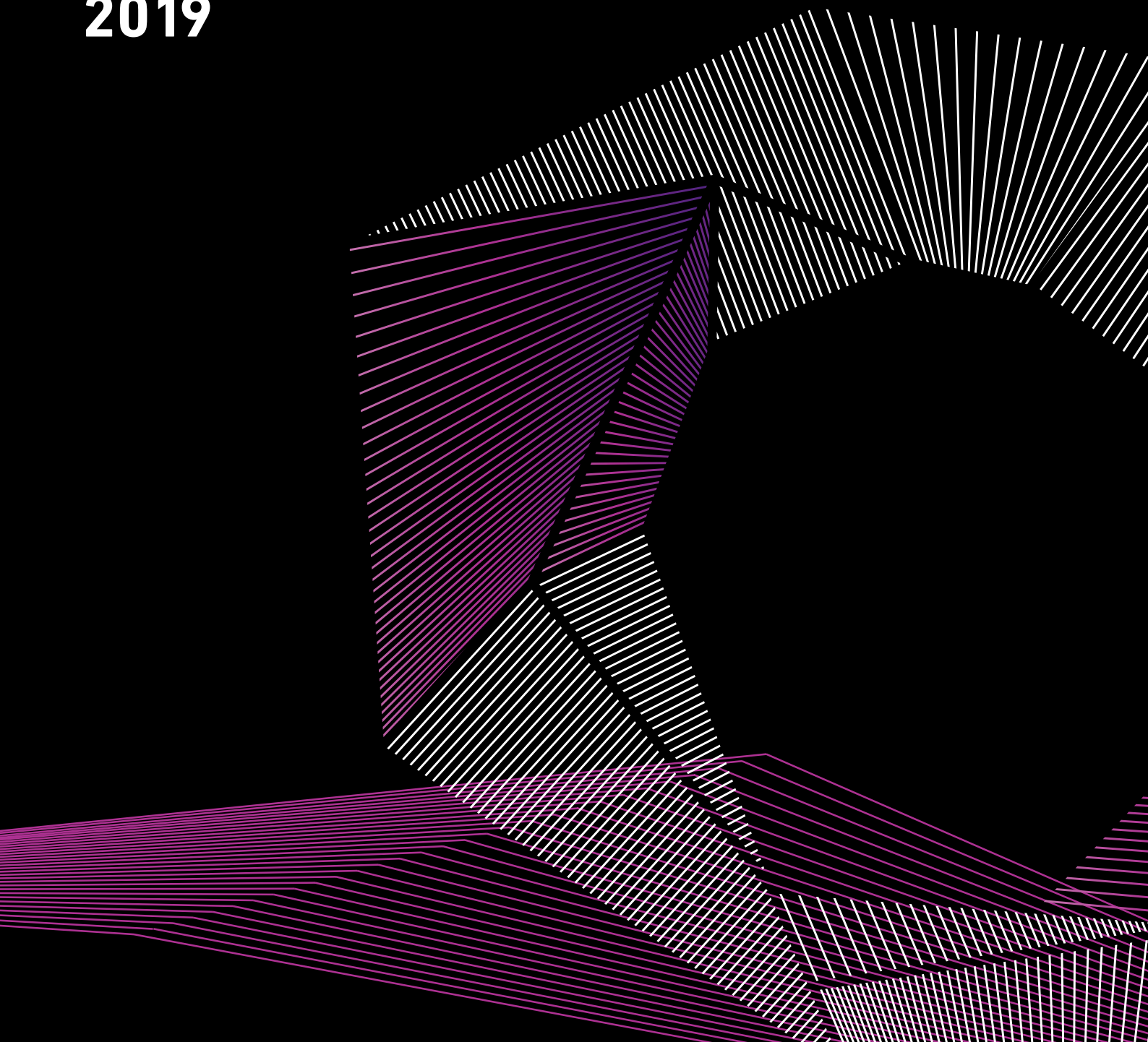
Peter Mac

Peter MacCallum Cancer Centre
Victoria Australia

CANCER RESEARCH
STUDENT PROJECTS
2019



FROM OUR CANCER RESEARCH EXECUTIVE DIRECTOR

For nearly 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 ransformation, translational studies that rovide 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.

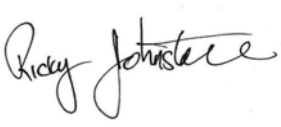
I firmly believe that our model of research-driven cancer care is the right one and Peter Mac is uniquely positioned to expand this paradigm both internally and with our external partners.

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 580 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.

ACCELERATE DISCOVERY AND TRANSLATIONAL RESEARCH

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

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

LABORATORY RESEARCH

The Cancer Research Division at Peter Mac is home to over 450 laboratory-based scientists and support staff, including more than 140 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:

- Organogenesis and Cancer
- Cancer Genetics & Genomics
- Cancer Immunology
- Cancer Therapeutics
- Translational Haematology
- Oncogenic Signalling and Growth Control
- Gastrointestinal Cancer
- Prostate Cancer
- Tumour Angiogenesis and Microenvironment
- Cancer Metabolism
- Computational Biology

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 not only our researchers, but researchers worldwide, access to a vast array of ethically collected clinical samples and associated clinical data.

ABOUT OUR RESEARCH

CLINICAL RESEARCH

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

At Peter Mac 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.

Research in the clinical services is included in 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 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.

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.

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

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 pre-clinical evaluation, novel biomarker development and early phase clinical trials of new drugs.

Biostatistics

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).

Clinical Trials Support

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.

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.

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

The Victorian Centre for Functional Genomics (VCFG) offers biomedical researchers Australia-wide the ability to perform novel discovery-based functional interrogation of all genes in the genome, or of selected boutique collections, using multiple platforms including:

- CRISPR screening (cas9/Pooled viral/Arrayed synthetic
- siRNA/miRNA/shRNA platforms
- Compound screening
- Reverse Phase Protein Array platform

The VCFG operates a 'researcher driven, staff assisted' model whereby the researcher is embedded in the facility, trained on appropriate equipment supported by the VCFG team.

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

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

Kieran Harvey Lab (Program head)

Louise Cheng: Lab

Andrew Cox Lab

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

David Bowtell Lab (Program head)

Ian Campbell Lab (Program head)

Kylie Gorringe Lab

Kara Britt Lab

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

Joe Trapani Lab (Program head)

Ilia Voskoboinik Lab

Phil Darcy Lab

Jane Oliaro Lab

Sarah Russell Lab

Paul Neeson Lab

Ricky Johnstone Lab

Tony Tiganis Lab

Paul Beavis Lab

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

Grant MacArthur Lab (Program head)

Sarah-Jane Dawson Lab

Ben Solomon Lab

Rodney Hicks Lab

Sherene Loi Lab

Charbel Darido Lab

Kristin Brown Lab

The Cancer Therapeutics Program aims to integrate various basic research activities, platform technologies, and pre-clinical 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

Mark Dawson Lab (Program head)

Ricky Johnstone Lab

Sarah-Jane Dawson Lab

Lev Kats Lab

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

Rick Pearson Lab (Program head)

Grant McArthur: Molecular Oncology Lab

Vihandha Wickramasinghe Lab

Ygal Haupt Lab

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

Wayne Phillips Lab (Program head)

Rob Ramsay Lab (Program head)

Alex Boussioutas Lab

Nicholas Clemons Lab

Focussing on clinical, preclinical, and basic science research across all cancers of the gastrointestinal ract (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 currently consists of four laboratory-based groups with a focus on (gastric, oesophageal, colorectal, and anal) cancers, and a surgical research team led by Professor Sandy Heriot. We also have strong clinical links with additional surgeons and oncologists with our Victorian Comprehensive Cancer Centre partners and other Melbourne hospitals 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

Marc Achen Lab (Program head)

Steven Stacker Lab (Program head)

Stephen Fox Lab

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

Gail Risridger Lab (Program head)

Ygal Haupt Lab

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

Tony Papenfuss Lab (Program head)

David Goode: Lab

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

Tony Tiganis Lab (Program head)

Rick Pearson lab

Andrew Cox Lab

Kristin Brown lab

Louise Cheng Lab

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
- ttargeting 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 140 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:

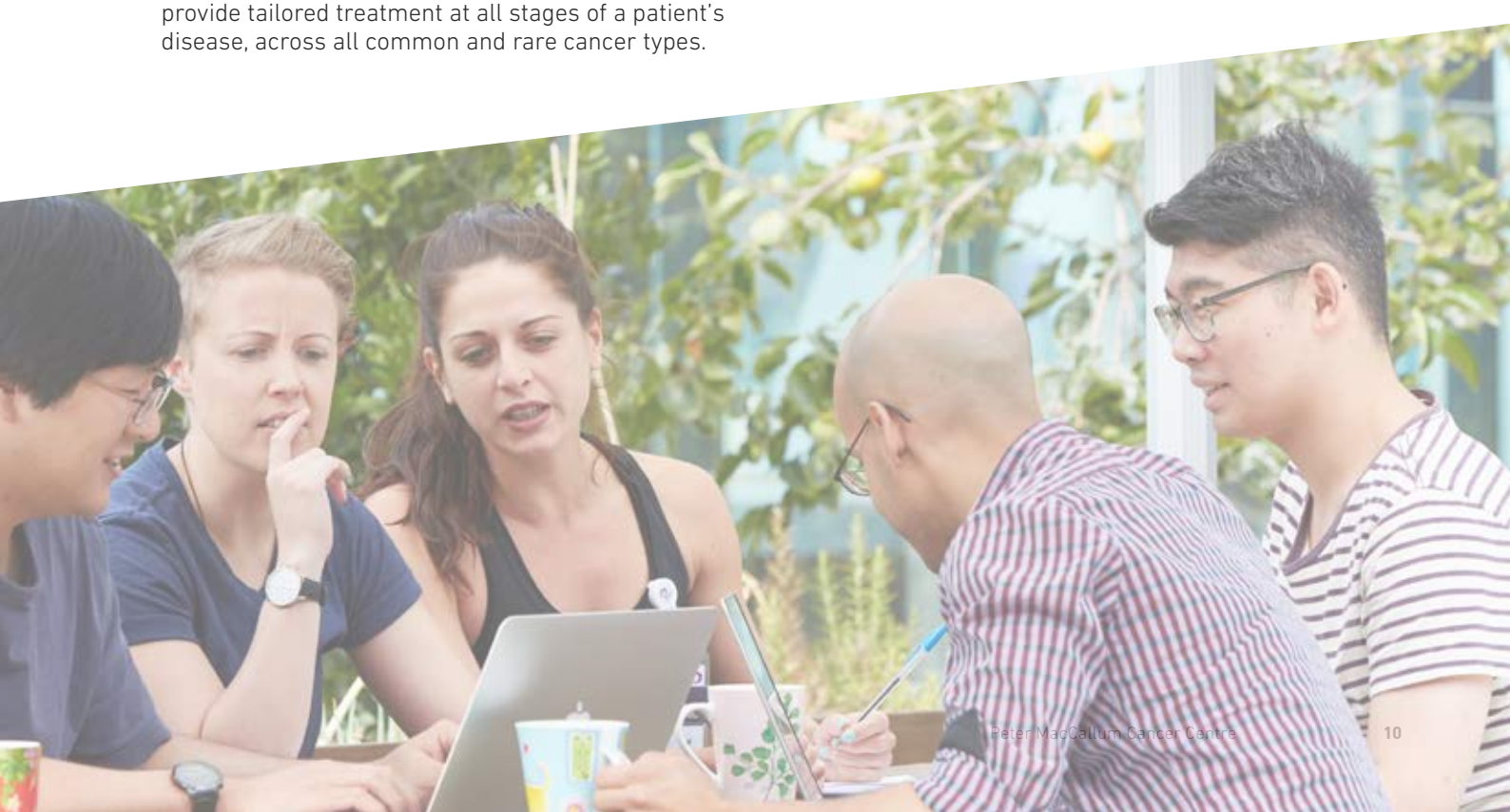
- the largest cancer research group in Australia, with laboratory-based researchers and clinicians working side-by-side;
- a strong academic program, driven by internationally renowned laboratory and clinical researchers, with a strong focus on educating future generations of cancer researchers;
- highly 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 recently approved Comprehensive Cancer PhD program, described in the following section.



COMPREHENSIVE CANCER PhD PROGRAM

The Comprehensive Cancer PhD program (The University of Melbourne) supports the acad 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 fulfill 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 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 transferrable 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**

- **Annual Thesis Bootcamp**

- **Topics in Cancer Seminar program**, with recent topic themes including:
  - Cancer Immunotherapy;
  - Oncogenes and Tumour Suppression;
  - Pillars of Cancer Care

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

For further information, email: ccphd@petermac.org

THE UNIVERSITY OF MELBOURNE

Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

VICTORIAN COMPREHENSIVE CANCER CENTRE

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

BECOMING A STUDENT AT PETER MAC

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

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

Students must:

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

2. Meet the University degree eligibility and entry requirements.

Postgraduate students

Applicants for postgraduate student positions at Peter Mac enrol through a University program that approves your project placement at Peter Mac. You must therefore satisfy the minimum entry requirements at the university through which they 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 phone or 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 univeristy eligibility requirements for postgraudate degree candidature.
- Apply for candidature at The University of Melbourne or at an equivalent university when supervisor and project are confirmed. Univeristy 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.

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 phone or 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 mulitdisciplinary and multicultural student cohort is at the heart of our research excellence.

WHAT ARE THE CAREER DESTINATIONS FOR OUR GRADUATES?

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.

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.

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

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.

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

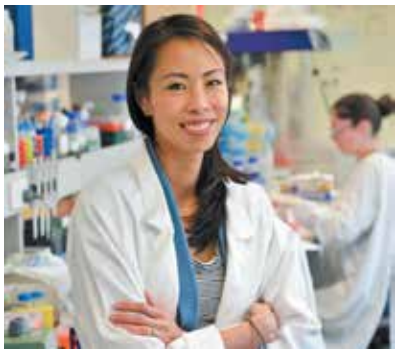
Collaborative interaction with national and international peers is a lynchpin of any vibrant program.

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.

"To make serious inroads against breast cancer, we are working to better understand its genetic make-up, how cancer genes can affect the effectiveness of breast cancer therapies, and how cancer genes alter over time."



Clinician-researcher Dr Sherene Loi completed her PhD in McArthur Lab at Peter Mac during the decade she spent at the prestigious Institute Jules Bordet in Brussels, Belgium. Returning to Peter Mac in 2013, she now heads the Translational Breast Cancer Genomics Laboratory, and will lead a number of international clinical trials of new combinations of therapies to promote enduring survival for women with HER2-positive breast cancer.

Prof. Sherene Loi

Consultatn Medical Oncologist, Breast Cancer Service; Group Leader, Research Faculty; National Breast Cancer Foundation Endowed Chair.

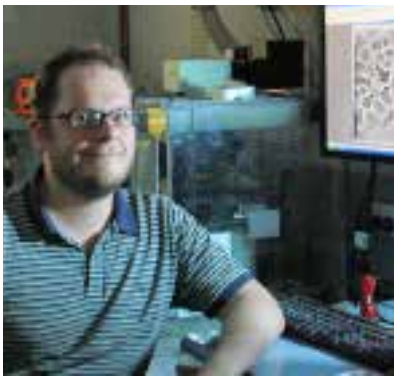
"Peter Mac's Department of Oncology provided a unique opportunity to balance patient-focused research with clinical practice and access to a supportive network of engaging supervisors."

Ben is an infectious diseases physician with primary clinical and research interests in the area of infections in cancer patients. He completed his PhD in advancing the management of infection in patients with myeloma through the Peter MacCallum Department of Oncology. He has continued progressing novel approaches utilising functional and numerical immune profiling to predict risk of infection in patients with cancer as a post-doctoral clinical research fellow at Peter MacCallum Cancer Centre.

Dr Ben Teh

Infectious Diseases physician, Peter MacCallum Cancer Centre. Recipient: 2018 Premier's Award for Clinical Research.

"I chose to study at the Peter Mac because not only does it have world class researchers working in conjunction with some of Australia's best clinical partners, but it also has the benefit of world leading core facilities run by experienced, knowledgable and friendly staff."



Alex commenced his PhD in 2014 after several years as a Research Assistant at Peter Mac. An important aspect of his reseach was made possible by the Advanced Micrsocopy Core facility, where Alex used live-cell microsocopy to investigate the biology of chimeric antigen receptor (CAR) T cells interacting with tumor target cells.

Dr Alex Davenport

PhD Student, Neeson & Darcy Labs.
Awarded a Fight Cancer PhD Scholarship through Melbourne Health.
Now a Postdoctoral Research at the Unversity of Cambridge, UK.

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: PhD/postgraduate, Honours.

For more information about this project contact:

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BOUSSIOUTAS, ALEX

GASTROINTESTINAL CANCER PROGRAM

Twist as a regulator of EMT in gastric cancer and its role in invasion

Supervisors: Prof. Alex Boussioutas, Dr. Rita Busuttil

Gastric cancer (GC) is often diagnosed at advanced stages, giving patients a 5-year survival of less than 20%. Advanced stage GC is directly correlated with increased local invasion of the cancer through the gastric wall and, at more advanced stages into adjacent structures Epithelial Mesenchymal Transition (EMT) is one mechanism which has been proposed as a modulator of invasion in GC as well as other cancer types.

This project seeks to expand on previous work in our laboratory exploring the role of TWIST, a master regulator of EMT, in gastric cancer. We have previously shown that TWIST is more highly expressed at the invasive front of the tumor compared to its core indicating that EMT is occurring in this area. It is conceivable that reducing TWIST expression could be used as a means to decrease the invasive capacity of a cancer. This project will aim to further explore the role of TWIST in the invasion of GC and its potential utility as a therapeutic target. A broad range of techniques including bioinformatics, cell culture, shRNA lentivirus mediated gene knockdown, and molecular biology will be applied.

Key Words: Gastric Cancer; Cancer Diagnosis; Cancer Genetics; Genomics; Upper Gastrointestinal Cancers.

Target Students: PhD/postgraduate, Honours.

Functional characterisation of genes involved in progression of gastric cancer

Supervisors: Prof. Alex Boussioutas, Dr. Rita Busutti

Gastric cancer (GC) is the fourth most common cancer globally. It has defined premalignant stages and progresses through Intestinal Metaplasia (IM) in the majority of cases. GC is diagnosed at advanced stage resulting in poor prognosis. Part of this is due to no means to identify and screen persons at risk of GC. Relatively little is known about the key genetic events leading to IM. Our laboratory is currently in the process of completing the first comprehensive analysis of IM in the world and we have identified a number of candidate genes which are likely to be involved in the progression of IM to GC. These could potentially be used to reliably predict the progression to GC in humans enabling clinical stratification of individuals into high-risk groups. This project would involve functional validation of these candidates using cell culture and organoid model systems

Key Words: Cancer Cell Biology, Gastric Cancer; Cancer Genetics; Genomics; Cancer Prevention, Organoid, Molecular Biomarkers, Upper Gastrointestinal Cancers.

Target Students: PhD/postgraduate, Honours.

Role of the tumour microenvironment in gastric cancer

Supervisors: Prof. Alex Boussioutas, Dr. Rita Busuttil

Gastric cancer (GC) is the fourth most common cancer globally and 7th in incidence in Australia. It has a poor survival rate which can be attributed to the advanced stage at diagnosis in most patients. The molecular and cellular mechanisms underlying the development of GC are not well described. Traditionally cancer research involved studying the cancer cell itself. More recently, there has been growing interest in studying the normal cells and molecules which surround the cancer cell. This tumor microenvironment consists of a variety of stromal cell types including cells such as fibroblasts. It is believed that

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the dynamic communication between tumor cells and the surrounding cell types may play a major role in cancer initiation, progression and establishment of metastatic disease.

The aim of this project is to investigate tumor-stromal interactions in gastric cancer utilizing established and primary cell lines. Once the molecular pathways by which a tumor cell progresses has been elucidated it is possible that these processes could be exploited in the development of novel therapeutics. Our previous genomic experiments have provided a number of exciting candidate genes that may be involved in this interaction. This is novel research that may have a major benefit to our understanding of cancer and improve patient outcomes.

Key Words: Gastric Cancer; Tumour Microenvironment; Cancer Diagnosis; Cancer Genetics; Genomics; Upper Gastrointestinal Cancers.

Target Students: PhD/postgraduate, Honours.

Investigating the innante and adaptive immune response in gastric cancer

Supervisors: Prof. Alex Boussioutas, Dr. Rita Busutti

Cancer is a disease involving complex interactions of the tumor cell along with a multitude of other cell types, including immune cells, which comprise the tumor microenvironment. It is this cross-talk that promotes cancer growth, invasion and metastasis. The immune system consists of an integrated system with two major components: the innate and adaptive response systems. Our laboratory is interested in examining the role of immune system in the context of gastric cancer (GC). We have individually characterized the spatial distribution of cells comprising both the innate and adaptive immune system.

This project aims to integrate these data to help elucidate the degree of cross talk between the two systems and to validate the findings using in vitro and in vivo model systems with the ultimate aim of developing novel therapeutic strategies for treating GC

Key Words: Cancer Cell Biology, Cancer Immunology, Immunotherapy, Innate Immunity, Terapeutics, Upper Gastrointestinal Cancers.

Target Students: PhD/postgraduate, Honours.

For more information about these projects contact:

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BOWTELL, DAVID

CANCER GENETICS AND GENOMICS PROGRAM

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

Pre-Clinical Models of Cyclin E1 Amplified High-Grade Serous Ovarian Cancer

Supervisors: Prof. David Bowtell, Dr. Jessica Beach

Despite aggressive surgery and chemotherapy, a majority of women with high-grade serous ovarian cancer (HGSC) recur. We have shown that amplification of the cyclin E1 gene (CCNE1) is associated with primary chemotherapy resistance in HGSC.

Honours project: Human HGSC cell lines will be used to evaluate the effectiveness of several small molecule inhibitors targeting cyclin E1 and/or its binding partners. The information obtained is important to the development of a currently funded clinical trial in patients with CCNE1 amplified tumors. Experimental techniques will include cell culture, qRT-PCR, drug sensitivity assays, and western blot analysis.

PhD project: Development and characterisation of patient derived xenografts and genetically engineered mouse models of CCNE1 amplified HGSC. Transgenic mice with 3 different knock-in alleles have already been generated by our lab. The study will also involve large-scale functional and genomic studies including high-throughput drug screens and next generation sequencing. Skills will be obtained in mouse genetics, tumour biology, somatic cell genetics, human genomics and bioinformatics.

Key words: Cancer Genetics, Genomics, Gynaecological Cancers

Target Students: PhD/postgraduate, Honours

For more information about this project contact:

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Dr. Jessica Beach
jessica.beach@petermac.org.

Analysis of heterogeneity and chemotherapy resistance in ovarian cancer

Supervisors: Prof. David Bowtell, Dr. Liz Christie, Dr David Goode

An excellent opportunity exists for a student wishing to pursue a Masters or PhD in computational biology and cancer genomics to investigate the effects of intratumoural heterogeneity in chemotherapy resistance in ovarian cancer using large next-generation sequencing data sets.

We are currently performing whole genome and single cell sequencing of tumour samples collected from patients at recurrence or autopsy to further our understanding of how high grade serous ovarian cancer, the most common histotype of ovarian cancer, evolves to become resistant to chemotherapy. In 2015, we published the largest whole genome analysis of high-grade serous ovarian cancer

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and described 4 mechanisms of acquired chemotherapy resistance (Patch et al Nature).

The project will involve analysis and integration of whole genome and RNA sequence data to (1) identify resistance mechanisms, (2) understand their heterogeneity within and between patients, and (3) examine how tumour subclones interact and evolve over time in response to chemotherapy. The project will involve using existing methods and development of new tools to identify changes driving chemotherapy resistance, to estimate tumour heterogeneity, and characterize evolution in ovarian cancer.

Key words: Bioinformatics, Cancer Genetics, Genomics, Gynaecological Cancers

Target Students: PhD/postgraduate

For more information about this project contact:

Prof. David Bowtell david.bowtell@petermac.org

Dr. Liz Christie liz.christie@petermac.org

Dr David Goode david.goode@petermac.org

Genomic determinants of long-term survival in high-grade serous ovarian cancer

Supervisors: Prof. David Bowtell, Dr. Dale Garsed, Dr. Jessica Beach

High-grade serous ovarian cancer (HGSC) 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 (AOCS), our laboratory is currently completing the world's first whole-genome and transcriptome analysis of HGSC tumours from 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, molecular biology techniques, genomics and bioinformatics..

Key words: Cancer Cell Biology, Cancer Genetics, Genomics, Gynaecological Cancers, Molecular Biomarkers,

Target Students: PhD/postgraduate

For more information about this project contact:

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Dr. Dale Garsed dale.garsed@petermac.org

Dr Jessica Beach jessica.beach@petermac.org

BRITT, KARA

CANCER GENETICS AND GENOMICS PROGRAM

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

Developing breast cancer preventatives by mimicking parity's protective role

Supervisor: Dr. Kara Britt

Women who have children (parous) have a reduced risk of breast cancer and this protection is strongest for those bearing children early. Women having children later in life are not protected against breast cancer, but instead at an increased risk. We have developed a mouse model to determine the role of mammary stem cells and stromal fibroblasts in parity-induced protection and will now test therapies aimed at modulating these cells.

Finding a therapy for triple negative breast cancer patients

Supervisors: Dr. Kara Britt, Prof. Robin Anderson, Prof. Kelly Phillips

Triple negative breast cancers are a poor prognosis breast cancer with limited therapeutic options as they do not express estrogen receptors, progesterone receptors or Her2. Recent clinical studies have shown that women who have triple negative breast cancers, but also express the alternate estrogen receptor, ERβ, respond well to Tamoxifen. We will use our mouse model of triple negative breast cancer, engineered to express ERβ, to determine how Tamoxifen exerts is benefits to these patients. This project will involve RNA sequencing of tumours.

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.

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

BROWN, KRISTIN

CANCER THERAPEUTICS PROGRAM, & CANCER METABOLISM PROGRAM

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

Metabolic reprogramming and chemotherapy resistance in triple-negative breast cancer

Supervisor: Dr. Kristin Brown

Treatment options for the triple-negative breast cancer (TNBC) subtype of breast cancer are limited to conventional chemotherapy agents. Chemotherapy resistance is a major barrier to the successful treatment of TNBC. There is a critical need to identify novel and actionable strategies to circumvent resistance and enhance the efficacy of chemotherapy.

There has recently been renewed interest in understanding how reprogramming of cell metabolism promotes tumourigenesis. Our studies suggest that metabolic reprogramming 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 when TNBC cells are exposed to chemotherapy, 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: PhD/postgraduate, Honours.

For more information about these projects contact:

Dr. Kristin Brown kristen.brown@petermac.org

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

Supervisors: Dr. Kristen 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: PhD/postgraduate, Honours.

For more information about these For more information about this project contact:

Dr. Kristin Brown kristen.brown@petermac.org

Dr. Andrew Cox andrew.cox@petermac.org

Elucidating the protein interaction network 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: PhD/postgraduate, Honours.

For more information about these projects contact:

Dr. Kristin Brown kristen.brown@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP

CHENG, LOUISE

ORGANOGENESIS AND CANCER PROGRAM, & CANCER METABOLISM PROGRAM

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

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 participating in this project 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.

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: PhD/postgrduate, Honours.

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: PhD/postgraduate, Honours.

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. This project will be jointly supervised by Louise Cheng (Peter Mac) and Christen Mirth (Monash). The techniques will involve: immunohistochemistry, tissue microdissection, metabolite measurements.

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

Target Students: PhD/postgraduate.

For more information about these projects contact:

Dr. Louise Cheng

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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: PhD/Postgraduate, Honours.

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: PhD/Postgraduate, Honours.

For more information about these projects contact:

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DARIDO, CHARBEL

CANCER THERAPEUTICS PROGRAM

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

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

Supervisor: Dr. Charbel Darido, Dr. Fiona Tan

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.

Here 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.

A wide range of skills will be taught including molecular biology, biochemistry, cell culture and knockout mice.

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

Target Students: Honours

Predicting the development of oral cancer

Supervisor: Dr. Charbel Darido, Dr. Fiona Tan

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

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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

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

Target Students: PhD/Postgraduate, Honours

Identification of the cell of origin of Grhl3-deficient head and neck squamous cell carcinoma

Supervisor: Dr. Charbel Darido

Head and neck squamous cell carcinoma (HNSCC) is the sixth leading cancer by incidence worldwide. The lack of appropriate animal models prevents the establishment of improved treatment options for HNSCC patients. The hosting laboratory has recently identified a novel factor, Grhl3, critical for tumour suppression in HNSCC in mice and humans.

Through the use of unique HNSCC mouse models that are driven by the exact cancer-causing molecular drivers found in patients, this project will enable delineation of the origin of HNSCC and testing of targeted therapies. Predicted outcomes have the potential to stratify treatment in HNSCC based on underlying molecular signatures.

A wide range of skills will be taught including molecular biology, biochemistry, cell culture and knockout mice.

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

Target Students: Honours.

For more information about these projects contact:

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Dr. Fiona Tan fiona.tan@petermac.org

DAWSON, MARK

TRANSLATIONAL HAEMATOLOGY PROGRAM

https://www.petermac.org/research/labs/mark-dawson

Discovering novel epigenetic therapies in Acute Myeloid Leukaemia

Supervisors: Dr. Omer Gilan, Prof. Mark Dawson

Acute leukemia is a devastating disease with a poor prognosis. The epigenetic enzyme, MLL, is translocated in around 70% of infantile leukaemia and 10% of adult leukaemia. These MLL-translocated leukemias display a poor response to conventional chemotherapy treatment, highlighting the urgent need for better targeted therapies for this aggressive disease. We have recently shown that this subtype of leukemia is particularly sensitive to inhibition of two key epigenetic proteins, BRD4 and DOT1L. However, targeting of these epigenetic proteins does not directly disrupt the MLL-fusion proteins and therefore results in many undesirable effects that limit the efficacy and increase the side effects of these treatments. The laboratory has recently been able to identify, at high resolution and on a genome-wide level, the subset of genes that are directly bound and regulated by MLL-fusion proteins. This has given us an unprecedent opportunity to uncover the mechanisms that regulate the recruitment and transcriptional activity of these potent oncoproteins.

We have a number of projects that utilize cutting edge molecular biology techniques, CRISPR-Cas9 technology and Leukaemia mouse models to provide insight into the intitiaton and progression of MLL-fusion driven leukaemia and potentially develop novel therapeutic approaches.

Key Words: Epigenetics (incl. Genome Methylation and Epigenomics), Haematology, Molecular Biology.

Target Students: Honours

For more information about these projectrs contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

ELLIS, SARAH

CENTRE FOR ADVANCED HISTOLOGY AND MICROSCOPY, & CANCER IMMUNOLOGY PROGRAM

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

Role of the Polarity Proteins, SCRIB and PAR3, in leukemia

Supervisors: A/Prof. Sarah Ellis, A/Prof. Phil Darcy

According to the Leukaemia Foundation, at least one Australian is diagnosed with leukemia or lymphoma every hour yet the cause of these blood cancers remains relatively unidentified. The evolutionary conserved polarity proteins, Partition Defective 3 (PAR3) and Scribble (SCRIB) act as tumour suppressors or tumour promoters in a variety of epithelial cancers yet their function in leukemia is largely unknown and is the focus of our laboratory.

We utilise conditional knockout mouse models to investigate how loss of PAR3 and/or SCRIB impact steady-state blood production and leukemia. Cutting edge technologies are employed to determine the intracellular signaling pathways that are deregulated upon loss of one or both of these polarity proteins. Depending upon the length of candidature, techniques will include RNAseq, quantitative reverse transcription PCR (RT-qPCR), multi-color flow cytometry, multiplex immunohistochemistry, and high content western blotting.

Changes in the bone marrow microenvironment during the development of leukemia in the presence or absence of SCRIB and/or PAR3 will be examined using state-of-the-art intravital microscopy. Importantly, expertise in all these methodologies exists within the laboratory or within Peter Mac's outstanding core facilities.

These pre-clinical studies will highlight the role of SCRIB and PAR3 in the onset and progression of leukemia with the ultimate aim of generating novel chemotherapeutic targets.

Key Words: Cancer Cell Biology; Cancer Epigenetics; Cancer Signalling; Cancer Therapy; Cell Cycle; Cell Growth, Proliferaiton and Death;. Cellular Immunity; Differentiation; Haematology; Haematological Cancers; Innate Immunity; Tumour Immunology; Tumour Suppression.

Target Students: PhD/Postgraduate, Honours

For more information about these projects 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: Dr. 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 problematical 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: PhD/Postgraduate, Honours.

Understanding mucinous ovarian cancer

Supervisors: Dr. Kylie Gorringe

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 a cohort of ~200 mucinous tumours, remarkable for such a rare disease, including with clinical, immunohistochemical, gene expression and genomics data (sequencing and copy number). We are also currently developing organoid and PDX models from primary patient material with which to test therapies.

Further investigations will be undertaken to understand the interaction of our research findings with clinical behaviour and response to treatment – this will be tailored to the interest of the student but could include bioinformatics/ data analysis, cell culture and drug screening and genetic analysis. Students with an interest in bioinformatics are especially encouraged to apply.

Key Words: Bioinformatics, Cancer Genetics, Gynaecological Cancers, Solid Tumours, Therapeutics.

Target Students: PhD/Postgraduate, Honours.

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AVAILABLE PROJECTS BY RESEARCH GROUP

HARVEY, KIERAN

ORGANOGENESIS AND CANCER PROGRAM

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

Control of tissue growth and cancer by the Hippo pathway

Supervisors: Prof. Kieran Harvey, Dr. Carole Poon

Our laboratory is focused on determining how the Hippo signalling pathway controls tissue growth during development and in cancer. The Hippo pathway is the most recently identified major signalling pathway and is a key regulator of organ size. We and others also discovered that the Hippo pathway is deregulated in many human cancers.

We currently have several different projects available aimed at studying the mechanism by which the Hippo pathway controls organ size and cancer, using an array of genetic, cell biological and biochemical techniques. The aims of our laboratory are to:

(1) Understand how the Hippo pathway controls organ size during development.

(2) Define the role of Hippo pathway in human cancers.

(3) Develop drugs to target the Hippo pathway for therapeutic benefit.

A broad range of cutting-edge techniques will be used, including confocal microscopy, immunohistochemistry, Drosophila genetics, molecular biology, cell biology. All techniques are routinely used by the laboratory and training will be provided. Our laboratory is looking for intelligent, motivated Honours students to join our team. You should have a willingness to learn a number of different biological techniques, and be able to integrate into a close team environment.

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

Target Students: Honours.

For more information about this project contact:

A/Prof. Kieran Harvey kieran.harvey@petermac.org

Watching the Hippo pathway in real time in growing organs

Supervisors: Prof. Kieran Harvey, Dr. Carole Poon

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.

You 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.

You 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.

You 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, Honours.

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

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: Dr. Sue Haupt, Prof. Ygal 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.

This project 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,

For more information about this project contact:

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Dr. Sue Haupt sue.haupt@petermac.org

Defining the role of p53 in cancer immunotherapy

Supervisor: Prof. Ygal Haupt, A/Prof. Paul Neeson

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: Bioinformatics; Cancer Cell Biology; Gene Expressions; Cancer Therapy; Genomics; Proteomics and Intermolecular Interactions; Tumour Suppression.

Target Students: PhD/postgraduate,

For more information about this project contact:

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A/Prof. Paul Neeson paul.neeson@petermac.org

HICKS, RODNEY

CANCER THERAPEUTICS PROGRAM

https://www.petermac.org/research/labs/rodney-hicks

Understanding the mechanisms of neuroendocrine tumour response to radionuclide therapy

Supervisors: A/Prof. Carleen Cullinane, Prof. Rod Hicks

Neuroendocrine tumours (NET) represent a heterogeneous group of tumours that arise in specialized cells found throughout the body. Peptide receptor radionuclide therapy (PRRT) is an emerging treatment modality for NET that involves the use of radiolabelled peptides to target the somatostatin receptor which is widely expressed on neuroendocrine cells. Despite its encouraging clinical activity, significant variability in tumour response to PRRT has been observed. These findings highlight the need to understand the mechanisms underlying tumour response to PRRT in order to identify better methods to select patients for treatment and to develop novel combination therapies to overcome resistance.

The aims of the project are to investigate the determinants of response to PRRT using a wide range of in vitro and in vivo techniques including cell culture, organoid culture, molecular biology, preclinical models of cancer and imaging.

Key Words: Cancer Cell Biology; Molecular Imaging; Molecular Targets; Radiation Therapy.

Target Students: PhD/postgraduate.

For more information about this project contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

JOHNSTONE, RICKY

TRANSLATIONAL HAEMATOLOGY PROGRAM

Investigating the role of CDK11 in haematological malignancies

Supervisor: Prof. Ricky Johnstone, Dr. Jennifer Devlin

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 analogue-sensitive CDK11 mutant which can be inhibited by a ATP-competitive inhibitory analogue and; ii) an auxin-inducible degradation CDK11 mutant.

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:

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Dr. Jennifer Devlin jennifer.devlin@petermac.org

KATS, LEV

TRANSLATIONAL HAEMATOLOGY PROGRAM

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

Development of targeted therapy for acute myeloid leukaemia with mutations in isocitrate dehysdrogenase

Supervisor: Dr. Lev Kats

Acute Myeloid Leukaemia (AML) is an aggressive disease with poor prognosis and development of novel treatment options is urgently needed. Isocitrate Dehydrogenase (IDH)-1 and -2 catalyse the conversion of isocitrate to a-ketoglutarate (a-KG), a crucial metabolite that is an intermediate in the TCA cycle and an essential co-substrate for >60 enzymes with a wide range of functions. IDH1 and -2 mutations occur in ~20% of AML as well as a range of other cancers and pre-malignancy syndromes. Mutations typically confer on the enzymes a novel ability to produce D-2-hydroxyglutarate (2-HG), a molecule that is structurally similar to a-KG and can act as an inhibitor or activator of a-KG-dependent enzymes.

We and others have recently shown that IDH mutations can contribute to leukaemia initiation and maintenance both in vitro and in vivo; and small molecule inhibitors that block production of 2-HG have recently entered clinical trials. However, the precise mechanism and genetic determinants of therapy response to IDH inhibition remain unknown.

The specific aims of this study are to:

(1) Develop clinically relevant, genetically engineered murine AML models wherein expression of mutant IDH is inducible;

(2) Evaluate the requirement for continued expression of mutant IDH for prolonged leukaemia growth and survival by genetically depleting expression (genetic de-induction) and pharmacologically inhibiting the mutant enzymes; and

(3) Understand the mechanism of disease regression following genetic de-induction and pharmacological inhibition of mutant IDH.

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

Target Students: PhD/postgraduate, Honours.

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AVAILABLE PROJECTS BY RESEARCH GROUP

LOI, SHERENE

CANCER THERAPEUTICS PROGRAM.

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

Understanding host anti-tumour immunity in preclinical models of breast cancer: biological interactions and mechanisms of PIK3CA mutations

Supervisors: Prof. Sherene Loi, Prof Wayne Phillips, Dr. Joyce Teo

We have characterised the alterations in 286 cancer-related genes in 538 luminal (estrogen receptor positive) breast cancer tumours from post-menopausal patients.

Overall, 28 genes were somatically altered at a frequency of >10%, with the most commonly mutated being PIK3CA. Interestingly, greater than 90% of PIK3CA mutations co-existed with another alteration. Additionally, we have found that the co-existence of alterations in PIK3CA together with certain genes significantly affected overall clinical outcome and response to treatment.

The biological interaction of these altered genes and the biological mechanism underlying their effect on tumour progression, metastasis and response to treatment is unknown. We propose to delineate these mechanisms/interactions, with use of genetic manipulation, in luminal breast cancer cell lines and xenografts in vitro and in vivo. Results from this project will guide future clinical trials of targeted-therapies in luminal breast cancer.

Students will learn about breast cancer biology, cell signaling, immunology, cell culture, mouse handling, therapeutics, flow cytometry, western botting, RT-PCR and genomic techniques.

Key Words: Breast Cancer; Cancer Genetics; Cell Biology; Bioinformatics; Genomics; Personalised Medicine.

Target Students: PhD/postgraduate, Honours.

For more information about this projects contact:

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Evolution of lethal breast cancer: understanding critical genomic and immune alterations in primary and metastatic breast cancer

Supervisors: A/Prof. Sherene Loi

Understanding the cancer genome is seen as a key step in improving outcomes for cancer patients. However, evolution of the cancer genome and how it evades host immunity during the natural history of lethal breast cancer is largely unknown.

The lab is studying in detail tumor and blood samples from human patients with primary and advanced breast cancers to answer these questions. We use a wide variety of cutting edge techniques including single cell sequencing technologies, CyTOF, flow cytometry and next generation sequencing. Validation of results may also occur, in vivo or in vitro as well as examining and developing novel therapeutics (such as immunotherapies).

We are looking for highly motivated students interested in cancer research: these projects may be focused on specific areas such as bioinformatics (honours and post graduate), immunology (post graduate) or cancer therapeutics (post graduate) or broadly encompass all areas.

Key Words: Applied Immunology (incl. Antibody Engineering, Xenotransplantation and T-cell Therapies), Bioinformatics, Breast Cancer; Cell Biology, Immunogenetics (incl. Genetic Immunology), Molecular Biuomarkers, Molecular Oncology, Tumour Immunology.

.Target Students: PhD/postgraduate, Honours.

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

https://www.petermac.org/research/labs/grant-mcarthur-0

Inhibition of PRMT5 as a cancer therapy

Supervisors: Dr. 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

AVAILABLE PROJECTS BY RESEARCH GROUP

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, Honours.

For more information about these projects contact:

Dr. Karen Sheppard karen.sheppard@petermac.org

Impact of targeted therapy on the melanoma immune microenvironment

Supervisors: Dr. Karen Sheppard, Prof. Grant McArthur

The treatment of melanoma is undergoing a fundamental change due to the success of both targeted therapies directed at the MAPK/ERK pathway and immunotherapies. Targeted therapies block essential cell signalling pathways that are required for tumour cell proliferation and survival, while immunotherapies promote the patient's own immune system to eliminate the cancer cells. Both approaches have their limitations. Targeted therapies initially elicit excellent tumour regression, but this response is generally short-lived due to the development of resistance. In contrast, immunotherapies lead to sustained tumour regression but are only effective in a small number of patients.

The difference in patient responses to these therapies suggests that the two approaches might have complementary roles in cancer treatment, and there are currently several clinical trials combining targeted and immune therapies. Targeted therapies can also enhance or diminish immune responses, thus understanding the effect of targeted therapies on immune cells is essential in advancing the combination of these agents into the clinic. Using melanoma cell lines, mouse models and patient samples, we are currently investigating the direct effect of these targeted therapies on immune cell function and how these targeted therapies impact on current immunotherapies.

This Honours/PhD project will initially assess the impact of several targeted therapies as single agents or in combination on tumour immunogenicity and on immune cell proliferation and function

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

Target Students: Honours.

For more information about this project contact:

Dr. Karen Sheppard
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MYC: oncogenic sensitisation of cancers to therapeutic inhibition of RNA polymerase I transcription

Supervisors: Dr. Gretchen Poortinga, Prof. Rick Pearson, Prof. Grant McArthur

Accelerated RNA polymerase I (Pol I) transcription of the ribosomal RNA genes is a common feature of many cancers. We have demonstrated that selective inhibition of Pol I transcription (via CX-5461) exclusively kills malignant cells and provides a significant survival benefit in preclinical cancer models. CX-5461 is now in a phase 1 clinical trial in haematologic malignancies (Peter Mac); however, our understanding of what drives sensitivity to Pol I transcription therapy is still unclear and presents a critical hurdle to predicting which patients will respond to CX-5461 in the clinic.The MYC oncoprotein and transcription factor is dysregulated in a majority of cancers and considered a major driver of malignancy. MYC plays a fundamental role in regulating Pol I transcription and ribosome biogenesis, a ubiquitously required cell process necessary for cancer cell survival. Our data in a MYC-driven model of lymphoma suggests that the MYC oncogene sensitises tumour cells to Pol I transcription inhibition and this is supported by preliminary data across several cancer types and in comparison to another critical oncogene, RAS.

This project will use isogenic cell lines/other model systems and a range of techniques to explore the interplay between oncogenic MYC function and heightened response to Pol I transcription therapy.

Key Words: Cancer Cell Biology; Cell Growth; Epigenetics (incl. Genome Methylation and Epigenomics) ; Gene Expression ; Gene Regulation; Molecular Oncology; Therapeutics; Transcription.

Target Students: PhD/postgraduate, Honours.

For more information about this project contact:

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Novel drug combinations targeting chromatin and RNA polymerase I transcription in multiple myleloma

Supervisors: Dr. Gretchen Poortinga, A/Prof. Simon Harrison, Prof. Grant McArthur

Multiple myeloma (MM) is an incurable cancer with currently available therapies. Single agent therapies rapidly lead to the development of drug resistance and clinical relapse, therefore combination therapies are necessary to provide a more durable response. Growing evidence supports that epigenetic dysregulation, i.e. abnormalities that impair DNA/chromatin function, is an important feature in MM development. Moreover, there are promising novel drugs that target these epigenetic factors entering the clinic for the treatment of MM, presenting an opportunity for investigation of innovative combination therapies.

Our preclinical studies established that selective inhibiton of RNA polymerase I (Pol I) transcription of the ribosomal genes provides a novel therapeutic window in many cancer types. We have intriguing data demonstrating that combining Pol I inhibition with several candidate "epi-drugs" elicits a surprisingly high level of synergy in models of MM.

Based on this impressive synergy, this Hons/PhD project aims to conduct epi-drug and genetic screens to not only identify novel drug targets but also uncover key

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chromatin factors driving the efficacy of these drug class combinations. We will use multiple approaches, including genome-wide, to interrogate the underlying mechanisms of synergy followed by validating promising combinations in mouse models to rapidly progress these findings towards the clinic.

Key Words: Cell Growth; Epigenetics (incl. Genome Methylation and Epigenomics) ; Gene Expression ; Gene Regulation; Haematological Cancers; Therapeutics; Transcription.

Target Students: PhD/postgraduate, Honours.

For more information about this project contact:

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Functional genomics of BRAF driven glycolysis in BRAFV600 melanoma

Supervisors: Dr. Lorey Smith, Prof. Grant McArthur

It has long been appreciated that cancer cells must rewire their metabolism in order to satisfy the demands of growth and proliferation. In aerobic conditions normal cells metabolize glucose through the tricarboxylic acid (TCA) cycle, whereas cancer cells metabolize glucose to lactate using a process known as aerobic glycolysis. More recently it has emerged that altered tumour metabolism lies downstream from various oncogenes or tumour suppressors such as RAS, PI3K, MYC and LKB1.

Our laboratory and others have now demonstrated that BRAFV600 regulates glycolysis in melanoma, and importantly, that BRAF inhibition via vemurafenib can suppress this glycolytic response. In order to further explore BRAF-mediated glycolysis in melanoma and how this relates to its anti-proliferative effects, we have now performed a whole genome siRNA screen to identify enhancers of BRAF inhibition within the context of viability and glycolysis in BRAFV600 melanoma cells. For this enhancement screen, WM266.4 cells were transfected with the human genome siRNA library and subsequently treated with either DMSO or vemurafenib in parallel for 48hrs. Both melanoma cell viability and glycolytic responses, as indicated by lactate production per cell, were assessed using a multi-parameter imaging and colorimetric screening approach. This Honours project will involve the functional validation and characterization of novel genes and pathways that were identified by the screen.

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

Target Students: Honours.

For more information about this project contact:

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OLIARO, JANE

CANCER IMMUNOLOGY PROGRAM

https://www.petermac.org/research/labs/jane-oliaro

Enhancing anti-tumour immune responses

Supervisor: Dr. Jane Oliaro, Dr. Conor Kearney

Immunotherapy is a new approach to treat cancer, and works by promoting the immune system to attack cancer. Immunotherapies, such as checkpoint blockade and adoptive T cell therapy, are proving to be very successful in certain human cancers. However, not all cancers are responsive to immunotherapy and combining immune-based therapies with drugs that cause direct cancer cell death may be more effective. Resistance to immunotherapy is also an issue, and identifying pathways that are modulated by tumour cells to avoid attack by the immune system is critical for optimising immunotherapy approaches.

We have projects available in the laboratory to investigate the potential of combining immunotherapy with novel anti-cancer drugs to enhance anti-tumour immune responses, in order to develop more effective treatments for cancers such as melanoma and breast. We also have projects designed to investigate novel genes and pathways that confer resistance in tumours to T cell mediated attack. The projects involve a strong immunology component, combined with molecular biology, cell biology, imaging and tumour immunology mouse models.

Key Words: Cancer Cell Biology; Cell Signalling; Cellular Immunology; Genetic Immunology; Immunotherapy; Innate Immunity; Skin Cancers (incl. Melanoma); Solid Tumours; Tumour Immunology; Pre-clinical Cancer models; Microscopy; Imaging.

Target Students: PhD/postgraduate, Honours.

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP

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.

Clinical cancer bioinformatics

Supervisor: Prof. Tony Papenfuss, Prof. Stephen Fox

This project will involve developing new bioinformatics methods for improved analysis of cancer gene hybridisation capture panels, particularly in the area of improved copy number analysis, and analysing the thousands of samples that have already been sequenced at Peter Mac.

Key Words: Bioinformatics, Computational biology; Genomics.

Target Students: PhD/postgraduate.

Formation and Evolution of Neochromosomes

Supervisor: Prof. Tony Papenfuss, Dr. Alan Rubin

Neochromosomes are giant super-numerary chromosomes that drive a variety of forms of rare cancer. We have previously shown that in liposarcomas neochromosomes form by a catastrophic process involving chromothripsis and hundreds of breakage-fusion-bridge cycles. Neochromosomes are a fascinating form of mutation and also represent a powerful model to student complex genomic rearrangements. This project will involve the use of short and long read sequencing, other omics, chromosomal imaging and bioinformatics approaches to develop better understanding of the molecular events that allow and direct neochromosome evolution.

Key Words: Bioinformatics, Computational Biology.

Target Students: PhD/postgraduate.

For more information about these projects contact:

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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 these projects contact:

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Dr. David Gyorki david.gyorki@petermac.org

PEARSON, RICK

ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM, & CANCER METABOLISM PROGRAM

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

Characterize the role of Treacle (TCOF1) in AKT-regulated ribosome biogenesis

Supervisors: Dr. Jian Kang, Prof. Rick Pearson

Ribosomes are essential for cell growth and proliferation, and their biogenesis requires exquisite regulation. Aberrant ribosome biogenesis underlies diseases of ribosomes, the so-called "ribosomopathies", and recently it has become evident that deregulated ribosome biogenesis is a characteristic of transformed cells that can be specifically targeted to treat cancer.

We have demonstrated that the kinase AKT mediates RNA Polymerase I (Pol I)-driven ribosomal RNA gene (rDNA) transcription and cooperates with MYC to achieve maximal activation of rDNA transcription, ribosome biogenesis and cell growth. Furthermore, we have identified the nucleolar protein Treacle (TCOF1) is present in the Pol I complex and is a direct AKT substrate. We hypothesized that AKT drives rDNA transcription and ribosome biogenesis through Treacle.

In order to establish phosphorylation of Treacle as a possible mechanism by which AKT regulates rDNA

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transcription, phosphoproteomics, immunoprecipitation, site-directed mutagenesis, real-time PCR, immunoblotting, immunofluorescence techniques will be utilized to uncover a key regulatory role of Treacle in AKT-driven ribosome biogenesis.

Key Words: Cancer Cell Biology; Cell Signalling; Cancer Therapy; Cell Growth; Cell Metabolism; Haematological Cancers; Ribosome Biogenesis.

Target Students: Honours.

For more information about this project contact:

Dr. Jian Kang
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Therapy-induced senescence and stemness in ovarian cancer

Supervisors: Dr. Keefe Chan, Prof. Rick Pearson

Cellular senescence is a stress response characterized by a robust cell cycle arrest and is a brake for malignant transformation. Recent evidence also suggests that senescent cells harbour gene signatures similar to stem cells, which has implications for tumour dormancy and resistance to anti-proliferative cancer therapies.

We have identified putative stemness biomarkers by using transcriptome profiling of oncogene-induced senescent cells. We hypothesise that these biomarkers may also be present in therapy-induced senescent cells and enriched in a therapy-resistant population of cancer cells. 70% of ovarian cancer patients have disease recurrence and emerging evidence suggests that ovarian cancer stem cells contribute to drug resistance and relapse. However, whether therapeutic targeting of ovarian cancer induces senescence and stemness is not well understood.

This project aims to test this hypothesis by utilising quantitative real-time PCR, immunoblotting, immunofluorescence, and flow cytometry techniques to:

1. Characterize the senescence phenotypes of a panel of human ovarian cancer cell lines in response to therapy.

2. Identify the presence of stemness biomarkers in therapy-induced senescent cells.

3. Determine the impact of targeting stemness biomarkers in therapy-induced senescent cells.

Key Words: Cancer Cell Biology; Cell Signalling; Cancer Therapy; Cell Cycle; Cell Growth; Cell Metabolism; Gynaeolcological Cancers; Molecular Oncology; Pharmacogenomics; Skin Cancers (incl. Melanoma); Solid Tumours; SenescenceN.

Target Students: PhD/postgraduate, Honours.

For more information about this project contact:

Dr. Keefe Chan
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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 are planning 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: PhD/postgraduate, Honours.

For more information about this project contact:

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RAMSAY, ROB

GASTROINTESTINAL CANCER PROGRAM

https://www.petermac.org/research/labs/rob-ramsay

Exploring the immunosuppressive microenvironment in colorectal and anal cancer

Supervisors: Dr. Sara Roth, Prof. Rob Ramsay

Immunotherapies have the potential to treat cancer mainly by educating and activating cytotoxic T cells, which are then able to recognize and eliminate the tumour cells. However, other components of the immune system, like myeloid derived suppressor cells (MDSC) and regulatory T cells (Tregs) are known to counteract this pathway, leading to immunotherapy resistance. The aim of this PhD study is to characterise the immunosuppressive microenvironment in colorectal and anal cancer, to explore the influence of current standard therapy, immunotherapy and new investigational treatment regimes. In this project, the student will perform preclinical studies using an innovative in-vitro platform with patient material and mouse models of colorectal and anal cancer. These studies will form the basis for translating the findings into a clinical trial in patients.

Key Words: Cancer; Immunotherapy, Immunosuppression

Target Students: PhD/postgraduate.

For more information about these projects contact:

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RISBRIDGER, GAIL

PROSTATE CANCER PROGRAM

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

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: PhD/postgraduate, Honours.

For more information about this project contact:

Dr. Roxanne Toivanen
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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: PhD/postgraduate, Honours.

For more information about this project contact:

Dr. Luc Furic luc.furic@petermac.org

New human models for rapid preclinical testing of prostate cancer

Supervisor: Prof. Gail Risbridger

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: PhD/postgraduate, Honours.

For more information about this project contact:

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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 ancestory, 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:

Dr. Sarah Russell sarah.russell@petermac.org

TIGANIS, TONY

CANCER METABOLISM PROGRAM

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

Metabolic Reprogramming in Liver Cancer

Supervisors: Prof Tony Tiganis, Dr. Florian Weide

Primary liver cancer is one of the world's deadliest cancers. It is the 5th most common cancer worldwide and represents the 3rd most common cause of cancer death. Hepatocellular carcinoma (HCC) accounts for 90% of primary liver cancers and is refractory to nearly all currently available anti-cancer therapies with a 5 year survival rate of <9%. In Australia HCC represents the most rapidly rising cause of cancer death. Worryingly the incidence of HCC in developed countries has been increasing driven by the obesity epidemic, the associated development of non-alcoholic fatty liver disease (NAFLD) and its progression to the more aggressive non-alcoholic steatohepatitis that results in liver fibrosis/cirrhosis. As the early stages of NAFLD/scarring are asymptomatic, patients with HCC typically present with advanced disease. Standard chemotherapy responses are poor, in most cases having no impact on overall survival rates, whereas the only targeted FDA-approved drug for HCC, Sorafenib (a multi-targeted oral tyrosine kinase inhibitor) prolongs survival by only 2-3 months. Thus there is an urgent need for new therapeutics.

Projects are available to delineate the role of reactive oxygen species (ROS) in tumour development and determine if selectively targeting redox pathways may be effective in suppressing HCC growth and maintenance. In particular we will take advantage of exciting new findings in the cancer field suggesting that the reliance of many tumours on ROS for their growth, may also be their Achilles' heel and that exacerbating the toxic effects of ROS may promote cell death and help eradicate tumours

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

Target Students: PhD/postgraduate, Honours.

For more information about this projects contact:

Prof. Tony Tiganis tony.tiganis@petermac.org

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 this projects contact:

Prof. Tony Tiganis tony.tiganis@petermac.org

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.

For more information about this projects contact:

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TRAPANI, JOSEPH

CANCER IMMUNOLOGY PROGRAM

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

Delineating transcriptional pathways that limit anti-cancer T cell function

Supervisors: Dr. Ian Parish

During cancer growth, cytotoxic T cells that would normally kill cancer cells lose their function in a process called exhaustion. The exhaustion process allows tumour growth, however we still understand relatively little about how the exhausted differentiation state is triggered and maintained. This is an important research area, as the immunotherapy approaches that have demonstrated spectacular success in cancer treatment are mainly thought to work by reinvigorating the exhausted T cell population.

By comparing cytotoxic T cell exhaustion with other processes that limit T cell function, we have identified a number of transcription factors that are critically important for both the exhaustion process, and the T cell response to immunotherapy. In this project, we will utilize both mouse tumour models, and mouse models of chronic viral infection that also induce T cell exhaustion, to examine how these transcription factors regulate exhaustion and the response to immunotherapy. We will also investigate whether manipulating these pathways can augment immunotherapy, and whether similar pathways are engaged in T cells found in the tumours of patients during both tumour growth and immunotherapy treatment.

This project will employ a range of cutting edge technologies, such as sophisticated animal models, genetic manipulation of T cells, transcriptional profiling and multi-parameter flow cytometry.

Key Words: Cancer Immunotherapy, Cancer Immunology, Viral Infection, T Cell Differentiation

Target Students: PhD/postgraduate, Honours.

For more information about this project contact:

Dr. Ian Parish ian.parish@petermac.org

Delineating transcriptional pathways that limit anti-cancer T cell function

Supervisors: Prof. Jospeh Trapani, Dr. Mohamed Ferah

Genetic aberrations drive pediatric cancers that are often correlated with poor prognosis, threatening the life of approximately 100,000 children per year worldwide. Recent advances in genomic technologies revealed the genomic landscape in pediatric neoplasms, and highlight an important genetic heterogeneity between various paediatric tumors. Given the genomic singularity of individual tumors, it is undeniable that personalized medicine will offer to individual child better survival chances.

We aim to exploit deep analyses of genomic data (from 400 tumors) to provide a comprehensive understanding of the molecular bases that drive the development of various paediatric tumors and its immunosuppressive microenvironment. We use different approaches to harness the power of our immune system to better recognize and eliminate malignant cells that otherwise would have escaped this natural surveillance mechanism. We believe the outcome of this project will lay the foundations for a new era of personalized therapies to treat kids cancers. This project will focus on:

1. Analysis of whole-genome and RNA sequencing data from approximatively 400 paediatric tumors.
2. Immunoprofiling of paediatric tumors using genomic and proteomic approaches to better understand the status of the immune system at the tumor site.
3. Tumor profiling to identify new markers that may represent potential targets for immunotherapies, particularly those that are predicted to be expressed on the surface of the cancer cell, and may thus be targets for antibodies or CAR T cells.
4. Development of personalized immunotherapies and RNA therapeutics based on the above.

We are able to offer a project in each of these areas, and a

AVAILABLE PROJECTS BY RESEARCH GROUP

specific topic will be selected depending on the interests and skills of a candidate.

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

Target Students: Honours.

For more information about this project contact:

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Dr. Mohamed Ferah mohamed.fareh@petermac.org

VOSKOBOINIK, ILIA

CANCER IMMUNOLOGY PROGRAM

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

Regulation and function of cytotoxic lymphocytes

Supervisors: A/Prof Ilia Voskoboinik, Prof. Joe Trapani

Cytotoxic lymphocytes recognize and kill cancerous and virus-infected cells through cytotoxic granule exocytosis pathway. Cytotoxic granules store a pore-forming protein, perforin, and serine proteases, granzymes. Once released, perforin transiently disrupts a target cell membrane thus permitting the delivery of granzymes into the cytosol, where they initiate various apoptotic death pathways. This is a fundamental homoeostatic process and, when disrupted, has catastrophic consequences: it either leads to fatal hyperinflammation or, in milder cases, results in haematological malignancies in childhood or adolescence.

We investigate:

1. The regulation of cytotoxic granule exocytosis,
2. The structural bases of perforin pore formation,
3. The biology of granzymes,
4. The molecular bases of congenital immune deficiency Familial Haemophagocytic Lymphohistiocytosis,
5. The genetic predisposition to haematological malignancies.

We offer project(s) in each of these areas, and a specific topic will be selected depending on the interests and skills of the candidate.

Lopez, J.A. et al and Voskoboinik, I. (2013) Blood, 121, 2659-2668; Brennan, A.J. et al and Voskoboinik, I. (2011) Immunity, 34, 879-892; Law, R.H.P.*, Lukoyanova, N.*, Voskoboinik, I.* et al. (2010) Nature, 468, 447-51

Key Words: Cancer Cell Biology, Cancer Immunotherapy, Cancer Immunology.

Target Students: PhD/postgraduate, Honours.

For more information about these projects contact:

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WICKRAMASINGHE, VIHANDHA

ONCOGENIC SIGNALLING AND GROWTH CONTROL PROGRAM

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

Mechanisms of regulating gene expression via selective mRNA transport

Supervisor: Dr. Vi Wickramasinghe

A critical step in the gene expression pathway that is altered in cancer is nuclear export of 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 aims to dissect the molecular mechanisms of regulating gene expression via selective mRNA transport. This will establish selective mRNA export as a novel area of research in cancer biology.

Key Words: Cancer Cell Biology; Cell Signalling; Cancer Therapy; Cell Cycle; Cell Growth; Cell Metabolism; Gene Expression (incl. Microarray and other genome-wide approaches); Gene Regulation; microRNA.

Target Students: PhD/postgraduate, Honours.

Impact of alternative mRNA splicing on the human proteome

Supervisor: Dr. Vi Wickramasinghe

Alternative splicing of RNA transcripts has emerged as a key mechanism for enabling biological complexity within the human genome. Alternative splicing has long been assumed to underlie the expansion of proteomic diversity. However, the extent to which this increased genomic complexity contributes to the generation of proteomic diversity is largely unknown. This fundamental biological question is of critical importance to human health, given the recent identification of perturbed RNA splicing as a causative factor in cancer.

We have developed an integrative approach to ask whether dynamic perturbations in mRNA splicing patterns alter the composition of the proteome. This project will reveal the impact of alternative splicing on the proteome.

Key Words: Cancer Cell Biology; Cell Signalling; Cell Metabolism; Genome Structure and Regulation; mRNA; Proteomics and Intermolecular Interactions (excl. Medical Proteomics)

Target Students: PhD/postgraduate, Honours.

For more information about these projects contact:

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AVAILABLE PROJECTS BY RESEARCH GROUP
CLINICAL RESEARCH GROUPS

AUSTRALIAN CANCER SURVIVORSHIP CENTRE

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

The Australian Cancer Survivorship Centre – A Richard Pratt legacy (ACSC) undertakes survivorship research with a range of collaborators. Contact us to find out more about our projects.

Facilitators, barriers and preferences around routine assessment of patient-reported outcomes for cancer survivors

Supervisors: Dr. Karolina Lisy, Prof. Michael Jefford

Substantial international evidence supports routine assessment of patient-reported outcomes (PROs) in oncology settings to inform health service delivery, research and policy, and ultimately to improve outcomes for people living with and beyond cancer. PRO measures allow patients to self-report the symptoms, issues and needs they are experiencing, and may be used to guide clinical consultation and subsequent intervention. PRO assessment within cancer services has numerous benefits for patients, including improved survival, treatment adherence, symptom identification, quality of life and patient satisfaction, and enhanced patient-provider communication. Despite the benefits PRO assessment in clinical practice and high rates of patient acceptability, this is not usual practice in Australia.

The aim of this project is to understand barriers, facilitators and preferences around PRO assessment for cancer survivors. This project will utilise qualitative research methodology (interviews and/or focus groups) to explore the experiences of healthcare professionals, including clinicians, administrators, researchers and policymakers, with implementing and delivering PRO assessment in local and interstate oncology settings.

Students will develop skills in literature review, ethical conduct of research, qualitative data collection and analysis, and writing for publication. It is anticipated that project results will be presented at national (and potentially international) meetings and lead to journal publication

Key Words: Cancer Experience; Patient-Reported Outcomes, Oncology, Patient Care, Quality of Care, Qualitative Research, Health Services Research.

Target Students: Honours.

For more information about these projects contact:

A/Prof. Michael Jefford michael.jefford@petermac.org

Quality cancer survivorship care

Supervisors: , Dr. Karolina LIsy, Prof. Michael Jefford

The aim of this PhD is to support development of an evidence-based quality framework for survivorship care.

Over 1 million Australians are living with or beyond their cancer diagnosis. Providing survivorship care for this growing population is a current challenge. There is limited guidance available to inform survivorship care, and where guidance does exist, it is fragmented and incomplete. Preliminary work conducted by the Australian Cancer Survivorship Centre (ACSC) has generated a set of high-level principles that may underpin quality survivorship care, including care that is based on evidence, integrated and coordinated, holistic and person-centred, and empowers people to live well long-term.

The successful PhD applicant will work closely with government, policy makers and healthcare professionals to define quality standards for survivorship care in Victoria, including a set of quality indicators to assess structural, resource, process and staff-related factors required for survivorship care, and to assess outcomes for both cancer survivors and staff.It is anticipated that project results will be presented to policy makers, at national meetings and lead to journal publications. This project will be based in the ACSC.

PhD scholarship of $30,000 p.a. tax free, funded by the Victorian Department of Health and Human Services.

Key Words: Cancer Experience; Survivorship; Quality of Life; Patient-Reported Outcomes, Oncology, Patient Care, Quality of Care, Qualitative Research, Health Services Research.

Target Students: PhD.

For more information about this project contact:

Dr. Karolina Lisy karolina.lisy@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP
CLINICAL RESEARCH GROUPS

NATIONAL CENTRE FOR INFECTIONS IN CANCER

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.

Epidemiology of Staphylococcus aureus bloodstream infections in patients with cancer

Supervisor: A/Prof. Leon Worth

Bloodstream infections due to Staphylococcus aureus (SAB) are a significant cause of morbidity and mortality, and are associated with increased healthcare costs. Patients with cancer are considered at high risk for infection due to a number of factors, including underlying malignant disease, the need for invasive procedures, and presence of indwelling medical devices (e.g. long-term central venous catheters for administration of chemotherapy). In Australia, the epidemiology of SAB in cancer populations has not been reported, and risks for infection are not well understood.

The objective of this project is to evaluate the risks, treatment and outcomes of SAB in cancer patients over a 7-year period, using historic surveillance data at Peter MacCallum Cancer Centre (2011-2017). Burden of illness will evaluated in terms of length of hospitalisation, ICU admission, complications and mortality. Community- and healthcare-associated events will be compared. The study will be structured as a case-control study, with the potential for economic analysis to also be performed. Findings will be published in peer-reviewed literature. Study outcomes will also be used to develop effective infection prevention strategies and guidelines, and to inform policy regarding use of SAB as a performance indicator.

Key Words: Epidemiology; Haematological Cancers; Infectious Disease and Control; Solid Tumours.

Target Students: PhD/Postgraduate.

For more information about this project contact:

A/Prof. Leon Worth leon.worth@petermac.org

Determination of the epidemiology and risk factors for infection in patients with peripheral and cutaneous T-cell lymphom

Supervisors: Prof. Miles Prince, Dr. Ben Teh, Dr. Carrie van der Weyden

Peripheral T cell lymphoma (PTCL) and cutaneous T cell lymphomas (CTCL) are types of non-Hodgkin lymphoma pose a treatment challenge. Patients with PTCL and CTCL are often at increased risk for infection due to disease related disruption in anatomical barriers and related immune deficits. Treatments for these diseases involve the use of chemo-immunomodulatory therapies, novel agents and monoclonal antibodies such as alemtuzumab, which have wide-ranging effects on the immune system and contribute to risk for infection. Infections in patients with PTCL and CTCL are not well characterised and this clinical project aims to determine the epidemiology, risk factors and outcomes of infection in patients with PTCL and CTCL which will guide development of better preventative strategies.

Key Words: Haematological Cancers; Infectious Disease and Control.

Target Students: PhD/Postgraduate.

For more information about this project contact:

Dr. Benjamin Teh ben.teh@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP
CLINICAL RESEARCH GROUPS

CANCER EXPERIENCES RESEARCH

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

The Cancer Experiences Research group at the Peter Mac is committed to improving care and treatment experiences, and health and wellbeing outcomes, for all people affected by cancer. Our multi-disciplinary research is focused on generating new and implementing existing knowledge, to the benefit of patients, their support networks and healthcare providers. Our research spans the cancer continuum from diagnosis through into survivorship, the management of advanced disease and end of life care.

Cancer patient experiences of guidelines for cancer-related fatigue

Supervisor: Dr. Elizabeth Pearson

The aim of this qualitative project is to understand the impact of undergoing screening, assessment or management of fatigue (tiredness) in cancer. This knowledge will contribute to design and delivery of patient-focused care for cancer-related fatigue. The project is aligned with the NEW Energy project, working to implement guidelines for cancer-related fatigue.

Data collection will be semi-structured interviews with patients receiving a particular recommendation of a guideline for cancer fatigue e.g. screening, assessment, treatment of contributing factors, exercise or psychosocial interventions (to be determined).

The student will be involved in an ethics application/ modification, recruitment and consenting of 10-15 participants, conducting qualitative interviews, analysis and manuscript writing. It will suit a clinical allied health professional who may be considering progressing on to a higher research degree.

Key Words: Cancer Experience; SLate Effects of Cancer, Palliative Care, Allied Health, Rehabilitation.

Target Students: Honours.

For more information about this project contact:

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PARKVILLE FAMILIAL CANCER CENTRE 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. Familial cancer researchers also investigate the wider psychosocial impact of these syndromes on the well-being of individuals and their families through the work of the Psychosocial Onco-Genomic Research Group.

Understanding Breast and Ovarian Cancer Families: the Variants in Practice (ViP) study

Supervisor: A/Prof. Paul James

Breast and Ovarian cancer both have a strong hereditary basis, the greatest part of which remains unexplained. We have assembled a unique cohort of hereditary breast and ovarian cancer (HBOC) families, known as the ViP study to investigate the clinical and genetic features of these cancers. This established, large cohort includes more than 4500 families with extensive pedigree, pathology, and clinical data along with in-depth sequencing of rare genetic variants and common polymorphisms and prospective follow-up data.

In this project, the candidate will be based in the Peter Mac Familial Cancer Centre and will use pedigree-based statistical techniques to mine this enormous data set with the aim of identifying novel genomic contributions to HBOC, combining complex genomic data into personalised risk assessments and creating the detailed information to use genomics in clinical practice.

This project is suitable for a candidate with a strong background in biostatistics or bioinformatics and an interest in clinical genomics..

Key Words: Biostatistics; Bioinformatics; Breast Cancer; Cancer Experience; Familial Cancer; Genomics; Health Service Research; Ovarian Cancer.

Target Students: Honours.

For more information about these projects contact:

A/Prof. Paul James paul.james@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP
CLINICAL RESEARCH GROUPS

Determining the Assessing the introduction of a novel personalized genome-based breast cancer risk assessment to women at a familial risk

Supervisors: A/Prof. Alison Trainer, A/Prof. Paul James, Health Economist

Familial cancer services (FCSs) evolved offering categorical risk assessments (high, moderate, low risk) based on family history or genetic tests for rare high-risk gene mutations such as in BRCA1/2. With the advent of massively parallel sequencing, came the ability to produce tailored personalized risk assessments by combining results from a spectrum of risk alleles, rare high-risk, and moderate risk as well as multiple low risk alleles (polygenic risk). This form of continuous risk assessment has potential to impact on cancer treatment as well as the cancer risk-specific management of healthy women. The Parkville familial cancer service has well-established clinical and research expertise in this exciting area.

This project will assess the impact of offering this form of comprehensive risk assessment to affected and healthy women attending the FCS, including its impact on clinical decision- making by both patient and clinician, as well as on clinical outcome. Part of the project will be to use these data to further refine an established health economic model to assess the cost effectiveness of this approach to risk assessment. Experience will be gained in discrete choice experiments as well as economic assessments.

Key Words: Biostatistics; Bioinformatics; Breast Cancer; Cancer Experience; Familial Cancer; Genomics; Health Service Research; Ovarian Cancer.

Target Students: Honours.

For more information about this project contact:

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

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

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

Supervisors: Dr. Laura Forrest

Young women aged 18-40 years who have a BRCA1/2 mutation have significantly increased risks of breast and ovarian cancer. These women have options to manage their risk of breast cancer including; breast screening, taking a medication to reduce their risk, or having risk reducing surgery that removes their breast tissue.

Women with a BRCA1/2 mutation are encouraged to at least consider starting screening from 25-30 years, and the other two options of medication and surgery are available, as well. The only option to reduce their risk of ovarian cancer is to have their ovaries and fallopian tubes removed, which is recommended between the ages of 40-45 years. These choices are complicated for young women who are simultaneously experiencing important life events, such as meeting partners and forming intimate relationships, and making decisions about having children and breastfeeding.

This research will involve recruiting young women with a BRCA1/2 mutation to take part in a survey that is being sent out nationally. Data collection is using an online platform..

Key Words: Breast Cancer; Cancer Risk, Familial Cancer; Genetic Counselling, Ovarian Cancer, Psychosocial, Young Women.

Target Students: Honours.

For more information about this project contact:

Dr. Laura Forrest laura.forrest@petermac.org

AVAILABLE PROJECTS BY RESEARCH GROUP
CLINICAL RESEARCH GROUPS

PHYSICAL SCIENCES

https://www.petermac.org/research/clinical-research-trials/clinical-research/physical-sciences-research

Medical physicists play a key role in underpinning high quality medical imaging and the planning and delivery of radiation therapy treatments at Peter Mac. We collaborate extensively with oncologists, radiation therapists, laboratory researchers, imaging scientists and cancer surgeons. A major strength of our research program is the ability of our medical physicists and biomedical engineers to turn ideas into evidence-based clinical practice. This has led to many successful innovations such as a computer controlled rotating turntable for whole body electron treatments, artificial intelligence for organ segmentation and image analysis, tools to ensure high quality clinical trials and the development of a device for tracking retinal motion during radiotherapy.

Radiomics for cancer diagnosis and patient outcome prediction

Supervisors: Dr. James Korte, Dr. Nick Hardcastle, Dr. Price Jackson

Radiomics is an emerging field that aims to extract vital information from growing collections of medical imaging and patient data. A large number of quantitative features are extracted from medical images, from basic features such as shape and size to more advanced texture analysis metrics. Radiomic signatures are constructed from these features across a patient cohort and are being investigated for tumor staging, treatment response and patient outcome prediction.

Whilst a range of radiomics feature analysis tools are available through the research community, a bottleneck for many studies is manual contouring or segmentation of the tumor volume. We propose the application of Deep Learning, which has recently shown excellent performance in many image analysis tasks, to develop an auto-contouring tool. Such a tool would automate our radiomics analysis and allow us to mine a much larger portion of the existing medical image database.

The project would suit a student with a background in medical imaging and analysis. The initial project has potential to focus on MRI data and developing a prediction model for brain tumors.

Key Words: Bioinformatics, Brain and Spine Cancers, Medical Imaging and Diagnostics, Deep Learning, Radiomics.

Target Students: PhD/Postgraduate, Honours.

For more information about this project contact:

Dr. James Korte james.korte@petermac.org

Efficient and effective adaptive radiotherapy

Supervisors: Dr. Nick Hardcastle, Dr. Adam Yeo

Approximately 40% of cancer patients benefit from radiotherapy. Radiotherapy involves highly targeted radiation beams directed at the tumour, whilst avoiding surrounding normal tissues. Anatomical variations introduce targeting uncertainty in the process. Adaptive radiotherapy incorporates medical imaging at multiple time points during radiotherapy delivery with adaptation of treatment geometry to allow improved targeting of the radiation. This project involves application of advanced image analysis and reconstruction to efficiently identify tumour and other anatomy in medical images, compute potential benefits of radiotherapy adaptation on a per-patient basis and generation of new radiotherapy treatment planning geometry.

This project would suit a masters or PhD student with a strong background in image analysis and or machine learning. Study results will directly improve our ability to target radiotherapy treatments and will have directly translatable outcomes into the clinic.

Key Words: Gynaecological Cancers, Haematological Cancers, Head and Neck Cancers, Lung Cancers, Medical Imaging and Diagnostics, Radiation Therapy, Sarcoma, Solid Tumours, Upper Gastrointestinal Cancers, Urological Cancers.

Target Students: PhD/Postgraduates.

For more information about this project contact:

Dr. Nick Hardcastle nick.hardcastle@petermac.org

WHY STUDY AT PETER MAC? WORDS FROM OUR 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.

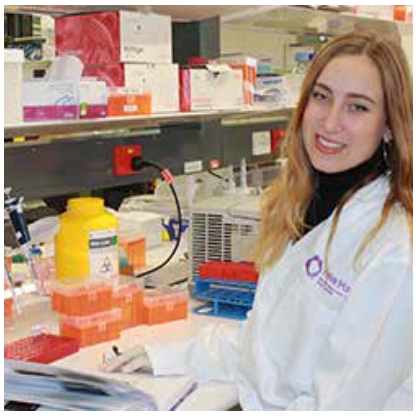
"Peter Mac is a very stimulating environment with such a wide array of cancer research being completed here, to an international standard. I'm so excited to be at one of the top-class research institutes in Australia and I'm looking forward to the adventures ahead."

Rosie completed her honours at Peter Mac in 2012. The cohort of honours students that year was a very tight-knit group who all helped each other throughout the course. The community of researchers, from Lab Heads to Research Assistants, also guided them through and this is one of the main reasons Rosie returned to Peter Mac for her PhD.

Rosemary Millen
PhD Student, **Ramsay Laboratory.** Awarded Peter Mac's Nicole Lundie Undergraduate Research Prize in 2012. President of the Postgraduaate Student Society, 2016. Awarded Harold Mitchell Trael Fellowship, 2018.

"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
PhD student, Dawson Laboratory.
Recipient of a Melbourne International Research Scholarship; Member, 2017 Postgraduate Student Committee.

"I was fascinated by the innovative ideas and research quality of Peter Mac labs publications. I was convinced that I could make a significant impact on the field by joining the Peter Mac and contributing to cancer research - the ultimate frontier. Today, my project supervisory team brings together significant combined expertise in subject areas relevant to my research and the Peter Mac state of the art facilities, sequencers and computing clusters empower me to achieve my goals."

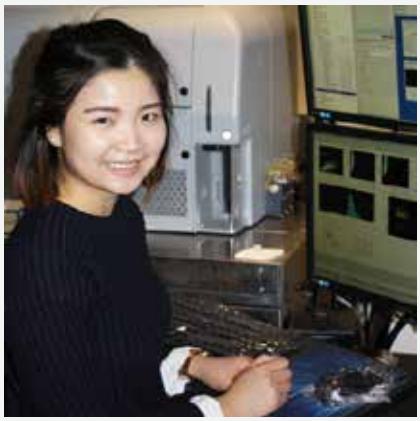
Luis completed his Master of Bioinformatics at The University of Melbourne, conducting his research placement at Peter Mac. He commenced his PhD in 2016, attracted to Peter Mac by the multidisciplinary projects and supervisory teams offered in their programs.

Luis Lara-Gonzalez

PhD Student, Goode Laboratory.
Recipient of a Melbourne International Research Scholarship, a Cancer Therapeutics Top-up Scholarship. President of the Postgraduate Student Society, 2017.

"My very first impression of Peter Mac was how there is a well-structured education and recruitment program for students, described on the website. It's very important and also encouraging to have project outlines, so students from the other side of the world know what people are currently doing and, more importantly, which researchers are recruiting students here."

Jirawas came to Australia to undertake a project targeting ribosome biogenesis in acute myeloid leukaemia.



Jirawas Sornkom
PhD student, Oncogenic Signalling and Growth Control Program
Recipient of an International Postgraduate Research Scholarship & Cancer Therapeutics Top-up Scholarship. President of the Postgraduate Student Society, 2015. Now postdoctoral researcher at Centre for Genomic Integrity, South Korea.

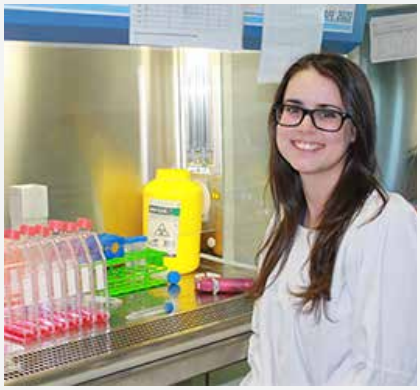
"Being able to conduct research alongside leading clinicians in the field of familial cancer is an invaluable aspect to my research. Having the opportunity to share research ideas with various active health professionals on a regular basis enables my research to have real impact on current practice. Daily interactions with patients attending the Familial Cancer Centre encourages me to understand the link between clinical research and how it impacts people's everyday lives."

After completing a Bachelor of Medical Sceince at ANU, Rowan moved into psychosocial research in cacner genetics. He wa attracted to Peter mac by its outstanding reputation in familial cancer clinical practice and research.

Rowan Forbes-Shepherd
PhD Student, Parkville Familial Cancer Centre.
Recipient of a Melbourne Research Scholarship; Member, 2017 Postgraduate Student Committee.

"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 strted 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.



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

"What drew me to Peter Mac was othe pportunity 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-institue 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 now is undertaking his Biomedical Science Honours project at Peter Mac.

Kenji Fujihama
PhD Student, Clemons Lab. Recipient of a Research Training Program (RTP)-Domestic Scholarship; Member, 2018 Postgraduate Student Committee

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