Line Trebananib Plus Sorafenib in Patients with Advanced Hepatocellular Carcinoma." *Oncologist* 22(7): 780-e765. (2017)

**2.** Adam, A., Hellig, J. C., Perera, M., Bolton, D. and Lawrentschuk, N. "'Prostate Cancer Risk Calculator' mobile applications (Apps): a systematic review and scoring using the validated user version of the Mobile Application Rating Scale (uMARS)." *World J Urol*. (2017)

**3.** Ahmed, A. U., Yim, H. C. H., Alorro, M., Ernst, M. and Williams, B. R. G. "Integrin-Linked Kinase Expression in Myeloid Cells Promotes Inflammatory Signaling during Experimental Colitis." *J Immunol* 199: 2128-2139. (2017)

**4.** Ahn, M. J., Kim, D. W., Cho, B. C., Kim, S. W., Lee, J. S., Ahn, J. S., Kim, T. M., Lin, C. C., Kim, H. R., John, T., Kao, S., Goldman, J. W., Su, W. C., Natale, R., Rabbie, S., Harrop, B., Overend, P., Yang, Z. and Yang, J. C. "Activity and safety of AZD3759 in EGFR-mutant non-small-cell lung cancer with CNS metastases (BLOOM): a phase 1, open-label, dose-escalation and dose-expansion study." *Lancet Respir Med* 5(11): 891-902. (2017)

**5.** Alchin, D. R., Murphy, D. and Lawrentschuk, N. "Predicting the risk of positive surgical margins following robotic-assisted radical prostatectomy (review)." *Minerva Urol Nefrol* 69(1): 56-62. (2017)

**6.** Alorro, M. G., Pierce, T. P., Eissmann, M. F., Dijkstra, C., Dickins, R. A., Ernst, M., Buchert, M. and Masson, F. "Generation of an inducible mouse model to reversibly silence Stat3." *Genesis*. (2017)

**7.** Anderson, R. L., Ingman, W. V. and Britt, K. L. "Editorial: How Reproductive History Influences Our Breast Cancer Risk." *Front Oncol* 7: 289. (2017)

**8.** Arulananda, S., Do, H., Musafer, A., Mitchell, P., Dobrovic, A. and John, T. "Combination osimertinib and gefitinib in C797S and T790M EGFR mutated non-small-cell lung cancer." *J Thorac Oncol* 12(11): 1728-1732. (2017)

**9.** Ayati, N., Jesudason, S., Berlangieri, S. U. and Scott, A. M. "Generalized Lymph Node Activation after Influenza Vaccination on 18F FDG-PET/CT Imaging, an Important Pitfall in PET Interpretation." *Asia Ocean J Nucl Med Biol* 5(2): 148-150. (2017)

**10.** Bjornmalm, M., Thurecht, K. J., Michael, M., Scott, A. M. and Caruso, F. "Bridging Bio-Nano Science and Cancer Nanomedicine." *ACS Nano* 11(10): 9594-9613. (2017)

**11.** Brouwer, J. M., Lan, P., Cowan, A. D., Bernardini, J. P., Birkinshaw, R. W., van Delft, M. F., Sleebs, B. E., Robin, A. Y., Wardak, A., Tan, I. K., Reljic, B., Lee, E. F., Fairlie, W. D., Call, M. J., Smith, B. J., Dewson, G., Lessene, G., Colman, P. M. and Czabotar, P. E. "Conversion of Bim-BH3 from Activator to Inhibitor of Bak through Structure-Based Design." *Mol Cell* 68(4): 659-672 e659. (2017)

**12.** Burr, M. L., Sparbier, C. E., Chan, Y. C., Williamson, J. C., Woods, K., Beavis, P. A., Lam, E. Y. N., Henderson, M. A., Bell, C. C., Stolzenburg, S., Gilan, O., Bloor, S., Noori, T., Morgens, D. W., Bassik, M. C., Neeson, P. J., Behren, A., Darcy, P. K., Dawson, S. J., Voskoboinik, I., Trapani, J. A., Cebon, J., Lehner, P. J. and Dawson, M. A. "CMTM6 maintains the expression of PD-L1 and regulates anti-tumour immunity." *Nature* 549(7670): 101-105. (2017)

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**15.** Candiloro, I. L. M., Mikeska, T. and Dobrovic, A. "Assessing alternative base substitutions at primer CpG sites to optimise unbiased PCR amplification of methylated sequences." *Clin Epigenetics* 9: 31. (2017)

**16.** Charmsaz, S., Al-Ejeh, F., Yeadon, T. M., Miller, K. J., Smith, F. M., Stringer, B. W., Moore, A. S., Lee, F. T., Cooper, L. T., Stylianou, C., Yarranton, G. T., Woronicz, J., Scott, A. M., Lackmann, M. and Boyd, A. W. "EphA3 as a target for antibody immunotherapy in acute lymphoblastic leukemia." *Leukemia* 31(8): 1779-1787. (2017)

**17.** Charmsaz, S., Scott, A. M. and Boyd, A. W. "Targeted therapies in hematological malignancies using therapeutic monoclonal antibodies against eph family receptors." *Exp Hematol* 54: 31-39. (2017)

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**21.** Christidis, D., McGrath, S., Perera, M., Manning, T., Bolton, D. and Lawrentschuk, N. "Minimally invasive surgical therapies for benign prostatic hypertrophy: The rise in minimally invasive surgical therapies." *Prostate Int* 5(2): 41-46. (2017)

**22.** Chueh, A. C., Liew, M. S., Russell, P. A., Walkiewicz, M., Jayachandran, A., Starmans, M. H. W., Boutros, P. C., Wright, G., Barnett, S. A., Mariadason, J. M. and John, T. "Promoter hypomethylation of NY-ESO-1, association with clinicopathological features and PD-L1 expression in non-small cell lung cancer." *Oncotarget* 8(43): 74036-74048. (2017)

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# ONJCRI SEMINARS

**Dr Silvia Alvarez-Diaz**
Walter and Eliza Hall Institute of Medical Research
*Deciphering the role of necroptosis in development, autoimmune disease and cancer.*

**Dr Miles Andrews**
MD Anderson Cancer Center, University of Texas, USA
*Waiter; there's a bug in my chemo - have microbes hit the prime time in cancer treatment?*

**Prof Eduard Batlle**
Institute for Research in Biomedicine, The Barcelona Institute of Science and Technology, Spain
*Mechanisms of immune evasion and metastasis in colorectal cancer.*

**Prof Gabrielle Belz**
Walter and Eliza Hall Institute of Medical Research
*Teasing apart innate lymphoid cell development and homeostasis.*

**A/Prof Claudine Bonder**
Center for Cancer Biology, University of South Australia & SA Pathology
*Vasculogenic mimicry; a bloody new way for cancer growth and spread.*

**Dr Kristin Brown**
Peter MacCallum Cancer Centre
*Metabolic reprogramming and chemotherapy resistance in breast cancer.*

**Dr Liz Christie**
Peter MacCallum Cancer Centre
*Evolution of chemoresistance in ovarian cancer.*

**Dr Melissa Davis**
Walter and Eliza Hall Institute of Medical Research
*Post-transcriptional regulation in a model of breast cancer epithelial-mesenchymal plasticity.*

**Dr Bedrich Eckhardt**
MD Anderson Cancer Center, University of Texas, USA
*Emerging therapeutic targets for aggressive breast cancers.*

**Prof Ulf Eriksson**
Karolinska Institute, Stockholm, Sweden
*VEGF-B signalling and metabolism.*

**Prof Dr Robert Feil**
University of Tübingen, Germany
*Viagra releases the brakes on melanoma growth.*

**Prof Peter Gibbs**
Walter and Eliza Hall Institute of Medical Research
*Beyond conventional clinical trials – biomarker and registry RCTs.*

**Prof John Hamilton**
The University of Melbourne
*A new GM-CSF-dependent pathway in inflammation.*

**Prof Andy Hill**
La Trobe University
*Extracellular vesicles – their role in health and disease.*

**Dr Damien Hudson**
Murdoch Children's Research Institute
*Chromosome structure, genome instability and disease.*

**Prof Bendan Jenkins**
Hudson Institute of Medical Research
*Uncovering the role of innate immune receptors in cancer.*

**Dr Angus Johnston**
Monash University
*Targeted drug delivery: understanding the secrets of nanoparticle cell interactions.*

**Prof Sharad Kumar**
University of South Australia
*Caspase-2, aneuploidy and tumour suppression.*

**Dr Najoua Lalaoui**
Walter and Eliza Hall Institute of Medical Research
*Targeting IAPs in cancer.*

**Dr Xia Li**
La Trobe University
*BIOSTATISTICS support for clinical research.*

**Dr Bruce Littlefield**
Eisai Inc.
*Eribulin (Halaven®) mechanisms of action: beyond antimitotic effects to complex changes in tumor biology.*

**Prof Roger Martin**
Peter MacCallum Cancer Centre
*New topical radioprotectors for cancer radiotherapy.*

**Prof Stephen Meyn**
The Hospital for Sick Children, Toronto, Ontario, Canada
*Diagnostic and predictive uses of whole genome sequencing in children.*

**Dr Lisa Mielke**
Walter and Eliza Hall Institute of Medical Research
*Transcriptional regulation of innate lymphocyte and T cell function in intestinal inflammation.*

**Dr Sandra Nicholson**
Walter and Eliza Hall Institute of Medical Research
*SOCS protein regulation of NK cell-mediated tumor immunity.*

**Dr Bhupinder Pal**
Walter and Eliza Hall Institute of Medical Research
*Construction of developmental lineage relationships in the mammary gland by single-cell RNA profiling.*

**Dr Con Panousis**
CSL
*Targeting Factor XIIa: Potential for safe anticoagulation and more.....*

**Prof Alain Puisieux**
Cancer Research Center of Lyon, France
*Differentiation status of the cell-of-origin and genetic routes toward tumorigenesis.*

**Dr Paul Ramsland**
RMIT University
*Structural and computational studies of protein-glycan interactions in cancer and infection.*

**Prof Bruce WS Robinson AM**
University of Western Australia
*Augmenting and broadening immune responses against mutated tumour neo-antigens - recent studies and translational implications.*

**Dr Elaine Sanij**
Peter MacCallum Cancer Centre
*Activation of nucleolar DNA damage response as a novel therapeutic strategy for ovarian cancer.*

**Dr Cyril Seillet**
Walter and Eliza Hall Institute of Medical Research
*Deciphering the innate lymphoid cell transcriptional program.*

**A/Prof Jake Shortt**
Monash Health
*Epigenetic meets immuno-oncology - therapeutic targeting of PDL1 transcription.*

**A/Prof Oliver Sieber**
Walter and Eliza Hall Institute of Medical Research
*What do proteomes of colorectal cancer cell lines tell us about primary cancer.*

**A/Prof Natalie Sims**
St Vincent's Institute
*Osteocytes: the multifunctional cellular network that controls bone strength.*

**Prof Melissa Southey**
University of Melbourne Centre for Cancer Research
*Preventing cancer in women who are at the highest risk of the disease.*

**A/Prof Alex Swarbrick**
Garvan Institute of Medical Research
*Exploring the breast cancer microenvironment for novel therapeutic targets at single cell resolution.*

**Dr Michele Teng**
QIMR Berghofer Medical Research Institute
*The science of cancer immunotherapy: where we are headed.*

**Dr Clare Weeden**
Walter and Eliza Hall Institute of Medical Research
*Understanding the formation and treatment of lung squamous cell carcinoma.*

**A/Prof Andrew Wei**
The Alfred Hospital
*Targeting the cell death machinery in AML: BH3-mimetics.*

**Prof Bryan Williams**
Hudson Institute of Medical Research
*Regulatory circuits in innate Immunity, inflammation and cancer.*

**Dr Jason Wong**
Lowy Cancer Research Centre
*Uncovering mutational and DNA repair processes in the search for cis-regulatory mutations in cancer genomes.*




# THE WELLNESS WALK AND RESEARCH RUN

A bright Sunday morning in September saw thousands gather at La Trobe University to be part of the Annual Wellness Walk and Research Run. More than 2,500 people walked or ran, cheered on by our Champion, Olivia Newton-John. Over 150 volunteers made the day possible, and our fabulous supporters **raised more than $400,000** for wellness and research programs.

Each of our laboratory and administration teams fundraised for the event. We were easily spotted in the crowd wearing matching Institute T-shirts, walking and running the 5km or 10km course.

Before and after the walk, our researchers met participants, explained their work and showed them what cancer cells look like under a microscope.

**The 2018 Wellness Walk and Research Run will be held at La Trobe University on 16th September.**

Olivia Newton-John
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