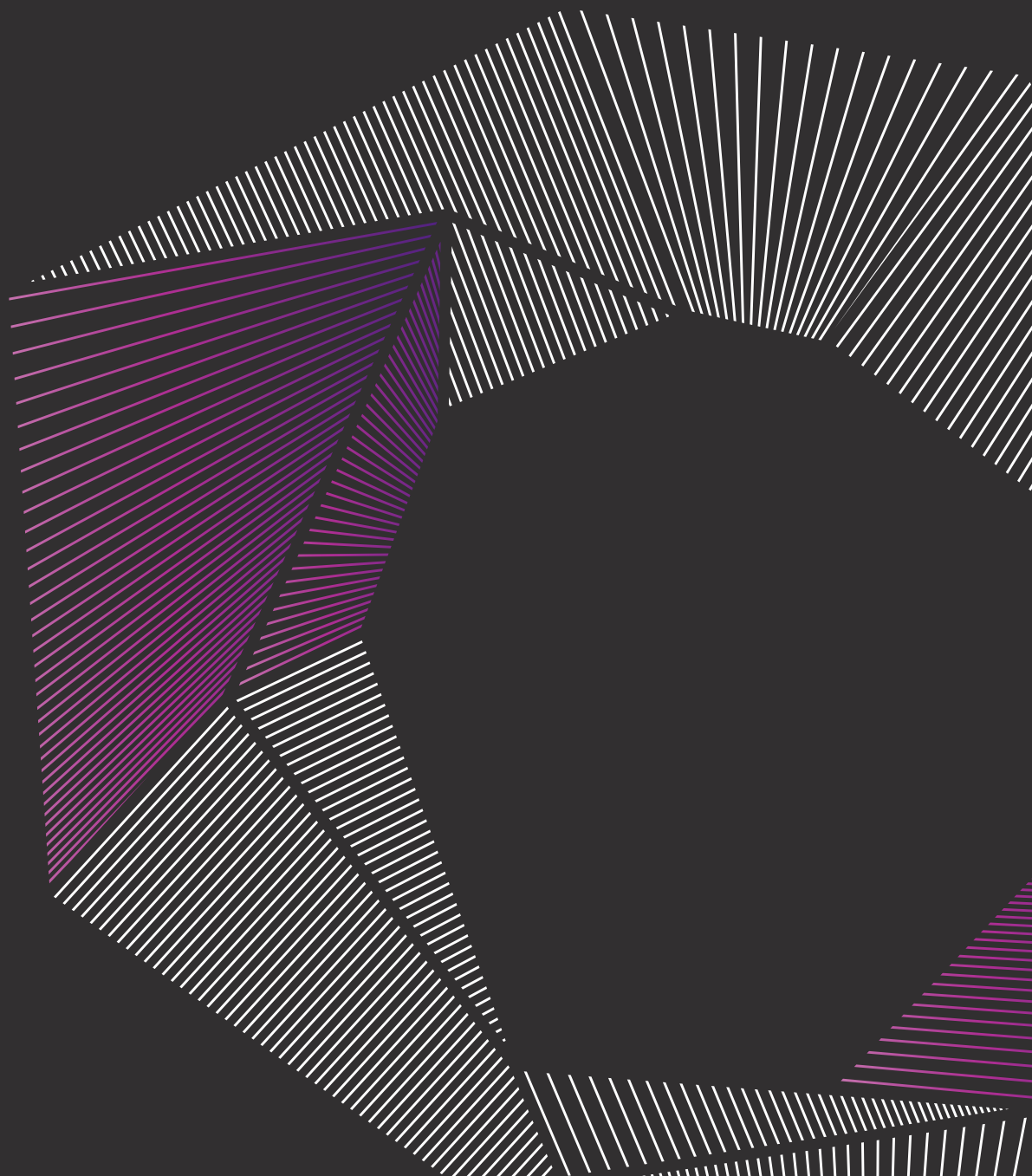**Peter Mac**

Peter MacCallum Cancer Centre
Victoria Australia

CANCER RESEARCH
STUDENT PROJECTS
2021

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

CONTENTS

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 600 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,

LABORATORY RESEARCH

https://www.petermac.org/research/labs

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.

Peter Mac is home to over 450 laboratory-based scientists and support staff, including more than 150 higher degree (mainly PhD) and Honours students.

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

• Cancer Genetics & Genomics

• Cancer Immunology

• Cancer Metabolism

• Cancer Therapeutics

• Computational Biology

• Gastrointestinal Cancer

• Organogenesis and Cancer

• Prostate Cancer

• Translational Haematology

• Tumour Angiogenesis and Microenvironment

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

https://www.petermac.org/research/programs/clinical-research-areas-programs

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.

ABOUT OUR RESEARCH

Treatment informed by research, and research informed by treatment, is the key to progressing better cancer care.

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.

Cancer Experiences Research

This group develops novel, patient-centred strategies and interventions. Their research focus is on communication, health literacy, emotional and physical functioning, care coordination, education information, well-being for survival and living well at the end of life.

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

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

- Optical Microscopy: including laser scanning confocal microscopes, a multi- modal super resolution microscope and multiphoton microscope, a dual laser multiphoton microscope, and a laser capture microscope.

- Electron Microscopy, inclusive of both transmission and scanning electron microscopy.

- Image Analysis, and Histology.

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

https://www.petermac.org/research/core-facilities/centre-advanced-histology-microscopy

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.

https://www.petermac.org/research/core-facilities/bioinformatics

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).

https://www.petermac.org/research/core-facilities/flow-cytometry

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 and specialised analysis pipelines, the world-first 3D bioprinter that embeds cells in a scaffold and our Reverse Phase Protein array platform. 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 to represent your cell biology and disease state. They have recently installed the 3D

bioprinter to grow cell lines and patient derived material in 3D in high throughput allowing personalised medicine approaches to drug discovery.

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!

https://www.petermac.org/research/core-facilities/victorian-centre-functional-genomics

Molecular Genomics

The Molecular Genomics Core facility offers researchers access to state-of-the-art genomics technology platforms, providing service and expertise in conducting genomics experiments. Genomics technologies are extremely powerful tools for discovering mutations in genes implicated in cancer. The facility operates three major platforms: Illumina Sequencing, Nanostring nCounter and QX200 Droplet Digital PCR.

https://www.petermac.org/research/core-facilities/molecular-genomics

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, 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 and general bioinformatics.

https://www.petermac.org/research/core-facilities/research-computing-facility

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.

https://www.petermac.org/research/core-facilities/tissue-bank

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

Organogenesis and Cancer Program

https://www.petermac.org/research/programs/organogenesis-cancer

Research Labs:

- Louise Cheng
- Andrew Cox
- Kieran Harvey
- Ben Hogan

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, mice 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.

Cancer Genetics and Genomics Program

https://www.petermac.org/research/programs/cancer-genetics-genomics-program

Research Labs:

- David Bowtell
- Kara Britt
- Ian Campbell
- Kylie Gorringe

Cancer is fundamentally a polygenic disorder, imparted by germline and somatic mutation. With advances in DNA sequencing and other genomic technologies, it is feasible to obtain high-dimensional genomic information about an individual patient's tumours and relate this to clinical outcome.

The Cancer Genetics and Genomics program applies genomic technologies to large patient cohorts, with a particular focus on breast, ovarian and prostate cancer. Familial (KConFab, ViP) and population-based (Lifepool) breast and ovarian (Australian Ovarian Cancer Study) cancer cohorts are embedded in the program and are highly enabling of the research program due to the large numbers of patient samples with rich clinical information and associated biospecimens.

More recently the program has established CASCADE, a unique rapid autopsy study that provides an enabling platform for a variety of solid and haematological malignancies. Sophisticated genomics, functional genetics and bioinformatics capabilities are also highly enabling of the program.

Cancer Immunology Program

https://www.petermac.org/research/programs/cancer-immunology-program

Research Labs:

- Paul Beavis
- Phil Darcy
- Belinda Parker
- Ricky Johnstone
- Paul Neeson
- Jane Oliaro
- Sarah Russell
- Tony Tiganis
- Joe Trapani
- Ilia Voskoboinik

The Cancer Immunology Program is identifying ways in which the immune system can be harnessed to prevent and control cancer.

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.

CANCER RESEARCH PROGRAMS

Cancer Therapeutics Program

https://www.petermac.org/research/programs/cancer-therapeutics-program

Research Labs:

- Kristin Brown
- Charbel Darido
- Sarah-Jane Dawson
- Shom Goel
- Rodney Hicks
- Sherene Loi
- Grant McArthur
- Belinda Parker
- Ben Solomon

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

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.

Translational Haematology Program

https://www.petermac.org/research/programs/translational-haematology-program

Research Labs:

- Mark Dawson
- Sarah-Jane Dawson
- Ricky Johnstone
- Lev Kats

The Translational Haematology Program contains a diverse set of laboratories that focus on understanding the molecular pathogenesis of a range of haematological malignancies.

The program spans the breadth of basic science and translational medicine with the goal of identifying novel therapies that will improve the outcome of patients with haematological cancers.

Oncogenic Signalling and Growth Control Program

https://www.petermac.org/research/programs/oncogenic-signalling-growth-control-program

Research Labs:

- Rick Pearson
- Grant McArthur: Molecular Oncology
- Vihandha Wickramasinghe
- Ygal Haupt

The global effort to understand the molecular drivers of cancer is now coming to fruition with the identification of specific genomic events that influence signalling through key oncogenic pathways.

A key feature of oncogenic signalling is a requirement for cells to grow and proliferate, processes that are intimately linked to protein synthesis and the provision of metabolic substrates for replication of cellular components. Specifically, increases in ribosomal assembly, mRNA translation and glycolysis are key downstream events in many of the most important pathways involved in malignant transformation. It is increasingly recognised that tumour heterogeneity both between lesions and within lesions in individual patients and the development of resistance, represent fundamental challenges to attainment of durable responses to targeted therapies. Unravelling the links between oncogenic signalling and their influence on cell biology will be critical to designing new therapeutic approaches and improving patient outcomes.

CANCER RESEARCH PROGRAMS

Gastrointestinal Cancer Program

https://www.petermac.org/research/programs/gastrointestinal-cancer-program

Research Labs:

- Wayne Phillips
- Rob Ramsay
- Nicholas Clemons

Focussing on clinical, preclinical, and basic science research across all cancers of the gastrointestinal tract (including oesophageal, gastric, colorectal and anal cancers).

This Program has developed a world-class multi- disciplinary translational research program that responds to the needs of patients by (i) addressing critical clinical questions related to treatment and management of gastrointestinal cancer, (ii) exploring the cellular and molecular biology underlying the development and progression of gastrointestinal malignancies, and (iii) actively translating laboratory findings into the clinic.

The program has a focus on gastric, oesophageal, colorectal, and anal cancers, and has strong clinical links with a surgical research team led by Professor Sandy Heriot and additional surgeons and oncologists within the Victorian Comprehensive Cancer Centre alliance, offering extensive training opportunities for postgraduate students, postdoctoral fellows and clinicians in basic, translational, and/or clinical research.

Tumour Angiogenesis and Microenvironment Program

https://www.petermac.org/research/programs/tumour-angiogenesis-microenvironment -program

Research Labs:

- Steven Stacker
- Stephen Fox

The program is interested in understanding the key role played by the non-malignant cells within the tumour microenvironment, which includes stromal cells, blood vascular endothelial cells, lymphatic endothelial cells and immune cells.

The interaction of these cells types with tumour cells can either support or inhibit tumour progression. The spread of cancer to lymph nodes and distant organs is a critical aspect of cancer progression and is facilitated by lymphatic and blood vessels. The cells that line these vessels (the endothelial cells) are the control points for changes to vessel structure and activity.

The program provides broad opportunities for training of postgraduate students, postdoctoral fellows, pathology fellows and clinically trained researchers in areas of basic scientific research, translational research and molecular pathology.

Prostate Cancer Program

https://www.petermac.org/research/programs/prostate-cancer -program

Research Labs:

- Ygal Haupt
- Gail Risbridger

The Prostate Cancer program aims to answer significant questions that arise at diagnosis and during treatment of men with Prostate 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. Research in this program includes but is not limited to:

- Which tumours are aggressive vs indolent and put men at high risk of progressing to aggressive disease?
- What returns predict tumour progression
- What treatments can prolong and improve patient survival?

The group uses patient specimens and clinically relevant models of prostate cancer to provide practice changing outcomes to benefit men with prostate cancer.

CANCER RESEARCH PROGRAMS

Computational Biology Program

https://www.petermac.org/research/programs/organogenesis-cancer

Research Labs:

- Alicia Oshlack
- David Goode
- Tony Papenfuss

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; and 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. Many researchers in the program hold joint appointment with other programs or institutes.

Cancer Metabolism Program

https://www.petermac.org/research/programs/cancer-metabolism-program

Research Labs:

- Kristin Brown
- Louise Cheng
- Andrew Cox
- Rick Pearson
- Tony Tiganis

The ability of tumour cells to reprogram key metabolic pathways to facilitate tumorigenesis and metastasis is now recognised as one of the hallmarks of cancer.

The Cancer Metabolism Program has been recently established at the Peter MacCallum Cancer Centre and aims to understand the influence of obesity and metabolism on the development and growth of cancer.

Areas of interest in the program include understanding:

- Obesity and the metabolic syndrome increasing the risk of cancer
- Obesity driving tumour growth
- Redox balance in tumour development
- Nutrient availability and utilisation driving tumour growth
- Metabolic heterogeneities in cancer
- Tumour metabolism altered to support cancer growth and spread
- Mechanisms by which oncogenic pathways reprogram tumour metabolism
- Alterations in tumour metabolism influencing the immune response
- Alterations in immune cell metabolism influencing tumour growth
- Tumour metabolism promoting therapy resistance
- Targeting tumour-specific metabolic vulnerabilities for cancer therapy

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 180 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 all Universities throughout Australia and overseas.

Our program provides all 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 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 and critical analysis through exposure to journal clubs.

2. Professional and career development, including generic and transferable skills, mentoring, networking, leadership, career opportunities, internships and placements.

3. Communication skills development, including thesis and journal writing skills, and oral or poster presentations skills.

4. Optional internships/placements tailored to the student's interests and relevance to their PhD.

Examples of student activities in this program:

• Annual Student Symposium

• Annual Debate

• 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

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

For further information, email:

ccphd@petermac.org

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 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. International students will 'meet' supervisors via skype 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 all of 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, 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 in 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 AND RECENT 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.

"The Peter MacCallum Cancer Centre is an excellent environment to conduct research because of its connections between the laboratory bench and the clinic. This important link gives me a sense that one day, my findings may be used to actually enhance human health and well being."

Katie completed her Masters in Neuroscience at The University of Melbourne in 2016 and decided to take the leap into cancer research for her PhD. She was attracted to the Peter Mac because of its reputation as a world leader in cancer research and its partnerships with other leading institutes. It is through a collaboration with The Walter and Eliza Hall that Katie is able to use cutting edge single-cell technology to investigate heterogeneity in acute myeloid leukaemia.

Katie Fennell: Postdoctoral Scientist, Dawson Laboratory. Recipient of a Melbourne International Research Scholarship; Member, 2017 Postgraduate Student Committee.
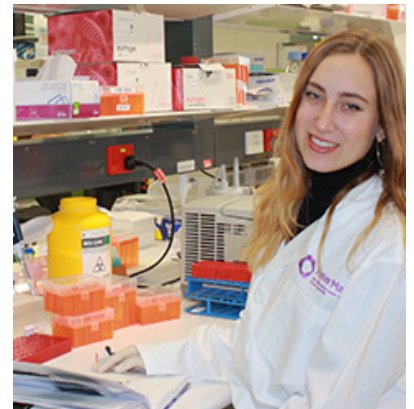
"The Peter Mac is a unique concept as our research division is directly embedded within the only dedicated cancer hospital in Australia, allowing unbridled potential for translationally relevant research. The thing I love most about Peter Mac is that expertise in practically any cancer field, tumour type or technology is literally just a short walk down the hall. Studying in this environment of brilliant minds pushes you to be a better student, and I so grateful to have had the privilege of completing my PhD at Peter Mac. We truly bat far above our weight on the global stage in terms of the quality and impactfulness of our research".

Stefan completed his Bachelor of Science degree (with Honours) in 2016 in the laboratory of Professor Ricky Johnstone, and continued his PhD in the same lab in 2017 investigating metabolic reprogramming events in acute myeloid leukaemia. He is currently in his final year of PhD studies and hopes to continue Post-Doctoral training overseas in the future.

Stefan Bjelosevic: PhD Student, Johnstone Laboratory. Recipient of a Research Training Program (RTP)-Domestic Scholarship (2017); the Robert Kirby Peter MacCallum Cancer Foundation Postgraduate Fellowship (2017); Member, 2018 Postgraduate Student Committee; the Picchi Award for Excellence in Cancer Research (Basic Science) (2020).

"Microscopy is at the core of my PhD. At Peter Mac, I am able to access the latest microscope equipment and expertise through the Centre for Advanced Histology and Microscopy (CAHM). This is vital for my research project, and enables me to investigate the most pressing questions in cell biology to date."

After completing an undergraduate degree in Genetics at the University of Melbourne, AJ joined the Harvey Lab at the Peter Mac as a summer student. He stayed in the lab to complete a Master of Biomedical Science, and worked as a Research Assistant. He commenced a PhD in 2020 to investigate Hippo pathway activity in real time in growing organs.

Abdul Jabbar (AJ) Saiful Hilmi: PhD Student, Harvey Laboratory. Recipient of the 2020 PeterMac Postgraduate Scholarship.
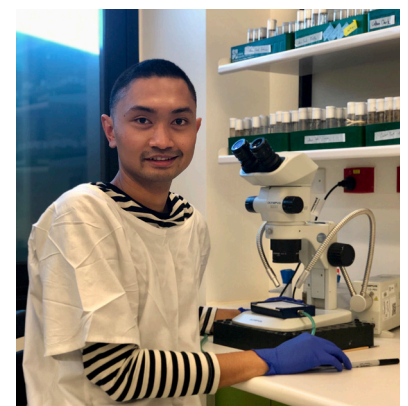
"The Peter MacCallum Cancer Centre has held a special place in my heart since I completed my Honours in 2016. I feel very lucky to be able to work with world-class scientists as well as up and coming young researchers in our diverse student cohort. In addition, I have built fantastic friendships that I know I will maintain for many years after Peter Mac. It is particularly gratifying to see the quality of research that is produced at Peter Mac and also the collaborative efforts between the hospital and research labs is what sets it apart from many other institutes."

Vicky completed her Honours in Immunology at Peter Mac in 2016 and worked 2 years as a Research Assistant. She commenced a PhD in 2019 investigating liver regeneration and cancer in zebrafish. Vicky loves being a part of the AFL and soccer teams and works alongside the Research Student Committee to help enhance the student experience at Peter Mac.

Vicky Tan: PhD student, Cox Laboratory. Recipient of the 2016 Nicole Lundie Undergraduate Award; Recipient of the 2019 PeterMac Postgraduate Scholarship; President of the 2020 Peter Mac Research Student Committee

"I was inspired by the passion and quality of cancer immunology research conducted by both staff and students at Peter Mac during my time as a Research Assistant. This led to my decision to undertake a PhD in the hopes of forming and answering my own research questions in this field. Peter Mac not only provides the facilities and latest technology to drive important discoveries in the laboratory, but also provides the perfect environment to allow these discoveries to be rapidly translated into the clinic to better treat patients burdened with cancer."

Andrew completed his Bachelor of Biomedical Science / Bachelor of Science (Honours) studies at Monash University. After completing his Honours year, Andrew started at Peter Mac as a Research Assistant in 2016. Andrew then commenced his PhD in 2018, which currently focuses on identifying and investigating novel ways to enhance the killing of tumour cells by natural killer cells, an immune cell critical to the innate immune system.

Andrew Freeman: PhD student, Oliaro Laboratory. Recipient of the 2018 Steer North VCCC PhD Scholarship; Recipient of the 2018 Rosie Lew Peter Mac Foundation Postgraduate Award.
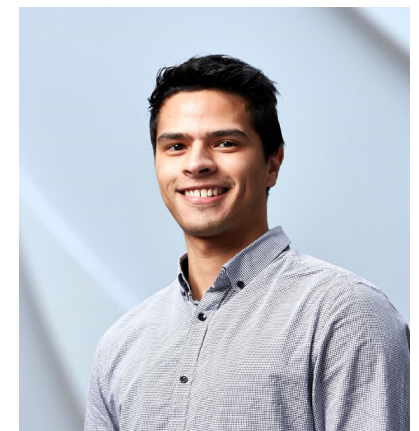
"I always wanted to work in translational research and here at Peter Mac I am able to work alongside world-renown oncologists and have the results of my research impact the ongoing treatment of patients and their overall prognosis. It's a thrilling and stimulating environment to work in, but Peter Mac has provided endless support and encouragement for me to continue on with my research and now undertake my PhD."

Courtney started at Peter Mac as a summer student, then completed her Honours and Master of Biomedical Science projects at Peter Mac before commencing her PhD in 2017, investigating endocrine resistance in oestrogen receptor positive metastatic breast cancer.

Courtney Van Geelan: PhD Student, Loi Laboratory. Recipient of a Research Training Program (RTP)-Domestic Schoalrship

"What drew me to Peter Mac was the opportunity to join a dedicated team of researchers and clinicians focused on improving cancer outcomes for patients. Being at the forefront of research into fundamental cancer biology in pursuit of developing new approaches to treat cancer has been an incredibly enriching experience. The unique culture of inter-institute collaboration empowers our ability to translate research findings directly into the clinic"

Kenji first came to Peter Mac for an undergraduate project, stayed as a research assistant and Summer student, and then completed his Biomedical Science Honours project at Peter Mac. He commenced his PhD in 2018, developing novel strategies to target mutant-p53 cancers.

Kenji Fujihara: PhD Student, Clemons Laboratory. Recipient of a Research Training Program (RTP)-Domestic Scholarship; Member, 2018 Postgraduate Student Committee; President, 2019 EMBL Australia Postgraduate Symposium Committee.

AVAILABLE PROJECTS BY RESEARCH GROUP

BEAVIS, PAUL

TUMOUR IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/paul-beavis

Enhancing lymphocyte trafficking to improve the Immunotherapy of Cancer

Supervisors: Dr. Paul Beavis, Dr. Imran House, Prof. Phil Darcy

Recent immunotherapy successes in the clinic have highlighted the potential of harnessing the immune system to target cancer. The number of tumour-infiltrating lymphocytes (TILs) positively correlates with disease outcome in cancer patients treated with standard chemotherapy or checkpoint inhibitor immunotherapy. In patients with low TILs, a group which constitutes the majority of cancer patients, immunotherapy with checkpoint inhibitors (e.g. anti-PD-1) has been largely ineffective to date, underlining the need to develop strategies to increase the recruitment of TILs. Trafficking of immune cells, including T cells, is modulated by a complex network of chemokine: chemokine receptor interactions. Chemokines interact with their respective chemokine receptors and binding results in the activation of intracellular signalling pathways which result in the migration of the target cells towards the source of the chemokine.

This project will employ state-of-the art technology to identify novel regulators of the key chemokines involved in this process and test the potential of targeting these to enhance lymphocyte infiltration into tumours and therefore increase the efficacy of checkpoint immunotherapy and chimeric antigen receptor (CAR) T cells. This approach has high translational potential and has the capacity to significantly enhance the effectiveness of Immunotherapy in cancer.

Key Words: Breast Cancers, Cellular Immunology, Genetic Immunology, Immunotherapy, Sarcoma, Skin Cancers (incl. Melanoma), Solid Tumours, Tumour Immunology.

Target Students: Honours, PhD/postgrduate

For more information about this project contact:

Dr. Paul Beavis   paul.beavis@petermac.org

Developing next generation Chimeric Antigen Receptor (CAR) T cells for enhanced therapeutic application in solid tumours

Supervisors: Dr. Paul Beavis, Dr. Imran House

Chimeric antigen receptor (CAR) T cells are a form of cancer immunotherapy whereby a patient's own T cells are genetically engineered to recognise, target and kill cancer cells through a defined cell surface antigen on the tumour cell surface. A CAR is comprised of an extracellular tumour antigen recognition domain and an intracellular region incorporating the CD3ζ chain and the signalling domains of CD28 or 4-1BB. Activation of the CAR therefore leads to robust T cell activation and induction of cytotoxic activity against tumour cells. Whilst CAR T cells are FDA-approved for the treatment of certain haematological malignancies, with clinical response rates >90% in some cases, they have

yet to achieve the same level of impact in the treatment of solid cancers. There are several unique challenges faced by CAR T cells in the solid tumour setting which contributes to this lack of efficacy, this includes tumour-mediated immunosuppression, tumour antigen heterogeneity, inefficient trafficking to the tumour site and limited persistence (Please see lab website for further details). Thus, our lab are committed to developing novel approaches to overcome these limitations.

This project will utilise state-of-the art technology that we have developed to generate 'next generation' CAR T cells. It has previously shown that constitutive expression of pro-inflammatory cytokines e.g. IL-12 by CAR T cells can enhance their therapeutic efficacy, but the clinical potential of this approach is limited by toxicities arising from systemic inflammation. Using 'knock in' CRISPR homology directed repair (CRISPR-HDR), we are now able to generate CAR T cells with the capacity for site-directed expression of cytokines. This enables CAR T cells to actively secrete pro-inflammatory cytokines at the tumour site, whilst sparing the toxicities associated with systemic inflammation.

To our knowledge, we are the first group in the world to successfully use CRISPR-HDR to insert large gene fragments into primary murine T cells and are therefore uniquely poised to develop this technology. Thus, this project will focus exploring the potential of this approach for therapeutic application by investigating the efficacy achieved with novel gene inserts in our established pre-clinical models.

The project will therefore encompass advanced molecular biology techniques, cell culture including generation of CRISPR-HDR modified CAR T cells, the use of syngeneic mouse models and flow cytometry analyses to determine effects of novel gene inserts on the phenotype of both CAR T cells and the host immune system. The project is highly innovative and so could make a significant impact in the CAR T cell field and, given the Peter Mac's well established clinical trial program for CAR T cells, has high potential to be translated into patients in the long-term.

Key Words: Breast Cancers, Cellular Immunology, Genetic Immunology, Immunotherapy, Sarcoma, Skin Cancers (incl. Melanoma), Solid Tumours, Tumour Immunology.

Target Students: Honours, PhD/postgrduate

For more information about this project contact:

Dr. Paul Beavis   paul.beavis@petermac.org

Dr. Imran House imran.house@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP

BOWTELL, DAVID

CANCER GENETICS AND GENOMICS PROGRAM

https://www.petermac.org/research/labs/david-bowtell

Genomic determinants of long-term survival in ovarian cancer

Supervisors: Prof. David Bowtell, Dr. Dale Garsed

High-grade serous ovarian cancer is an aggressive disease in which only ~30% of women survive 5 years or more. Despite a poor prognosis, a subset of patients are highly responsive to chemotherapy, and some become long-term survivors (>10 years survival). This spectrum of treatment responses suggests fundamental differences in tumour biology that are not yet understood. In collaboration with the Australian Ovarian Cancer Study, our laboratory is currently performing whole-genome sequencing, transcriptome sequencing and immune profiling of high-grade serous ovarian cancer in long-term survivors. We have identified a number of candidate genomic alterations that may be associated with exceptional outcomes.

This project will involve verification of candidates using DNA sequencing, and functional validation using pre-clinical models of ovarian cancer. Students will gain experience in human tissue culture, tumour biology and immunology, molecular biology techniques, genomics and bioinformatics.

Key words: Cancer Cell Biology, Cancer Genetics, Genomics, Ovarian Cancer, Molecular Biomarkers, Tumour Immunology

Target Students: PhD/postgraduate

For more information about this project contact:

Dr. Dale Garsed dale.garsed@petermac.org

Prof. David Bowtell david.bowtell@petermac.org

BRITT, KARA

CANCER GENETICS AND GENOMICS PROGRAM

https://www.petermac.org/research/labs/kara-britt

The role of the immune system in early breast cancer

Supervisors: Dr. 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. This project will determine whether immune changes occur early in the tumorigenic process of and whether this can be treated with immunotherapy to inhibit cancer development.

Key Words: Breast Cancers, Cancer Cell Biology, Immunotherapy, Tumour Immunology.

Target Students: PhD/postgraduate.

A mouse model of endocrine therapy for breast cancer prevention and treatment.

Supervisors: A/Prof Kara Britt, Prof. Kelly Phillips

Endocrine therapy has been successful for inhibiting the growth of existing breast cancers and in women and is also approved for breast cancer prevention. Despite this, there are limited mouse models of endocrine therapy and prevention which can be used to aid in the development of pre-clinical experiments that are able to test current standard of practice with emerging early treatments and preventatives. This project will develop a mouse model of endocrine therapy and use it to test the effectiveness of emerging novel therapies from the lab.

Key Words: Breast Cancers, Cancer Cell Biology, Cancer Therapy

Target Students: Honours

For more information about these projects contact:

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

BROWN, KRISTIN

CANCER THERAPEUTICS PROGRAM, &

CANCER METABOLISM PROGRAM

https://www.petermac.org/research/labs/kristin-brown

Fueling chemotherapy resistance in triple-negative breast cancer

Supervisor: Dr. Kristin Brown

Triple-negative breast cancer (TNBC) is a molecularly heterogeneous group of diseases 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. Approximately 30% of TNBC patients respond to chemotherapy. Unfortunately, the long-term prognosis for the majority of patients with residual disease after chemotherapy is poor.

Identification of novel and actionable strategies to sensitize cancer cells to chemotherapy would represent a major advance for the management of TNBC. Cancer cells exhibit dramatic alterations in cell metabolism, which support cell growth, proliferation and survival. Indeed, metabolic reprogramming is a recognized hallmark of cancer induced by numerous genetic or epigenetic alterations. Our recent studies suggest that reprogramming of cellular metabolism is also a component of the highly coordinated response to chemotherapy exposure. The aims of this project will be to:

1) identify adaptive metabolic reprograming events triggered upon chemotherapy exposure, and

2) identify novel therapeutic approaches to exploit adaptive metabolic reprogramming events and sensitize TNBC cells to chemotherapy.

This research will lead to the identification of critical mechanisms driving chemotherapy resistance in TNBC and establish combination therapy strategies with potential to have a major impact on patient survival. Students will gain experience in mammalian cell culture, molecular biology techniques, metabolomics and stable-isotope labelling techniques.

Key Words: Breast Cancers, Cancer Therapy, Molecular Biomarkers, Molecular Targets.

Target Students: Honours, PhD/postgrduate

Unravelling the oncogenic activities of serum- and glucocorticoid-regulated kinase 1 (SGK1)

Supervisor: Dr. Kristin Brown

The phosphoinositide 3-kinase (PI3K) pathway is a master regulator of numerous cellular phenotypes associated with cancer including cell survival, proliferation, growth, altered metabolism and malignant transformation. Deregulation of the PI3K pathway is implicated in virtually all human cancers and the pathway has been aggressively targeted for cancer therapy. Although most work has focused on the Akt kinase family as major downstream effectors of PI3K, the closely related serum- and glucocorticoid-regulated kinase (SGK) family of serine/threonine kinases has by comparison received little attention.

Recently, SGK1 has been shown to play a critical role in driving the expansion of tumour cells and promoting resistance to conventional chemotherapy and targeted therapy agents. However, the molecular mechanisms underlying the oncogenic activities of SGK1 are poorly characterised. In this project, we will identify SGK1 substrates and interacting proteins using the proximity-dependent biotin identification (BioID) method. Students will gain experience in mammalian cell culture and proteomics (mass spectrometry) techniques. Targets identified in the BioID screen will be validated using a variety of biochemical and molecular biology techniques.

Key Words: Breast Cancers, Cancer Therapy, Molecular Biomarkers, Molecular Targets.

Target Students: Honours, PhD/postgrduate

For more information about these projects contact:

Dr. Kristin Brown kristin.brown@petermac.org

Cutting off the Fuel Supply to Starve Cancer: Identifying metabolic vulnerabilities in cancer

Supervisors: Dr. Kristin Brown, Dr. Andrew Cox

A universal characteristic of all cancer cells is the reprogramming of cell metabolism to provide the energy and building blocks necessary to support proliferation and survival. Reprogramming of cell metabolism occurs as a consequence of oncogenic mutations and renders cancer cells dependent on a unique set of nutrients. It is now widely recognized that the altered metabolic activity of cancer cells provides a window of opportunity to develop tumour-specific anticancer therapies.

Using transcriptomic and metabolomic approaches, the aims of this project will be to: (1) compare and contrast metabolic reprogramming induced by well-described oncogenes, (2) compare and contrast the nutrient requirements of cancer cells dependent on well-described oncogenes and (3) identify and validate key metabolic vulnerabilities that can be targeted for the preclinical development of novel anticancer strategies. Students will gain experience in mammalian cell culture, molecular biology techniques, metabolomics and stable-isotope labelling techniques.

Key Words: Breast Cancers, Cancer Therapy, Molecular Biomarkers, Molecular Targets.

Target Students: Honours, PhD/postgrduate

For more information about this project contact:

Dr. Kristin Brown kristin.brown@petermac.org

Dr. Andrew Cox andrew.cox@petermac.org

CAMPBELL, IAN

CANCER GENETICS AND GENOMICS PROGRAM

https://www.petermac.org/users/prof-ian-campbell

High throughput discovery of synergistic drug combinations for patients with low-grade serous ovarian cancer

Supervisors: Dr. Dane Cheasley, Prof. Ian Campbell

Low-grade serous ovarian carcinomas (LGSOC) represent 5-8% of all epithelial ovarian cancers and are largely unresponsive to standard ovarian cancer chemotherapy. Little is known about alternative treatment strategies for LGSOC, and yet these are urgently needed. As cancer treatment becomes increasingly personalised, there is growing emphasis on drugs that target specific cancer-causing mutations and aberrant signalling pathways. However, clinical experience has shown that even when these drugs are effective in the short-term, tumours can rapidly develop resistance. A fundamental problem is that cancers are genetically heterogeneous, and as a result there is inevitably a small population of cells within each tumour that is resistant to any given treatment. While a single drug is unlikely to eradicate a cancer, combinations of drugs targeting multiple mutations and cancer pathways offer a higher chance of long-term efficacy and even cure.

We hypothesise that discovery of synergistic drug combinations for LGSOC will be achieved by high-throughput testing of clinically approved drugs on an outstanding collection of LGSOC cell lines capturing the molecular diversity of the disease. This study involves three aims:

1. Funnelled and unbiased discovery of synergistic drug combinations in a large panel of LGSOC cell lines.

2. Identification of biomarkers predicting treatment response.

3. Testing drug combinations in prospective patients.

Key Words: Genomics, Drug screening, Biomarkers, Genetics, Ovarian cancer.

Target Students: Masters, PhD/Postgraduate

For more information about this project contact:

Dr. Dane Cheasley dane.cheasley@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP

Exploration of alternative mechanisms of hereditary breast cancer

Supervisors: Prof. Ian Campbell, A/Prof. Paul James, Dr. Na Li

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: Honours, Masters, PhD/Postgraduate

For more information about this project contact:

Dr. Na Li na.li@petermac.org.

CHENG, LOUISE

ORGANOGENESIS AND CANCER PROGRAM, & CANCER METABOLISM PROGRAM

https://www.petermac.org/research/labs/louise-cheng

How do tumours grow at the expense of other tissues?

Supervisors: Dr. Francesca Froldi, Dr. 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 calchexia, 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 utilise a brain tumour model to study how tumour cells communicate with other tissues to gain a growth advantage, and utilise Drosophila genetics, transplantation assays, confocal microscopy, FACS analysis and molecular techniques to address this question.

Key Words: Cancer Cell Biology, Cell Metabolism, Differentiation, Molecular Imaging, Stem Cells.

Target Students: Honours, PhD/postgrduate

How does nutrition affect stem cell proliferation?

Supervisors: Dr. Louise Cheng, Dr. Francesca Froldi, Dr. Christen Mirth (Monash)

The evolutionary size of animals and plants is determined by cell intrinsic regulation and constrained by nutrient availability, and brain size is perhaps the most profound example of this. Understanding at the molecular level how stem cells respond to nutrients will provide foundation for the understanding of how nutrient availability impacts on size and growth in multicellular organisms. Once thought to be a mere consequence of the state of a cell, metabolism is now known to play a pivotal role in dictating whether a cell proliferates, differentiates or remains quiescent.

This project will investigate how metabolic rewiring operates in the neural stem cells using Drosophila as a model organism, and more specifically how metabolic pathways can influence body size, organ shape and whether neural stem cell proliferates or remain quiescent. The techniques will involve: immunohistochemistry, tissue microdissection, metabolite measurements.

Key Words: Cell Growth, Cell Signalling, Stem Cells.

Target Students: PhD/postgraduate.

Identification of factors mediating dedifferentiation in regeneration

Supervisors: Dr. Louise Cheng, Dr. Patricia Jusef

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, and in this project, the student will test the idea that these dedifferentiation regulators are also involved in neural regeneration using the Drosophila adult CNS. The candidate genes identified in the Drosophila will then be tested for their significance in a neural regeneration model mediated by Muller glia stem cells in the zebrafish vertebrate.

Key Words: Cancer Cell Biology, Differentiation, Stem Cells

Target Students: Honours, PhD/postgrduate

AVAILABLE PROJECTS BY RESEARCH GROUP

How does amino acid metabolism affect tumour growth?

Supervisors: Dr. Francesca Froldi, Dr. Louise Cheng

The effect of diet on tumour growth is hotly debated but poorly characterized. Due to the heterogeneous nature of the tumours, dietary studies in patients with varied genetic background often led to inconclusive outcome. Dedifferentiation is a cellular process by which a partially or terminally differentiated cell reverts to a less differentiated, more multipotent state. The bidirectional conversion between differentiated cells and stem cells often underlies carcinogenesis. Cancer such as glioblastoma, the most aggressive subtype of the gliomas are thought to originate from terminally differentiated cortical astrocytes and neurons. Similarly, through expressing the right combination of transcription factors, non-cancer stem cells can also convert to highly proliferative cancer stem cells found in intestinal tumours.

Using a combination of genetics, metabolic and genomic techniques, the student will address the knowledge gap of how diet, in particular amino acid metabolism, impacts on cellular dedifferentiation, and tumour growth. These studies will allow us to quickly and systematically identify tumour metabolic dependencies, and shed light on important metabolic targets, which can be assessed in other stem cell and tumour settings.

The student will use a combination of Drosophila genetics, confocal microscopy, FACS analysis and molecular biology techniques to address this question.

Key Words: Cancer Cell Biology, Cell Metabolism, Differentiation, Molecular Imaging, Stem Cells.

Target Students: Honours.

For more information about these projects contact:

Dr. Louise Cheng   louise.cheng@petermac.org

CLEMONS, NICHOLAS

GASTROINTESTINAL CANCER PROGRAM

https://www.petermac.org/research/labs/nicholas-clemons

Supervisor: Dr. Nicholas Clemons

The Clemons Laboratory incorporates fundamental cancer biology research, pre-clinical development of innovative therapeutic strategies and translational research, with a focus on upper gastrointestinal cancers.

Our research integrates novel in vitro and in vivo models to functionally characterise drivers of tumour development and progression, and identify and test new therapeutic approaches for these cancers.

Current research topics we are focusing on include:

- Developing therapeutic strategies for targeting mutant p53 cancers including understanding the effect of mutant p53 on oxidative stress and metabolism
- Understanding mechanisms that regulate a form of cell death called "ferropotosis" for exploitation as a process to kill cancer cells
- Performing in vitro and in vivo genome wide CRISPR-Cas9 screens in models of oesophageal cancer to identify drivers of the disease and novel therapeutic targets.

Defining the functional drivers of oesophageal tumourigenesis

Supervisors: Dr. Nicholas Clemons, Prof. Wayne Phillips

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/postgrduate

For more information about this research project contact:

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

AVAILABLE PROJECTS BY RESEARCH GROUP

COX, ANDREW

ORGANOGENESIS AND CANCER PROGRAM, & CANCER METABOLISM PROGRAM

https://www.petermac.org/research/labs/andrew-cox

Fishing for metabolic clues: Role of the Hippo/Yap pathway in reprogramming metabolism in liver cancer

Supervisor: Dr. 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 the Yap target genes responsible for tissue growth. Using a combination of metabolomic and transcriptomic approaches in zebrafish, we have discovered that Yap reprograms glutamine metabolism in vivo to stimulate nucleotide biosynthesis and fuel premalignant liver growth.

Building on this initial investigation, we currently have research projects that aim to 1) Examine how Yap coordinates nutrient sensing to metabolic output in the liver. 2) Elucidate the mechanisms by which Yap reprograms metabolism to fuel liver growth in the context of regeneration and cancer.

The students will use a combination of innovative biochemical, genetic and imaging approaches in zebrafish to identify the metabolic dependencies of tissue growth during regeneration and cancer.

Key Words: Cancer Cell Biology, Cancer Therapy, Cell Growth, Cell Metabolism, Gene Expression, Solid Tumours, Stem Cells.

Target Students: Honours, PhD/Postgraduate

Metabolic rewiring in liver cancer: Role of oxidative stress and the Nrf2 pathway

Supervisor: Dr. 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 activated by oxidative stress that orchestrates an adaptive response remodeling metabolism and promoting cytoprotection.

Recent studies have identified that the Nrf2 pathway is frequently mutated in liver cancer (~12% tumors), causing activation of the pathway in the absence of oxidative stress. We have used transcriptomic and metabolic profiling in Nrf2-/- zebrafish to examine the role Nrf2 plays in remodeling metabolism during liver development and regeneration.

Building on these preliminary studies, we currently have research projects that aim to 1) Generate a gain of function Nrf2 mutant (Nrf2D29H), frequently recovered in cancer, and characterize the effect the mutation has on metabolic reprogramming. 2) Examine how deregulation of Nrf2 remodels metabolism to stimulate liver tumorigenesis.

The students will use a combination of innovative biochemical, genetic and imaging approaches in zebrafish to identify the

metabolic dependencies of tissue growth in liver regeneration and cancer.

Key Words: Cancer Cell Biology, Cancer Therapy, Cell Growth, Cell Metabolism, Gene Expression, Solid Tumours, Stem Cells.

Target Students: Honours, PhD/Postgraduate

Exploring the role of metabolic reprogramming in liver regeneration

Supervisor: Dr. Andrew Cox

The liver is an essential organ that exhibits the remarkable capacity to regenerate. The process of liver regeneration is multifaceted, as it requires a complex tissue comprised of multiple cell types to sense the extent of injury and mount an appropriate compensatory regrowth response. However, despite decades of research, the molecular underpinnings of liver regeneration are poorly understood. In this project we will perform a boutique phenotype-driven chemical genetic screen using CRISPR/Cas9 approaches to identify the metabolic requirements for liver regeneration.

The students will use a combination of innovative metabolomic, transcriptomic and multiphoton imaging approaches in zebrafish to identify the metabolic dependencies of tissue growth in liver regeneration.

Key Words: Regenerative Medicine, Cell Growth, Cell Metabolism, Gene Expression, Stem Cells.

Target Students: Honours, PhD/Postgraduate

For more information about these projects contact:

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DARCY, PHILLIP

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/users/prof-phillip-darcy

Engaging host anti-tumour immunity to overcome tumour antigen heterogeneity during CAR T cell therapy

Supervisors: Dr. Junyun Lai, Dr. Paul Beavis, Prof. Phil Darcy

Adoptive cellular therapy involving chimeric antigen receptor (CAR) T cells have achieved high clinical response rates in B cell malignancies, leading to FDA and Australian TGA approval for the treatment of haematological cancers such as pre-B acute lymphoblastic leukemia. However, CAR T cells have yet to achieve the same therapeutic efficacy against solid cancers. A major hurdle that has prevented the successful utility of CAR T cells in treating solid tumours is tumour antigen heterogeneity, clinical observations indicate that antigens targeted by the CAR T cells are only expressed on 20 – 80% of the cancer cells found within tumour tissues. As a result, CAR T cell treatment may lead to subsequent tumour relapse involving antigen-low/negative tumour cells.

We hypothesize that engineering CAR T cells to engage the host immune system will enable them to overcome this barrier and allow for effective treatment of heterogeneous

tumours. Our recent work, published in Nature Immunology, has highlighted a novel strategy to achieve this by engineering CAR T cells to secrete a dendritic cell growth factor Flt3L. This project will focus on investigating strategies to further leverage this axis and address the issue of tumour antigen heterogeneity and improve CAR T cell efficacy in solid cancers. Students will gain experience in cell culture, CAR T cell transduction, molecular biology techniques, as well as flow cytometry and working with in vivo tumour models. The cancer immunology program at the Peter Mac encompasses over 60 staff and provides a terrific learning environment and collegial atmosphere for new students.

Key Words: Breast cancer, Immunotherapy, CAR T cells, Solid tumours, Tumour immunology

Target Students: Honours, PhD/Postgraduate

For more information about these projects contact:

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DARIDO, CHARBEL

CANCER THERAPEUTICS PROGRAM

https://www.petermac.org/research/labs/charbel-darido

Predicting the development of oral cancer

Supervisors: Dr. Charbel Darido, Dr. Promoda Perera

Human head and neck cancer is a devastating disease with poor survival rates. Oral cancer (OC) is the most common type of head and neck cancer affecting the oral cavity where it is driven by the continuous exposure to risk factors including tobacco use, alcohol abuse, infection with high-risk human papilloma viruses (HPV) and genetic pre-disposition. Over the last thirty years, improvements in survival rates of oral cancer patients have remained modest, hampered by the late diagnosis of the disease. In this project, we will use mouse models of OC that mirror the human malignancy to identify initial molecular changes that predict cancer development. We expect that analysing the tissue integrity in these models of the OC risk factors will provide a window for disease initiation. Discoveries in these models will lead to identification of biomarkers for early diagnosis and disease progression in OC patients. A wide range of skills will be taught including biochemistry, molecular biology, cell culture and knockout mice. This is an ideal project for a student who wishes to pursue higher studies in cancer research.

Skills to be taught include biochemistry, molecular biology, cell culture and knockout mice. This is an ideal project for a student who wishes to pursue higher studies in cancer research.

Key Words: Cancer, Treatment, Head and Neck Cancer, Inflammation, Signalling Pathways, Skin.

Target Students: Honours/Masters, PhD/Postgraduate

Identification of biomarkers of response to therapies against head & neck cancer

Supervisors: Dr. Charbel Darido, Dr. Promoda Perera

Human head and neck cancer is a devastating disease with poor survival rates. Inter-patients, intra-patients as well as intra-tumour heterogeneity limit the response to advanced therapies resulting in mortality and morbidity. Using a combined approach of molecular profiling, proteomics, bioinformatics, drug sensitivity to inhibitors of oncogenic pathways, and mutational analysis, we identified potential biomarkers of response to treatment. This project aims to:

- Assess potential biomarkers related to resistance or response using in vitro and in vivo laboratory systems and animal models that are designed specifically to investigate heterogeneous head & neck cancer.

- Understand why some patients respond well to targeted therapies and other patients, who clinically appear to have the same type of cancer, respond poorly or not at all.

Successful completion of this project will pioneer novel therapeutic approaches and will determine the merit to explore genomic biomarkers paired with targeted therapies to improve clinical outcomes in this disease.

This research will benefit from collaborative research across several members of the VCCC alliance members and will contribute to the growing knowledge of response and resistance to targeted therapies. Skills to be taught include drug assays, biochemistry, molecular biology, cell culture and muse models.

Key Words: Cancer, Treatment, Head and Neck Cancer, Inflammation, Signalling Pathways, Mouse Models.

Target Students: Honours.

Investigating the requirements of pro-inflammatory signaling in skin and head & neck Squamous Cell Carcinomas

Supervisors: Dr. Charbel Darido, Ms Yuchen Bai

Squamous cell carcinomas (SCC) are amongst the most common cancer types afflicting man. SCCs most frequently arise from stratified squamous epithelia such as the epidermis or the mucosae of the head and neck. We have recently identified two novel microRNA-21 (miR-21)-dependent proto-oncogenic networks that underpin SCC in skin and head & neck in both mice and humans.

We hypothesize that inflammation in SCC occurs in a tissue-specific manner leading to miR-21 induction. The project is designed to investigate which upstream pro-inflammatory pathways promote dysregulation of miR-21 in skin versus head & neck. Successful completion of this project will pioneer novel therapeutic approaches and will determine the merit to explore tissue-specific targeted therapies of human SCC to improve clinical outcomes in this disease. Skills to be taught include molecular biology, biochemistry, cell culture and knockout mice.

Key Words: Cancer, Treatment, Head and Neck Cancer, Inflammation, Signalling Pathways, Skin.

Target Students: Honours/Masters

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

GOEL, SHOM

CANCER THERAPEUTICS PROGRAM

https://www.petermac.org/research/labs/shom-goel

Dr Goel has recently been recruited to the Peter Mac from Harvard Medical School, where he developed a number of innovative cell line and transgenic mouse models of breast cancer. He has already used these models to uncover previously unappreciated mechanisms of CDK4/6 inhibitor activity (Goel, Cancer Cell 2016, Goel, Nature 2017).

Discovering better therapies for ER-positive metastatic breast cancer

Supervisors: Dr. Shom Goel

Each year, over 3000 Australians lose their life to breast cancer. The majority of these women suffer from metastatic estrogen receptor-positive (ER-positive) breast cancer, the commonest subtype of the disease. Unfortunately, metastatic ER-positive breast remains invariably fatal, largely because cancers develop resistance to existing therapies over time. Furthermore, efforts to understand why this resistance develops using next generation DNA sequencing have been unrewarding, as the majority of tumours have not acquired new genetic mutations at the time of acquiring resistance.

In the Goel lab, we are focused on identifying the fundamental biological mechanisms that underlie therapeutic resistance in ER-positive breast cancer. More specifically, we study why breast cancers develop resistance to a class of cell cycle targeting drugs called CDK4/6 inhibitors, which are routinely used in this disease.

In this project, you will have access to these same models and will use them to explore why breast cancers acquire resistance to CDK4/6 inhibition. The project will focus on epigenetic and immunologic mechanisms of drug resistance, both novel concepts that have not been explored in breast cancer thus far.

In the lab, you will have unrestricted access to the Goel lab's cutting-edge transgenic mouse models of breast cancer, and will perform sophisticated molecular biology assays including epigenetic profiling of cancer cells and genome editing using CRISPR-Cas9 technology. In addition, you will have access to a unique collection of tumour samples from breast cancer patients, which will allow you to validate your laboratory findings in a clinical context.

Key Words: Cancer Cell Biology, Immunology, Immune Checkpoint Inhibitors, Mouse Models.

Target Students: PhD/postgraduates.

For more information about these projects contact:

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GOODE, DAVID

COMPUTATIONAL BIOLOGY PROGRAM , & PROSTATE CANCER PROGRAM

https://www.petermac.org/research/labs/david-goode

Intratumoural transcriptional heterogeneity and cellular plasticity in prostate cancer

Supervisors: Dr. David Goode, Dr. Shivakumar Keerthikumar

Tumours are a highly heterogeneous mix of multiple cellular subpopulations, each with their own unique molecular and biological properties. Studying intratumoural heterogeneity (ITH) is crucial for understanding the acquisition of drug resistance in tumours.

This project will apply single-cell RNA sequencing to characterize ITH at the transcriptional level in patient-derived xenograft (PDX) models of prostate cancer and track how ITH changes in response to treatment with commonly used drugs for prostate cancer. We will also investigate how cellular plasticity, the ability of tumour cells to change molecular states, may act as a means for prostate cancer cells to adapt to drug treatment.

Students will be trained in the analysis and interpretation of single-cell RNA sequencing data using R, gain expertise in statistics, genomics and cancer biology and work with a team of computational and wet-lab biologists.

Key Words: Cancer Genomics, Bioinformatics, Computational Biology, Single Cell Sequencing.

Target Students: Honours, PhD/Postgraduate

Discovering biomarkers of treatment response in castration-resistant prostate cancer

Supervisors: Dr. David Goode, Dr. Shivakumar Keerthikumar

Androgen deprivation therapy (ADT) is an important last-line treatment for advanced prostate cancer. ADT initially works well but eventually fails in most patients, leading to castration-resistant prostate cancer (CRPC). There are currently no effective therapies for CRPC and overall patient survival is poor.

To identify better treatments for CRPC, we have performed RNA-sequencing and exome sequencing on a large cohort of patient-derived xenograft (PDX) models of CRPC that have been screened for response to a panel of existing and experimental cancer drugs.

This project will develop and apply methods for combining gene expression, mutation and experimental data from PDXs to search for biomarkers that predict response to specific drugs, to identify additional candidate drugs to screen and to shed light on potential mechanisms of drug resistance in prostate cancer.

In this way, we aim to develop personalized therapies for CRPC patients to improve their prospects for long-term survival.

Students will receive training in bioinformatics, statistics, genomics and cancer biology and work with a team of computational and wet-lab biologists.

AVAILABLE PROJECTS BY RESEARCH GROUP

Key Words: Cancer Genomics, Bioinformatics, Biomarkers, RNA sequencing.

Target Students: Honours, PhD/Postgraduate

Computational simulation of tumour formation and progression

Supervisors: Dr. David Goode, Prof. Howard Bondell (Uni Melb Math & Stats)

Tumours comprise a complex mix of related but distinct cellular subpopulations that both compete with and complement one another. We have developed sophisticated computational simulations that accurately recreate the growth and evolution of real tumours. By matching our simulated results to data from cancer patients, we aim to understand how early events in tumour formation drive later outcomes and devise improved therapeutic strategies.

This project will extend and improve on our existing models to:

1. Simulate different treatment regimes, to investigate how the timing and intensity of drug dosing affects the growth and evolution of tumours under different settings.

2. Model the role of epigenetics alterations in drug resistance, by modelling the non-genetic processes of evolution.

This project provides a unique opportunity to work at the intersection of mathematics, biology, medicine and genomics.

Key Words: Cancer Genetics, Mathematical Modelling, Bioinformatics, Evolution.

Target Students: PhD/Postgraduate

For more information about these projects contact:

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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.

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

For more information about this project contact:

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GORRINGE, KYLIE

CANCER GENETICS AND GENOMICS PROGRAM

https://www.petermac.org/research/labs/kylie-gorringe

Personalised risk evaluation in DCIS

Supervisors: A/Prof. Kylie Gorringe, Prof. Ian Campbell

Breast screening using mammography has seen an increased detection of not only invasive breast cancer, but also pre-invasive lesions such as ductal carcinoma in situ (DCIS). The clinical management of DCIS is problematic due to a lack of accurate prognostic and predictive tests. If recurrence risk could be accurately estimated, those with low risk disease could be offered surgery only, and those with high risk of recurrence have excision plus radiotherapy or a full mastectomy, thus optimising patient outcomes while minimising treatment toxicity. Thus, our principal research question is: are there molecular biomarkers that can predict which DCIS are at higher risk for recurrence?

The project will involve molecular analysis of DCIS cases both with and without later recurrence to identify potential biomarkers, which may include DNA mutations, copy number changes, and gene expression. Techniques will include DNA/RNA extraction from tumour tissue, analysis by next-generation sequencing and/or a Nanostring expression assay. Analysis using in situ methods such as immunohistochemistry and FISH may also be undertaken.

Key Words: Breast Cancers, Cancer Genetics, Cancer Genomics, Molecular Biomarkers, Pathology, Precision Medicine, Mammography, CLinical Management.

Target Students: Honours, PhD/Postgraduate

Understanding and treating mucinous ovarian cancer

Supervisors: A/Prof. Kylie Gorringe, Prof. Ian Campbell

The Gorringe lab has an ongoing project 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 completed extensive genomic characterisation and now want to translate these findings into the clinic. We plan to interrogate patient data for treatment responses, evaluate potential therapies in our unique tumour organoid and xenograft models, and discover new treatment approaches based on our genomics data.

AVAILABLE PROJECTS BY RESEARCH GROUP

Key Words: Gynaecological cancers, Solid tumours, Therapeutics

Target Students: Masters, PhD/Postgraduate

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HARVEY, KIERAN

ORGANOGENESIS AND CANCER PROGRAM

https://www.petermac.org/research/labs/kieran-harvey

Watching the Hippo pathway in real time in growing organs

Supervisor: Prof. Kieran Harvey

A new frontier in biomedical research will involve watching individual proteins work in real time, in living organs. Traditionally, researchers have drawn conclusions about gene function using indirect techniques that only allow us to infer what a gene normally does, without actually watching it work. For example, we create organisms that lack a particular gene and determine whether something goes wrong. If the loss of gene X causes organs to overgrow then we assume that gene X normally limits organ size. This has been an extraordinarily powerful approach for interrogating gene function but it cannot substitute the ability to watch gene products executing their function in real time, which allows determination of exactly when, where and how they work.

This project will investigate the role Hippo tumour suppressor pathway in organ growth by watching, for the first time, its, in growing organs, in real time. This will provide novel insights into normal organ growth and pathogenic organ growth in diseases such as cancer.

Students will observe Hippo pathway activity in real time in the following situations:

a.   When organs are actively growing

b.   When organs stop growing

c.   In regions of organs that are subject to mechanical compression

d.   throughout the cell cycle

Students will be taught an array of techniques including ex vivo organ culture, live multi-photon microscopy, image analysis and Drosophila genetics.

Key Words: Cancer Cell Biology, Cell Signalling, Cell Development, Proliferation and Death, Skin Cancers, Solid Tumours, Developmental Biology.

Target Students: PhD/postgraduate.

For more information about this project contact:

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HAUPT, YGAL

PROSTATE CANCER PROGRAM, & ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM

https://www.petermac.org/research/labs/ygal-haupt

Exploration of novel approaches to anti-cancer treatment: manipulation of mutant p53

Supervisors: Prof. Ygal Haupt , Dr. Sue Haupt

P53 is the most mutated gene in human cancer, affecting about half the cases of cancer, and involved in every cancer type. We have recently identified novel regulators of mutant p53 using sophisticated loss of function whole genome high content screen.

In this project the candidate will study a key novel regulator derived from this screen to explore the interplay with mutant p53, and to define novel target for anti-cancer drugs. The student will explore the efficacy of manipulating these regulators as a novel approach to treating cancer cells bearing mutant p53 (majority of human cancers).

The project will involve work with cancer cell lines, transgenic mouse models, and human samples. In addition the project will expose students to a variety of molecular, cellular biochemical techniques, as well as to genomic and bioinformatics analyses.

Key Words: Breast Cancers, Cancer Cell Biology, Cancer Therapy, Therapeutics, Tumour Suppression.

Target Students: PhD/postgraduate

Cancer Sex Disparity: a computational approach.

Supervisors: Prof. Ygal Haupt , Dr. Sue Haupt

For the vast majority of non-reproductive cancers, there is a higher rate of cancer incidence and morbidity in males than females. The molecular basis for this disparity is yet to be properly understood. We recently made a breakthrough in this field by identifying sex-specific genomic alterations, through our computational interrogation of The Cancer Genome Atlas (TCGA) (Haupt et al 2019, Nature Communications). This study opened many windows through which to better understand this major variance in cancer.

In this project, the candidate Master student will pursue this topic further. Specifically, the candidate will use unique data sets that have been generated in the Peter MacCallum Cancer Centre using information derived from the clinics including clinical trials. This information will be tested against publicly available databases to validate and test the findings. The candidate will use a variety of computational approaches, programming languages, and be exposed to statistical analysis tools. Advance knowledge of stats and ability to interrogate large data sets will be advantageous but is not a prerequisite. Information derived from this project will form the basis for the understanding of the sex-disparity in other cancer types and is likely to have important clinical implications.

Key Words: Computational Biology, Cancer Genetics, Bioinformatics, Epigenteics,

Target Students: PhD/postgraduate

AVAILABLE PROJECTS BY RESEARCH GROUP

Defining the role of p53 in cancer immunotherapy

Supervisor: Prof. Ygal Haupt, Dr. Sue Haupt

Despite clear evidence of an association between the tumour suppressor p53 and immunity, a gap in knowledge exists regarding its role in modulating immune responses, or its value in predicting patient responses to immunotherapy. Given the unprecedented frequency of p53 mutation in cancers and the heterogeneous responses to immunotherapy, this question deserves rigorous exploration.

P53 activity has been associated with tumour-infiltration and immune activation. Despite the prevalence of p53 mutations in human cancers (>50%) and its link to immune regulation, the impact of p53 status on the immune response, and on the response to immune checkpoint inhibitors has not been explored. These fundamental questions, which potentially affect many cancer types and a large proportion of cancer patients, form the basis of this study.

The project will involve work with cancer cell lines, transgenic mouse models, and human samples. In addition, the project will expose students to a variety of molecular, cellular biochemical techniques, immune profiling, and to genomic and bioinformatics analyses.

Key Words: Cancer Cell Biology, Cancer Therapy, Immunotherapy, Radiation Therapy

Target Students: PhD/postgraduate

For more information about these projects contact:

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HOGAN, BEN

ORGANOGENESIS & CANCER PROGRAM

https://www.petermac.org/research/labs/ben-hogan

Zebrafish models of vascular disease: lymphatic malformation

Supervisors: Prof. Ben Hogan, Dr. Kazuhide Okuda

Lymphatic malformation (also known as lymphangioma) is a rare childhood disease caused by uncontrolled proliferation of the lymphatic endothelium. These malformations are typically present at birth, or soon after, and are largely treated with surgery when possible. The genetic causes of lymphangioma remain to be fully understood but somatic mutations in PIK3CA, impacting the AKT-mTOR pathway, have emerged as causative in many cases. Several potential molecular therapies have been proposed but their relative utilities remain to be fully assessed.

The project will generate genetic, inducible, models of lymphangioma in zebrafish and attempt to generate CRISPR-induced models. These will drive vascular malformation by expression of mutant PIK3CA expression. Phenotype will be assessed with molecular markers and confocal imaging. The models generated will ultimately be used to assess the efficacy of a series of candidate therapeutic molecules. The project will employ transgenesis, pharmacology, live-imaging of development (confocal) and molecular biology approaches.

Key Words: Development, Cell biology, Disease, Zebrafish, Genetics.

Target Students: Honours.

Cell fates and cell states: analysis of enhancer dynamics during angiogenesis and lymphangiogenesis

Supervisors: Prof. Ben Hogan, Dr. Lizzie Mason

Cellular fates are regulated by key transcription factors during vascular development, angiogenesis and lymphangiogenesis. In recent decades, analysis of vascular cell fates, such as artery, vein and lymphatic fates, has uncovered key transcription factors and target enhancer elements that regulate tissue identity. Nevertheless, how transcription factors drive dynamic changes in vessel growth, dynamic enhancer activities, dynamic cell behaviours and cellular heterogeneity in the growing vasculature, remains to be determined. Live imaging reporters of enhancer activity during zebrafish vascular development offers a unique opportunity to approach these fundamental questions.

This project will take advantage of a large-scale data set recently generated in the Hogan lab using single cell ATAC-seq data to assess the developing vasculature of the zebrafish embryo. The project will clone and assess functional enhancers that are lineage specific, evolutionarily conserved and candidate elements that may control dynamic cell behaviours during new vessel formation. Transgenesis, molecular genetics and cellular resolution confocal imaging of zebrafish vasculature will be coupled with bioinformatics studies of enhancer conservation and prediction of key functional regulators.

Key Words: Development, Cell biology, Angiogenesis, Genomics, Bioinformatics.

Target Students: Honours.

For more information about these projects contact:

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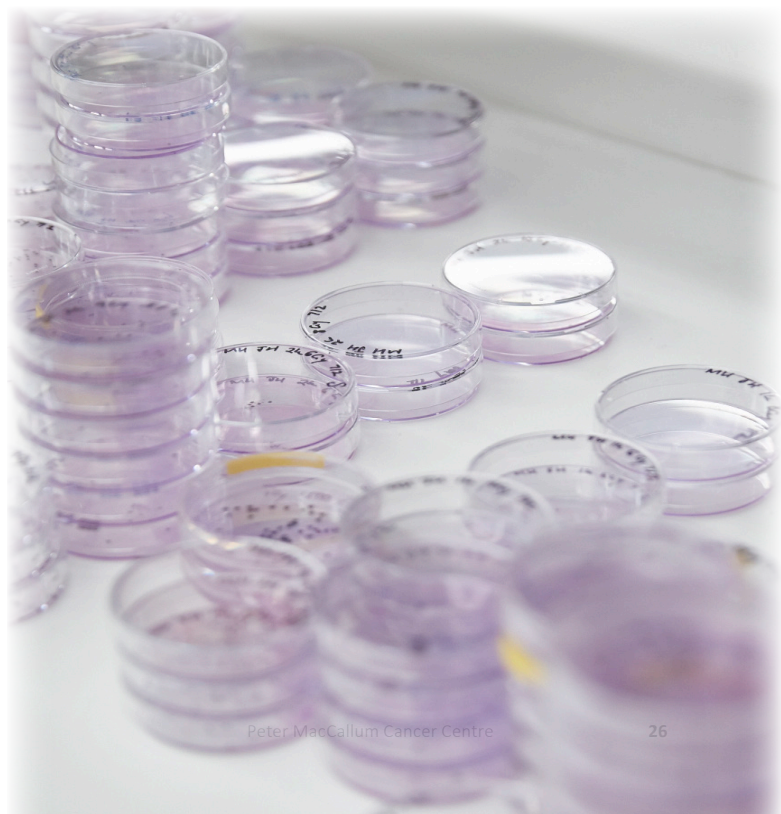
AVAILABLE PROJECTS BY RESEARCH GROUP

JOHNSTONE, RICKY

TRANSLATIONAL HAEMATOLOGY PROGRAM
CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/ricky-johnstone

Investigating the role of CDK11 in haematological malignancies

Supervisor: Dr. Jennifer Devlin, Prof. Ricky Johnstone

Coordinated gene expression requires exquisite regulation of transcriptional initiation, pausing, elongation and termination, as well as co-transcriptional mRNA processing, controlled by a class of cyclin-dependent kinases including CDKs 7, 8, 9, 10, 11, 12 and 13. Subversion of these fundamental molecular processes disrupts gene expression programs and drives tumorigenesis, Our lab has demonstrated that small molecule inhibitors of transcriptional CDKs including CDK7 (initiation), CDK9 (pausing) and CDK12/13 (elongation) induce anti-tumour responses in haematological malignancies and we have subsequently utilized these inhibitors to investigate the molecular processes that control cellular transcription.

Our lab has shown using short-hairpin RNA (shRNA) screens and CRISPR-Cas9 knockout experiments that CDK11 is essential for the survival of acute myeloid leukaemia and multiple myeloma cells. Biochemical studies have demonstrated a role for CDK11 for the control of gene expression at the level of transcription regulation and pre-mRNA processing (e.g. splicing, polyadenylation, export). However, the exact mechanisms through which CDK11 functions are as yet unknown, as no small molecule inhibitor of CDK11 has yet to be developed. Therefore, our lab has been developing chemical genetic models in order to acutely study the activity of CDK11, including i) an auxin-inducible-degron CDK11 mutant system to rapidly deplete CDK11 protein and, ii) an analogue-sensitive CDK11 mutant which can be inhibited by a ATP-competitive inhibitory analogue.

This project aims to use novel chemical genetic systems to study the functions of CDK11, in order to evaluate its potential as a therapeutic target in haematological cancers, as well as to investigate its role in the regulation of gene expression.

Key Words: Haematological Cancers, Cancer Cell Biology, Gene Expression, Gene Regulation.

Target Students: PhD/Postgraduate, Honours.

For more information about this project contact:

Dr. Jennifer Devlin   jennifer.devlin@petermac.org

Targeting epigenetic deregulated mechanisms in lymphoma

Supervisors: Dr. Pilar Dominguez, Prof. Ricky Johnstone

Our project focuses on diffuse large B-cell lymphoma (DLBCL), an aggressive form of lymphoma. Despite progress in the treatment of DLBCL, approximately 40% patients relapse or do not respond to the chemotherapy, which usually has fatal consequences. Therefore, there is an urgent need to find better treatments for this disease.

DLBCLs are characterized by profound alterations in epigenetic mechanisms (i.e. DNA methylation and chemical modifications of histones), which correlate with poor outcomes for patients. We hypothesise that therapies aimed at reversing abnormal epigenetic changes will increase survival of DLBCL patients. We are investigating the efficacy and underlying mechanisms of action of a new therapy consisting of a novel inhibitor of histone deacetylase 3 (HDAC3) in combination with hypomethylating agents (HMA). For that, we are generating mouse models of lymphoma and in vitro (organoids) and in vivo models (xenografts) derived from primary patient samples and cell lines to:

1. Explore the therapeutic potential of HDAC3 inhibitors and HMA to treat DLBCL,

2. Characterise in detail the effects of these epigenetic drugs at the molecular level, through genome-wide epigenomic and transcriptional studies,

3. Analyse their effect on the tumour microenvironment using single cell technologies and flow cytometry.

Key Words: Haematological Cancers, Lymphoma, Epigenetics, Targeted therapies, Personalised medicine

Target Students: Honours, Masters, PhD/Postgraduate

For more information about this project contact:

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KATS, LEV

TRANSLATIONAL HAEMATOLOGY PROGRAM

https://www.petermac.org/research/labs/lev-kats

RNA Methylation in normal and malignant blood development

Supervisors: Dr. Lev Kats, Dr. Joan So

As is the case with DNA and histones, RNA can also be modified and indeed more than 100 chemical groups that decorate all four canonical RNA nucleotides have been described. While these modifications undoubtedly carry genetic information, their study has lagged far behind that of DNA and histone modifications and their functional relevance remains largely unknown. Methylation of the N6 position of adenosine (m6A) is the most common alteration on eukaryotic messenger RNA (mRNA).

Recent studies have begun to identify writers, readers and erasers of this epigenetic mark and have demonstrated that it has broad physiological roles in splicing, RNA stability and microRNA processing. As m6A does not affect Watson-Crick base pairing, specialised sequencing methods are required to determine its precise localisation in the genome.

We are investigating how regulators of the m6A pathway control RNA methylation, gene expression and cellular behaviour in normal and malignant blood cells.

Key Methodologies: CRISPR gene editing, RNAseq, m6Aseq.

Key Words: Haematological Cancers, Cancer Cell Biology, Gene Expression, Gene Regulation, Animal Models.

Target Students: PhD/postgraduate, Honours

AVAILABLE PROJECTS BY RESEARCH GROUP

Targeting IDH mutations in acute myeloid leukaemia

Supervisor: Dr. Lev Kats, Dr. Joan So

Acute Myeloid Leukaemia (AML) is an aggressive disease with poor prognosis and development of novel treatment options is urgently needed. Approximately 20% of AML patients carry mutations in genes that encode the metabolic enzymes IDH1 and-2. Mutant IDH proteins possess a neomorphic enzymatic activity and produce the onco-metabolite D-2-hydroxyglutarate (2-HG) that modulates numerous pathways implicated in cell fate decisions and cancer.

Using advanced mouse models we are investigating the molecular mechanisms of response and resistance to IDH inhibitors. Key Methodologies to be used: CRISPR gene editing, RNAseq, m6Aseq.

Key Words: Haematological Cancers, Cancer Cell Biology, Gene Expression, Gene Regulation, Animal Models.

Target Students: Honours, PhD/Postgraduate

For more information about these projects contact:

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LOI, SHERENE

CANCER THERAPEUTICS PROGRAM.

https://www.petermac.org/research/labs/sherene-loi

Manipulation of tumour microenvironment to enhance anti-tumour immunity in breast cancer: from bench to bedside.

Supervisor: Prof. Sherene Loi

Our lab is studying the breast cancer immune microenvironment mechanisms to modulate with therapeutics in order to improve survival from breast cancer. We use in vitro and in vivo models, as well as patient tissue and blood samples to understand the mechanisms of immune responses. We use a wide variety of cutting edge techniques including single cell sequencing technologies, multi-parameter flow cytometry, CRISPR, and next generation sequencing on in vivo or in vitro platforms.

Students will learn about breast cancer biology, cell signalling, immunology, cell culture, mouse handling, therapeutics, flow cytometry, western blotting, genomic techniques, biostatistics, bioinformatics. Particularly suited for students interested in translational research, novel therapeutics and clinical applications.

Current projects:
- Dissect mechanisms driving progression of early stage in situ cancers to invasive breast cancers.
- Identifying factors regulating differentiation and longevity of tumor specific T cells and use therapeutic strategies to lodge these cells at tumor site.

Key Words: Breast Cancer, Cancer Genetics, Cell Biology, Tumour Immunology, Bioinformatics, Genomics, Personalised Medicine.

Target Students: Honours, Masters PhD/postgraduate

For more information about this project contact:

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McARTHUR, GRANT

ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM, & CANCER THERAPEUTICS PROGRAM

https://www.petermac.org/research/labs/grant-mcarthur

Inhibition of PRMT5 as a cancer therapy

Supervisors: A/Prof. Karen Sheppard, Prof. Grant McArthur

Targeted therapy has had profound impact on outcomes for cancer patients. Nonetheless significant challenges remain to maximize the clinical benefit of targeted therapies including the discovery of targets beyond driver oncogenes, overcoming or preventing resistance, the combination with immunotherapies, and extending their benefit to cancers with poor outcomes.

We have been at the forefront of development of targeted therapies for melanoma through targeting of BRAF, MEK and more recently CDK4. This work has led to a global standard of care for BRAF-mutant melanoma of BRAF + MEK inhibitors and the progress of the combination of BRAF, MEK and CDK4 inhibition into clinical trials. Our recent preliminary studies have identified Protein Arginine Methyltransferase 5 (PRMT5) as a new target for melanoma and potentially oesphageal and pancreatic cancer. In preclinical studies using melanoma cell lines and mouse models we have demonstrated that PRMT5 inhibition synergises with CDK4 and BRAF/MEK inhibitors leading to sustained inhibition of melanoma cell proliferation.

This project will assess the ability of PRMT5 inhibition to be combined with RAF/MEK/CDK4 pathway inhibitors in several cancers and investigate the mechanisms leading to the robust response.

In summary this proposal is aimed at improving the clinical benefit of BRAF/MEK and CDK4 inhibitors by combining with PRMT5 inhibition and extending these combination therapies into cancers with poor outcomes (pancreatic and oesophageal).

These studies will provide mechanistic insight into the action of PRMT5 inhibitors in RAS/RAF/CDK4 driven tumours and identify patients that will likely benefit from PRMT5 therapy including combination therapy.

Key Words: Melanoma, Targeted Therapies, Acquired Resistance, Metabolism, Molecular Oncology.

Target Students: PhD/postgraduate

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

Overcoming therapy induced reprogramming of metabolism in melanoma

Supervisors: Dr. Lorey Smith, Prof. Grant McArthur

Therapies that target oncogenes in cancer have revolutionised cancer care. The major benefits of targeted therapies are high response rates and manageable toxicities, however they do not result in cures in the vast majority of patients. Clinical outcomes of these therapies are limited by cellular adaptation and drug tolerance that allows persistence of residual disease that ultimately results in relapse. This project will take a new approach to address this problem by understanding how cancer cells adapt to targeted therapy, prior to development of overt drug resistance.

Cellular adaptation induced by targeted therapy is characterised by oncogenic network rewiring following initial pathway inhibition. In both preclinical and clinical studies of melanoma, drug induced adaptation reprograms metabolism however whether this creates unique metabolic liabilities that can be targeted to prevent resistance, and the underlying mechanisms that control it, are unknown.

We hypothesise that targeting metabolic alterations underlying cancer cell plasticity in response to targeted therapy will offer new opportunities to treat minimal residual disease to improve response and delay or prevent resistance.

This project will investigate mechanisms underlying drug-induced cellular adaptation with a focus on metabolism, using MAPK targeted therapy in melanoma as a paradigm.

Key Words: Melanoma, Metabolism, Targeted Therapies

Target Students: PhD/Postgraduate

For more information about this project contact:

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NEESON, PAUL

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/paul-neeson

CAR-T therapy for cold tumours

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

Cold tumours are advanced solid cancers with no tumour infiltrating lymphocytes, e.g. Advanced metastatic prostate/breast cancer. Cold tumours are poorly responsive to immunotherapy, including adoptive cell transfer and immune checkpoint blockade. Patients with cold tumours have a poor clinical outcome, with high morbidity and mortality.

For these patients, chimeric antigen receptor (CAR)-T cells are a potential treatment as they target tumour antigen expressed on the cell surface. Additionally, CAR-T cells survive long term in patients and provide long-term remission. However, to date, CAR-T efficacy in cold tumours has been poor. Barriers to CAR-T cell success in cold tumours include poor T cell trafficking, tumour derived immunosuppressive microenvironment and immune checkpoint-mediated T cell suppression.

In this project, we will develop and evaluate novel CAR-T design and combination therapy to address these barriers. This project will provide sufficient pre-clinical and translational data to drive the novel therapy into clinical trials for patients with advanced tumours.

Key Words: CAR-T therapy, Cold tumours, Immune suppression, Tumour microenvironment, T cell trafficking, Immune checkpoint blockade.

Target Students: Honours, PhD/Postgraduate

For more information about these projects contact:

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Dr. Criselle DSouza   criselle.dsouza@petermac.org

In-depth immune profiling of oral cavity squamous cell carcinoma

Supervisors: A/Prof. Paul Neeson, Dr Minyu Wang

The oral cavity is the most common site for head and neck squamous cell carcinoma, and nearly half of new cases present with advanced-stage disease. Despite aggressive therapy, the disease outcomes have remained poor, with less than 40% five-year survival. The success of immune checkpoint inhibitors for the treatment of recurrent metastatic head and neck squamous cell carcinoma highlighted the role of the tumour microenvironment in carcinogenesis. The tumour microenvironment contains a wide range of cells: including tumour, stromal, and immune cells.

In this project, we will collect human tumour samples to define the immune composition, immune gene expression, and spatial organisation of the immune cells in the tumour. Each tumour sample will be analysed by flow cytometry, transcriptional profiling, and fluorescent multiplex immunohistochemistry. Importantly, patient outcomes will also be tracked, allowing for the identification of immune parameters that regulate protective immune responses to cancer. By in-depth immune profiling these oral cavity carcinomas, we aim to identify markers that will assist in a more targeted approach to treat these patients.

Key Words: Tumour microenvironment, Immune checkpoint blockade, Immune gene expression, Immune composition, Patient outcome

Target Students: Honours, PhD/Postgraduate

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

OSHLACK, ALICIA

COMPUTATIONAL BIOLOGY PROGRAM

Finding cancer drivers in long-read transcriptomes

Supervisors: A/Prof. Alicia Oshlack, Dr. Nadia Davidson

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 methods for identifying these important events are not available. This project aims to develop bioinformatics approaches to analyse and explore long read transcriptome data and identify cancer driver events.

Key Words: Bioinformatics, Transcriptomics, Sequencing technologies

Target Students: PhD/Postgraduate

For more information about these projects contact:

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Is RNA methylation disrupted in cancer?

Supervisors: A/Prof. Alicia Oshlack, Dr. Lev Kats

It is well known that methylation of DNA is associated with cancer and can play important roles in cancer progression such as suppressing the expression of tumour suppressor genes. However methylation of RNA is much less understood and its association with disease has not yet been established. In this project we plan to develop bioinformatics analysis methods for using direct RNA sequencing to understand the role of RNA methylation in cancer.

We will generate data using new technologies that can detect methylation during direct sequencing of RNA. Oxford Nanopore technologies will be used to sequence RNA in cancer and normal cells. This project will develop pipelines to analyse this cutting edge data for the purpose of looking at differential methylation between samples. We will be able to apply our methods to many data sets in disease and development.

Key Words: Bioinformatics, Transcriptomics, Sequencing technologies

Target Students: PhD/Postgraduate

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PAPENFUSS, TONY

COMPUTATIONAL BIOLOGY PROGRAM

https://www.petermac.org/research/labs/anthony-papenfuss

Analytic methods for detecting and making sense of somatic genomic rearrangements

Supervisor: Prof. Tony Papenfuss, Dr. Daniel Cameron

Building on state-of-the-art methods that the lab has previously created, this project involves the development of a variety of new bioinformatics methods to cancer genome sequencing data, including copy number analysis techniques and methods for the refinement, visualisation and classification of genomic rearrangements, and their application to clinical cancer samples.

Key Words: Bioinformatics, Computational biology, Genomics.

Target Students: PhD/postgraduate

Immunostaging for melanoma to accurately predict the risk of relapse after surgery

Supervisor: Prof. Tony Papenfuss, Dr. David Gyorki

This project will utilise a large biobank of clinically annotated samples from patients with melanoma at high risk of relapse after surgery to develop a signature that predicts risk of relapse. By combining readouts from various platforms that measure immune-tumour engagement as well as known clinicopathological staging information, the project seeks to develop an accurate immune-staging algorithm. The project will build on prospective data collected through Melanoma Research Victoria and biomarker analysis using a number of platforms including circulating tumour DNA, other circulating biomarkers (microRNA, autoantibodies) as well as genomics analysis. New bioinformatics methods will be used to develop a clinically meaningful risk prediction signature.

Key Words: Bioinformatics, Melanoma, Translational Immunology.

Target Students: PhD/postgraduate.

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

PARKER, BELINDA

CANCER IMMUNOLOGY PROGRAM, & CANCER THERAPEUTICS PROGRAM

https://www.petermac.org/research/labs/belinda-parker

Testing the function of immune suppressive cytokines and cells in bone metastasis

Supervisors: A/Prof. Belinda Parker, Dr. Damien Zanker, Dr Katie Owen

Bone metastasis is a common occurrence in breast and prostate cancer that leads to patient morbidity and, in many cases, mortality. Treatments that target bone metastases long-term are lacking and, to date, immunotherapeutics including checkpoint inhibitors have met with underwhelming responses. In fact, our laboratory has discovered that immune control of tumour growth in bone is unique and this has highlighted the need for bone-specific studies that dissect the tumour cytokines that lead to immune suppression by altering the balance of immune suppressor and effector cells that promote cancer outgrowth. This is an extremely understudied area of research.

This project will measure and manipulate immune suppressive cytokines (including IL-10), checkpoint proteins (such as PD-1/L1) and immune suppressor cells (such as regulatory T cells) in syngeneic mouse models of breast and prostate cancer to identify prognostic and therapeutic opportunities to predict, prevent or target bone metastasis. This will be linked to analysis of primary and metastatic patient tissues to validate findings in mouse models. Techniques for this project include cell culture, CRISPR-cas9 gene editing, RNA extraction and analysis (using quantitative reverse transcription PCR (RT-qPCR)), western blotting, flow cytometry, multiplex cytokine analysis, multiplex immunohistochemistry, induction and monitoring of tumorigenesis and metastasis in vivo, immune activation and cytotoxicity assays.

Key Words: Bone Metastasis, Breast Cancer, Prostate Cancer, Cytokines, Immune Suppression, Biomarkers, Precision Medicine, Immune Suppressor cells, Metastasis-Targeted Therapeutics, Innate Immunity, Adaptive Immunity, Checkpoint Proteins, Immunotherapy

Target Students: Honours, PhD/Postgraduate

Investigating the function of a novel cytokine in immune regulation of breast cancer

Supervisors: A/Prof. Belinda Parker, Prof. Paul Hertzog (Hudson Institute)

Immune therapy is currently being trialled for aggressive types of breast cancers that fail on conventional therapies, such as chemotherapy. To date, response to checkpoint-based immunotherapies have been underwhelming, despite their success in other malignancies such as melanoma. Our laboratory has discovered that a class of cytokines called the type I interferons (IFNs) are secreted from tumour cells to promote anti-cancer immunity and that loss of IFN production is closely linked to an increased risk of rapid metastasis in breast cancer. A new type I IFN has now been identified by Paul Hertzog's group (IFN epsilon) that is expressed in the reproductive tract and is regulated by estrogen. We now want to determine is this IFN could actually promote an anti-cancer response in aggressive breast cancer models, as a less toxic alternative to use of other classical type I IFNs that have been trialled in the clinic.

This project will utilise mouse models of triple negative breast cancer and cell lines derived from patients to test the expression and therapeutic implications of IFN epsilon, including whether this cytokine can promote anti-tumour immunity, enhance response to other therapeutics and suppress metastasis. Techniques for this project include cell culture, RNA extraction and analysis (using quantitative reverse transcription PCR (RT-qPCR)), ELISA, western blotting, multiplex flow cytometry, immunohistochemistry, induction and monitoring of tumorigenesis and metastasis in vivo, immune activation and cytotoxicity assays, and in vitro cell proliferation and apoptosis assays.

Key Words: Breast Cancer, Interferons, Immunotherapy, Metastasis, Innate Immunity, Memory T Cells, Checkpoint Proteins, Anti-Tumour Immunity.

Target Students: Honours, PhD/Postgraduate

The role of the breast microenvironment in suppressing early cancer invasion

Supervisors: A/Prof. Belinda Parker, Prof. Bruce Mann (RMH), Dr. Natasha Brockwell

Ductal carcinoma in situ (DCIS) is a pre-invasive stage of breast cancer, whereby the tumour cells remain restrained by myoepithelial cells that surround breast ducts. Predicting which cases of DCIS will later develop invasive cancer is difficult, meaning that the majority of patients have treatment that may not benefit them. The aim of this project is to assess changes to the myoepithelial cells and the surrounding immune cells that are associated with disease recurrence, with the ultimate objective of identifying prognostic biomarkers that will enable individualised treatment options for patients diagnosed with early stage breast cancer.

Our laboratory has developed a 3D model that mimics the earliest stages of tumour cell invasion beyond the myoepithelial layer. Using this model and high throughput screening, we have identified candidate tumour suppressors in myoepithelial cells and now want to confirm their functional role.

This project will combine use of this model with a large cohort of patient DCIS tissues to identify myoepithelial and immune markers/cells that have important roles early invasion and could serve as candidate biomarkers of risk of invasive relapse after DCIS diagnosis.

Techniques for this project include 3D cell culture, live cell imaging, confocal microscopy/immunofluorescence, RNA extraction and analysis, western blotting, gene editing, multiplex flow cytometry, immunohistochemistry, immune activation assays, and in vitro cell proliferation and apoptosis assays.

AVAILABLE PROJECTS BY RESEARCH GROUP

Key Words: Breast Cancer, Invasion, Immune activation, Myoepithelial Cells, INovel Prognostic Markers, Precision Therapy.

Target Students: Honours, PhD/Postgraduate

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PEARSON, RICK

ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM, & CANCER METABOLISM PROGRAM

https://www.petermac.org/research/labs/rick-pearson

Targeting the ribosome to treat oncogene-driven blood cancer

Supervisors: Dr. Jian Kang, Prof. Rick Pearson

Most human tumours exhibit deregulated signalling through the PI3K/RAS/MYC network, leading to increased ribosome synthesis and hence elevated protein synthesis. We developed the "first-in-class" selective inhibitor of ribosome biogenesis, CX-5461. Targeting ribosome biogenesis has shown remarkable potency in mouse models of solid and blood cancers with deregulated MYC activity and the treatment efficacy is largely dependent on an intact immune system. Critically, our first-in-human trial of CX-5461 demonstrated single-agent efficacy in patients with refractory blood cancers. However, patients' disease still progresses revealing acquired resistance is the major challenge for maximizing the clinical efficacy of this novel therapy.

This research will identify the novel points of therapeutic vulnerability and provide new therapeutic strategies and biomarkers of response to improve the efficacy of ribosome-targeting therapy in oncogene-driven blood cancers.

Eventually it will provide novel understanding and therapeutic approaches to accelerate this new treatment option into standard of care for blood cancer patients.

Our Specific Aims are to:

1. Evaluate new combination therapies that improve the efficacy of ribosome-targeting therapy.

2. Identify and characterize the novel targets that drive resistance to ribosome-targeting therapy.

3. Define the role of anti-tumour immunity in the response and resistance to ribosome-targeting therapy.

Key Words: Drug resistance, Haematological cancer, Ribosome

Target Students: PhD/Postgraduate

For more information about this project contact:

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Activation of targeted DNA Damage Response as a novel therapy for Ovarian Cancer

Supervisors: Dr. Elaine Sanij, Prof. Rick Pearson

High-grade serous ovarian cancer (HGSOC) is the most common and aggressive subtype of ovarian cancer and accounts for 70% of all ovarian cancer deaths. HGSOC patients are treated by surgery and/or chemotherapy, yet within 5 years most of these women relapse making new treatment options essential.

We developed a "first in class" drug, CX-5461 that activates DNA damage response, selectively kills cancer cells and is in clinical trials in haematologic (Peter Mac) and breast cancers (Canada). Importantly, our studies demonstrate substantial efficacy of CX-5461 in HGSOC, which is the basis of a new trial in ovarian cancer we planned in 2018/19.

50% of HGSOC is characterized by defects in the homologous recombination (HR) DNA repair pathway. Aberrations in DNA repair provide a weakness that can be exploited therapeutically with genotoxic chemotherapy and inhibitors of DNA repair such as PARP inhibitors (PARPi), now approved in the clinic. Our data demonstarte that CX-5461 in combination with PARPi has significant therapeutic benefit against HGSOC patient-derived xenograft models.

This project aims to investigate the efficacy of CX-5461 in combination with chemotherapy and inhibitors of DNA repair and DNA damage response in pre-clinical models of HGSOC to facilitate clinical trials of effective combination therapies.

Key Words: Cancer Cell Biology, Cell Signalling, Cancer Therapy, Cell Cycle, Cell Growth, Cell Metabolism, Gynaeoncological Cancers, Molecular Oncology, Pharmacogenomics, Solid Tumours.

Target Students: Honours, PhD/Postgraduate

For more information about this project contact:

Dr. Elaine Sanij elaine.sanij@petermac.org

A multiple modality approach for targeting treatment-resistant ovarian cancer

Supervisors: Dr. Elaine Sanij, Prof. Rick Pearson

High-grade serous ovarian cancer (HGSOC) accounts for 70% of ovarian cancer (OvCa) deaths and its five-year survival rate is 43%. 50% of HGSOC demonstrate deficiencies in the homologous recombination (HR) DNA repair pathway, most commonly mutations in BRCA1/2, which underpin favourable responses to chemotherapy and Poly-(ADP-ribose) polymerase (PARP) inhibitors (PARPi). However, most women relapse within three years and succumb to chemo- and PARPi-resistant disease.

Immunotherapy has emerged as a new promising therapeutic approach in cancer care, however, the response to single immunotherapy agents in OvCa is modest (6-30%). OvCa is considered immunologically "cold" and immunosuppressed due to decreased expression of Type I interferon (IFN) genes, low level of T cell infiltration and poor response to T cell checkpoint inhibitors. This proposal addresses a significant clinical need in developing effective treatments for refractory OvCa and in applying immunotherapy to "cold" OvCa tumours.

AVAILABLE PROJECTS BY RESEARCH GROUP

This project aims to identify efficacious combination therapy regimens that incorporate the novel RNA polymerase I (Pol I) transcription inhibitor CX-5461 and DNA damage response inhibitors for treatment of relapsed OvCa. We aim to identify strategies that enhance anti-tumour immunity, and to design optimal combination therapies with immunotherapies to enhance anti-tumour efficacy and improve survival in ovarian cancer.

Key Words: Ovarian Cancer, DNA Repair, Immunology, Novel Combination therapies.

Target Students: Honours, PhD/Postgraduate

For more information about this project contact:

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Targeting the DNA damage response in relapsed ovarian cancer

Supervisors: Dr. Elaine Sanij, Prof. Rick Pearson

Acquired resistance to chemotherapy and PARPi represent a fundamental barrier to the cure of high-grade serous carcinoma (HGSOC), the most common and aggressive subtype of ovarian cancer. New effective treatment options are urgently needed to tackle resistant disease.

Combining agents targeting different pathways in the DNA damage response (DDR) has great potential in relapsed ovarian cancer. Therapies that target the G2/M cell cycle checkpoint show great promise, as they target the cell cycle delay required for DNA repair and replication fork stability in PARPi resistant cells. We will assess the therapeutic benefit of combining inhibitors of DDR targeting ATM, DNA-PK, ATR with inhibitors of the G2M checkpoint targeting AURKB and WEE1 in vitro in patient-derived cell lines of PARPi- and chemotherapy-resistant high-grade serous ovarian cancer. We will also assess the benefit of combining a novel inhibitor of RNA Polymerase I, which activates the DDR with DDR inhibitors in models of relapsed ovarian cancer. The evidence generated will provide the basis for translation into clinical trials.

Key Words: Novel therapy, Drug resistance, DNA damage response

Target Students: Honours, Masters, PhD/Postgraduate

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PHILLIPS, WAYNE

GASTROINTESTINAL CANCER PROGRAM

https://www.petermac.org/research/labs/wayne-phillips

The role of oesophageal submucosal glands in epithelial homeostasis and the development of Barrett's oesophagus

Supervisors: Prof. Wayne Phillips, Dr. Nick Clemons

Barrett's oesophagus, the premalignant precursor of oesophageal adenocarcinoma, is a metaplastic condition where the normal stratified squamous epithelium that lines the oesophagus is replaced by an intestinal-like columnar epithelium. Barrett's oesophagus arises as a result of chronic reflux but the cellular origin of the intestinal-like metaplastic cells that characterise this condition is contentious. The current prevailing view, based almost exclusively on rodent models, is that they arise from cells residing at the squamo-columnar junction, where the oesophagus joins the stomach. However, using pig oesophagus (which is structurally more similar to human oesophagus than rodents) as a model, we have shown that specialised glands in the oesophageal sub-mucosa contain progenitor cells that we believe are responsible for the maintenance of the normal squamous mucosa and may also be the potential cell of origin of Barrett's oesophagus in humans.

This project will define the heterogeneity, hierarchy and functional relationships of cell populations in these glands at the single cell level to identify these progenitor cells, and use our novel organoid culture systems to demonstrate their potential to differentiate into either normal squamous epithelium and/or Barrett's-like intestinal epithelium. The study will also investigate the ability of acid and bile (components of refluxate) and/or inflammatory mediators to control the fate of submucosal gland progenitor cells thus demonstrating an important physiological role for the submucosal glands and providing important new knowledge about the mechanisms of both normal oesophageal homeostasis and the development of Barrett's oesophagus.

Key Words: Cancer Cell Biology, Oesophageal Cancer, Intestinal Metaplasia, Barrett's Oesophagus, Epithelial Homeostasis.

Target Students: PhD/postgraduate.

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AVAILABLE PROJECTS BY RESEARCH GROUP

RISBRIDGER, GAIL

PROSTATE CANCER PROGRAM

https://www.petermac.org/research/labs/gail-risbridger

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. In addition, we are also developing and testing therapeutic antibodies and a new vaccine technology.

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

Target Students: Honours, PhD/postgraduate

For more information about this project contact:

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Analysing the progression of neuroendocrine prostate cancer

Supervisor: Prof. Gail Risbridger, Dr. Roxanne Toivanen

One-in-seven men will be diagnosed with prostate cancer (PC) in their lifetime. As the majority of prostate tumours are dependent on androgens for growth, androgen deprivation is the gold standard treatment for metastatic disease. However all patients inevitably acquire resistance to androgen deprivation, and this most aggressive state is referred to as castration-resistant prostate cancer (CRPC).

While, new anti-androgen treatment regimens have delayed the onset of metastatic CRPC (mCRPC), it remains a lethal condition with limited treatment options, which at best provide short-term disease control. Furthermore, in an increasing subset of PC patients, androgen-targeted treatment selection pressure leads to the emergence of CRPC with neuroendocrine features. Indeed, the prognosis of patients with neuroendocrine differentiation (NEPC) is extremely poor owing to the resistance to conventional therapies. Consequently, new therapeutic strategies to target CRPC in general and NEPC in particular, are critical to improve outcomes for PC patients, including the use of combination therapies to better target tumour heterogeneity.

This project will characterise the progression of NEPC using patient-derived models (xenografts and organoids), and test new treatment strategies for this aggressive prostate cancer subtype.

Key Words: Cancer Cell Biology, Endocrinology, Pathology, Prostatre Cancer, Solid Tumours, Therapeutics, Urological Cancers.

Target Students: Honours, PhD/postgraduate

For more information about this project contact:

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New human models for rapid preclinical testing of prostate cancer

Supervisor: Prof. Gail Risbridger, Dr. Luc Furic

Prostate cancer is the most commonly diagnosed cancer in Victoria. Unfortunately, our ability to pre-clinically test new therapies is constrained by the paucity of experimental human models because prostatic tumours are more difficult to grow in the laboratory than many other types of cancer. However, our laboratory has successfully developed in vivo and in vitro systems to maintain viability of rare and valuable patient samples as "patient-derived xenografts and explants/organoids". These samples represent an invaluable resource for testing novel therapeutics for prostate cancer.

The goal of this project is to use patient-derived xenografts as ex vivo explant cultures or organoids to test drugs of interest that are in development and identify the most promising compounds for further in vivo studies.

The project will involve a variety of techniques including tissue pathology, tissue culture and handling, immunohistochemistry, automated image analysis and qPCR.

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

Target Students: Honours, PhD/postgraduate

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AVAILABLE PROJECTS BY RESEARCH GROUP

RUSSELL, SARAH

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/sarah-russell

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

Supervisor: Dr. 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 ancestry, intrinsic and extrinsic cues.

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

Target Students: PhD/postgraduate

For more information about this project contact:

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STACKER, STEVEN

TUMOUR ANGIOGENESIS PROGRAM

https://www.petermac.org/research/labs/steven-stacker

Novel regulators of lymphangiogenesis and lymphatic remodelling in tumour metastasis

Supervisors: Prof. Steven Stacker, Dr. Rae Farnsworth

The ability of tumour cells to escape the primary tumour site and metastasise to distant organs is the most lethal attribute of solid cancers. There is now extensive evidence from clinical and experimental studies that the growth and remodelling of tumour-associated lymphatic vessels is linked with increased metastasis to lymph nodes and distant organs, and overall to poorer prognosis[1]. Inhibition of key pathways regulating this tumour-associated lymphangiogenesis inhibits metastasis in experimental models. However, clinical experience with anti-angiogenesis drugs indicates that targeting multiple pathways may be necessary to fully inhibit tumour-associated lymphangiogenesis and thereby lymphogenous metastasis.

Migration of lymphatic endothelial cells (LECs) – the cells lining lymphatic vessels – is an essential process in lymphangiogenesis. We used a genome-wide siRNA screen combined with in vivo-derived datasets to identify dozens of candidate genes involved in LEC migration2. This project will involve characterising one or more of these candidates, which can be selected according to the student's interests and skills. Students will use advanced microscopy, multiplex immunohistochemistry, analysis of cancer patient samples, functional cell biological assays, molecular biology techniques and preclinical models to determine the function and therapeutic tractability of these genes.

1. Stacker SA et al. (2014) Nat Rev Cancer 14(3):159-72, 2Williams SP et al. and Stacker SA (2017) Sci Signal 10(499):eaal2987

Key Words: Metastasis, Solid Tumours, Vascular Biology, Cancer Therapy.

Target Students: Honours, PhD/postgraduate

Understanding tissue-specific vasculature in cancer metastasis

Supervisors: Prof. Steven Stacker, Dr. Rae Farnsworth

Cancer is a diverse disease, with each tumour differentiated by the organ and cell type of origin, the patient's genetic and clinical background, and the non-mutated cells that comprise the tumour microenvironment. Blood and lymphatic vessels serve important physiological functions in almost all tissues and organs of the body, and can be hijacked by tumours to aid in tumour growth, metastasis and regulating immune responses[1,2]. The heterogeneity of blood and lymphatic vessels and their component endothelial cells in different organs is only partially characterised, and less still is understood about how these differences contribute to tumour behaviour and therefore to cancer outcomes in patients.

This project will use cutting-edge technologies such as single-cell RNA-Seq to elucidate the unique molecular profiles of organ-specific lymphatic and blood endothelial cells in mouse models of cancer. The project will then utilise cell sorting, multiplex immunohistochemistry, organotypic co-culture assays, molecular and cell biological techniques, analysis of human tumour samples and preclinical models to understand the role of tissue-specific features of the blood and lymphatic vasculature in tumour progression.

1. Farnsworth RH, Achen MG and Stacker SA (2018) Curr Op Immunol 53:64-73, 2. Hendry SA, Farnsworth RH et al. (2016) Front Immunol 7:621

Key Words: Solid Tumours, Vascular Biology, Transcriptomes, Cancer Microenvironment, Metastasis.

Target Students: Honours, PhD/postgraduate

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

TIGANIS, TONY

CANCER METABOLISM PROGRAM

https://www.petermac.org/research/labs/tony-tiganis

Targeting immune checkpoints in obesity-driven HCC

Supervisors: Prof. Tony Tiganis and Dr. Florian Wiede

Hepatocellular carcinoma (HCC) is the most rapidly rising cause of cancer death in Australia. The obesity epidemic and the accompanying development of non-alcoholic fatty liver disease (NALFD) have become major drivers of HCC in the developed world. It is estimated that >85% of overweight individuals and 25.2% of the general population have NAFLD. If left unresolved, NAFLD can progress and result in severe fibrosis or cirrhosis and HCC. At present there are no effective therapies for advanced NAFLD with severe fibrosis/cirrhosis. Moreover, although surgical resection and liver transplantation are effective for early stage HCC, the majority of patients present with advanced disease, when neither surgery, chemotherapy, ionizing radiation or targeted therapies (Sorafenib) are effective. Thus, there is an urgent need for the development of effective therapeutics. Pre-clinical studies point towards the suppression of the immune system being fundamental for HCC development in obesity/NAFLD. However, recent phase III trials for HCC have been disappointing, with the Merck's PD-1 blocking antibody Keytruda (pembrolizumab) failing to achieve any significant improvements in survival.

Our pilot studies suggest that the lack of efficacy of anti-PD-1 monotherapy in HCC might be due to HCC engaging multiple redundant immune checkpoints and posit that the combinatorial targeting of several immune checkpoints will be necessary to combat HCC in obesity. Projects are available to assess the therapeutic potential of targeting multiple immune checkpoints in the context of NAFLD driven HCC.

Key Words: Cancer Cell Biology, Cancer metabolism, Cell Growth, Solid Tumours

Target Students: PhD/postgraduate.

Using T cells to eradicate cancer

Supervisors: Prof Tony Tiganis, Dr. Florian Weide

The inability of the adaptive immune system to initiate a robust anti-tumour response is often linked to the poor prognosis of patients. Immunotherapy is poised to play a central role in the treatment of varied human cancers. The project will take advantage of multidisciplinary techniques and utilise both cell-based and animal models to develop novel approaches for enhancing cytotoxic T cell responses in the context of T cell adoptive immunotherapy.

Key Words: Cancer Cell Biology, Cancer metabolism, Cell Growth, Solid Tumours

Target Students: PhD/postgraduate

Understanding how obesity drives the development of liver cancer

Supervisors: Prof Tony Tiganis, Dr. Florian Weide

Obesity is a leading factor in the development of liver disease, with >85% of overweight individuals developing non-acloholic fatty liver disease (NAFLD). NAFLD encompasses a broad spectrum of liver conditions ranging from simple steatosis, to the more severe and progressive non-alcoholic steatohepatitis (NASH), a condition that results in fibrosis and if left unresolved, cirrhosis (late-stage liver disease) and/or liver cancer.

Obesity-associated NASH is currently the third leading cause for liver transplantation and is expected to soon surpass hepatitis C as the principal cause for liver transplantation and hepatocellular carcinoma (HCC) in the developed world.

Projects are available to determine the mechanisms by which obesity drives the development of NASH, fibrosis and HCC.

Key Words: Cancer Cell Biology, Cancer metabolism, Cell Growth, Solid Tumours

Target Students: PhD/postgraduate.

For more information about these projects contact:

Prof. Tony Tiganis tony.tiganis@petermac.org

TRAPANI, JOSEPH

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/joseph-trapani

Reengineering of CRISPR–CAS effectors for targeted cancer therapy

Supervisors: Prof. Jospeh Trapani, Dr. Mohamed Fareh

Genetic aberrations drive high-risk pediatric cancers that are often correlated with poor prognosis. Recent advances in genomic technologies revealed the genomic landscape in pediatric neoplasms and highlight an important intra- and inter-tumour genetic heterogeneity. Given the genomic singularity of individual tumors and/or tumour subclones, it is undeniable that targeted therapies will offer better survival chances to individual child.

Recent breakthrough discoveries have identified a new subclass of bacterial CRISPR–CAS effectors that target bacteriophages genes with incredibly high fidelity. These discoveries open the possibility of reprogramming CRISPR–CAS effectors to target any disease-related gene in a sequence-specific manner. A single guide RNA (gRNA) loaded into CRISPR-CAS effectors mediates the sequence specificity through the base-pairing with the target, making these nucleoprotein complexes promising programmable tools to achieve specific-specific and efficient targeting of various tumour drivers. This project will focus on:

1. Understanding the molecular basis of CRISPR–CAS target recognition.

2. Reengineering CRISPR-CAS effectors to silence tumour-associated genes with single-nucleotide accuracy.

AVAILABLE PROJECTS BY RESEARCH GROUP

In this proof-of-concept project and through our collaboration with the Zero Childhood Cancer program, we will exploit whole-genome sequencing data and patients' samples (400 paediatric tumors) to reprogram CRISPR–CAS effectors to silence drivers of paediatric tumours such as gene-fusions and single-nucleotide variants. We believe the outcome of this project will help to lay the foundations of a new era of targeted cancer therapies.

A prospective student will have the opportunity to use cutting-edge interdisciplinary approaches including molecular cloning, CRISPR–CAS genome editing, single-molecule super-resolution microscopy, RNA/protein purification and labeling, high-throughput cell-based assays, preparation of DNA libraries, RNA-seq, FACS, RT-PCR, and targeted delivery assays. We offer project(s) in each of these areas, and a specific topic will be selected to cater for the interests and skills of a candidate.

Key Words: Cancer Immunology, Cancer Immunotherapy, Paediatric tumors, Personalized Immunotherapy, RNA Therapeutics, Immunoprofiling, Genomics

Target Students: Honours, PhD/postgraduate

For more information about this project contact:

Dr. Mohamed Fareh mohamed.fareh@petermac.org

VOSKOBOINIK, ILIA

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/ilia-voskoboinik

Understanding cytotoxic lymphocyte biology in health and disease.

Supervisors: A/Prof Ilia Voskoboinik, Prof. Jospeh 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:

- The mechanisms that regulate the transition from a quiescent naïve lymphocyte to a potent killer cell,
- Novel therapeutic strategies aimed at improving immunotherapy,
- 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/postgraduate

For more information about this project contact:

A/Prof. Ilia Voskoboinik   ilia.voskoboinik@petermac.org

WICKRAMASINGHE, VIHANDHA

ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM

https://www.petermac.org/research/labs/vihandha-wickramasinghe

RNA in 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. This project will use cutting-edge cell biology, molecular biology and genetic approaches to understand how mRNA export is altered in cancer. Our ultimate goal is to use these fundamental biological insights to develop novel first-in-class inhibitors to treat cancer.

Key Words: Cancer Cell Biology, RNA, Gene Regulation, Cell Signalling, Cancer Therapy, Cell Growth, Gene Expression.

Target Students: Honours, Masters, PhD/postgraduate

For more information about this project contact:

Dr. Vihandha Wickramasinghe vi.wickramasinghe@petermac.org

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CANCER NURSING RESEARCH

https://www.petermac.org/research/CANCER%20NURSING

Located within Cancer Experiences Research, our 'Cancer Nursing Research' program focuses on practice-relevant studies that address care and treatment issues known to impact on the quality of life of people affected by a cancer diagnosis.

Is Fatigue a useful flag for risk of fall in people with cancer?

Supervisors: Prof. Mei Krishnasamy

Cancer related fatigue (CRF) is defined as a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functioning. It affects significant numbers of patients across all disease stages, from pre-diagnosis to survivorship. The cause is often multifactorial with genetic, biological, psychosocial, and behavioural risk factors identified.

Whether CRF contributes to falls in people with cancer remains unclear. Falls increase morbidity and mortality rates in older adults with cancer. Therefore, further investigation of fatigue as a predeterminant factor, and a potentially useful flag for individuals at risk of falls, is warranted.

This prospective, exploratory study investigates whether patients reporting higher fatigue on admission have a higher proportion of falls compared to those reporting low fatigue but are identified as a falls risk on established screening. It involves collecting subjective and objective measures of fatigue, including patient reported outcome measures and biomarkers from blood tests. It offers students the opportunity to interact with patients in a clinical setting and provides experience in both quantitative and qualitative methodology. Findings will be prepared for publication in a peer-reviewed journal and presented at relevant conferences.

Key Words: Cancer, Fatigue, Falls

Target Students: Honours

For more information about this project contact:

Prof. Mei Krishnasamy Meinir.Krishnasamy@petermac.org

NATIONAL CENTRE FOR INFECTIONS IN CANCER

- https://cancerandinfections.org/
- https://www.petermac.org/research/clinical-research-trials/clinical-research/infectious-diseases-infection-prevention

The National Centre for Infections in Cancer (NCIC) is an integrated health care program for reducing infections in cancer. Cancer patients are a unique population with specialised needs. There is compelling evidence that infection in cancer patients remains a leading cause of death and a significant cost to the healthcare system. Our research group aims to optimise patient outcomes using a health services approach to prevent and manage the critical and growing problems of healthcare associated and antibiotic resistant infection, poor sepsis and antimicrobial management and late recognition of infection in this vulnerable population.

Improving management of sepsis, fever and neutropenia after chemotherapy in cancer patients

Supervisor: Prof. Monica Slavin

Fever and neutropenia are complications of cancer therapy which may represent infection or side effects of chemotherapy. Antibiotic resistance is a major threat in this group. Clinical parameters collected in a prospective study of patients with fever and neutropenia after chemotherapy will be explored to better define use of antibiotics in this population.

Key Words: Sepsis, Fever, Neutropenia, Chemotherapy, Haematological cancers, Solid tumours

Target Students: Honours, Masters, PhD/postgraduate

For more information about this project contact:

Professor Monica Slavin Monica.Slavin@petermac.org

Investigation of the incidence and predictive factors of osteoradionecrosis (ORN) of the jaw in the treatment of head and neck cancer

Supervisors: Dr. Sophie Beaumont, Prof. Karin Thursky, Dr. Lachlan McDowell

Osteoradionecrosis (ORN) of the jaw is a serious complication secondary to treatment of head and neck cancer. ORN can occur spontaneously or in relation to oral cavity trauma, including dental procedures or irritation from an ill-fitting dental prosthesis. Currently, the management of patients with ORN is heterogeneous, owing to differing referral patterns and the variable involvement of multiple clinical teams.
The classification and care pathway of ORN is not universally agreed upon. leading to variations in outcomes and management. Typical management strategies range from simple, local management of oral hygiene, to debridement, surgical excision, antimicrobial therapy, medical therapy and hyperbaric oxygen treatment. Failure

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to identify early cases of ORN and suboptimal management may lead to mandibular fracture, necessitating wide field excision of necrotic bone with a large soft tissue and bony defect requiring reconstruction, heralding a significant decline in survivors' quality of life.

This project will analyse the population of patients with a diagnosis of osteoradionecrosis (ORN) seen at Peter MacCallum Cancer Centre to gain an understanding of their cancer treatment history including surgery and radiation therapy, comorbidities and other factors that might influence the risk of developing ORN.

This project will be conducted through the Melbourne Dental School.

Key Words: Head and Neck Cancers; Infectious Disease

Target Students: Honours/Masters.

For more information about this project contact:

Dr. Sophie Beaumont sophie.beaumont@petermac.org

PARKVILLE FAMILIAL CANCER CENTRE

https://www.petermac.org/research/clinical-research-trials/clinical-research/familial-cancer-research-centre

Familial cancer research at Peter Mac combines clinical and laboratory-based research to: identify new hereditary cancer predisposition genes; improve the identification of people with hereditary cancer syndromes; and develop new strategies for cancer risk management and personalising cancer treatments.

Integrating genome-based breast cancer risk prediction models with evidenced-based clinical outcomes and patient values to empower women considering riskreducing contralateral and bilateral mastectomy

Supervisors: A/Prof. Alison Trainer, Lara Petelin, A/Prof. Paul James, Prof. Bruce Mann

There is increasing demand for contralateral risk-reducing mastectomy(CRRM)in women with breast cancer(BC), despite the majority having a low future BC risk, whilst many women with high-risk BRCA mutations do not pursue risk-reducing surgery. Studies indicate women are fully informed of risk and benefits but overestimate the benefit of CRRM as they struggle to synthesis the information they are given; conflating issues such as BC recurrence with second primary BC risk. Asking women to determine their personal values when making decisions has been shown to improve decision-making and reduce decisional regret. This proposal will develop an on-line tool which integrates state-of-the-art genome-based BC risk prediction (high and moderate risk genes and polygenic risk scores) with evidenced based clinical outcomes through microsimulation modelling. The tool will allow women to determine their optimal clinical decision based on best

clinical evidence, a personalised BC risk assessment and the clinical outcomes that they personally value and wish to optimise.

Aim. To facilitate evidence— and personal values-based decision-making in women contemplating risk-reducing BC surgery.

Skill set gained: Computer coding and microsimulation modelling; Multicriteria decision analysis; Genomic BC risk modelling; BC health services clinical research.

Key Words: Breast Cancer; Familial Cancer; Genomics.

Target Students: Honours.

For more information about this project contact:

A/Prof. Alison Trainer alison.trainer@petermac.org

PROSTATE THERANOSTICS AND IMAGING CENTRE OF EXCELLENCE: ProsTIC

https://www.petermac.org/ProsTIC

ProsTIC comprises a multidisciplinary team led by Professor Michael Hofman and include nuclear medicine, medical oncology, radiation oncology, urology and laboratory-based doctors and researchers with a strong patient-centred philosophy.

Theranostic treatment for prostate cancer involves targeting prostate specific membrane antigen (PSMA) on prostate cancer cells – first with a radioactive molecule to reveal the cancer's spread via a PET scan and then a similar radioactive molecule that kills cancer cells.

Our Discovery research aim is to further investigate next generation targets, develop biomarkers to predict and monitor response to PSMA therapy, optimise new combinations with PSMA therapy in pre-clinical models, explore the use of radio-guided surgery and artificial intelligence image interpretation.

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

Supervisors: Prof. Michael Hofman, Prof. Declan Murphy, A/Prof Arun Azad

Prostate Cancer is a leading cause of death in men. ProsTIC 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 use 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. We have a portfolio of clinical trials generating large volumes of imaging data and blood biomarker data which can be analysed to optimise application of this novel treatment in the future.

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CLINICAL RESEARCH GROUPS

There are several opportunities for research in different domains including:

1. Advanced imaging analysis techniques using radiomics or computer-deep learning, to better personalise care, or enable response better response assessment.

2. Using post-therapy imaging (SPECT/CT) to determine dosimetry (radiation dose to tumour and normal tissue) and establish how to best use this imaging as a prognostic marker or to better personalise therapy.

Project (1) will involve software development to extract tumour data from complex DICOM image datasets. Suitable for students with a background in computer science, engineering or computational biology. You would closely work with our nuclear medicine physicians and medical physicist to achieve project goals.

Project (2) will involve using existing tools to determine the dose of radiation delivered to tumour and normal tissues. You will correlate dosimetry output with patient outcomes to see if dosimetry can be used as a prognostic tool, predict toxicities or better personalise care. This project may be suitable for a medical student or physician who has an interest in medical imaging.

Key Words: Prostate cancer, Radiology, Artificial intelligence, Deep learning

Target Students: Honours, Masters, PhD/Postgraduate

For more information about this project contact:

Prof. Michael Hofman   michael.hofman@petermac.org

RADIATION ONCOLOGY

https://www.petermac.org/research/clinical-research-trials/clinical-research/radiation-oncology-research

Radiation Oncology at Peter Mac is the largest and most academically active radiotherapy treatment centre in Australia. Our research aims to provide the most up-to date and effective evidence-based treatment for patients who require radiotherapy.

IMaging of cancer imMUNOtherapy targets with Positron Emission Tomography: Characterising PD-L1 with 89Zr-Durvalumab

Supervisors: Dr. Fiona Hegi-Johnson and Prof. Michael MacManus

There is a compelling unmet need to develop imaging techniques for immunotherapy targets in humans with cancer, especially the immune checkpoint programmed cell death ligand (PD-L1) and its receptor (PD1). Checkpoint blockade immunotherapies (CBI), such as durvalumab, targeting PD-L1, and nivolumab/pembrolizumab (targeting PD1) are revolutionising the management of common cancers, including lung carcinomas1,2 head and neck3 and skin cancers4.

Although it is known that radiotherapy and chemotherapy can up-regulate PD-L1 expression, potentially increasing response rates to CBI and increasing the number of patients who may benefit, the dynamics of PD-L1 expression in response to chemotherapy, radiotherapy and CBI have never been systematically explored. Patient selection for treatment with CBI often relies on pre-treatment PD-L1 status of a single, potentially non-representative, tumour biopsy and may not correlate strongly with efficacy, or with the global level of PD-L1 expression. Currently, without repeated biopsies of multiple lesions, we cannot tell who may become eligible for treatment after other lines of therapy have upregulated PD-L1, or which individual lesions are most likely to respond or progress.

The imaging of molecular targets of immunotherapy has rapidly become a critically important area of cancer research. The recent publications of a first-in-human studies of 89Zr-atezolizumab5 and 89Zr-nivolumab PET tracers have demonstrated the feasibility and potential robustness of 89Zr -durva PET to assess PD-L1 levels in comparison with established methodologies such as immunohistochemistry and RNA-sequencing (13). In this study, we will characterise the dynamics of PD-L1 upregulation using durvalumab, a human derived PD-L1 antibody that currently is the only therapeutic agent shown to confer an additional survival benefit in NSCLC patients treated with radical chemoradiation, and we expect that this information will help us develop novel, personalized treatment approaches for cancers where PD-L1 is a potential therapeutic target.

This PhD project is based on a fully-funded clinical trial aimed at establishing the feasibility of 89Zr- Durvalumab as a novel imaging biomarker of PD-L1 activity during treatment for lung

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cancer, and embraces both clinical and translational research in novel-tracer PET/CT and molecular biology.

The core skills that will be acquired by the research candidate 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- Durvalumab-PET/CT

2. Molecular biology: analysis of data acquired from the molecular translational work

3. Bioinformatic analysis of the relationships between imaging and molecular data

Key Words: Radiation Oncology, Immunotherapy, Imaging, Lung Cancer, Clinical and Translational Research, Biomarkers

Target Students: PhD/postgraduate

For more information about this project contact:

Dr. Fiona Hegi-Johnson   Fiona.Hegi-Johnson@petermac.org
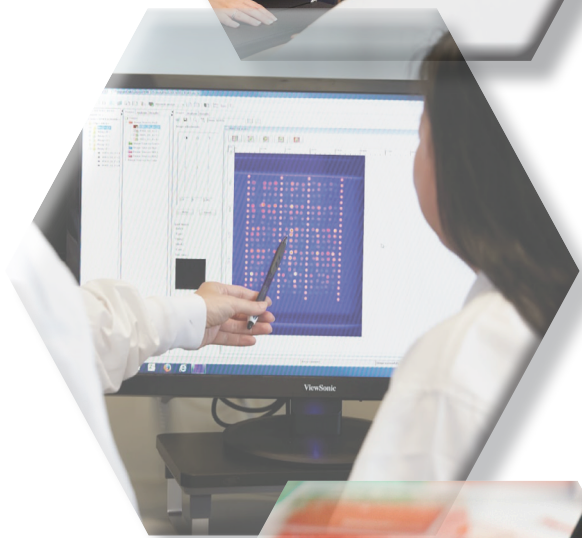
WHY STUDY AT PETER MAC?
WORDS FROM OUR PAST RESEARCH STUDENTS

Collaborative interaction with national and international peers is a lynchpin of any vibrant program.

Peter Mac is continually seeking to work with the best worldwide and the world's best are increasingly seeking out Peter Mac researchers to interact with.

In speaking to past research students, it is immediately evident that the two factors most strongly influencing their decision to join and stay at Peter Mac are firstly, the opportunity to be mentored by a strong and collegiate group of senior researchers and secondly, the well-established research infrastructure that enabled them to perform virtually any type of experiment they required at affordable cost.

This is a strong vindication of our strategy of identifying, seeding and supporting the growth of an enabling environment, both in terms of talented senior personnel and a first-class research infrastructure.

"I have been incredibly fortunate to be part of a dynamic and supportive research group at The National Centre for Infections in Cancer at Peter Mac. My inspiring PhD supervisors Prof Karin Thursky and Prof Monica Slavin have taught me to think beyond the hospitals walls, to collaborate across disciplines and to translate my research into practice."

Gabrielle's research encompasses three domains: risk prediction, health-services utilisation and implementation. Her vision is to lead national knowledge translation studies to improve the management of infections in cancer with a focus on standardising practice, reducing unwarranted variation and improving efficiencies within the healthcare system. Results of Gabrielle's PhD have already been implemented across Victoria and have resulted in significant reductions in hospital length of stay for children with cancer and febrile neutropenia (FN).

Dr. Gabrielle Haeusler: Infectious Diseases Physician and Clincial Researcher, Peter MacCallum Cancer Centre. Recipient: 2018 Premier's Award for Health Service Research; 2019 Chancellor's Award, The University of Melbourne; 2019 Peter Mac Postgraduate Research Medal.

"Doing a PhD at Peter Mac surrounded by a critical mass of world-class cancer researchers is invaluable experience for any young investigator and certainly was for me. Apart from learning an array of scientific techniques, it honed my ability to critically evaluate data, to present my own data verbally and in writing, and allowed me to get my first independent funding (a CJ Martin Fellowship) to undertake postdoctoral training at the British Columbia Cancer Agency."

Arun is a clinician-researcher with a focus on urological cancers and especially prostate cancer. He has a key role in early- and late-phase clinical trials in prostate cancer, including investigator-sponsored studies, and leads a lab team focused on characterising circulating blood-based biomarkers in advanced prostate cancer. His work is supported by research grants and fellowships from NHMRC, Victorian Cancer Agency and other funding bodies including industry partners. He is co-PI of the Upfront-PSMA Movember/Cancer Australia Prostate Cancer Research Alliance.

A/Prof. Arun Azad: Medical Oncologist and Clinician Researcher, Peter MacCallum Cancer Centre.

"I was attracted by Peter Mac's reputation as a holistic cancer centre with everyone striving towards one goal. In this supportive and collaborative environment I developed my potential towards making a significant contribution to the field of cancer research."

Nimali completed a postdoctoral position at Stanford School of Medicine. She is now a Clinical Scientist at Genentech/Roche working in Product Development Oncology, responsible for developing and executing the late stage (Phase II – IIIA) clinical strategies and plans, to help deliver novel therapies that provide significant improvement to patient health. Her goal is to translate promising, innovative scientific breakthroughs to global health that impacts patients.

Dr. Nimali Withana, Clinical Scientist, Genentech/Roche, USA

"Undertaking a PhD at the Peter MacCallum Cancer Centre was critical to the development of my career. Being immersed in an institute dedicated to cancer research gave me a wide and diverse exposure to different aspects of cancer biology, enabling me to tap in to different areas of expertise whenever I needed it. The PhD education program and interaction with scientists across the institute (especially other PhD students) provided me with a solid foundation across multiple areas of cancer biology from cancer genetics, metastasis, immunology and more."

Nick's research interests in upper GI cancers were developed during research fellowships in the Surgical Oncology Research Lab at Peter Mac and the MRC Cancer Cell Unit at the University of Cambridge. Throughout his career, collaboration with clinicians (especially surgical oncologists, medical oncologists and gastroenterologists) has been critical to his research by enhancing the relevance of his work to the most critical issues facing patients with oesophageal cancer. Nick's research group focuses on understanding the tumourigenic process in oesophageal cancer and they use this knowledge to investigate opportunities to improve clinical management of this disease, including the identification of new therapeutic approaches.

A/Prof. Nicholas Clemons: Head, Tumourigenesis & Cancer Therapeutics Laboratory, Peter MacCallum Cancer Centre; Senior Honorary Fellow in the Sir Peter MacCallum Department of Oncology at The University of Melbourne.

"I was very fortunate to do my PhD doing something I was really passionate about – cancer immunotherapy. I had a wonderful time during my PhD at Peter Mac, not only because it is a great place to work in with all the amazing people and staff, but also because of all the opportunities I got as a PhD student. Peter Mac always brings in the best scientists from various fields in cancer research, and all those seminars definitely helped me learn so much about exciting current research outside of my own. All the training I had at Peter Mac definitely has helped equip me with important skills that I need here as a scientist, not only laboratory skills but also communication and presentation skills."

Sherly's PhD My research focused on T cell immunotherapy, in particular chimeric antigen receptor (CAR) T cell therapy which involves genetic engineering of T cells to redirect their specificity to target tumour antigen(s). Sherly made the most of the opportunities for personal development throughout her PhD; she developed from being a timid first year student into to a mature confident scientist in her final year, presenting at international conferences and labs in the US. After these conferences and lab visits, she was offered a few post-doctoral positions in a number of institutes in Canada and the US, which then led her to her current role as a post-doctoral scientist at the University of Pennsylvania in Philadelphia.

Dr. Sherly Mardiana: Postdoctoral Scientist, University of Pennsylvania, USA.

"Attending a Peter Mac Student Open Day in the 3rd year of my undergraduate degree, I was struck by the enthusiasm and the collaborative environment at the open day, and on subsequent visits to the labs. More so than other institutes that I'd visited and work at, I didn't really notice a clear distinction between RAs, students and post-docs. I felt that everybody had an opportunity to contribute to the discussion around the experiments."

Don completed his Honours year at Peter Mac in 2010, following which he worked in various RA roles in the Oncogenic Signalling and Growth Control Program before commencing his PhD in 2014. He remained at Peter Mac throughout these stages of his early research career because he enjoyed the excellence of the research environment and facilities, and he was learning a lot from the people at Peter Mac. After completing his PhD, he commenced a postdoctoral position at the Karolinska Institute, Sweden, in June 2018.

Dr. Don Cameron: Postdoctoral Scientist, Karolinska Institute, Sweden
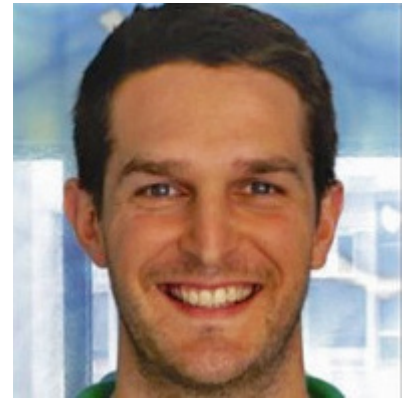
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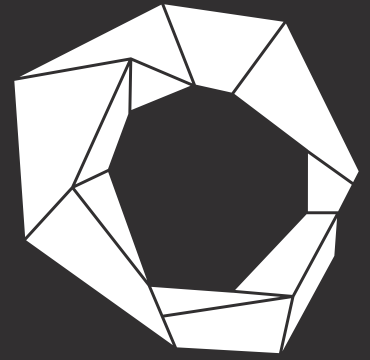Melbourne Victoria
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