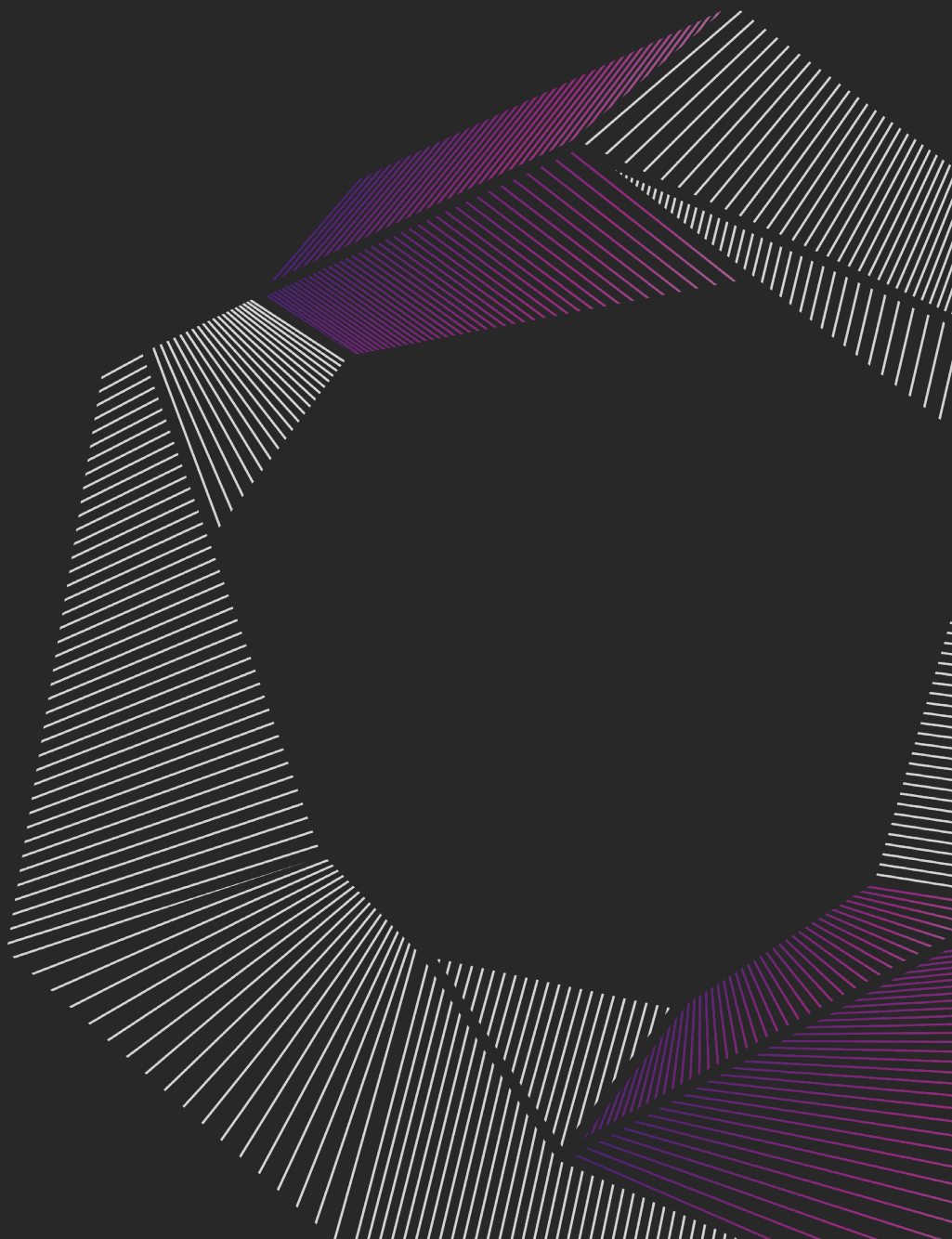
Peter Mac

Peter MacCallum Cancer Centre
Victoria Australia

CANCER RESEARCH STUDENT PROJECTS 2025



FROM OUR CANCER RESEARCH EXECUTIVE DIRECTOR

For over 70 years, Peter Mac has been providing high quality treatment and multidisciplinary care for cancer patients and their families. Importantly, we house Australia's largest and most progressive cancer research group, one of only a handful of sites outside the United States where scientists and clinicians work side-by-side.

Our research covers a diversity of topics that range from laboratory-based studies into the fundamental mechanisms of cell transformation, translational studies that provide a pipeline to the patient, clinical trials with novel treatments, and research aimed to improve supportive care.

The proximity and strong collaborative links of clinicians and scientists provides unique opportunities for medical advances to be moved from the 'bench to the bedside' and for clinically orientated questions to guide our research agenda. As such, our research programs are having a profound impact on the understanding of cancer biology and are leading to more effective and individualised patient care.

As Executive Director Cancer Research, it is my mission to strategically drive Peter Mac's standing as one of the leading cancer centres in the world by enhancing our research outputs, increasing our talent pool and enabling existing and new areas of research excellence.

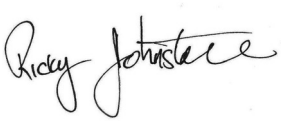
I firmly believe that our model of research-driven cancer care is the right one and Peter Mac is uniquely positioned to expand this paradigm both internally and with our external partners.

Peter Mac is committed to continue to support and build our broad research enterprise including fundamental research, and I am in no doubt that strong discovery-based research labs and programs are essential for us deliver the best care for our patients.

If you undertake your research at Peter Mac, you will be supported by a pre-eminent academic program, driven by internationally renowned laboratory and clinician researchers, with a strong focus on educating future generations of cancer clinicians and researchers.

You have the opportunity to work at the forefront of cancer care and make a contribution to our research advances.

Welcome to Peter Mac Cancer Research.



Professor Ricky Johnstone
Executive Director, Cancer Research

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Peter Mac's comprehensive and internationally renowned cancer researchers seek fundamental biological and biomedical discoveries, and aim to facilitate the development and application of these discoveries to their full therapeutic potential.

Critical to this aim is our ability to recruit outstanding staff and students to drive our innovative basic and translational research.

This book provides an overview of project directions available for students across different disciplines, all with a focus on cancer and changing treatment outcomes for patients.

'Nothing but the best is good enough for the treatment of cancer'

Sir Peter MacCallum

ABOUT OUR RESEARCH

Peter Mac is one of the world's leading cancer research, education and treatment centres globally and is Australia's only public hospital solely dedicated to caring for people affected by cancer. We have over 2,500 staff, including more than 700 laboratory and clinical researchers, all focused on providing better treatments, better care and potential cures for cancer.

Dedicated research is the key to better treatments, better care and cures for cancer. This is a place where normal days are extraordinary – as are the people we care for. Each day our team strives to provide the very best in cancer care, better treatments and potential cures for all people affected by cancer.

Globally, we are facing one of the most pivotal times in the pursuit of cancer cures, and Peter Mac stands at its forefront. Together, we aim to lead a new era of cancer prevention, care and discovery, supported by state-of-the-art facilities at our home within the Victorian Comprehensive Cancer Centre building.

Peter Mac is home to over 700 researchers, including more than 250 students (PhD, MPhil, Honours and others).

LABORATORY RESEARCH

Peter Mac's comprehensive and internationally renowned cancer research laboratories seek fundamental biological and biomedical discoveries, and aim to facilitate the development and application of these discoveries to their full therapeutic potential.

Supported by core technology platforms, our research laboratories are organized into programs of laboratory-based and translational research:

- Cancer Biology & Therapeutics Program
- Cancer Evolution & Metastasis Program
- Cancer Immunology Program
- Computational Biology Program
- Organogenesis & Cancer Program

Peter Mac is home to many large, group [cohort] studies collecting biospecimens, blood samples and survey data from people with cancer to build large open-access resources for innovative research projects. Some studies also collect information from people who have never had cancer.

Cohort studies give our researchers, and researchers worldwide, access to a vast array of ethically collected clinical samples and associated clinical data. Our cohort studies include:

- Australian Ovarian Cancer Study (AOCS)
- BROCADE- BReast Origin CAncer tissue DonatEd after death
- CASCADE- Cancer Tissue Collection After Death
- Cancer 2015
- International Sarcoma Kindred Study
- kConFab
- Lifepool
- Melanoma Research Victoria (MRV)
- SUPER- Solving cancer of unknown primary
- ViP: Variants in Practice

CLINICAL RESEARCH

Peter Mac is committed to linking patient care with cancer research. Our clinician researchers take their observations from the clinic and plan their research directions with patients in mind.

There are many specialised groups actively engaged in clinical research. Our aim is to improve treatment, and care and experience outcomes of cancer patients and their support networks.

Our clinician researchers work across all tumour types and services: the Bone and Soft Tissue, Breast, Cancer of Unknown Primary, Colorectal, Gynae-Oncology, Haematology, Head and Neck, Lung, Melanoma and Skin, Neuro-Oncology, Paediatric and Late Effects, Upper Gastrointestinal, and Uro-Oncology Services.

Clinical services research includes the following areas:

Australian Cancer Survivorship Centre (ACSC)

The ACSC aims to better understand the issues that survivors experience and their needs, and develop and test interventions that improve survivors' well-being.

Cancer Allied Health (CAH)

CAH research is focused on delivering high-quality evidence-based services to our patients, their families and carers.

Familial Cancer Centre (FCC)

The Parkville FCC works with families to investigate hereditary cancer syndromes and how they can better manage their cancer risk.

Imaging and Diagnostic Research

Imaging and diagnostic research is conducted in Peter Mac's Centre for Cancer Imaging. Our researchers image tumours to develop new therapies and improve imaging technologies for cancer patients.

Infectious Diseases & Infection Control (IDIC)

Peter Mac's IDIC research group aims to improve cancer outcomes through enhanced infection services. This group is home to the NHMRC National Centre for Infections in Cancer - an integrated health care program for reducing infections in cancer.

ONTrac

This multidisciplinary research group is committed to improving the understanding and knowledge of the health outcomes of young people living with cancer.

Pain & Palliative Care (PPC) Research

PPC research focuses on symptom control, end-of-life care including advance care planning, and models of integration of palliative and acute care.

Physical Sciences Research

Physical sciences research is focused on the delivery of cancer radiotherapy treatments that increase tumour exposure to effective therapy while reducing exposure to normal tissue.

Radiation Oncology Research

Radiation oncology research aims to provide the most up-to-date and effective evidence-based treatment for patients with cancer who require radiotherapy as part of their treatment.

Cancer Surgery & Anaesthesia Research

This clinical research group is working to improve the technical aspects and impact of cancer surgeries, and to improve the delivery and efficacy of anaesthesia and interventional pain medicine.

Victorian Epigenetics Group (VEG)

The VEG supports clinical trials of "epigenetic drugs" for patients with blood cancers through preclinical evaluation, novel biomarker development and early phase clinical trials of new drugs.

Biostatistics and Clinical Trials (BaCT)

Peter Mac is the leading biostatistical centre focusing on cancer clinical trials in Australia. The centre provides statistical expertise for national cancer trials groups including the Trans Tasman Radiation Oncology Group (TROG) and the Australasian Leukaemia and Lymphoma Study Group (ALLG).

Radiation and Cancer Imaging

State-of-the-art radiation and imaging equipment underpins Peter Mac's efforts to enhance the delivery of radiation therapy, both as a single modality and, increasingly, as a combined modality therapy using novel chemotherapy and targeted therapy agents.

Clinical Trials

Clinical trials are central to Peter Mac's commitment to finding more effective cancer treatments and improving care for people with cancer, their families and carers.

With more than 200 clinical trials active every year, Peter Mac has a comprehensive network of clinical trials support in place, bringing together laboratory researchers, medical, surgical and radiation oncologists, many of whom are clinician-researchers, pathologists, pharmacists, geneticists and clinical trials nurses.

The Parkville Cancer Clinical Trials Unit (PCCTU) incorporates the cancer clinical trials services of Peter Mac, the Royal Melbourne Hospital, and the Royal Women's Hospital.

HEALTH SERVICES RESEARCH

The Department of Health Services Research supports the broader health services research and implementation science portfolio. The new department reinforces Peter Mac's investment in health services research and implementation science as a new major research theme in the 2020- 2025 Research Strategic Plan.

The focus of the health services research and implementation science portfolio is to bring together Peter Mac researchers, clinicians and patients to deliver world class, equitable, and evidence-based patient-centred cancer treatments and care.

Health services research and implementation science, or HSRIS, complements Peter Mac's other major research themes to deliver a comprehensive 'bench to bedside and beyond' program of research.

Some of the department's strategic imperatives include:

- Leading data-driven priority setting for improving clinical care through assessment of needs, gaps and key outcomes;
- Identifying and harnessing existing research capacity, networks and relationships;
- Embedding a co-design model across all health services research, implementation science, and clinical trial activities;
- Facilitating high quality knowledge translation into policy and practice.

PLATFORM TECHNOLOGIES

Our core facilities and platform technologies are the backbone of our research and ensure that the researchers are outfitted with the equipment and expertise needed to facilitate their research.

An important role of the core platform technologies is to also identify, import, and develop new technologies.

Peter Mac's core technologies and expertise are also made available to external researchers on a collaborative or cost recovery basis, thereby increasing research output in the wider bioscience community.

Centre for Advanced Histology and Microscopy

The Centre for Advanced Histology and Microscopy (CAHM) underpins a multitude of cancer research projects with four core platforms:

- Histology – including tissue embedding and sectioning, slide staining, immunohistochemistry and multiplex immunohistochemistry
- Optical Microscopy- including widefield, slide scanning, confocal microscopy, super-resolution microscopy, multiphoton microscopy and spatial proteomics platforms
- Electron Microscopy- including sample preparation and acquisition for both transmission and scanning electron microscopy
- Image Analysis- including freeware and licensed software for the analysis of multiparameter microscopy data

Researchers utilising CAHM receive support, training and advice from expert technical scientists.

Bioinformatics Consulting Core

The Bioinformatics Consulting Core provides services and know-how for the analyses of high-throughput genomics data. Our team of bioinformaticians and postdoctoral scientists work alongside laboratory and clinical researchers and contribute to their experimental design, grant applications and the analysis and publication of genomic and transcriptomic data. Data types analysed by the core include whole-exome sequencing, targeted re-sequencing, RNA-sequencing, ChIP-sequencing, NanoString and various types of microarray data.

Flow Cytometry and Cell Sorting

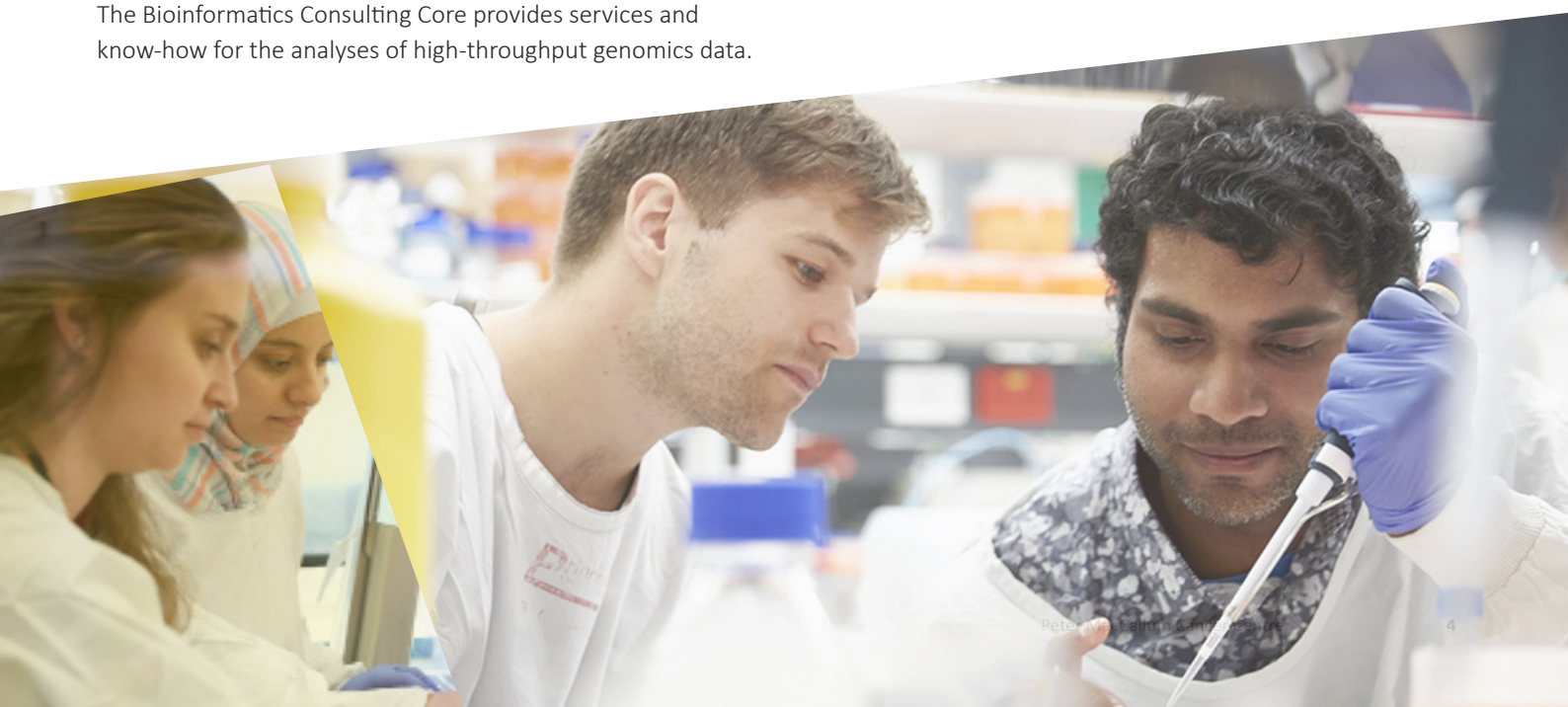
This facility provides researchers with access to state-of-the-art equipment and expertise that enables isolation, separation and analysis of cell populations based on their biological and therapeutic properties.

Flow cytometry is a powerful technique for the analysis of individual cells within complex populations. It is used in both research and clinical settings, and has an important role in the translation of knowledge from the research setting to the clinical area (translational research).

Victorian Centre for Functional Genomics

Want to work with CRISPR? Want to knock down gene expression? Interested in growing your cells in 3D? Thinking about finding the next generation drug that targets your disease of interest? How about quantifying that cellular phenotype you are working on or the expression of a series of proteins? You can do all this and more in the Victorian Centre for Functional Genomics (VCFG) on Level 11 using the sophisticated liquid handling automation, high content microscopy, live cell imaging and specialised analysis pipelines.

The VCFG team are highly experienced technical experts in the areas of high throughput RNAi, CRISPR and compound screening coupled with many different types of functional readouts that best represent your cell biology and disease state. They revel in the challenge to take a regular bench



experiment and transpose it to a high throughput multiplexed approach.

The VCFG has developed an automated 3D cellular characterisation, imaging and screening pipeline that can be adapted to analyse cell lines and patient derived materials. This is the start of significant steps towards providing personalised medicine approaches. The VCFG operates a 'researcher-driven-staff assisted' model whereby someone from the team works with you through the process of your project, trains you to run some of the instrumentation and assists in analysis and interpretation. The opportunities are vast, it really just requires your imagination!

Molecular Genomics

The Molecular Genomics Core is an exciting space with the most relevant state-of-the-art genomics technologies and highly skilled staff to support researchers conduct genomics experiments. At the MGC we process samples according to established methods and work with researchers to develop and implement the latest genomics tools and niche protocols. We also team up with other Core Facilities at PeterMac to integrate all aspects of sample processing and analysis, giving the researcher technical confidence to focus on the biology is trying to answer. Via the MGC the researcher has expert access to:

- **NGS, MiSeq, NextSeq and NovaSeq (Illumina):** whole genome sequencing, whole exome sequencing, targeted DNA sequencing, RNA-Seq, ChIP-Seq, ATAC-Seq, CRISPR-Seq, etc.
- **Single Cell Sequencing, Chromium (10x Genomics):** Single-cell gene expression, single-cell immune profiling, single-cell ATAC-Seq, etc.
- **Spatial Transcriptomics, GeoMX DSP (Nanostring) and Visium (10x Genomics):** gene expression with tissue information from FFPE or FF sections.
- **Others:** Nanostring for hybridization-based gene expression; DRUG-seq for high-throughput RNA-Seq; TapeStation for nucleic acid QC; liquid handlers for high throughput sample processing, etc.

Research Computing Facility

The Research Computing Facility is responsible for administering Peter Mac's Computing Cluster and Linux environment, providing leadership in the area of data governance, managing the Research Data Repository/Archive and REDCap, administering cloud computing resources, and providing specialised software solutions and/or systems to support research. The facility also provides training for the software systems they administer as well as general bioinformatics and statistics.

Tissue Bank

The Tissue bank is a member of the Victorian Cancer Biobank, providing researchers with ethically collected, high quality human tissue, blood and data samples for their investigative projects. It also supports clinical trials at Peter Mac by processing and storing blood and tissue specimens in accordance with trial-specific protocols.

Research Laboratory Support Services

Research Laboratory Support Services (RLSS) provides a centralised, comprehensive range of services that support the researcher's needs in a timely and cost effective manner. This includes Media Kitchen, Labware Services and Research Store.

Transgenic and SPF Facility

We currently breed and maintain approximately 20,000 mice, representing over 130 different strains of transgenic and gene-targeted mice.

Peter Mac's Animal Ethics Committee (AEC) has an important role in overseeing the ethical conduct of any work involving the use of animals for scientific purposes, conforming to the NHMRC Australian Code of Practice for the Care and Use of Animals for Scientific Purposes.

CANCER RESEARCH PROGRAMS

Cancer Biology and Therapeutics Program

Research Labs:

- Sarah-Jane Dawson
- Mark Dawson
- David Bowtell
- Kristin Brown
- Charbel Darido
- Melanie Eckersley-Maslin
- Shom Goel
- Lev Kats
- Ricky Johnstone
- Grant McArthur
- Vihandha Wickramasinghe

The Cancer Biology & Therapeutics Program aims to integrate various basic research activities, platform technologies and pre-clinical model systems available within Peter Mac to discover, develop, characterise and refine novel cancer therapeutics for clinical use for solid tumours.

This integrated program allows insight into fundamental aspects of cancer biology through the identification of novel tumour-suppressor and tumour-initiating genes. We explore the functional relationships between altered cancer genetics and aberrations to the cancer epigenome, and a deeper understanding of the molecular events that drive oncogenic signalling networks. These findings serve as a basis for extensive translation-based studies to determine the potential therapeutic benefit of interfering with or augmenting the activity of key proteins involved in these signalling networks through pharmacological intervention.

Find Projects

Cancer Evolution and Metastasis Program

Research Labs:

- Belinda Parker
- Kylie Gorringe
- Steven Stacker
- Ian Campbell
- Wayne Phillips
- Stephen Fox
- Nicholas Clemons
- Kara Britt
- Elizabeth Christie

The Cancer Evolution & Metastasis Program focuses on understanding the mechanisms of cancer initiation, progression and metastatic spread.

The program works across multiple tumour streams to ultimately uncover markers of risk and to develop precision therapeutics. The program encompasses three main themes:

- Risk and Prevention (Britt and Campbell labs)
- Therapy and Resistance (Christie, Clemons, Gorringe, Phillips and Ramsay labs)
- Progression and metastasis (Fox, Parker and Stacker labs)

The constituent laboratories explore these themes using a wide variety of approaches and technologies including whole-genome and single-cell genomics and transcriptomics; in vitro and in vivo tumour models, including patient-derived and animal models; high-content and spatial imaging; and high-throughput functional genomics, small molecule screening and biomarker discovery platforms.

Find Projects

CANCER RESEARCH PROGRAMS

Cancer Immunology Program

Research Labs:

- Joe Trapani
- Phillip Darcy
- Paul Beavis
- Sherene Loi
- Jane Oliaro
- Ian Parish
- Sarah Russell
- Gail Risbridger
- Ilia Voskoboinik
- Ben Solomon
- Paul Neeson
- Riccardo Dolcetti
- Luc Furic
- Paul Ekert

Harnessing the power of the immune system to fight cancer through research into cancer immune surveillance and chemo/immunotherapy, defining key cells and molecules that can elicit an effective response to tumours.

We are interested in the very early stages of how immune cells can pick up and respond to the presence of cancer cells. We have demonstrated that specific toxins made by "killer T cells" can prevent the onset of certain cancers (immune surveillance), and are developing genetic technologies to modify and expand the activity of these cells to treat established malignancies. In addition, we are defining the molecular means by which new classes of anti-cancer drugs kill cancer cells, so that rational choices can be made on the most appropriate cancer chemotherapy for a patient.

Find Projects

Computational Biology Program

Research Labs:

- Alicia Oshlack
- Anna Trigos
- Gerry Tonkin-Hill

The Computational Biology Program uses mathematics, statistics and computing to generate new discoveries in cancer. We develop new models, algorithms and software tools, and apply these to make sense of cancer data. This includes whole genome, exome, transcriptome and epigenome sequencing data.

Our research interests encompass:

- bioinformatics algorithm and methods development
- computational cancer biology
- cancer evolution and genomics
- software tool development
- personalised medicine.

The program includes research laboratories, as well as the Bioinformatics Consulting Core and the Research Computing Facility. Scientists come from a range of disciplines including biology, computer science, mathematics and statistics, as well as software engineering.

Find Projects

CANCER RESEARCH PROGRAMS

Organogenesis & Cancer Program

Research Labs:

- Kieran Harvey
- Ben Hogan
- Louise Cheng
- Andrew Cox
- Najoua Lalaoui
- Sarah Russell

The primary focus of the Organogenesis & Cancer Program is to investigate the process of organ development and how failure of organogenesis contributes to cancer.

Despite being a fundamental part of life, we still lack a clear understanding of how individual organs know how to grow to the right size and maintain this size. The roles of stem and progenitor cells in the growth of different organs are also unclear, as is the impact of diet and nutrition on organ growth. To investigate these questions, our program leverages the unique strengths that are offered by different experimental systems, including Drosophila, zebrafish and organoid cultures. We also collaborate with clinicians from within the VCCC network to examine how deregulation of organogenesis signalling networks drive cancers such as melanoma, mesothelioma, glioblastoma and hepatocellular carcinoma.

We have specific interests in the following topics:

- How the Hippo pathway controls normal, neoplastic and regenerative tissue growth.
- The impact of diet and nutrition on organogenesis.
- The metabolism of cells in normal and neoplastic tissue.
- How deregulation of organogenesis signalling networks drive cancer.
- How the growth of different organs are coordinately regulated during development.
- How the proliferative potential of stem cells is controlled.

Find Projects

RESEARCH EDUCATION PROGRAM

With strong links to local and international universities and research institutes, our research education program provides a training and support framework for the academic and professional development of our staff and students.

Peter Mac is home to over 250 research students undertaking postgraduate and honours research programs. Most students completing projects at Peter Mac are enrolled through The University of Melbourne. We also host students from Universities throughout Australia and overseas.

Our program provides students with the opportunity to expand their research knowledge and skills, while also developing important transferable skills that will make an important contribution to their future career directions.

We provide a structured yet flexible program to meet the varied needs of our students. This research environment supports all students during the development of the important research and professional skills that will allow our graduates to demonstrate their development as efficient researchers, and makes a significant contribution to improving the quality of research coming out of our Centre.

Sir Peter MacCallum Department of Oncology, The University of Melbourne

The University of Melbourne's Sir Peter MacCallum Department of Oncology is located within the Peter MacCallum Cancer Centre.

The Sir Peter Mac Department brings to the university the strengths of world-class laboratory and clinical research conducted within a public cancer hospital, including:

- The largest cancer research group in Australia, with laboratory-based researchers and clinicians working side-by-side;
- A strong academic program, driven by internationally renowned laboratory and clinical researchers, with a strong focus on educating future generations of cancer researchers;
- Highly sophisticated equipment and technology, enabling complex research projects through access to cutting-edge core research technology platforms
- A cancer stream-based and holistic model of care where multi- disciplinary experts come together to provide tailored treatment at all stages of a patient's disease, across all common and rare cancer types.

Peter Mac and the Sir Peter MacCallum Department of Oncology also provide research placements for medical research programs, for international postgraduate students, for undergraduate students associated with the Summer Vacation Research Program, undergraduate work experience and undergraduate research projects undertaken in the laboratories.

Postgraduate research students based in clinical settings are supported by the Cancer Research Education program in addition to the support offered by their clinical service teams.

The co-location of research and research training capability with a hospital dedicated to cancer treatment enables researchers and clinicians to work side-by-side to make significant contributions to basic research, translational research and clinical trials for cancer.

The Peter Mac Research Education program formed the basis of The University of Melbourne's Comprehensive Cancer PhD program, described in the following section.

COMPREHENSIVE CANCER PhD PROGRAM

The Comprehensive Cancer PhD program (The University of Melbourne) supports the academic and professional development of students undertaking cancer-related research within the Victorian Comprehensive Cancer Centre (VCCC) Alliance.

This innovative and integrated program aims to produce graduates ready to conduct world-class cancer research and set them on a path to a broad range of career options.

The Comprehensive Cancer PhD (CCPhD) Program is designed to complement existing PhD activities by providing eligible students with opportunities to broaden the scope of their research knowledge, professional development and career training, and to develop research and professional skills that will help students to fulfil their career ambitions.

The Comprehensive Cancer PhD Program builds on established conventional training for cancer research students providing a coordinated program of skills, research and career training in addition to usual PhD activities.

Tapping into the depth and breadth of knowledge and experience of the VCCC alliance partners, the program provides a unique opportunity for multidisciplinary cancer-related PhD candidates to experience clinical and research activities across the alliance.

The program is managed by the Sir Peter MacCallum Department of Oncology (University of Melbourne), and is based on the gold-standard postgraduate program offered by Peter Mac.

All students engaged in postgraduate research studies at Peter Mac are enrolled in the CCPhD program, regardless of which university they are enrolled through.

The program includes:

1. Research skills development, including mastery of core technologies, cancer-specific seminars and presentations.
2. Professional and career development, including generic and transferable skills, mentoring, networking, leadership and career opportunities.
3. Communication skills development, including thesis and journal writing skills, and oral or poster presentations skills.

Examples of student activities in this program:

- Annual Student Symposium
- Thesis Bootcamp
- Annual Chat with a Nobel Laureate
- Topics in Cancer Seminar program, with recent topic themes including:

  Cancer Immunotherapy;

  Oncogenes and Tumour Suppression;

  Pillars of Cancer Care

  Cancer Genetics and Genomics

  Hallmarks of Cancer

- Workshops, including presentation skills, communication skills, candidature management, CV preparation.

For further information, email: ccphd@petermac.org

THE UNIVERSITY OF MELBOURNE

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

VICTORIAN COMPREHENSIVE CANCER CENTRE

The Comprehensive Cancer PhD Program is supported by academic partner the University of Melbourne, Peter MacCallum Cancer Centre and the Victorian Comprehensive Cancer Centre alliance

BECOMING A STUDENT AT PETER MAC

We provide a world-class research education program at a leading Australian cancer research institution for students from The University of Melbourne and other national and international universities.

There are two general stages in preparing to become a student in our postgraduate and honours programs.

Students must:

1. Find a project and supervisor for their research program, and

2. Meet the University degree eligibility and entry requirements.

Postgraduate students

Applicants for postgraduate student positions at Peter Mac enrol through a university program that approves your project placement at Peter Mac. You must therefore satisfy the minimum entry requirements at the university through which you plan to enrol.

Entry to the Peter Mac postgraduate program is based on the availability of projects, student suitability and academic background.

To undertake a postgraduate project at Peter Mac, students need to:

- Demonstrate a genuine interest in biomedical research.
- Be happy to conduct your research candidature off-campus at Peter Mac.
- Look through the available project summaries and contact the project supervisor directly by email.
- Discuss your interest in the project with the supervisor.
- Meet with potential supervisors at Peter Mac to discuss the project, your interests, visit the lab and meet others in the research group. At this meeting, supervisors will also want to view your academic record. International students will 'meet' supervisors via zoom or similar.
- Meet university eligibility requirements for postgraduate degree candidature.
- Apply for candidature at The University of Melbourne or at an equivalent university when supervisor and project are confirmed. University of Melbourne students enrol with The Sir Peter MacCallum Department of Oncology, through the Faculty of Medicine, Dentistry and Health Sciences.
- Apply for a postgraduate scholarship. Note the different deadlines that apply to different scholarships, different universities, and for local versus international scholarships.

Peter Mac staff will work with students to facilitate these processes.

Applications for candidature/scholarships for all universities are online processes, requiring a letter of support from the proposed supervisor.

Honours students

Each year we accept students from biomedical science and science programs to undertake one-year, full time Honours projects in cancer-related biomedical research.

Students undertake their scientific research work on site at Peter Mac, while undertaking their course work at the university department through which they are enrolled.

Our honours students come to us with a range of majors and backgrounds including biochemistry, chemistry, biomedical science, immunology, cell biology, medicine, pharmacology, molecular biology, pathology, physiology, anatomy and other similar subjects.

Most of our Honours students are enrolled at The University of Melbourne through departments of the Faculty of Medicine, Dentistry and Health Sciences, such as: Biochemistry & Molecular Biology, Clinical Pathology, Microbiology & Immunology, Anatomy & Cell Biology and Pharmacology.

Students who have completed their undergraduate degree at another university in Australia or overseas are also encouraged to contact us directly for further information on how to apply.

Students interested in undertaking an Honours project at Peter Mac need to:

- Demonstrate a genuine interest in biomedical research.
- Ensure their university/department approves them conducting their research project full time off-campus at Peter Mac.
- Look through the available project summaries and contact the project supervisor directly by email.
- Discuss your interest in the project with the supervisor.
- Meet with potential supervisors at Peter Mac to discuss the project, your interests, visit the lab and meet others in the research group. At this meeting, supervisors will also want to view your academic record.
- Apply for candidature at the University, meeting the university's application and eligibility requirements.

Assistance with the application process

Further information about the postgraduate and honours projects, supervisor contact details and the application process is available online at:

www.petermac.org/education/research-education

For application assistance, contact:

Research.EducationAdmin@petermac.org

WHERE DO OUR STUDENTS COME FROM TO STUDY AT PETER MAC?

We host students from countries and universities all over the world to undertake their research studies at Peter Mac. Our multidisciplinary and multicultural student cohort is at the heart of our research excellence.

WHERE DO ARE OUR GRADUATES GO AFTER THEY COMPLETE THEIR DEGREES?

Our graduates have taken up research positions across the world at leading research institutes and universities as post-doctoral researchers and academic leaders, including:

USA: Memorial Sloan Kettering Cancer Center, Dana-Farber Cancer Center, MD Anderson Cancer Center, Stanford University, Harvard University, University of California (LA, Irvine, SF), St Jude's Children's Research Hospital, University of Pennsylvania, Mount Sinai Hospital, University of Pittsburgh, Medical College of Wisconsin Cancer Centre, University of Texas Health Science Center, Brigham and Women's Hospital, Boston; British Oregon Health and Science University, NYU School of Medicine, Colorado Cancer Centre, John Hopkins School of Medicine, Roswell Park Cancer Institute; Northwestern University; Columbia University.

CANADA: University of Toronto, British Columbia Cancer Agency, Vancouver.

UK: Cambridge University; Cancer Research UK; University College London; University of Dundee; The Beatson Institute for Cancer Research, Glasgow; Nottingham University Hospitals NHS Trust; St Andrews University Edinburgh; Sanger EBI; Medical Research Council; University of Birmingham.

EUROPE: Research Institute of Molecular Pathology, Austria; University of Zurich, Switzerland; NKI, Amsterdam; Max Planck Institute of Immunobiology and Epigenetics, Frieberg, Germany; Ludwig-Maximilians Universität München, Germany; Institute for Molecular Medicine, Finland; Karolinska Institute, Sweden; Stockholm University, Sweden; Gustav Roussy, France; University of Paris Sud XI, France; Antoni van Leeuwenhoek, Netherlands,

ASIA: Center for Genome Integrity, Institute for Basic Science, Korea; Nanyang University Hospital, Singapore.

Our graduates have taken up research positions across Australia and the world at leading companies including:

Amgen, Roche, Pionyr Immunotherapies, Comugen Ltd, GSK, Seres Therapeutics, Genesearch, Geneworks, Australian Department of Health (PBS), Davies Collison Cave Intellectual Property, Merck, QIAGEN.

WHY STUDY AT PETER MAC? WORDS FROM OUR CURRENT RESEARCH STUDENTS

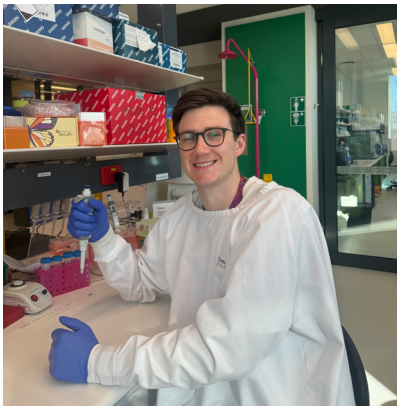
We are proud to offer a supportive and nurturing environment for our students throughout their degrees. Our researchers mentor and support our students throughout their research and towards their careers. Our student committee provides peer-to-peer mentoring opportunities through scientific and social events including an annual retreat and our annual student symposium.

"Being a student Peter Mac over the past year has been so fulfilling, with the ability to work alongside a team of passionate researchers in a field so close to home. Every day brings a new opportunity to learn new skills and network with amazing researchers, allowing me to get the most out of my project. At Peter Mac, I have the chance to be at the forefront of exciting research that could one day save many lives"

Ryan's first experience in the lab was as a summer student in 2018/19, followed by the completion of Honours in 2019 at The Institute for Molecular Biosciences. He moved to Melbourne in 2020 to begin his PhD investigating lymphatic recovery and regeneration in the zebrafish model.

Ryan Brown: PhD Student, Hogan Laboratory, Recipient of a Research Training Program (RTP)-Domestic Scholarship, Member, 2021 Postgraduate Student Committee.

"There's no better place to research cancer in Australia than Peter Mac, and I have had an amazing time so far in my PhD. The combination of state-of-the-art technology and passionate researchers situated within a world-class cancer hospital makes this a fantastic place to learn and produce meaningful translational research. I'm grateful for the endless support and opportunities that are presented to me every day as a PhD student at Peter Mac, and I'm looking forward to continuing my research here for years to come"



Tom completed his undergraduate degree at King's College London in 2020, before moving home to Melbourne and completing a Masters in Biomedical Science at UniMelb in 2022. Tom then moved across the road to Peter Mac to begin his PhD in 2023, focusing on identifying novel therapies to target bone metastasis in breast cancer.

Tom Chadwick: PhD Student, Parker Laboratory, Recipient of a Research Training Program (RTP)-Domestic Scholarship and the 2024 Tour de Cure PhD Support Scholarship. Member, 2024 Postgraduate Student Committee.

"I have always wanted to work in a place doing cutting-edge research, and getting the opportunity to do my PhD at Peter Mac has truly been a dream come true. Despite being a relatively new student here, Peter Mac has already offered me numerous opportunities to grow as a person and as a researcher through the many seminars, retreats and symposiums they've held. The passion and drive everyone here hold towards research continues to amaze and encourage me every day, where I work with the hope that my findings too would one day be translational."

The time Shenali spent working as a Research Assistant at the Institute of Biochemistry, Molecular Biology and Biotechnology (IBMBB), Sri Lanka was what made her fall in love with research in the first place. This then led her to complete her Honours degree in Immunology and integrative Molecular Biology at the University of Colombo and make the big move to Melbourne for her PhD at Peter Mac. She is now working on the molecular regulation and therapeutic vulnerabilities of RNA polymerase II transcription in cancer.

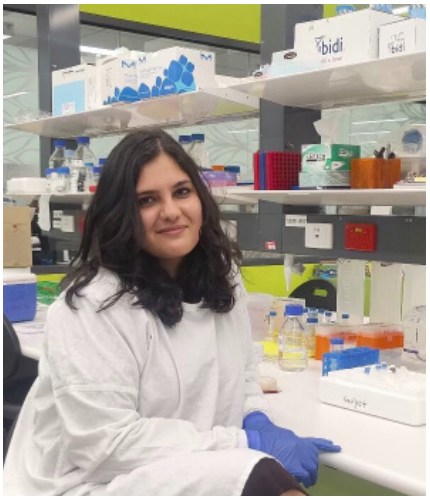
Shenali Avishka Ranasinghe: PhD student, Johnstone laboratory. Recipient of an International Melbourne Research Scholarship.

"Peter Mac is one of the top research institutes in Australia. Through my time at Peter Mac I have been supported and encouraged which has helped to foster and advance my development as a research scientist. At Peter Mac there is no shortage of equipment, services and help available to expand and innovate within your research. It is an incredibly rewarding feeling to be a part of the fight to cure cancer, with the hopes that all of us, through each bit of our research, can help to save the lives of many."

After graduating from UoM, Madeline conducted Honours in Cancer Cachexia at Peter Mac in 2021. She worked as a research assistant for 1 year (2022) before commencing her PhD in 2023 within the Cox lab investigating cancer cachexia and liver cancer in the zebrafish.

Madeline Webb: PhD Student, Cox Laboratory. Recipient of 2023 Peter Mac Foundation Postgraduate Award and a Melbourne Research Scholarship.

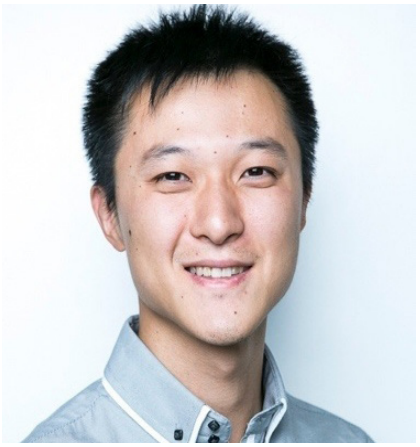
"At Peter Mac, I am able to work with such passionate and driven research scientists as well as access world class facilities and equipment, especially the CAHM facility, which is where I carry out most of my work! The highly accessible, collaborative, and diverse community as well as being surrounded by such an encouraging and supportive environment is what I think sets Peter Mac apart. We're at the forefront of cancer research, from basic discovery to applied and translational research, and I can't wait to keep seeing more of the amazing work that's being done here!"



Gurjeet completed her bachelor's in science in Biochemistry and Molecular Biology and took a year off to explore more options. She was an intern at the Brain Research Institute Monash Sunway (Malaysia) and this is where she first fell in love with research. She did her Masters and continued on as a PhD student in the Trapani lab where she is currently working on developing a new tool for RNA visualisation in live cells using CRISPR, to study RNA dynamics.

Gurjeet Jagjeet Singh: PhD Student, Trapani Laboratory. Recipient of an International Melbourne Research Scholarship. Peter Mac Student Society co-President.

"PeterMac is Australia's best location for conducting cancer research. I started working on my PhD in the Eckersley-Maslin Lab in January 2023. My research focuses on the link between developmental plasticity and cancer. The environment and culture of PeterMac is quite motivating. Everyday I get to interact with people who truly embody the true characteristics of a scientist."



Tongtong completed a Bachelor of Science (Honours) at the University of Adelaide and has worked in 6 different laboratories, either as a research assistant or a student prior to his PhD.

Tongtong Wang: PhD Student, Eckersley-Maslin Laboratory. Recipient of a 2023 Peter Mac Foundation Postgraduate Award.

"Peter MacCallum Cancer Centre prides itself in profound collaboration between world-class basic science researchers and clinicians and state-of-the-art facilities. The translational prowess of the research outcome attracted me to Peter Mac. I have benefited immensely from the supportive environment at Peter Mac research-wise and for personal development."

Having worked as a clinician in Nigeria, Ibukun's daily encounter with patients with advanced cancer with no hope of survival informed his decision to pursue a career in cancer research. He then obtained an MSc in Biomedical Science (cancer biology) from The Hebrew University of Jerusalem, Israel. Ibukun commenced his PhD in 2022 to uncover the cell of origin of Barrett's metaplasia and its progression.

Ibukun Adesoji Adejumobi: PhD student, Clemons laboratory. Recipient of an International Melbourne Research Scholarship.

AVAILABLE PROJECTS BY RESEARCH PROGRAM

Cancer Biology and Therapeutics Program

BROWN, KRISTIN

Targeting cell metabolism to overcome chemotherapy resistance in triple-negative breast cancer

Supervisor: A/Prof Kristin Brown

Triple-negative breast cancer (TNBC) is defined by the lack of estrogen receptor (ER), progesterone receptor (PR) and absence of human epidermal growth factor receptor-2 (HER2) amplification. Consequently, TNBCs are impervious to therapies commonly used in other breast cancer subtypes and treatment options are largely limited to conventional chemotherapy agents that are only effective in approximately 30% of patients. Identification of novel and actionable strategies to treat TNBC would represent a major advance for the management of this deadly disease. Cancer cells exhibit dramatic alterations in cell metabolism, which support cell growth, proliferation and survival. Our studies have revealed that reprogramming of cellular metabolism is also a component of the highly coordinated response to chemotherapy exposure. Moreover, we have shown that the unique metabolic requirements of chemotherapy treated cancer cells can be targeted for therapeutic gain. The aims of this project will be to:

1. Identify adaptive metabolic reprogramming events triggered by chemotherapy exposure

2. Determine how these metabolic reprogramming events drive chemotherapy resistance

3. Identify novel therapeutic approaches to exploit adaptive metabolic reprogramming events and sensitise TNBC cells to chemotherapy.

Students will gain experience in a variety of biochemistry and molecular biology techniques including metabolomics, transcriptomics and CRISPR-Cas9 genetic screens.

Key Words: Cell metabolism, Breast cancer, Therapy resistance

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof. Kristin Brown kristin.brown@petermac.org

Metabolic regulation of antigen presentation and tumour immune escape

Supervisor: A/Prof Kristin Brown

Tumour development and progression are dependent on the ability of cancer cells to evade immune control. The strategies employed by cancer cells to escape immune control are diverse but one of the primary mechanisms involves loss of immune recognition as a result of dysfunctions in antigen processing and presentation (APP). APP is the process by which antigenic peptides are generated and loaded onto MHC-I molecules for display on the cell surface. Reduced MHC-I expression has been observed across diverse tumour types and is associated with poor prognosis. Cancer cells are dependent on reprogramming of cellular metabolism to promote cell growth, proliferation and survival. Surprisingly, the contribution of metabolism to the regulation of APP and immune escape is poorly understood. The aims of this project will be to:

1. Identify specific metabolic pathways that contribute to the regulation of MHC-I expression

2. Determine how these metabolic pathways impact APP

3. Identify strategies to target metabolism to overcome immune escape and enhance the efficacy of currently existing immunotherapies.

Students will gain experience in a variety of biochemistry and molecular biology techniques including metabolomics, transcriptomics and CRISPR-Cas9 genetic screens.

Key Words: Cell metabolism, Immune escape, Antigen processing and presentation

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof. Kristin Brown kristin.brown@petermac.org

Can antioxidants accelerate cancer? Exploring the role of reductive stress in cell fate plasticity.

Supervisors: A/Prof. Kristin Brown A/Prof. Andrew Cox Dr. Athena Ong

A balance between oxidants and antioxidants, known as redox homeostasis, is crucial for many cellular processes. The biological consequences of redox imbalance have been extensively investigated in the context of oxidative stress. In contrast, the impact of reductive stress on cell function and tumourigenesis is poorly understood. Reductive stress is characterised by accumulation of reducing equivalents (e.g. NADPH, GSH) in excess of levels required to manage

intracellular oxidants. Our recently published studies demonstrate an underappreciated role for reductive stress in mediating the downstream consequences of oncogenic NRF2 pathway activation. Specifically, our data suggest that reductive stress plays a critical role in the regulation of cell fate plasticity. This project will seek to:
1. Generate novel in vitro and in vivo models to investigate reductive stress.
2. Examine reductive stress as a novel cue in the regulation of lysosomal biogenesis and cell fate plasticity.
3. Investigate the impact of reductive stress on cancer development and progression.

Students will gain experience in a variety of biochemistry/cell biology/molecular biology techniques including CRISPR/Cas9-mediated gene editing, metabolomics, transcriptomics and confocal microscopy.

Key Words: Reductive stress, Cancer metabolism, antioxidants, Cell fate plasticity, Cancer development, Cancer progression

Target Students: Honours, Masters, PhD, MPhil

For more information about these projects contact:

A/Prof. Kristin Brown kristin.brown@petermac.org

ECKERSLEY-MASLIN, MELANIE

Investigating a novel epigenetic regulator using embryonic stem cell models.

Supervisors: Dr Melanie Eckersley-Maslin

Epigenetics helps define current cell states, yet also shapes how cells respond to external cues such as differentiation or stress. The epigenetic plasticity of a cell describes how flexible this regulation is. Early embryonic cells are highly plastic in that they are able to generate all adult cell types. As development progresses, this plasticity is lost as normal healthy adult cells are locked in their identity. Crucially, aberrant reactivation may contribute to pathologies such as cancer. Our laboratory explores how epigenetic plasticity is controlled and regulated in development, applying these principles to understand how it is exploited by cancers. This project will investigate a poorly understood epigenetic regulator that is associated with severe developmental disorders. Interestingly this protein is also implicated in cancer where its upregulation is associated with reduced patient survival. The project will use embryonic stem cell models to uncover the molecular mechanism of this epigenetic regulator in shaping developmental processes. The prospective student will have the opportunity to use a range of cutting-edge technologies including chromatin assays, CRISPR-Cas genome engineering, epigenomic and transcriptomic analyses, cell culture and molecular biology techniques.

The project is suitable for a student wishing to be solely lab based or those who also wish to do both experiments and bioinformatic analysis.

Key Words: Epigenetics, Stem Cell Biology, Chromatin, Plasticity, Next generation sequencing, bioinformatics

Target Students: Honours, Masters, PhD, MPhil

For more information about these projects contact:

Dr Melanie Eckersley-Maslin melanie.eckersley-maslin@petermac.org

JOHNSTONE, RICKY

Molecular interrogation and therapeutic exploitation of dysregulated RNA Pol II transcription-cycles in cancer.

Supervisors: Dr Jennifer Devlin, Prof. Ricky Johnstone

Tightly controlled gene expression is essential for normal cellular development and homeostasis, and the dysregulation of gene expression is a universal feature of human disease and a hallmark of cancer. RNA polymerase II (Pol-II) dependent transcription of protein-coding genes is a highly coordinated, multi-stage process that is controlled by an expansive range of epigenetic and non-epigenetic regulators. Mutations impacting the expression and/or function of these regulators can lead to aberrant Pol-II transcriptional activity resulting in oncogenic gene expression and tumorigenesis. Pol-II progression through distinct transcriptional checkpoints (recruitment, initiation, pausing, elongation, termination) is controlled by a family of transcriptional-cyclin-dependent-kinases (tCDKs) including CDK7, CDK8, CDK9, CDK10, CDK11, CDK12, CDK13, CDK19 and CDK20. This project will use complementary genetic and pharmacological systems, and molecular biology and biochemistry experimental approaches, to investigate the mechanisms through which tCDKs regulate Pol-II transcription in normal and cancer cells.

Key questions this project can address are:

1. How do independent tCDKs co-operate to modulate Pol-II transcription?

2. What are the molecular functions of understudied tCDKs (CDK10, CDK19, CDK20) for the control of gene expression in normal and cancer cells?

3. How can pharmacological inhibitors of tCDKs most effectively be used as therapeutic strategies for aggressive solid and blood cancers?

Key Words: Transcription and gene regulation; cancer cell biology; biochemistry and molecular biology; next-generation-sequencing; proteomics; CRISPR-CAS9 gene-editing; anti-

AVAILABLE PROJECTS BY RESEARCH PROGRAM

cancer therapeutics.

Target Students: PhD, MPhil

For more information about this project contact:

Dr. Jennifer Devlin jennifer.devlin@petermac.org

Investigating the molecular mechanism of mRNA stability in leukemia

Supervisors: Dr Mary-Jane Tsang, Prof. Ricky Johnstone

Messenger RNA (mRNA) is the fundamental link between the genetic information stored in DNA and the production of proteins necessary for cellular activities. Once produced, mRNA molecules persist for some time before being destroyed. This balance of synthesis and decay determines how much mRNA is present for each gene and that dictates cell identity and whether a cell is "normal" or cancerous. Aberrant levels of the oncogene c-MYC have been implicated in cancer formation and progression. Our lab developed a reporter system using a stabilized chimeric c-MYC mRNA transcript that decouples effects on c-MYC transcription from those on mRNA stability. Surprisingly, differences in mRNA stability are observed between global transcription inhibition and inhibition of selective targets using epigenetic drugs. This project will use molecular biology, genetics, biochemistry, and cell biology to identify novel or alternative mRNA decay pathways that either specifically target c-MYC or target a broad range of substrates.

Key questions that will be addressed are:

- How do cells respond differently to global transcriptional inhibition and selective inhibition by epigenetic drugs by focusing on c-MYC transcription and mRNA stability?
- What are novel cellular factors mediating mRNA decay upon transcriptional inhibition and how do they regulate mRNA stability in leukemia?

Key Words: Transcription and gene regulation, mRNA stability, RNA decay, epigenetics, molecular biology, CRISPR/Cas9 gene-editing

Target Students: Honours

For more information about these projects contact:

Dr Mary-Jane Tsang maryjane.tsang@petermac.org

Manipulating T cell differentiation for more effective anti-cancer immunotherapies

Supervisors: Dr Dane Newman, Prof. Ricky Johnstone

The clonal expansion of CD8+ T cells upon antigen activation is a remarkable process, with a single naïve T cell capable of producing thousands of activated progeny. Naïve T cells have stem-like properties and following antigen-induced expansion, they impute a complex array of environmental and cell-intrinsic stimuli and differentiate into a functionally diverse mix of T cell phenotypes. Notably, from a clinical perspective, the different T cell subsets also display different levels of anti-cancer activity, with those exhibiting stem-like or memory attributes being therapeutically superior to their more terminally differentiated counterparts. Understanding the environmental signals and epigenetic processes that influence T cell differentiation trajectories and 'fate-decisions' is therefore critical in the design and development of potent anti-cancer immunotherapies. Our team has recently developed a unique cytokine-conditioning approach that promotes the differentiation of a distinct form of stem-like CD8+ T cell with potent anti-tumour activity. We now aim to interrogate the environmental cues and underlying molecular signals that are necessary for the formation and propagation of these stem-like T cells, with the ultimate aim of increasing their abundance in cancer patients and transforming clinical outcomes. In this honours project, the student will employ sophisticated molecular biology techniques, high-throughput screening methods, multiplexed flow cytometry, T cell activation and cytotoxicity assays, and mouse tumour models to better understand the formation of stem-like CD8+ T cells in vitro and in vivo and discover new strategies to harness their therapeutic potential.

Key Words: CD8+ T cells, T cell differentiation, epigenetics, cell signalling, cytokines, immunotherapies.

Target Students: Honours

For more information about these projects contact:

Dr Dane Newman dane.newman@petermac.org

AVAILABLE PROJECTS BY RESEARCH PROGRAM

KATS, LEV

Understanding and targeting heme metabolism in acute myeloid leukaemia

Supervisors: Dr Alexander Lewis and A/Prof Lev Kats

Acute myeloid leukaemia (AML) is an aggressive and deadly blood cancer and is the most common acute leukaemia in adults. Identification of metabolic pathways that are dysregulated in AML offers significant promise for the development of new therapeutic strategies. Heme is an essential metabolite with broad biological activity that is required and produced by all cells. In addition to its catalytic role as a cofactor in hemoproteins, heme also directly regulates signalling and gene expression. We and others have shown that heme biosynthesis is transcriptionally suppressed to varying degrees by AML driver mutations, but whether or not this results in reduced heme levels in leukaemic cells has not been systematically analysed. Moreover, the implications for metabolomic and transcriptional pathways that are controlled by heme remain unexplored. In this project we aim to:

1. characterise heme metabolism in AML using metabolomics and functional genomics;
2. investigate the function of heme in regulating self-renewal and leukaemic stem cells (LSCs); and
3. develop new treatment paradigms for selective targeting of low heme AML cells.

Key Words: Haematological cancers, Cancer metabolism, Leukaemic stem cells, Targeted therapies

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof. Lev Kats lev.kats@petermac.org

A Swiss Army knife approach for targeting therapy resistant multiple myeloma

Supervisors: Dr Emily Gruber and A/Prof Lev Kats

Multiple Myeloma (MM) is a common, incurable plasma cell malignancy with an urgent unmet need for new therapies. MM cells are peculiar in their susceptibility to drugs disrupting protein homeostasis, such as proteasome inhibitors and immunomodulatory thalidomide analogues (IMiDs; e.g. lenalidomide). IMiDs modulate cereblon (CRBN), a substrate recognition subunit of the CRL4 E3 ubiquitin ligase complex that regulates proteasomal degradation of various client proteins. IMiDs engage CRBN and redirect the CRL4-CRBN complex to ubiquitinate neosubstrates, most notably the essential MM transcription factors IKZF1 and-3. The finding that IMiDs can induce targeted proteolysis represented a paradigm shift not only for MM, but for drug design more generally, and led to the development of a novel class of small molecules termed PROTACs. PROTACs are hetero-bifunctional compounds that link E3 ligase complexes with protein targets promoting their ubiquitination and degradation via the ubiquitin proteasome system. Although still in their infancy, PROTACs hold significant promise for drugging non-enzymatic proteins that may be difficult to modulate using more traditional drug design.

We reasoned that the identification of further E3 ligase substrate receptors that are essential in MM cells would enable a 'Swiss Army knife' approach to the development of novel anti-myeloma agents that would significantly increase the efficiency of our medicinal chemistry efforts. Not only could molecules that effectively bind to such proteins directly kill MM cells, but they could also be leveraged to design PROTACs with CRBN-independent anti-MM activity. We have identified VPRBP as a pan-essential gene in MM. VPRBP is a highly unusual substrate receptor that can direct ubiquitination of target proteins via two distinct E3 ubiquitin ligase complexes, the RING-type CRL4 complex and the HECT-type DYRK2/UBR5 complex. As VPRBP is a multi-domain, multi-functional molecule it can potentially be targeted by a range of medicinal chemistry strategies. Notably however, lack of fundamental knowledge of VPRBP biology in MM is a significant obstacle to these endeavours. In this project, we posit that VPRBP represents a distinct 'druggable' vulnerability in MM that may be orthogonally targeted in a domain-specific manner by distinct small molecules, and seek to define key mechanistic determinants by which loss of VPRBP function induces MM cell death.

Key Words: Haematological cancers, Cancer cell biology, Functional genomics, Proteomics

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof. Lev Kats lev.kats@petermac.org

MCARTHUR, GRANT

Combining Novel Targeted Therapies With Immunotherapies in Melanoma

Supervisors: A/Prof Karen Sheppard Dr Reem Saleh

The development of both targeted and immune therapies has revolutionized the treatment of advanced-stage melanoma and improved the outcomes of patients. Unfortunately, the current BRAF/MEK targeted and immune therapies have limitations. Typically, targeted therapies are associated with very high initial response rates, followed by drug tolerance and then tumour progression. In contrast, immunotherapies

AVAILABLE PROJECTS BY RESEARCH PROGRAM

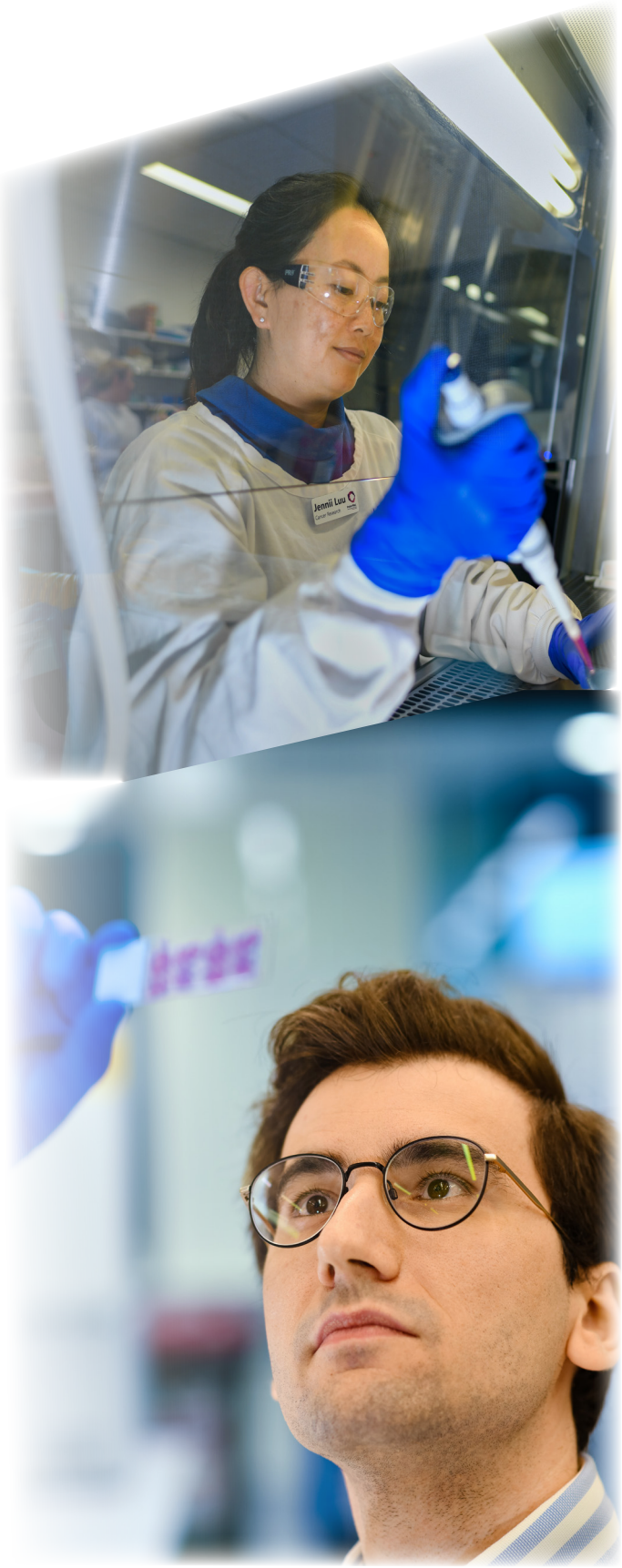
provide more durable responses but have lower response rates. Current BRAF/MEK targeted therapies can alter the melanoma immune microenvironment, likely making it more amenable to immunotherapy. Thus, combining targeted therapy with immunotherapies might overcome the clinical limitation of the individual classes of therapy and potentially lead to more durable responses and even cure. Furthermore, novel targeted therapies are being developed that may overcome the development of resistance. This study aims to understand therapy-induced time-dependent changes in tumour cells and their microenvironment with both current and novel targeted agents. Understanding these changes will assist in the development of optimal scheduling strategies for combining targeted and immune therapies.

Key Words: Melanoma, Cancer cell biology, Animal models

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof Karen Sheppard karen.sheppard@petermac.org



WICKRAMASINGHE, VIHANDHA

Uncovering new links between the cell cycle, DNA damage and mRNA export that drive cancer

Supervisor: Dr. Vihandha Wickramasinghe

Nuclear export of messenger (mRNA) is extensively connected to transcription and processing of mRNA throughout the cell cycle. Little is known about how cancer cells regulate mRNA export during DNA replication which occurs during S-phase of the cell cycle. Using CRISPR screening approaches, we have unexpectedly discovered that cell cycle regulated proteins regulate mRNA export during the DNA damage response.

This project will use cutting-edge cell biology, molecular biology, genetic and computational biology approaches to understand why these biological processes are linked and how they drive cancer. As several promising cancer therapies target these cellular pathways, this project will reveal new cancer sub-types that may be suitable for treatment

Key Words: Cancer Cell Biology, DNA Damage, RNA, Cell Cycle, Cancer Treatments.

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Vihandha Wickramasinghe vi.wickramasinghe@petermac.org

AVAILABLE PROJECTS BY RESEARCH PROGRAM

New RNA-targeting therapeutics to treat cancer

Supervisor: Dr. Vihandha Wickramasinghe

A critical step in the gene expression pathway that is altered in cancer is nuclear export of messenger RNA (mRNA). We have demonstrated that mRNA export is not constitutive, but highly selective and can regulate distinct biological processes through poorly understood mechanisms.

The extraordinary success of RNA based therapeutics to treat COVID-19 has dramatically increased interest in other types of RNA targeting therapies. We have developed a completely new mRNA targeting therapy that works in the nucleus of cells and has the potential to be an exciting new frontier in cancer therapeutics.

This project will use cutting-edge cell biology, molecular biology and genetic approaches to understand how RNA export is altered in cancer and how our novel first-in-class inhibitors can be used to treat cancer.

Key Words: New Cancer Treatments, Cancer Cell Biology, RNA, Gene Regulation, Cell Signalling.

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Vihandha Wickramasinghe vi.wickramasinghe@petermac.org

Uncovering the promise of circular RNA in next generation RNA based therapeutics

Supervisor: Dr. Vihandha Wickramasinghe

RNA stability is a key determinant in improving the efficacy of RNA based therapeutics. Through our pioneering work on nuclear export of RNA over the past 15 years, we have uncovered key mechanisms that modulate RNA export and the stability of RNA in the nucleus and the cytoplasm. Many of these proteins are amplified in various types of cancer, underlying the importance of this cellular process in both fundamental RNA biology and in disease. Recently, we have applied these principles to work out how circular RNAs, a subtype of RNA with great therapeutic potential, are exported from the nucleus. This work has uncovered a completely new mechanism for export that is distinct from export of mature mRNA. Our findings have important implications for the potential use of circular RNAs in therapeutics. This project aims to make further advances in how biogenesis of circular RNAs is coupled to their export and stability to be at the forefront in determining how circRNAs may play a role in the next generation of RNA based therapeutics.

Key Words: RNA, Therapeutics, Cancer

Target Students: Honours, PhD, MPhil

For more information about this project contact:

Dr. Vihandha Wickramasinghe vi.wickramasinghe@petermac.org

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Cancer Evolution and Metastasis Program

BRITT, KARA

The role of the macrophages in early breast lesions

Supervisors: A/Prof. Kara Britt/Prof Phil Darcy

Breast cancer is not considered immunogenic, as its incidence is not increased in immune suppressed patients (transplant patients and HIV patients). However, irrefutable data now show that the immune cell infiltrate of a breast cancer affects its growth and metastasis. Only limited data exist on the role of immune cells in the early stages of BCa. We have preliminary data showing that macrophages are important during the development of breast cancer. This project is focussed on testing macrophage targeting therapies in preclinical models to determine if we can block/delay cancer initiation. In addition to understanding the immune control of early cancer development, our goal is to delay tumour onset by orchestrating an anti-tumour immune microenvironment.

Key Words: Immune cells, Breast Cancer

Target Students: PhD

For more information about this project contact:

A/Prof. Kara Britt kara.britt@petermac.org

Deciphering the mechanism between the APOBEC deletion polymorphism and breast cancer risk and mutagenesis.

Supervisors: A/Prof. Kara Britt, Dr Conor McGuinness and A/Prof. Laura Forrest

APOBEC enzymes are known to cause somatic mutagenesis in breast cancer. A polymorphism that affects the APOBEC3B gene is associated with heightened breast cancer risk and a greater number of APOBEC mutations in breast tumours. This polymorphism is found at a relatively high frequency in non-European populations, including Indigenous Australians. APOBEC mutagenesis has been associated with poor response to standard of care treatments such as hormone therapy, but potentially enhanced response to immune checkpoint blockade. Therefore, we hypothesise that carriers of the polymorphism could benefit from targeted immunotherapy responses. Using cutting edge genomic techniques such as deep mutation profiling, scRNAseq, and multiplex immunofluorescence, we will decipher exactly how the polymorphism breast epithelial and immune cells. Additionally, there is an opportunity for engagement with Indigenous communities to inform governance of tissue and genomic data associated with this project. This process will follow guidelines for the establishment of partnerships between researchers and donors and use a qualitative approach to determine tissue and data governance for this research program. Students with Aboriginal/Torres Strait Islander background are strongly encouraged to apply.

Key Words: Indigenous health, breast cancer, immunotherapy

Target Students: Honours, PhD

For more information about these projects contact:

A/Prof. Kara Britt kara.britt@petermac.org

Determine how obesity impacts the breast to drive an increase in cancer risk

Supervisors: A/Prof. Kara Britt, Prof Phil Darcy, A/Prof Kristin Brown

Obesity doubles the risk of developing hormonally driven breast cancer (75% of all breast cancers) yet we still do not know how it increases risk. This project will use our expertise in breast cell isolation, single cell sequencing and functional assays to determine how the breast epithelial and immune cells change in obese compared to lean women. The project involved collecting fresh human breast tissue and processing with numerous protocols to obtain cell number, activity and transcriptional changes. We will also work with international clinical collaborators to further our research using clinical samples from obese and lean women and those treated with anti-obesity drugs and surgery.

Key Words: breast cancer, human samples, scRNAseq, cancer prevention

Target Students: PhD

For more information about these projects contact:

A/Prof. Kara Britt kara.britt@petermac.org

Develop a pre-clinical model to study obesity driven ER breast cancer

Supervisors: A/Prof. Kara Britt, Prof Phil Darcy, A/Prof Kristin Brown

Whilst hormonally responsive breast cancer is the most common cancer and our rising obesity levels is in part helping to drive the increased incidence, we do not have a pre-clinical model with which to study this disease. This project will develop a model of diet induced obesity in mouse breast cancer models and assess the impact on the latency and growth of the tumours. It will also assess the impact of anti-obesity drug Ozempic on the breast cancer latency, but also the breast epithelial and immune cells.

Key Words:breast cancer, preclinical models, breast cancer

therapeutics

Target Students: PhD

For more information about these projects contact:

A/Prof. Kara Britt kara.britt@petermac.org

CAMPBELL, IAN

Exploration of alternative mechanisms of hereditary breast cancer

Supervisors: Prof. Ian Campbell, A/Prof. Paul James

Pathogenic variants in BRCA1, BRCA2 and PALB2 are major contributors to hereditary breast and ovarian cancer (HBOC) but collectively explain less than a quarter of the families tested in clinical practice, leaving the majority with no identifiable genetic defect to inform cancer prevention strategies. Other HBOC genes explain only a small fraction (<5%) of families. In contrast to the intensive international efforts aimed at discovering new predisposition genes, little attention has been given to the potential for alternative pathogenic mechanisms in the already established HBOC genes. In this project bioinformatics approaches will be used to mine the large-scale genetic/epigenetic data available in the BEACCON study of 12,000 hereditary breast cancer (BC) cases and controls to explore the contribution of non-coding variants and inherited promoter hypermethylation silencing in BC predisposition. The proposed study is also underpinned by the unrivalled clinical and biospecimen resources of the Variants in Practice (ViP) study where data from thousands of hereditary BC family members are accessible for analysis. This study will advance the knowledge in the under-studied field of alternative mechanisms of HBOC predisposition

Key Words: Familial breast cancer, Genetics, Bioinformatics.

Target Students: PhD

For more information about this project contact:

Prof. Ian Campbell : ian.campbell@petermac.org

Genetic mosaicism as a stable and robust blood DNA biomarker for precision risk assessment for cancer

Supervisors: Prof. Ian Campbell, A/Prof. Paul James,

A major goal of genomic precision medicine in cancer is to identify early detection modalities and treatments that are specific to the unique situation of each individual. This project will elucidate and validate blood DNA genetic biomarkers to identify individuals who are at higher risk of developing cancer. This will be achieved through assessment of the burden of somatic genetic mutations in DNA from peripheral blood lymphocyte (PBL) DNA. This biomarker is expected to be a stable reflection of the cumulative exposure to DNA damaging factors in an individual's lifetime and has the potential to identify, through a simple PBL DNA genetic test, people who are at risk of future cancer development. The ultimate aim of the study is to develop a genomic screening tool for testing PBL DNA to accurately identify genetic predisposition to cancer that will enable targeted intervention and enhanced screening to prevent disease. The proposed study is underpinned by the resources of the Lifepool cohort (www.lifepool.org) and funded through an MRFF genomics health futures grant.

Key Words: Genetic risk factors, Cancer prevention, Cancer screening, Somatic mutation, Risk prediction, Bioinformatics

Target Students: PhD

For more information about this project contact:
Prof. Ian Campbell : ian.campbell@petermac.org

Novel cellular models to investigate the mechanism of polygenic risk of breast cancer

Supervisors: Prof Ian Campbell and Prof Paul James

A large number of common genomic variants have been identified that are associated with differences in the risk of breast cancer (BC) in the general population. In combination these variants explain a large proportion of the heritable component of BC. Combined PRS influences major functional pathways involved in carcinogenesis and also modifies the established functional effects of known BC predisposition genes. Progress toward a functional understanding of these variants has been slow and focused on dissecting variants one locus at a time, despite the fact that it is only through their combined effect- as measured in a Polygenic Risk Score (PRS)- that they have significant impact. This project will take an entirely novel approach by studying induced pluripotent stem cell (iPSC) lines from women who have exceptional BC PRS results that put them into either the lowest or highest 0.1%. The molecular features of these model lines will be characterised, through gene expression studies and mutational signature analysis to measure the effect of polygenic risk on the hallmark pathways of cancer. Finally, mutations in BRCA1 and CHEK2 will be introduced by to examine the modifying effect of the PRS on these established BC genes.

Key Words: Familial Breast Cancer, Cancer Genetics, polygenic risk

Target Students: PhD

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Poor outcome breast cancer: Identifying genetic risk factors and new treatments

Supervisors: Prof Ian Campbell and Prof Paul James

Women diagnosed with breast cancer (BC) at a very early age or during pregnancy have particularly poor outcome compared to patients diagnosed over >40 years. In addition, because of the young age of onset, the impact on life can be particularly devastating, including issues related to contraception, management of menopausal symptoms and pregnancy. These issues are compounded for women with a pregnancy associated BC because of fears of the effects of treatment to the baby. The clinical and genetic features of early-onset and pregnancy-associated BC suggest they are quite different from BCs that occur in older patients, but these differences have not been properly explained. We will apply integrated germline and tumour whole genome sequencing (WGS) to our large and unique cohort of early onset BC (EOBC) and pregnancy associated BCs (PABC) to identify unique hereditary and somatic genetic features that confer their aggressive phenotype. Aim 1. Identify novel genes predisposing to EOBC and PABC through integration of tumour and germline WGS data from women diagnosed <30 years for whom all known genetic causes have been excluded. Aim 2. Create a somatic genomic landscape of EOBC and PABC to identify unique therapeutic vulnerabilities through comparison with BCs diagnosed >55 years.

Key Words: Breast cancer, familial cancer, genomics

Target Students: PhD

For more information about this project contact:

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CHRISTIE, ELIZABETH

Analysis of heterogeneity and chemotherapy resistance in women's cancers

Supervisors: Dr Elizabeth Christie

Acquired treatment resistance, whereby patients respond well to primary treatment but eventually develop drug resistance, is common across a range of cancer types.

This study aims to

(1) identify acquired resistance mechanisms,

(2) understand their heterogeneity within and between patients, and

(3) examine how tumour cells interact and evolve over time in response to chemotherapy.

This project will involve analysis of DNA and RNA sequencing data from primary, recurrent and end-stage patient samples to identify mutations and expression changes that lead to resistance, and may also involve cell culture and other molecular biology techniques. Students will receive training in genomics, bioinformatics and cancer cell biology, working with a team of wet-lab and computational biologists and clinicians.

Key Words: Ovarian cancer, Endometrial cancer, Genomics

Target Students: Honours, Masters, PhD/Mphil

For more information about this project contact:

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CLEMONS, NICHOLAS

Defining the functional drivers of oesophageal tumourigenesis

Supervisors: A/Prof. Nicholas Clemons

Oesophageal adenocarcinoma develops in a step-like fashion from Barrett's oesophagus, a benign intestinal-like metaplasia that arises as a consequence of chronic gastro-oesophageal reflux. Recent genomic studies have shown there are few common oncogenic drivers of this progression, whilst loss of tumour suppressor genes (e.g. TP53 and SMAD4) and genomic instability is common. Recently, we have demonstrated that loss of SMAD4 on a background of mutant p53 induces tumourigenesis in Barrett's oesophagus in in vivo models.

The aim of this project is to determine the functional drivers of oesophageal carcinogenesis. The project will utilise gene editing technologies (e.g. CRISPR/Cas9) and lentiviral expression systems to target candidate drivers (e.g. knockout putative tumour supressors or overexpress candidate oncogenic drivers). The functional effects of these events will be studied in models of Barrett's oesophagus, including human cell lines and primary organoid cultures derived from Barrett's oesophagus grown in vitro and as xenografts, to determine whether they contribute to disease progression.

This project will make a significant contribution to our understanding of how this disease develops at the fundamental level and thereby enhance our ability to develop new management strategies for patients with this disease.

Key Words: Cancer Cell Biology, Cancer Therapy (excl. Chemotherapy and Radiation Therapy), Molecular Biomarkers, Molecular Oncology, Molecular Targets, Solid Tumours, Therapeutics, Upper Gastrointestinal Cancers

Target Students: Honours, PhD, MPhil

For more information about this research project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

GORRINGE, KYLIE

New therapies for mucinous ovarian cancer

Supervisor: A/Prof Kylie Gorringe

The Gorringe lab has an ongoing program of research investigating a rare ovarian cancer subtype, mucinous ovarian carcinoma. This disease has no effective chemotherapies and women with advanced disease have dire clinical outcomes. We have a cohort of ~200 mucinous tumours, remarkable for such a rare disease, including with clinical, immunohistochemical, ene expression and genomics data (sequencing and copy number). We have an active tumour organoid program and are developing PDX models from primary patient material with which to test therapies. Funded by NHMRC and the US Dept of Defense, we will test existing therapies and combination in these new patient models and discover new ones using our unique data set.

This program would best suit a student looking for hands-on laboratory experience in cell culture, cancer drug discovery and 3D screening. In addition, we are collating data from multiple patient registries to investigate whether we can answer chemotherapy efficacy questions using real patient data. This alternative approach would best suit a student interested in clinical trials and biostatistics.

Key Words: Cancer, Ovarian, Therapy

Target Students: Masters, PhD, MPhil

For more information about this project contact:

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PARKER, BELINDA

Enhancing immune targeting of metastatic cancers

Supervisors: Prof. Belinda Parker, Dr Nicole Haynes

Despite high 5-year survival rates, breast and prostate cancer remain the second leading cause of cancer-related deaths in Australia due to metastatic recurrence. Upon diagnosis of metastatic disease, the 5-year survival rate drops to less than 30%, emphasising the critical need for strategies to target metastases. A common feature of metastatic cancers is reduced cancer cell immunogenicity, rendering aggressive cancers invisible to the immune system and resistant to immunotherapy. Our laboratory has uncovered the key pathways in cancer cells that control cancer cell visibility and we now want to harness these discoveries to develop novel metastasis-specific therapies for breast and prostate cancer patients. This project utilizes preclinical metastasis models along with patient-derived tissues to dissect mechanisms of reduced immunogenicity and new therapeutic strategies to restore immune signaling and response to radiotherapy and immune checkpoint inhibitors.

Key techniques include cell culture, organoid culture, mouse models of metastasis, histopathology, Opal multiplex immunostaining, T cell derivation and anti-tumour function assays, therapeutic screening, preclinical radiotherapy delivery, in vivo imaging, flow cytometry.

Key Words: Immune therapies, metastasis, prostate cancer, breast cancer, organoids, cytokines

Target Students: Honours, PhD

For more information about these projects contact:

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Use of a new bone bioscaffold model to test anti-metastatic therapies

Supervisors: Prof Belinda Parker and Dr Nicole Haynes

Bone is the most common site of metastasis in breast and prostate cancer patients. Unlike soft tissue metastases, bone metastases commonly fail to grow outside a patient in typical organoid and mouse xenograft models. This has drastically hampered the discovery of biology-guided therapies for the effective management of metastatic disease, an urgent requirement given that bone metastases are associated with terrible morbidity and eventual mortality. This project aims to link biological discoveries uncovered using metastatic samples with a recently developed patient-derived bone metastasis bioscaffold model to uncover new therapeutic strategies to combat this deadly disease. This model offers exciting avenues for testing therapies against human samples taken directly from the patient. Further development utilising match patient T cells is also an exciting opportunity. This project could be modified for an honours or PhD project. Key techniques include multi photon microscopy, tissue culture, flow cytometry, immunohistochemistry, microfluidics, cytokine analysis, qRT-PCR.

Key Words: metastasis, breast cancer, prostate cancer, immunotherapy, bone

Target Students: Honours, PhD

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

STACKER, STEVEN

Understanding tissue-specific vasculature in cancer metastasis

Supervisors: Dr. Aadya Nagpal Malhotra, Dr. Rae Farnsworth and Prof. Steven Stacker.

Metastatic spread of cancer cells to distant sites is the most lethal aspect of cancer. It has long been observed that certain tumour types metastasise preferentially to particular distant organs. More recently, evidence has emerged that tumours can pre-emptively remodel these distant tissue environments to promote the future arrival and survival of metastatic cells, generating supportive "pre-metastatic niches"(1,2). Blood and lymphatic vessels throughout the body are frequently hijacked by tumours to promote tumour growth and metastasis. However little is understood about the underlying mechanisms, and how tissue-specific heterogeneity of these vessels affects tumour behaviour at different stages of progression. We have recently conducted single-cell RNA-sequencing to elucidate the unique molecular profiles of organ-specific lymphatic and blood endothelial cells in mouse models of cancer during early stages of metastasis, focussing on lymph node, lung and brain as important metastatic sites. In this project, students will functionally investigate one or more candidate genes arising from these studies using flow cytometry, multiplex immunohistochemistry, organotypic co-culture assays, integrated bioinformatics and molecular and cell biological techniques. Analysis of human tumour samples and preclinical models will further support understanding of the role and therapeutic or prognostic tractability of these candidates.

Key Words: Solid Tumours, Vascular Biology, Transcriptomics, Cancer Microenvironment, Metastasis

Target Students: Honours, Masters, PhD

For more information about these projects contact:

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Dr. Rae Farnsworth rae.farnsworth@petermac.org

Prof. Steven Stacker steven.stacker@petermac.org

Role of the RYK receptor in cancer therapy resistance and epithelial-to-mesenchymal transition

Supervisors: Dr. Aadya Nagpal Malhotra and Prof. Steven Stacker.

Acquired resistance to cytotoxic therapies becomes a major cause of therapy failure in patients with advanced metastatic cancer. Accordingly, the identification and targeting of novel signalling pathways involved in mediating drug resistance is essential to improving patient responses. Our lab has previously demonstrated a role of the WNT receptor and pseudokinase "RYK" in cancer growth and progression. Importantly, our findings identified a link between the RYK receptor and TGFb-mediated epithelial to mesenchymal transition (EMT), a process that is crucial to cancer metastasis and therapy resistance. This project will utilise advanced cellular and molecular biology techniques to identify the direct role of the RYK receptor in mediating therapy response and EMT. Students will use functional cell biological assays, molecular biology techniques, advanced microscopy, multiplex immunohistochemistry, analysis of cancer patient samples, and preclinical models to dissect the function and therapeutic benefit of targeting the RYK receptor.

Key Words: Therapy resistance; Epithelial to mesenchymal transition (EMT); Cancer cell signalling; Cancer therapeutics; Growth factor receptors

Target Students: Honours, Masters, PhD

For more information about these projects contact:

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Prof. Steven Stacker steven.stacker@petermac.org

Developing a CAR T cell targeted to the Wnt receptor RYK

Supervisors: Dr. Rae Farnsworth and Prof. Steven Stacker.

RYK is a member of the Wnt-binding family of growth factor receptors involved in development and cancer. Using a human monoclonal antibody, we have demonstrated a role for tumour-expressed RYK in TGFβ-mediated epithelial to mesenchymal transition, migration and metastasis. Furthermore, RYK is highly expressed in a broad range of human cancer cell types, and is upregulated in cancer relative to normal tissues, making it a promising therapeutic target. We have now developed a novel chimeric antigen receptor (CAR) T cell targeting the RYK receptor. This project will involve engineering and testing the RYK CAR T cells for optimal efficacy against tumour cells in vitro and in mouse tumour models. Students will utilise molecular biology techniques, viral vector systems, flow cytometry and advanced real-time microscopic imaging techniques to generate and test CAR T cells in vitro. The anti-tumour efficacy of these RYK CAR T cells may also be assessed in mouse models of solid tumours or leukemias, using in vivo imaging, multiplex flow cytometry and multiplex immunohistochemistry to assess their effects and their therapeutic potential.

Key Words: CAR T cells; Immunotherapy; Cancer therapeutics; Growth factor receptors

Target Students: Honours, Masters, PhD

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Cancer Immunology Program

BEAVIS, PAUL

Enhancing CAR T cell therapy with CRISPR/Cas9 engineering

Supervisors: A/Prof. Paul Beavis and Dr. Yu-Kuan (Tony) Huang

Chimeric antigen receptor (CAR) T cell therapy involves genetic engineering of patients' own immune cells to express a synthetic receptor that recognises tumour antigens. This drives potent tumour killing in these CAR T cells and has proven to be efficacious against certain leukemias. However, CAR T cell therapy has limited effects in solid tumours. Our lab has established an innovative CRISPR/Cas9 homology-directed repair (Knock-in) technology to generate armed-CAR T cells to enhance their efficacy in targeting solid tumours via facilitating their interactions with host immunity. These approaches include, but are not limited to, activating host T cells and antigen-presenting cells with bi-specific T-cell engager, relevant ligands and proinflammatory cytokines. In this project, the student will (i) use viral transduction protocols to generate CAR T cells, (ii) arm these CAR T cells using CRISPR/Cas9 technology, (iii) test their function and ability to target tumour cells and activate immune cells in vitro, and (iii) treat tumours in mouse models to assess their therapeutic efficacy and underlying mechanisms. The results of this project are critical for generating the next generation of CAR T cells to fight solid tumours.

Key Words: CAR T cells, solid cancers, CRISPR/Cas9

Target Students: PhD

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DARCY, PHIL

Targeting the epigenome to 'armour' CAR-T cells against solid tumours

Supervisors: Dr Kevin Sek and Prof Phil Darcy

Chimeric antigen receptor (CAR) T cell therapy involves genetic engineering of a patients' own immune cells to express a synthetic receptor that recognises tumour antigens and drives potent tumour killing. CAR T cell therapy is highly efficacious against certain leukemias. However, it has shown only moderate effects in solid cancers. Our lab has established state-of-the-art technologies to enhance CAR-T cell function, including Single-cell resolution sequencing, CRISPR/Cas9 gene-editing and Viral or non-viral Lipid Nanoparticle gene-delivery platforms. In this project, the student will (i) explore the transcriptome and epigenome (multi-ome) of CAR-T cells at the single-cell level, (ii) utilize the aforementioned tools to 'armour' CAR-T cells, and (iii) demonstrate their enhanced ability to treat cancer in both mouse models and with patient-derived products. The outcomes of this project could lead to the development of a novel next-generation CAR-T cell product with potential for rapid clinical translation.

Key Words: Multi-omics, Epigenetics, CAR-T cells, CRISPR/Cas9

Target Students: Honours , PhD

For more information about these projects contact:

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Prof Phil Darcy Phil.Darcy@petermac.org

Idenitification of novel gene targets for enhancing the persistence and function of CAR T cells for cancer therapy

Supervisors: Dr Christina Scheffler, Prof. Phillip Darcy, A/Prof. Paul Beavis

Despite the immense promise of adoptive CAR T cell immunotherapy in treating blood cancers, its efficacy in targeting solid cancers is limited by a number of metabolic and immune-suppressive hurdles present in the tumour microenvironment. Thus, identifying the gene targets that connect metabolic and epigenetic pathways represents a novel avenue in preparing CAR T cells to overcome these metabolic challenges. We have recently performed a CRISPR/Cas9 screen in naive human T cells and identified several new target genes regulating T cell persistence, function and exhaustion. This exciting new project will now validate these targets in both mouse and human CAR T cells through a series of in vitro functional assays and adoptive transfer mouse models. Project design/Methodology The graduate undertaking this new PhD project will become familiar with a number of techniques including flow cytometry, tissue culture, CRISPR/Cas9 gene editing and biological functional assays in T cells including evaluation of cytokine production (CBA's), cytotoxicity (Inucyte, 51Cr release), Seahorse assays and proliferation (CTV). The project will undertake preclinical in vivo testing of gene-edited CAR T cells in mice and explore novel mechanisms of action uisjng bioinformatics (ie. RNA-Seq analysis) to gain insight into improved therapeutic outcomes. Results of this project can be further developed for future testing in patients.

Key Words: Cell based therapy, CAR-T Cells

Target Students: PhD

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

DOLCETTI, RICCARDO

Development of improved cancer vaccines to enhance the efficacy of immunotherapy combination strategies

Supervisors: Prof. Riccardo Dolcetti, Dr Roberta Mazzieri, Dr Bijun Zeng

Despite the ability of cancer vaccines to generate brand new and strong anti-tumour immune responses, their therapeutic efficacy is still unsatisfactory. This is due to the limited potency and antigen-specificity of available cancer vaccines, which need to be combined with other treatments to overcome the local immune suppression of tumour microenvironment. This project aims at developing new classes of clinically applicable cancer vaccines targeting tumours with limited inherent immunogenicity by exploiting our recently developed nanoparticle-based vaccination platform targeting cross-presenting dendritic cells in vivo. Novel and more immunogenic antigen formulations will be identified and therapeutically validated in different preclinical cancer models. To overcome immunotherapy resistance and local immunosuppression typically associated with tumour progression, the project will explore mechanism-based combination therapies, also including cell- and gene-based strategies for the tumour targeted delivery of biomolecules. Proof of feasibility, efficacy, and safety, as well as insights into therapy induced immune modulation will be provided using both murine and humanised models of primary and metastatic tumours, including melanoma, breast, liver and brain cancers.

Key Words: Cancer vaccines, anti-tumour immunity, immunotherapy, tumour antigens, adaptive immunity, immunogenicity, neo-antigens, brain metastasis, melanoma, brain tumour, breast cancer, humanised mouse models.

Target Students: PhD

For more information about these projects contact:

Dr. Roberta Mazzieri Roberta.Mazzieri@petermac.org

Identification and characterisation of novel classes of therapeutically relevant tumour neo-antigens.

Supervisors: Prof. Riccardo Dolcetti, Dr Pouya Faridi, Dr Roberta Mazzieri

Knowledge about the peptide repertoire presented by human leukocyte antigens (HLA) holds the key to unlock target-specific cancer immunotherapies as vaccines and adoptive cell therapies. The recent advances in mass spectrometry approaches have greatly improved our ability to comprehensively characterise the HLA immunopeptidome of tumour cells. However, only a fraction of tumour peptides identified by immunopeptidomics strategies are real immunogenic epitopes able to elicit therapeutically relevant immune responses. Through the combination of immunopeptidomics and an advanced immunogenicity screening pipeline, this project aims at identifying and characterising novel classes of tumour neo-antigens suitable for therapeutic purposes. The immunogenicity of the tumour neo-antigens identified will be also validated by detecting specific T-cell responses in the blood of cancer patients, thus paving the way for the development of new immunoassays for improved monitoring of tumour antigen-specific immune responses in patients treated with immunotherapies. The project will also exploit our nanoparticle-based vaccination platform targeting cross-presenting dendritic cells in vivo to investigate the feasibility and efficacy of vaccination approaches targeting the new antigens identified in suitable humanised mouse models.

Key Words: Anti-tumour immunity, immunotherapy, tumour antigens, adaptive immunity, immunogenicity, immunopeptidome, neo-antigens, cancer vaccines, immunomonitoring, humanised mouse models.

Target Students: PhD

For more information about these projects contact:

Dr. Roberta Mazzieri Roberta.Mazzieri@petermac.org

Characterisation of immune responses specific for preneoplastic lesions predisposing to oesophageal adenocarcinoma

Supervisors: Prof. Riccardo Dolcetti and A/Prof. Nicholas Clemons

Esophageal adenocarcinoma (EAC) arises from Barrett's esophagus (BE), a precancerous replacement of squamous by columnar epithelium in response to chronic inflammation due to gastro-oesophageal reflux. Once diagnosed, patients with BE are kept on surveillance to detect progression so that timely intervention can occur with endoscopic therapy. Although several demographic and clinical risk factors are known to increase progression toward EAC, a reliable identification of patients at risk of malignant progression is still unavailable. Considering the inflammatory microenvironment that characterises BE, these patients may mount an abnormal immune response against proteins that are aberrantly overexpressed in these lesions. We will therefore identify immunogenic epitopes provided by proteins aberrantly overexpressed in BE and belonging to signaling pathways involved in the pathogenesis of BE, such as the Hedgehog pathway. Immunogenicity of these epitopes will be functionally validated using a reliable pipeline established in the lab. The presence of T cell responses specific for these epitopes will be investigated and characterised in blood samples prospectively collected from patients with BE or overt EAC representative of different stages of these diseases. A cohort of healthy donors will be also investigated as a negative control. The results

obtained will allow us to assess whether these abnormal immune responses may serve as biomarkers predictive of the evolution of BE towards overt EAC. The immunogenic epitopes identified may be also exploited to develop vaccines potentially able to prevent this malignant evolution in patients at high risk.

Key Words: Anti-tumour immunity, immunotherapy, tumour antigens, Barret's oesophagus, oesophageal adenocarcinoma, adaptive immunity, immunogenicity, cancer vaccines, immunomonitoring

Target Students: PhD

For more information about this research project contact:

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A/Prof. Nicholas Clemons nicholas.clemons@petermac.org

Next generation humanised mouse platform to study tumour immunology

Supervisors: Prof Riccardo Dolcetti and Dr Roberta Mazzieri

Immunotherapies are emerging as promising strategies to treat both primary and metastatic tumours. The development and deployment of novel therapies requires rigorous research in preclinical animal models before moving into clinical trials and gaining regulatory approval. Despite the unparalleled importance of animal models such as murine models in drug discovery, critical differences in the genetics and immune systems of mice and those of humans provide an important barrier to study the complex and dynamic interactions between a human tumour and the human immune system. Models involving humanised mice (Hu-mice) have evolved as a powerful tool to close this gap and are emerging as fundamental preclinical platforms for drug testing and therapeutic screening as recently stated by the FDA (Rouse, Ther Innov Regul Sci 52, 244-255, 2018). Hu-mice are created by introducing human immune cells, tissues, or genes into immunodeficient mice, enabling the preclinical study of human immune responses, tumour-host interactions, and evaluation of novel immunotherapies. Key limitations still restrict the use of Hu-mice in studying tumour immunology and preclinical testing of novel therapies including the limited development of innate immune cell populations, or the lack of renewable source of HSCs to humanise the mice. In this project the student will explore novel approaches to develop more advanced humanised models for the preclinical testing of emerging cancer immunotherapies, including cancer vaccines, or gene- and cell-based therapies.

Key Words: tumour immunology, preclinical models, immunotherapies

Target Students: PhD

For more information about this research project contact:

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EKERT, PAUL

Using CRISPR technology to model novel oncogenic gene fusions

Supervisors: Dr. Teresa Sadras, Prof. Paul Ekert

In many patients with acute lymphoblastic leukaemia, a frequent event is the fusion of 2 genes to form a novel active oncogene which then drives unregulated proliferation and a resistance to cell death (apoptosis). We have identified several novel fusions which drive the expression of genes normally expressed during early development. In this project, the student will use the tools of molecular and cellular biology determine the mechanisms by which these novel oncogenes function to drive proliferation, repress cell death, regulate differentiation and activate oncogenic signalling pathways. The student will explore some of the fundamental molecular mechanisms that characterise cancer cell. This project will engage the student in cancer biology and the generation of new models to study these fusion genes. As well as the many techniques of molecular biology, the student will have the opportunity to develop skills in advanced sequencing techniques to determine where these fusion bind in the genome and the genes they regulate. Ultimately, the student will try to identify potential ways in which these novel fusions can be therapeutically targeted.

Key Words: Leukaemia, CRISPR, gene fusions

Target Students: Honours, Masters, PhD, MPhil

For more information about these projects contact:

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Dr. Teresa Sadras teresa.sadras@petermac.org

Investigating leukemic intrinsic mechanisms of relapse after immunotherapies

Supervisors: Dr. Teresa Sadras

Chimeric Antigen Receptor T-cell (CAR-T) therapy targeting the CD19 antigen has become a promising therapeutic option for the treatment of relapsed/refractory B cell acute lymphoblastic leukemia (B-ALL) and some lymphomas. Despite some remarkable success for CD19 targeting CAR-T products, 30-50% of B-ALL patients will relapse with limited therapeutic options remaining1. Relapse after CAR-T cell therapy falls into two broad classes, 1. CD19 positive (CD19+/+) relapse, largely due to poor CAR-T persistence, or 2. CD19 negative (CD19-/-) relapse, associated with loss of the CD19 antigen in the leukemic cells. This project will investigate mechanisms by which the leukemic cells adapt to resist therapy and relapse. The student will learn and perform a combination of molecular biology techniques (including flow cytometry, drug screens and western blotting) and advanced microscopy approaches to understand how patients relapse after CAR-T cell therapy.

AVAILABLE PROJECTS BY RESEARCH PROGRAM

This project will also make use of unique mouse models of leukaemia development which will allow important discoveries which may aid the development of improved therapies for patients who relapse.

Key Words: Immunotherapy, Leukemia, Relapse, Molecular Biology, B cell Biology

Target Students: Honours, Masters, PhD, MPhil

For more information about these projects contact:

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FURIC, LUC

Pre-clinical testing of novel combination therapies in mouse models of prostate cancer

Supervisor: Dr. Luc Furic

The prostate requires androgens for normal growth and functioning and the vast majority of prostate cancer (PC) are dependent on the androgen receptor (AR) for growth and proliferation. Androgen-deprivation therapy (ADT) remains the mainstay of therapy for advanced PC, but the disease invariably progress to a stage known as castration-resistant PC (CRPC). The last decade has seen the development of many new therapeutic agents targeting AR activity directly by inhibiting its transcriptional activity or indirectly by inhibiting the enzymes responsible for androgens synthesis. These agents have successfully increased survival in CRPC, but resistance emerges in a matter of months. It is therefore urgent to develop and validate new therapeutic targets in PC which are independent of AR activity.

This project will use genetically modified mouse models (GEMM) of PC to test novel small molecule inhibitors targeting key vulnerabilities of PC cells.

Key Words:Cancer Cell Biology, Cell Signalling, Cancer Therapy, Cell Growth, Molecular Targets, Solid Tumours, Therapeutics, Prostate Cancer.

Target Students: Honours, PhD,MPhil

For more information about this project contact:

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Targeting tRNA modification enzymes in prostate cancer

mRNA translation, also known as protein synthesis, is a key step in gene expression and is often dysregulated in cancer. During translation, mRNA codons are recognised by their corresponding tRNA anticodons. Chemical modification of tRNA bases is an important factor affecting codon recognition and mRNA translation efficiency. In addition to the standard Watson-Crick base pairing, the pairing between the 3rd nucleotide of the codon and the first nucleotide of the anticodon (N34) allows for non-standard “wobble” base pairing. A uridine at position 34 (U34) is often modified to stabilise wobble position base pairing, which subsequently affects decoding and translation rates. One of the best characterised tRNA modification pathway is the three-step modification of U34: firstly, the Elongator complex made up of six proteins (ELP1-6) adds a cm5 moiety; next, the methyltransferase ALKBH8 transfers a methyl group to generate mcm5U34; and lastly, the thiouridylases CTU1/2 catalyses the formation of the mcm5s2U34. Recent studies from our group and others have demonstrated that tRNA modifications can readily be altered in response to various stimuli by modulating the activity of the U34-modifying enzymes. The aim of this project is to investigate whether the activity of U34-modifying enzymes can be targeted to suppress translation and inhibit prostate cancer growth. This project will apply techniques including but not limited to CRISPR gene editing, mammalian cell culture and mass spectrometry to characterise the role(s) of U34-modifying enzymes in prostate cancer aetiology.

Key Words:Cancer Cell Biology, Cell Signalling, Cancer Therapy, Cell Growth, Molecular Targets, Solid Tumours, Therapeutics, Prostate Cancer.

Target Students: Honours, PhD,MPhil

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

NEESON, PAUL

Unveiling the role of CD4+ T cells in glofitamab treatment of Diffuse Large B-cell lymphoma

Supervisors: Prof. Paul Neeson and Dr. Thiago Maass Steiner

Diffuse Large B-Cell lymphoma (DLBCL) is an aggressive type of non-Hodgkin lymphoma. Around 50% of high-risk DLBCL patients fail standard chemoimmunotherapy. Response rates to further treatment are particularly poor (Overall Survival: 6.3 months). Bispecific antibodies (bsAb) have emerged as a novel off-the-shelf therapy for the treatment of cancers. An effective class of bsAb for treating malignancies is the T-Cell Engagers (TCEs), which have two binding sites, simultaneously targeting the immune system's T cells and tumour. Upon activation, engaged T cells can kill their target. One such successful TCE is glofitamab. When glofitamab was administered in heavily treated, refractory or relapsed DLBCL, 39% of patients achieved a complete response rate (median follow-up of 12.6 months). T cells can be divided into two populations, CD8+ and CD4+ T cells, the former are known for their target-killing capacity while the latter have a wider range of actions. CD4+ T cells can differentiate into distinct subsets. Some subsets have tumour-killing capacity; others have anti-tumour activity mainly due to the secretion of anti-inflammatory molecules (cytokines). It is still unclear how CD4+ T cells contribute to killing DLBCL tumour cells after glofitamab treatment and if, in some circumstances, they have deleterious effects leading to disease progression or relapse. This research aims to dissect CD4+ T cell responses to glofitamab, proposing new immune targets for future combination therapies for DLBCL patients.

Key words: Diffuse Large B-cell lymphoma, bispecific antibodies, T-Cell Engagers, glofitamab

Target Students: Honours, PhD

For more information about this project contact:

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Improving CAR-T cell therapy efficacy against multiple myeloma

Supervisors: Dr. Criselle DSouza, Dr. Joe Zhu and Prof. Paul Neeson

Multiple myeloma (MM) is characterized by a clonal expansion of plasma cells in the bone marrow. Australia's MM incidence rate has been rising over the past few years. MM patients are treated with multiple treatments. . Although CAR-T cell therapy has a positive outcome in MM, patients eventually relapse. To ensure that CAR-T cells can have long-term responses in MM, we need new strategies to overcome resistance. In this project, we propose multiple approaches. The first approach is to understand the TME of treated patients at the tumour site. The second approach is to use engineered switch CAR-T cells in combination with certain existing drugs that can specifically function in an immunosuppressed TME. These approaches will overcome issues such as CAR-T cell trafficking into the tumour and immunosuppression. The third approach is to test a novel CAR target and test the efficacy in pre-clinical models and against patient MM samples using autologous CAR-T cells.

Key Words:Multiple myeloma, Immunotherapy

Target Students: PhD

For more information about this projects contact:

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Improving CAR-T cell therapy efficacy against solid tumors

Supervisors: Dr. Joe Zhu, Dr. Criselle DSouza and Prof. Paul Neeson

Immunotherapy uses a patient's own immune system to fight cancer. There are two major types of immunotherapies, i.e. immune checkpoint blockade and chimeric antigen receptor T (CAR-T) cell therapy. CAR-T cell therapy involves the adoptive transfer of autologous T cells that have been genetically engineered with a CAR to target tumor cells. CAR-T cell therapy has been successful in treating patients with relapsed/refractory B-cell malignancies. However, this success has not occurred in patients with solid tumors. The reasons for this poor outcome include tumor heterogeneity, an immunosuppressive tumor microenvironment (TME), insufficient T-cell trafficking to the tumor site, and poor T-cell persistence post-infusion. In this project, we will develop and evaluate new strategies for CAR-T cells to overcome these barriers. This project will provide sufficient pre-clinical and translational data to drive the novel therapy into clinical trials for patients with solid tumors.

Key Words: CAR-T therapy, Solid tumors, Immune suppression, Tumour microenvironment, CAR-T cell trafficking

Target Students: Honours

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Characterisation of tissue-resident memory T cells in melanoma disease

Supervisors: Prof Paul Neeson and Dr. Andrea Di Pietro

Melanoma, a disease characterised by the growth of malignant tumours in the skin, elicits an immune response that evolves as the tumour progresses. Among melanoma-reactive immune cells, T cells can be found in three distinct locations:

1. within the tumour itself, referred to as tissue resident T cells,
2. in nearby or distant lymph nodes as memory T cells, and
3. traversing between these two sites via the bloodstream.

The tissue-resident memory T cells (TRMs) are the most crucial and effective cells for controlling melanoma. Interestingly, previous research indicates a correlation between increased numbers of TRMs and enhanced clinical outcomes. Therefore, it is crucial to explore whether an abundance of resident memory T cells can serve as a predictive factor for favourable outcomes in individuals with early-stage or metastatic disease. By conducting this project, we aim to

1. Investigate the density and location of TRMs in primary and metastatic disease and
2. Investigate the phenotype and genealogy of TRMs by utilising a multiomic approach at a single-cell level.

The findings will provide valuable insights into the prognostic significance of increased TRMs in melanoma and it will empower melanoma oncologists to make informed decisions regarding patient treatment.

Key words: Melanoma, Cancer immunology, Tumour microenvironment, Tissue-resident memory T cells

Target Students: Honours

For more information about this project contact:

Dr. Andrea Di Pietro andrea.dipietro@petermac.org

Investigating the Diffuse Large B cell Lymphoma tumour microenvironment following treatment with a novel bispecific antibody concomitantly targeting tumour cells and T cells

Supervisors: Prof. Paul Neeson and Dr. Thiago Maass Steiner

More effective treatments are needed for patients with high-risk Diffuse Large B cell Lymphoma (DLBCL), where response at 3-years is approximately 50%. Intensification of standard chemoimmunotherapy has not translated to improved outcomes. Glofitamab is a novel CD20/CD3 bispecific antibody achieving a 39% complete remission rate in refractory or relapsed DLBCL patients. We have now started an ongoing multi-centre phase I/II study of glofitamab in combination with standard chemoimmunotherapy in younger patients with high-risk DLBCL patients. The aim of this trial is to evaluate the potential benefits provided by glofitamab at the start of treatment alongside standard chemoimmunotherapy. In this project, we are particularly interested in the translational aspect of this trial. We aim to investigate the tumour microenvironment evaluating the location and state of key immune cells, such as T cells at baseline in the tumour microenvironment. We will also investigate potential immune escape mechanisms to glofitamab in refractory or relapsed patients. For this purpose, we will perform flow cytometry, mass cytometry, bulk-RNAseq and scRNA-seq, alongside multiplex imaging for an in-depth analysis of the tumour immune cell landscape. Ultimately, the goal is to identify potential biomarkers for the selection of patient cohorts that will benefit from glofitamab.

Key words: DLBCL, T cells, Immunotherapy, Bispecific antibodies, Clinical trial.

Target Students: Honours

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Investigating CAR-T cell therapy for Acute Myeloid Leukemia

Supervisors: Prof Paul Neeson, Dr Deborah Meyran, Prof Joe Trapani

Acute myeloid leukemia (AML) is a heterogeneous disease comprising multiple sub-groups of disease derived from an AML cancer stem cell. Unfortunately, AML patients who relapse after stem cell transplantation have a poor clinical outcome. Chimeric antigen receptor (CAR)-T cells provide a potential opportunity for patients with refractory AML. However, there are issues with designing CAR-T cells to be specific for the AML blasts, and not antigens expressed by normal haemopoietic stem cells which could lead to bone marrow toxicity. In this project we will address this issue by targeting an onco-fetal antigen (Lewis Y) which is heterogeneously expressed on AML blasts. In this project, we will use a CRISPR editing screen (KI or KO) to define the molecules which control LeY expression on AML lines. Using this data, we will use a drug screen to target these pathways and investigate LeY-CAR-T cell killing, proliferation and cytokines in AML cell lines and then extend this to patient AML blasts and LeY-CAR-T cells. Finally, we will explore gene editing and drug targeting to increase LeY expression in an in vivo AML model; we will also combine this with LeY-CAR-T therapy to assess AML disease control.

Key words: Acute myeloid leukemia, chimeric antigen receptor T cells

Target Students: Honours, PhD/MPhil

For more information about this project contact:

Dr. Deborah Meyran Deborah.Meyran@petermac.org

TRAPANI, JOSEPH

A New Era of Precision Medicine: CRISPR Therapeutics against Oncogenes and Pathogenic Viruses

Supervisors: Dr. Mohamed Fareh and Prof. Joseph Trapani

Recent breakthrough discoveries have revealed that CRISPR effectors can function as programmable molecular scissors, allowing precise editing of the human transcriptome and genome. These revolutionary CRISPR technologies have opened up possibilities for targeting specific disease-causing genes. Our group is fully dedicated to the development of next-generation CRISPR therapeutics that specifically target pathogenic oncogenes and infectious viruses. We successfully reprogrammed a novel CRISPR protein called Cas13 to silence oncogenic RNA drivers (Hu et al, under review) and SARS-CoV-2 viral strains (Fareh et al, Nature Comms, 2021). We believe that these CRISPR therapeutics have the potential to revolutionize personalized medicine. Our current projects encompass several key areas:

1. We aim to comprehensively understand the underlying mechanisms of target recognition and editing exhibited by newly discovered and poorly characterized CRISPR effectors.
2. We aim to reengineer CRISPR-Cas effectors to achieve single-base accuracy in silencing tumor drivers, enabling highly precise and specific therapeutic interventions.
3. By leveraging "Big data" and high-throughput screening techniques, we aim to design multiplexed CRISPR tools capable of targeting entire families of pandemic viruses, such as Betacoronaviruses.
4. We are actively working on the engineering of mRNA and lipid-nanoparticles as delivery vehicles, paving the way for the next generation of CRISPR therapeutics.

A prospective student will have the opportunity to use cutting-edge interdisciplinary approaches including computational data mining, molecular cloning, CRISPR-Cas editing, CRISPR screens, super-resolution microscopy, RNA-seq, Mass Spec proteomics, FACS, RT-PCR, mRNA synthesis, and lipid nanoparticle-based deliveries.

Key words: CRISPR, Gene editing, Personalized therapy, RNA Therapeutics, AI, SARS-CoV-2, Molecular biology, Genetic screens

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Mohamed Fareh Mohamed.fareh@petermac.org.

AVAILABLE PROJECTS BY RESEARCH PROGRAM

VOSKOBOINIK, ILIA

Understanding cytotoxic lymphocyte biology in health and disease.

Supervisors: Prof Ilia Voskoboinik, Prof. Joseph Trapani

Cytotoxic lymphocytes – cytotoxic T lymphocytes and natural killer cells- are essential for our immune defence against disease, as they recognise and kill virus-infected or cancer target cells. The health consequences of cytotoxic lymphocyte dysfunction are catastrophic, and range from uncontrolled hyperinflammation to cancer.

Using a wide range of immunological, biochemical, molecular, biophysical and cellular approaches, and in collaboration with clinicians, we investigate:

1. The mechanisms that regulate the transition from a quiescent naïve lymphocyte to a potent killer cell,
2. Novel therapeutic strategies aimed at improving immunotherapy,
3. Mechanisms of primary immunodeficiencies and other disorders that can affect cytotoxic lymphocyte function in humans.

Key Words: Cytotoxic lymphocytes, Immunotherapy, Cell biology, Immunodeficiency.

Target Students: Masters, PhD, MPhil

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Computational Biology Program

OSHLACK, ALICIA

Cell free RNA sequencing: New approaches to liquid biopsies

Supervisors: Prof Alicia Oshlack and Dr Jovana Maksimovic

Most RNA-seq analysis extracts RNA from intact cells. However RNA can be released into fluids such as blood and amniotic fluid during cell death. This RNA can be measured using RNAseq. This project aims to characterise the technical features of cell free RNA that we have collected from amniotic fluid. In addition, several published studies have shown that RNA from tumours can been found in patient plasma. We will look at data quality features such as fragment length, transcript positions of reads and ribosomal contamination. We will also look at detecting fusion genes in plasma cell free RNA as a new type of liquid biopsy. This project has several alternative avenues of extension based on the result of initial analysis.

Key Words: RNA-seq, computational biology

Target Students: PhD

For more information about this project contact:

Prof. Alicia Oshlack Alicia.oshlack@petermac.org

Characterising transcriptional diversity in cancer using long-read sequencing

Supervisors: Prof Alicia Oshlack and Dr Jovana Maksimovic

Cancer is a disease of the genome which occurs from an accumulation of mutations at a range of scales from single nucleotides to chromosomal rearrangements. The functional consequences of mutations can be transcribed into RNA and detected through transcriptome sequencing. Events that alter the function of genes by driving novel transcript structures can be detected using RNA sequencing and we have been working on methods and approaches for this with traditional sequencing. New long read sequencing technologies promise to provide a richer source of information about novel transcripts that drive cancer. However there are limited computational methods for identifying these important events. Further approaches to characterise the features and rates at which novel splicing occurs are needed. This project aims to develop bioinformatics approaches to analyse and explore long read transcriptome data and identify important events in cancer.

Key Words: Computer science, Statistics or similar quantitative science

Target Students: PhD

For more information about this project contact:

Prof. Alicia Oshlack Alicia.oshlack@petermac.org

TONKIN-HILL, GERRY

Patterns of Microbial Evolution in Human Hosts

Supervisors: Dr Gerry Tonkin-Hill, Dr Sudaraka Mallawa Arachchi

Deciphering how bacteria evolve within humans is crucial for understanding critical health issues, including the rise of antibiotic resistance and the interactions between the microbiome and cancer immunotherapies. By analysing large metagenomic datasets (sequencing all bacterial genomes within a sample), it is possible to track bacterial evolution and transmission patterns across multiple species. However, there are limited computational and statistical methods for performing these analyses. This project will develop and apply new computational techniques to examine large patient sample collections, enhancing our understanding of how therapeutics and the host environment influence the evolution of pathogenic and commensal bacterial species. The project is ideal for students interested in developing new computational and statistical methods as well as applying existing techniques to large, unique datasets that are critical for public health.

Key Words: metagenomics, microbiome, statistics, machine learning, bioinformatics

Target Students: Masters, PhD, MPhil

For more information about this project contact:

Dr Gerry Tonkin-Hill gerry.tonkin-hill@petermac.org

TRIGOS, ANNA

Using a combination of genomics, single-cell and spatial technologies to understand prostate cancer heterogeneity

Supervisor: Dr. Anna Trigos

While prostate cancer is generally considered a highly manageable disease, a subset of patients develops metastatic disease unresponsive to treatment. Tumours acquire a diversity of genetic and transcriptional changes during their evolution, many of which promote treatment resistance. Beyond these tumour-intrinsic factors, the surrounding microenvironment may promote or inhibit distinct tumour populations. All these factors act in combination to promote tumour heterogeneity during metastasis.

This project aims to understand the role of genetics, transcriptional programs and the microenvironment in driving tumour heterogeneity using a combination of genomics, single-cell gene expression and spatial technologies. Our projects are computational and can be tailored to the student's interest. There is scope for algorithm-development, data analysis and integration, or a mixture of computational and laboratory work.

AVAILABLE PROJECTS BY RESEARCH PROGRAM

Students are expected to have extensive programming experience and be comfortable in at least one language (preferably R). The student will be part of a highly multidisciplinary team of bioinformaticians, computational biologists, medical oncologists and immunologists.

Key Words: Prostate cancer, Bioinformatics, Single-cell gene expression, Spatial tissue analysis, Heterogeneity, Tumour evolution

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Anna Trigos Anna.trigos@petermac.org

Cancer evolution using multi-omics

Supervisor: Dr. Anna Trigos

Cancer evolution and heterogeneity limit the success of personalised medicine. These processes have traditionally been studied under the lens of genetic Darwinian evolution. However, recent technological developments have brought to light that beyond the presence of multiple clones, genetically identical cells often have different epigenomes. This project aims to elucidate how tumour cell states result from plasticity and clonal evolution and communication with the environment, and how these co-evolve during disease progression and the development of resistance. There is a wealth of opportunities for projects in this space, from understanding how tumour cells alter their own phenotype in response to genetic alterations, how they adapt to the microenvironment, how cell-cell communication between tumour cells and with the microenvironment is fundamental for the emergence of specialised tumour cell populations, and how the composition of tumour populations changes with treatment. For this, we use single-cell multi-omics, spatial transcriptomics, spatial proteomics, liquid biopsies and DNA sequencing data together with a combination of a diversity of data analyses techniques, such as bioinformatics, simulations, modelling and machine learning.

Key Words: cancer, multi-omics, bioinformatics, data analysis, machine learning

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Anna Trigos Anna.trigos@petermac.org

Development of methods to analyse the spatial distribution of tumour and microenvironment cells in tissues

Supervisor: Dr. Anna Trigos

Cancers are composed of a myriad of cell types, such as tumour cells and immune cells. However, rather than a homogeneous mixture of cells, cells are organised in biologically meaningful ways. For example, immune cells that are close to tumour cells might be recognising and killing tumour cells, whereas the absence or the random location of immune cells in the tissue might mean that such recognition is not taking place. Our group develops and applies computational approaches that allow us to quantify, compare and simulate such patterns from spatial proteomics and transcriptomics data. Techniques to be used include algorithm development, machine learning, data analysis and software development.

Key Words: spatial analysis, method development

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Dr. Anna Trigos Anna.trigos@petermac.org

Deep learning to analyse patient imaging

Supervisor: Dr. Anna Trigos

During treatment, cancer patients often receive a wealth of imaging, including PET scans, CT scans and MRIs. To date, these have been largely used to understand the extent of disease and tumour location and size. However, there is a clear potential of further information contained in these imaging modalities that can help understand disease evolution, development of resistance, and predict patient treatment response and survival. In this project we will extract imaging features from a diversity of imaging modalities of large patient imaging datasets, and associate with mutation, epigenetic and transcriptional information derived from tissue and liquid biopsies, and rich clinical data. The project will primarily involve the use of deep learning methods and would suit a student with a strong computer science background.

Key Words: patient imaging, deep learning

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

Organogenesis and Cancer program

CHENG, LOUISE

How do tumours grow at the expense of other tissues in cancer cachexia

Supervisors: A/Prof Louise Cheng

Cancer cells are known to drive altered metabolic circuits to meet the bioenergetic and biosynthetic demands of increased cell growth and proliferation. Under nutrient restriction, when growth of most organs shut down, cancer cells can bypass these brakes imposed on cellular growth, thus gaining a growth advantage under these conditions. Furthermore, during cachexia, which causes more than one third of cancer death, tumour derived factors can also induce the break down of fat and skeletal muscles, in order to generate metabolic intermediates necessary for the preferential tumour growth. The signalling between tumours and other tissues is highly complex, and the adaptations that allow cancer cells to preferentially activate growth are largely unknown. The student will work within a existing team to discover some of the mediators of cancer cachexia using Drosophila genetics, confocal microscopy, proteomics, metabolomics; the findings will be further validated in human samples.

Key Words:Cachexia, interorgan crosstalk

Target Students: Honours, Masters, PhD

For more information about this project contact:
A/Prof Louise Cheng : louise.cheng@petermac.org

Discovering mechanisms of dedifferentiation.

Supervisors: A/Prof Louise Cheng

Dedifferentiation is a fundamental process, which allows post-mitotic (non-dividing, mature) cells to revert to a stem cell-like state. It is an important mechanism, which allows mature cells to re-enter the cell cycle to generate additional stem cells, and the regulation of this process has important implications for regenerative medicine, where it is not well understood how stem cells can be activated upon injury (in order to carry out repair). Deregulation of dedifferentiation also has important implications for tumour formation, as generation of ectopic stem cells can cause uncontrolled proliferation and cancer. We have so far identified a number of transcription factors important for dedifferentiation in the developing Drosophila CNS, in this project, we aim to explore how dedifferentiation is regulated, what types of cells are produced during dedifferentiation, how is the balance between dedifferentiation and tumour growth regulated. The student will use Drosophila genetics, genomics and imaging to answer some of these questions.

Key Words: Neural stem cells, dedifferentiation

Target Students: PhD

For more information about this project please contact:
A/Prof Louise Cheng : louise.cheng@petermac.org

AVAILABLE PROJECTS BY RESEARCH PROGRAM

Non-autonomous regulation of tumour growth

Superviors: A/Prof Louise Cheng, Dr Joanna Dong

How tumours communicate with tissues to trigger their breakdown is a key unresolved question. We have generated novel genetic tools that allow independent spatial and temporal overexpression or knockdown of genes in multiple tissues simultaneously. Using these tools, this project aims to look at how brain tumours can interact with other tissues.

Key Words: brain tumour, inter-organ communication

Target Students: Honours, PhD

For more information about this project please contact:
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Dr. Joanna Dong Qian.Dong@petermac.org

COX, ANDREW

Role of the Hippo-YAP pathway in tumour initiation.

Supervisor: A/Prof Andrew Cox

The Hippo-YAP pathway is an evolutionarily conserved cascade that plays a fundamental role in governing organ size control, stem cell homeostasis and cancer. The Hippo-YAP pathway is regulated by a range of environmental cues including nutrient status. Although many of the inputs into the Hippo pathway have been identified, less is known about how YAP drives tumourigenesis. Our previous studies revealed that the oncogenic Hippo-YAP pathway reprograms anabolic metabolism (nucleotide and lipid biosynthesis) to fuel liver cancer. Building on these studies, we currently have research projects that aim to 1. Examine how YAP initiates liver tumour formation. 2. Elucidate the mechanisms by which YAP reprograms metabolism 3. Examine role of YAP in regulating cancer-associated cachexia. Students will gain experience in a variety of biochemistry/cell biology/molecular biology techniques including CRISPR/Cas9-mediated gene editing, Next generation sequencing (transcriptomics), Mass Spectrometry (metabolomics), tissue clearing and advanced microscopy.

Key Words: Liver Cancer, YAP, CRISPR, Zebrafish, Metabolism, Cachexia.

Target Students: Honours, Masters, PhD/MPhil

For more information about this project please contact:

A/Prof Andrew Cox andrew.cox@petermac.org

Investigating the interplay between oxidative stress and oncogenic KEAP1-NRF2 pathway in liver cancer.

Supervisor: A/Prof Andrew Cox

Many of the major risks factors for developing liver cancer such as alcohol, obesity, smoking and toxin exposure share in common a role for oxidative stress. NRF2 is a transcription factor that plays a pivotal role in the cell's adaptation to oxidative stress. The NRF2 pathway is frequently mutated in solid tumours, leading to NRF2 activation. Despite the high prevalence of NRF2 activation in cancers, we still lack a clear appreciation of how this major oncogene drives tumorigenesis. We have recently used transcriptomic and metabolic profiling in zebrafish models to examine the role NRF2 plays in remodeling metabolism during liver development, regeneration and cancer. Building on these preliminary studies, we currently have research project that aims to

1. Develop new zebrafish models of liver cancers driven by oncogenic NRF2 activation.
2. Identify the metabolic dependencies of NRF2-driven liver cancer.
3. Reveal therapeutic vulnerabilities of NRF2-driven liver cancer.

Students will gain experience in a variety of biochemistry/cell biology/molecular biology techniques including CRISPR/Cas9-mediated gene editing, transcriptomics, tissue clearing and advanced microscopy.

Key Words: Liver Cancer, YAP, CRISPR, Zebrafish, Metabolism, Cachexia.

Target Students: Honours, Masters, PhD/MPhil

For more information about this project please contact:

A/Prof Andrew Cox andrew.cox@petermac.org

HARVEY, KIERAN

New treatments for mesothelioma

Supervisors: Prof Kieran Harvey, Dr Aishwarya Kulkarni

Mesothelioma is a terrible disease that is most commonly caused by exposure to asbestos. There are limited treatment options for mesothelioma patients and survival rates are very low compared to most other cancers. Therefore, the need for new and effective mesothelioma treatments is urgent. Importantly, over the past 5 years, cancer genome sequencing studies have revealed that a particular signaling pathway – the Hippo pathway – is mutated in more than half of all mesotheliomas.

AVAILABLE PROJECTS BY RESEARCH PROGRAM

We are searching for ways by which we can modulate Hippo pathway activity to treat mesothelioma. Importantly, to ensure the potential of Hippo targeted therapies is met, we must gain a deeper understanding of exactly how they work. This project will investigate:

1. How targeting the Hippo pathway kills mesothelioma cells
2. How mesothelioma cells become resistant to Hippo targeted therapies
3. Potential combination therapies that work together with Hippo therapies to kill mesothelioma cells

You will work as part of a collaborative team and receive excellent training in cell and molecular biology skills and advanced microscopy techniques. You will also receive training in problem solving, scientific writing, delivering oral presentations and how to critically appraise data.

Key Words: Mesothelioma, Cancer, Hippo pathway

Target Students: Honours, PhD, MPhil

For more information about this project contact:

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Dr Aishwarya Kulkarni Aishwarya.Kulkarni@petermac.org

Investigating how the TNF and Hippo pathways co-regulate genes to control neoplastic tissue growth

Supervisors: Prof Kieran Harvey, Dr Katrina Mitchell

Organ size control, tissue damage and tumour growth are all tightly linked processes. Animals have evolved complex mechanisms to remove damaged or abnormal cells from a tissue in order to prevent tumour growth. We use Drosophila melanogaster to understand the mechanisms by which epithelial tissues can prevent tumours from growing. Neoplastic cells, which have mutations in conserved apical polarity genes (e.g. scribble), can form malignant tumours. Interestingly, if a tissue contains only a small number of these neoplastic cells they are eliminated. We have identified that both the Tumour necrosis factor pathway (TNF pathway - also known as JNK pathway) and Hippo pathway play important roles in eliminating neoplastic cells. This project will involve investigating how these pathways can regulate the transcription of genes to control neoplastic tissue growth. You will use the following techniques: 1. Drosophila organ growth assays 2. Confocal microscopy analysis of gene and protein expression 3. Molecular biology 4. Genomics and bioinformatics You will work as part of a collaborative team and receive excellent training in the techniques listed above. You will also receive training in problem solving, scientific writing, delivering oral presentations and how to critically appraise data.

Key Words: Organ size control, Hippo pathway, TNF pathway, Cancer, Transcription

Target Students: Honours, Masters, MPhil

For more information about this project contact:

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Dr Katrina Mitchell Katrina.Mitchell@petermac.org

HOGAN, BEN

Understanding the roles of novel membrane receptors in lymphangiogenesis and tumour vasculature

Supervisors:Prof Ben Hogan and Dr Wei Chen

Lymphangiogenesis is the formation of new lymphatic vessels from pre-existing vessels. This process is crucial in both development and the metastatic spread of cancer. The transcription factor Prox1 has been shown to play important roles in the specification, transdifferentiation and maintenance of lymphatic endothelial cells (LECs) across species. A recent single cell transcriptomic atlas of lymphangiogenesis in zebrafish identified novel membrane receptor genes expressed specifically in lymphangiogenesis. CRISPR-Cas9 knockout of the candidate genes led to defects in lymphangiogenesis in development, but their mechanistic roles and contribution in disease have yet to be characterised. This project will use CRISPR-Cas9 generated stable knockout mutants of novel receptors important for lymphangiogenesis. Detailed characterisations of the mutants' lymphatic phenotypes will be conducted using state-of-the-art spinning disc confocal microscopy. Specific drugs for the target receptors will be applied to examine molecular pathways that are involved following receptor(s) activation. The results obtained will be validated using human lymphatic cell lines, genomics will be used to probe receptor roles in cancer and homology modelling is an optional approach to further shed light on receptor/ligand interactions. This project has translational potential and can enhance our understanding of lymphangiogenesis in both development and disease settings.

Key Words: Lymphangiogenesis, CRISPR-Cas9, Development, Microscopy, Homology modelling

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH PROGRAM

LALAOUI, NAJOUA

Inflammatory cell death in cancer and inflammatory diseases

Supervisor: Dr Najoua Lalaoui

Cell death programs are crucial processes in development, tissue homeostasis and immunity. 'Too much' cell death can lead to neurodegenerative and immune diseases and 'too little' cell death causes cancer. Consequently, re-activation of cell death within tumours is one of the major goals of cancer therapies. Until recently, it was thought that the unique purpose of programmed cell death was to kill cells. However, it has become clear that dying cells release a variety of signals that communicate with the microenvironment and the immune system. Thus, how the body responds to dying cells can influence cancer progression and cancer treatments. RIPK1 and RIPK3 are crucial kinases that regulate inflammatory cell death downstream of various innate immune ligands (e.g. TNF or TLR ligands). The student will work within an existing team to investigate the causes and consequences of cell death induced by RIPK1/3 using a range of cellular, and molecular techniques and in vivo models. This fundamental knowledge will be applied to design new therapeutic strategies for cancer and inflammatory diseases and to understand the impact of inflammatory cell death on cancer immunity and progression.

Key Words: cell death, inflammation, cancer, innate immunity, RIP kinases

Target Students: Honours, Masters, PhD

For more information about this project contact:

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RUSSELL, SARAH

How is fate determined during T cell development, leukemogenesis and responses

Supervisor: Prof. Sarah Russell

Understanding how cell fate programming works will lead to improved diagnostic and therapeutic opportunities for leukemia, and to improved immunotherapies for cancer and infectious disease. We have developed new methods for imaging single cells and their progeny through many generations of T cell development and activation. These methods mean that we can now assemble pedigrees that describe both the relationships between different differentiation stages, and molecular and behavioral attributes of their ancestors and progeny. The next step is to use these pedigrees and the wealth of information associated with them to determine the relative contributions of genetic, epigenetic, extrinsic and stochastic influences on fate determination. This PhD project will involve development of new computational approaches to determine how behaviours in the T cell progeny (differentiation, growth, death, division) are influenced by ancestory, intrinsic and extrinsic cues.

Key Words: Cell Signalling,Cellular Immunology, Differentiation, Haematology, Haematological Cancers, Immunotherapy, Tumour Immunology.

Target Students: PhD

For more information about this project contact:

Prof. Sarah Russell sarah.russell@petermac.org

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AVAILABLE PROJECTS BY CLINICAL RESEARCH PROGRAM

FAMILIAL CANCER RESEARCH CENTRE

Co-design and feasibility piloting of PERSONA (Precision prEvention of bReaSt and OvariaN cAncer), a personalised breast cancer risk assessment

Supervisors: A/Prof Laura Forrest, Dr Sibel Saya, and Dr Michelle Tew

Personalising the early detection and prevention of breast cancer would reduce the significant cancer burden experienced by Australian women and reduce the burden on the Australian healthcare system. This study will deliver key evidence to inform the development of PERSONA, a risk assessment intervention, that is critical to the precision prevention program. PERSONA uses the latest understanding of genomic risk markers combined with non-genomic cancer risk factors to define a personalised, comprehensive breast cancer risk assessment.

The study aims include:

1. to co-design the development and refinement of PERSONA, and
2. to pilot PERSONA and associated study procedures in primary care.

The students will be involved in the co-design process collecting qualitative data from stakeholders. During the second stage of research, the student will be involved in conducting an early value assessment of PERSONA to establish the clinical potential of PERSONA and explore what is needed to provide the most value for money.

The outcome of co-designing and feasibility testing PERSONA with end-users, will be a fit-for-purpose, tailored intervention that will be implementation-ready.

Key Words: Precision prevention, breast and ovarian cancer, cancer risk assessment

Target Students: Honours, PhD, MPhil

For more information about this project contact:

A/Prof Laura Forrest Laura.Forrest@petermac.org

POSTATE THERANOSTICS AND IMAGING CENTRE OF EXCELLENCE: ProsTIC

Advanced Image and Biomarker Analysis to Better Personalise Care of Men with Prostate Cancer undergoing Radionuclide Therapy

Supervisors: Prof. Michael Hofman

Prostate Cancer is a leading cause of death in men. ProsTIC is a clinical and laboratory research program which comprises a multi-disciplinary team including nuclear medicine, medical oncology, radiation oncology, urology and laboratory-based doctors and researchers with a strong patient-centred philosophy. We see radioactive molecules that target a unique receptor on the cell surface of prostate cancer cells called prostate specific membrane antigen (PSMA) for both imaging with positron emission tomography (PET) and also therapy. There are several opportunities for research in different domains including:

- Advanced imaging analysis techniques using radiomics or computer-deep learning, to better personalise care, or enable response better response assessment.
- Analysing data from a registry of patients undergoing Lutetium-PSMA therapy to identify prognostic biomarkers and/or patterns of response.
- Experience in analysing DICOM imaging datasets will be helpful for candidates with background in computer science or computational biology.
- Registry analysis may be suitable for medical students or physicians with an interest in nuclear medicine or medical oncology.

Key Words: Prostate Cancer, PSMA, Radioligand Therapy, Artificial intelligence, Deep learning

Target Students: Honours, Masters, PhD, MPhil

For more information about this project contact:

Prof. Michael Hofman michael.hofman@petermac.org

AVAILABLE PROJECTS BY CLINICAL RESEARCH PROGRAM

RADIATION ONCOLOGY RESEARCH

Immune-PET: Characterising the Immunophenotype with Novel PET Tracers

Supervisors: Dr Fiona Hegi-Johnson, Prof Michael MacManus

Immune-PET is a multidisciplinary collaboration led by Dr Fiona Hegi-Johnson and Professor Michael MacManus. We are a group of radiation oncology and medical oncology clinicians at Peter Mac that in partnership with the research group of Professor Andrew Scott at the Olivia Newton John Cancer Research Institute (ONJCRI) and the Donnelly Laboratory at the University of Melbourne develop novel PET tracers to characterise the immune system. We work closely with our laboratory colleagues, including Dr Magnus Dillon
at the ICR in London and Dr Harriet Gee at the University of Sydney,
to understand the mechanisms that underpin radiotherapy-induced
immunotherapy responses, and our clinical trials couple novel imaging approaches with interrogations in tumour and host immunity through our collaboration with Professor Stephen Fox and Paul Neeson.

Key words: Lung Cancer, Immunotherapy, Nuclear Medicine

Target students: Honours, Masters, PhD

For more information please contact

Dr Fiona Hegi-Johnson Fiona.Hegi-Johnson@petermac.org.

Imaging of cancer immunotherapy targets with Positron Emission Tomography: Characterising PD-L1 with 89Zr-Durvalumab

Supervisors: Dr Fiona Hegi-Johnson and Prof Michael MacManus

This PhD project is based on a clinical trial aimed at establishing the feasibility of 89Zr- Durvalumab as a novel imaging biomarker of PD-L1 activity during treatment for lung cancer, and embraces both clinical and translational research in novel-tracer PET/CT and molecular biology.

The project consists of a 20 patient Phase I study in which patients undergo sequential PD-L1 imaging before and during radical chemoradiation for Stage III NSCLC. This project runs in tandem with a translational analysis analysing serial liquid biopsies for circulating tumour cells (CTC), circulating tumour DNA (ctDNA) and changes in host immunity, as well as analysis of serial tissue biopsies of irradiated tumour that will characterise the T-cell repertoire and PD-L1 dynamics during treatment.

Key words: Lung Cancer, Immunotherapy, Nuclear Medicine

Target students: PhD, MPhil

For more information please contact

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AVAILABLE PROJECTS BY CLINICAL RESEARCH PROGRAM

Defining the Immunophenotype of PD-L1 resistance with durvalumab and CD8 PET/CT: pathways to the development of novel treatment strategies

Supervisors: Dr Fiona Hegi-Johnson and Prof Michael MacManus

This PhD project is based on a series of small clinical trials that will characterise the biology of PD-L1 resistance in the following patient cohorts.

1. Patients with oligoprogressive disease during PD-L1 therapy
2. Patients with PD-L1 positive incurable NSCLC who are planned to receive palliative radiotherapy

Novel tracer PET imaging of CD8, and other immune pathways will be used in conjunction with molecular analyses of liquid and tissue biopsy to characterise the biology of patients with disease progression during PD-L1 therapy, and to investigate whether radiotherapy can be used to modulate host and tumour immune responses

The core skills that will be acquired by research candidates are:

1. Advanced skills in image analysis of PET/CT and the ability to interrogate the impact of radiotherapy treatment on dynamic changes on both FDG and 89Zr- based monoclonal antibody PET and other novel tracers
2. An understanding of clinical trial design for novel-PET tracer multicentre studies
3. Molecular biology: analysis of data acquired from the molecular translational work, including RNA-sequencing and ctDNA.
4. Bioinformatic analysis of the relationships between imaging and molecular data

Key Words: Lung Cancer, Immunotherapy, Nuclear Medicine

Target Students: PhD, MPhil

For more information about this project contact:

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