Diamantina Institute

The University of Queensland Diamantina Institute (UQDI) is a modern research facility where clinical and basic science are used to study cancer, immunology and genomic medicine.

The Institute has a vibrant community of over 300 researchers, students and support staff. We have delivered global, world-changing discoveries to humanity, such as the world’s first cervical cancer vaccine.

Based at the Translational Research Institute (TRI) beside the Princess Alexandra Hospital, UQDI has strong clinical interactions and world-class facilities that enable researchers to be at the forefront of their fields. UQDI’s position within the TRI allows for a much greater collaborative research environment, allowing our researchers to focus their efforts on turning their scientific discoveries into new treatments for diseases including a variety of cancers, arthritis and other autoimmune diseases.

UQDI focuses on bringing the discoveries of basic science to the patient.

We aim to translate the greatest opportunities for research discoveries into the cause, mechanism, prevention and treatment of major disease.

As part of The University of Queensland’s prestigious Faculty of Medicine, UQDI is committed to making a global difference to health outcomes.

For further information visit di.uq.edu.au

Key research themes:

- Blood cancer
- Immune and Inflammation
- Genomic medicine
- Immunotherapy
- Skin and skin cancer
Undergraduate research projects

UQDI offers various opportunities for undergraduate students to gain research experience in biomedical research facilities including Summer and Winter research projects.

For further information visit: di.uq.edu.au/study/undergraduate

Summer research projects

For further information visit: medicine.uq.edu.au/research/research-strategy-and-support-office/summer-research-program

Winter research projects

For further information visit: medicine.uq.edu.au/research/research-strategy-and-support-office/winter-research-projects

In July of each year UQDI offers a one week course in advanced immunology.

For further information visit: di.uq.edu.au/event/2293/advanced-immunology-course

Honours program

UQDI hosts honours students enrolled through other schools within the Faculties of Science or Medicine at UQ or affiliated Institutions. These include (but are not limited to) the School of Chemistry and Molecular Biosciences, or the School of Biomedical Sciences at UQ.

The Honours Program is a one year full time course. Students must fulfill the prerequisites of the undergraduate Faculty/School through which they are enrolled.

For further information visit: di.uq.edu.au/study/honours

MD student research experience

UQ Medicine is committed to enhancing the research training and experience for students in the Medical Program.

There are a number of ways students can incorporate research training and experience into their medical degree.

For further information visit: medicine-program.uq.edu.au/research/research-your-medical-degree

Research higher degree

UQDI is an internationally recognised research facility where clinical and medical sciences converge in the translational research of cancer, disorders of immune regulation and genomic medicine.

For more information on starting a Higher Degree by Research with us, please visit: medicine.uq.edu.au/future-students#qt-study-foundation-tabs-4
Dr Anne-Sophie Bergot

Research Field
Immunology and pathogenesis of type 1 diabetes

Research Synopsis
Anne-Sophie is working with Prof. Ranjeny Thomas on Immunotherapy for type 1 diabetes (T1D).
We are investigating the use of a liposome based strategy to develop an antigen-specific therapy for TID. Immunologically, it has a dual role of fostering regulatory T cell function and terminating pathogenic T cells.

Research Projects
• “Analysis of effector and regulatory T cells in type 1 diabetes” using various genetic, immunological or cell based assays
Research Field
Innate immunity and infectious diseases

Research Synopsis
With resistance to antibiotics on the rise, new insights into host defence mechanisms that control pathogenic bacteria are vital for the development of novel therapeutic interventions. Our research focuses on molecular pathways that are important for the recognition and control of bacterial pathogens as well as those that orchestrate inflammatory responses during infection.

Students are part of a dynamic research team to maximise their research training and experience. The research employs a series of molecular, cell biological and immunological techniques to define novel molecular and cellular aspects of the host response to infection.

Research Projects
• Innate immune recognition of pathogenic bacteria
• Molecular regulation of host anti-microbial defence mechanisms
Dr Andrew Brooks

Research Field
Class I cytokine receptor signalling and HLA-G regulation of inflammation

Research Synopsis
Our research focuses on understanding the mechanisms of cytokine receptor signalling and how these receptors regulate cell behavior and functions such as inflammation, blood cell formation, postnatal growth, obesity, and lactation. Dysregulated cytokine receptor signalling leads to many diseases such as cancer and inflammatory diseases such as liver fibrosis, inflammatory bowel disease, and arthritis. The development of novel molecules that target cytokine receptors or their signalling pathways may lead to important therapeutics for a wide variety of clinically important diseases.

Research Projects
• Understanding dysregulated cytokine receptor signalling in leukaemia
• Defining the mechanisms of cytokine receptor signalling
• Developing novel therapeutic peptides targeting cytokine receptors
• Defining the mechanism of HLA-G inhibition of NK cell activation
Dr Janin Chandra

Research Field
Immunobiology of antigen-presenting cells in health and disease

Research Synopsis
Immunotherapy aims to correct a malfunctioning immune system to combat a variety of diseases including cancer, autoimmunity or allergies. Many immunotherapy targets have been identified and some have been developed into powerful treatments. Immunotherapy largely targets effector T cell responses which are either suppressed or falsely activated. Professional antigen-presenting cells such as dendritic cells (DCs) play a pivotal role in T cell fates and are hence a desired immunotherapy target. Immunotherapy has the potential to effectively harness DCs to prime e.g cancer-specific cytotoxic T cell responses or shut-down self- or allergen-reactive T cells. My research focusses on understanding dendritic cell diversity and fate, and how manipulation of dendritic cells can improve disease outcomes.

Research Projects
• Characterizing the diversity of dendritic cells in steady state and disease
• Defining and optimizing the mechanisms of action of therapeutic vaccine candidates

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Professor Paul Clarke

Research Field
Cell cycle control in cancer

Research Synopsis
Paul Clarke is working on the role of cell division in the development of cancer and in the response of cancer cells to cancer therapies. His research group investigates the role of tumour suppressors and oncogenes that control mitosis and mitotic cell death. His group study the function of proteins in tumour cells using biochemical techniques to identify their post-translational modifications (phosphorylation, ubiquitylation) and advanced microscopy to analyse their localisation and stability in live cells. The group aim to understand why tumour cells often have abnormal numbers of chromosomes and why they become resistant to cell death. This work will improve our understanding of how cancer develops and will provide new strategies for cancer therapy.

Research Projects
• The role of tumour suppressors in mitosis
• Control of mitotic cell death
• The relationship between cellular ageing and cancer

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Research Field
New strategies to improve cancer immunotherapy and immunomonitoring

Research Synopsis
Cancer immunotherapy harnesses and enhances the power of the immune system to fight cancer and represents the most promising new cancer treatment approach. Indeed, immunotherapy constitutes an effective treatment for patients with certain types of cancer that have been resistant to chemotherapy and radiation treatment (e.g. melanoma). Nevertheless, the clinical benefit provided by current immunotherapeutic approaches is still limited to 25-30% of treated cancer patients. By exploiting the most advanced technologies (nanoparticle-based vaccines, neo-antigens identification and validation, etc.) and suitable preclinical models, we are developing innovative strategies potentially able to improve current approaches. We are also investigating a range of different combinations of immunotherapeutic approaches and conventional treatment modalities to identify the most effective and tailored therapeutic schedule. Our final goal is to provide effective personalised treatments for cancer patients with reduced non-specific side-effects.

Research Projects
• Cancer vaccines exploiting the in vivo delivery of tumour specific (neo-)antigens to cross-presenting dendritic cells to improve the immunotherapy for melanoma, breast cancer, lymphoma, glioblastoma and virus-driven tumours

• Development and validation of clinically applicable protocols able to identify tumour-specific immunogenic neo-epitopes to be exploited in personalised vaccination approaches

• Identification and exploitation of new modalities to induce immunogenic cell death for immunotherapeutic purposes
Professor David Evans

Research Field
Genetics of complex traits and diseases; statistical genetics and genetic epidemiology

Research Synopsis
Our group aims to elucidate the genetic and environmental basis of complex traits and diseases using statistical approaches that are applied to “big data”.

We work on a diverse range of diseases and phenotypes including (but not limited to) osteoporosis, autoimmune disease, perinatal phenotypes like birthweight, and systemic sepsis (infection).

Our research involves many of the world’s largest datasets (some >500,000 individuals) and a variety of different technologies including RNA-Seq, genome-wide association (GWAS) SNP arrays, epigenome-wide methylation arrays, meta-genomic community profiling, and NMR metabolomics.

We are also very active in the development of new statistical models to answer interesting questions about biology. We regularly publish in top tier journals like Nature and Nature Genetics and are proud of our perfect record of 1st class honours students.

We are searching for high quality students that are highly numerate ideally with a background in genetics, statistics, epidemiology, psychology and/or computer science.

Research Projects
• Using genetics to unravel the relationship between low birthweight and future risk of cardio-metabolic disease in later life
• Investigating the genetic and genomic basis of septic shock
• The genetic basis of osteoporosis

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Research Field
Tumour immunology

Research Synopsis
As immunologists, we work on the skin immune system and how the immune responses at squamous epithelial surfaces are influenced by epithelial proliferative disease and by the skin microbiome.

We work with animal models of human squamous skin cancer, and with patients with human squamous skin cancers, as part of a consortium including experts in microbiology, ecogenomics, genomics, proteomics and clinical management.

Research Projects
• Effects of epithelial proliferation on local immune effector function in skin
• Bacterial colonisation as a driver of epithelial proliferation and inflammation
• Influence of viral infection on local immune responses and epithelial proliferation
Professor Nikolas Haass

Research Field
Melanoma cell biology and experimental melanoma therapy

Research Synopsis
Using cutting-edge technology, including real-time cell cycle and cell death imaging in several three-dimensional cell culture and in vivo models, we investigate the biology of tumour heterogeneity with the goal to develop novel therapeutic approaches by simultaneously targeting different melanoma subpopulations.

Research Projects
• The role of the MITF/BRN2 axis in dynamic melanoma heterogeneity and in sensitivity to targeted therapy
• The role of the MITF/BRN2 axis in an EMT/MET switch in 3D melanoma spheroids
• The role of microtubule-dependent ‘mechanosensing’ in melanoma plasticity and invasion
• The role of NDRG1 and canonical WNT signaling in dynamic melanoma heterogeneity
• Characterisation of the intrinsic, non-phototoxic, effects of Rose Bengal on melanoma
• The role of Noxa and Puma on melanomagenesis
Dr Emma Hamilton-Williams

Research Field
Immunology and pathogenesis of type 1 diabetes

Research Synopsis
The Hamilton-Williams laboratory currently has two major areas of focus.

(1) Immunotherapy for type 1 diabetes. We are investigating the use of a liposome system for antigen-specific therapy in type 1 diabetes. Our goal is to restore tolerance in autoreactive islet-specific T cells. In concurrent studies we are testing novel combination therapies aimed at simultaneously improving regulatory T cell function while terminating T effectors.

(2) The role of the microbiota in type 1 diabetes. Using patient stool samples and a novel proteomic approach we seek to understand how changes in the gut microbiota in type 1 diabetes alter the islet immune response.

In complementary studies, we are using animal disease models to understand the link between the gut and type 1 diabetes.

Research Projects
• Metaproteomic profiling for prediction of type 1 diabetes
• Host-microbiota interactions in the pathogenesis of type 1 diabetes
• Nanoparticle based immune therapies for tolerance induction in type 1 diabetes

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**Professor Kiarash Khosrotehrani**

**Research Field**
Skin regeneration, skin cancer

**Research Synopsis**
The Experimental Dermatology Group has three main streams focused on regenerative medicine and cancer in Dermatology and skin biology.

**Research Projects**
(1) Keratinocyte cancers are the most frequent malignancy in humans. In particular, basal cell carcinomas affect one in 3 Australian from age 70. The main morbidity of basal cell carcinoma is related to the onset of new tumours in the same sun-exposed skin field. It is therefore essential to develop new strategies to prevent the onset of new basal cell carcinomas. Proposed projects:
   a - Developing a preventive immunotherapy against Basal cell carcinoma
   b - Epidermal ablation to reduce skin cancer incidence

(2) Melanoma is the most lethal form of skin cancer. The development of metastases is reliant on the activation of vascular stem cells in the tumour and in the site of future metastases. Proposed projects:
   a - To develop biomarkers for the identifications of patients at risk of melanoma progression and metastases.
   b - To develop inhibitors of vascular stem cells to prevent melanoma metastasis.

(3) Skin wound vascularization is an essential step of the healing process to supply oxygen and nutrient to the surrounding cells. Upon wound closure, most endothelial cells from blood vessels undergo a mesenchymal transition and contribute to scarring. In this project we aim to evaluate the impact of IL6 signalling on vascular stem cells’ transition towards a mesenchymal and pro-fibrotic fate.

In all projects there are ample opportunities for strong clinical linkage and PhD or MD PhD.
Dr Xiaowen (Tina) Liang

Research Field
Liver diseases, liver cancer

Research Synopsis
Liver cancer is the second most common cause of death from cancer worldwide. The most common type of primary and secondary liver cancer is hepatocellular carcinoma (HCC), and colorectal cancer liver metastases (CLM), respectively. According to current clinical practice guidelines, patients with advanced-stage liver cancer are candidates for chemotherapy. However, response rates of current conventional chemotherapy are only 10% to 20% for HCC, and 7% to 51% for CLM. Therefore, we have to develop and improve methods for liver cancer chemotherapy.

Reactive oxygen species (ROS) are chemically reactive molecules containing oxygen, including hydrogen peroxide (H2O2), hydroxyl radical (•OH), hypochlorous acid (HOCl), singlet oxygen (1O2), and superoxide (O2-). It is well known that levels of ROS are associated with cancer progression, metastases and apoptosis. ROS levels change rapidly during anti-cancer therapy. ROS levels before and after chemotherapy in cancer cells can be an early indicator of treatment efficacy, which has the potential to shed new light on the ROS-mediated therapies. This critical research aims at developing a novel technology to enable prediction of response to anti-cancer treatment early and guide personalized medication. We will monitor and quantify the specific ROS levels before and after various chemotherapeutic regimens in liver cancer cells and orthotopic mouse model using biological or chemical probes.

Research Projects
• Novel approaches to assessing chemotherapy efficacy in liver cancer
Dr Samuel Lukowski

Research Field
Cellular and computational genomics, genomic medicine and regulation of gene expression

Research Synopsis
My research sits at the intersection of computational genomics, molecular biology and medical genetics. I am interested in mechanisms of genetic and genomic regulation and I use wet- and dry-lab approaches to investigate how altered gene expression contributes to human disease and development. Many of my current research projects utilise genomics techniques such as high-throughput single cell RNA-seq, ‘bulk-tissue’ RNA-seq and bioinformatics.

Research Projects
• Developing computational tools for single cell RNA-seq analysis
• Prediction of tumour neoantigens from next-gen sequencing data
• Systems biology of skin and skin cancer
• Cellular and genetic heterogeneity in healthy and diseased tissues
Dr Johan Medina

Research Field
HLA-G/H2Bl role in the inflammatory process that affects liver regeneration and growth hormone induction and inflammatory factors response in in vitro and in vivo models

Research Synopsis
HLA-G/H2Bl is a molecule belonging to the non-classical MHC class Ib family which is best known for its immunotolerance properties. Our laboratory is interested in studying the significance of HLA-G effect in the inflammatory process that regulates liver regeneration. It has been reported that HLA-G plays an important role in liver disease, especially cancer as it may allow tumoral cells to escape from the tight control exerted by immune cells via the overexpression on HLA-G/H2Bl. That is explained by the fact that although HLA-G is not expressed in the liver in physiological conditions, it has been detected in human hepatocellular carcinoma cells and in the hepatocytes and biliary epithelial cells of the livers of patients with chronic hepatitis B. It is clear that this protein is a main player in the mechanism of cell survival under physiological (maternal-foetal interface) and pathological (tumoral cells) conditions. Additionally, we have found that growth hormone has a role in the production of this protein. Assessing the significance of these factors in liver regeneration will give us clues for the development of new therapies for liver diseases and for a better response to liver transplantations.

Research Projects
• HLA-G/H2Bl role in the liver regeneration: Effect in inflammatory factors
• Growth hormone function in the expression of HLA-G/H2Bl
• Characterisation of HLA-G/H2Bl sources and targets in the liver
Dr Ahmed Mehdi

Research Field
Genomic medicine, computational immunology and genomics and linear modeling

Research Synopsis
Type-1 diabetes (T1D) is a chronic autoimmune disease that leads to the destruction and dysfunction of the insulin producing beta cells. The clinical presentation of T1D is preceded by a prodromal period that can last from months to years post birth and is characterised by the production of islet autoantibodies or seroconversion, reflecting loss of immune tolerance to beta cells. Over the last decade, significant advances in T1D research have occurred through studying HLA high risk individuals at familial risk of T1D into cohorts followed from birth, with concomitant exploration of biomarkers associated with preclinical development of autoantibodies and eventual progression to T1D. Our vision is that a better understanding of T1D progression mechanisms can be established by integrating the huge resource of the heterogeneous data that is available from preclinical studies of T1D development.

Through successful collaborations, we have access to longitudinal microarray data from German BABYDIET, the US DAISY and Finnish DIPP study cohorts from individuals who are at risk of T1D. Some of these individuals progressed to develop T1D. By using this huge resource of data, we aim to find differentially expressed genes in children at risk of T1D. We also aim to link clinical and gene expression data by developing probabilistic models would predict T1D onset.

Research Projects
• Developing computational methods to predict type-1 diabetes onset
• Developing connectivity maps of type-1 diabetes associated drugs-genes interactions
Professor Mark Morrison

Research Field
Microbial biology and metagenomics

Research Synopsis
The microbiome is a new frontier in biomedical research. It is the fusion of the traditional fields of medical microbiology (pathogenesis and epidemiology) with environmental microbiology and ecology (the study of microbial diversity and function in their natural environment).

We are investigating and defining the roles of the microbiome in unique clinical studies of Asian and Australian cohorts to advance a pathophysiology-based classification of gastrointestinal diseases, such as Crohn’s disease.

To do this, we use innovations in microbial genomics and metagenomics to better characterize the metabolic and bioactive landscape of the gut microbiome during health and disease; and how diet modulates the ecological drivers of the microbiome.

Our overarching objective is to better treat and prevent these diseases by thwarting the underlying mechanisms, rather than controlling symptoms.

Research Projects
• Not all methane is created equally: the role of methanogens and the consequences of a diet-induced inflammatory microbiota
• Epithelial metabolism as a mediator of host-microbiome interactions in inflammatory bowel disease
• The Eastern IBD Gut Microbiota (ENIGMA) project – a comparative study of diet x microbiome interactions in the East and West as drivers of Crohn’s disease incidence
• The bioactive landscape of the skin microbiota

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Dr Leisl Packer

Research Field
Chromosome instability in cancer

Research Synopsis
Leisl Packer is interested in how mutant FBW7 (a tumour suppressor) causes chromosomal instability, which ultimately leads to cancer formation. FBW7 binds to protein substrates (such as cyclin E) to enable their ubiquitination and degradation by the proteasome. Therefore loss of FBW7 results in the upregulation of these proteins, many of which are critical regulators of the cell cycle and cell survival. Mutant FBW7 has also been linked with resistance to anti-cancer therapies. By understanding how mutation of FBW7 leads to tumorigenesis, Leisl hopes to find ways to selectively treat these cancers. This research involves in vitro techniques such as cell culture, cloning, lentiviral production, western blotting, microscopy, immunoprecipitations and proteomics to name a few.

Research Projects
• Understanding the role of FBW7 during cell division
• Identification of FBW7 substrates during mitosis
• Regulation of cyclin E during in FBW7 mutant cells

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Dr Gabriel Cuellar Partida

Research Field
Genetics of complex traits and diseases, data mining and cloud computing

Research Synopsis
In the last few years, initiatives such as UK Biobank and international genetics research consortia have fueled the rapid increase of data and discoveries on the genetic basis of complex traits and diseases. Novel computational methods and infrastructure is needed to cope with this massive amount of data. To this end, our group is developing the Complex-Traits Genetics Virtual Lab (CTG-VL), a user-friendly and high performing cloud computing platform that aggregates and analyze these kinds of data. The CTG-VL will connect to hundreds of biological databases that together with the data derived from genetic studies stored in the CTG-VL will lead to the generation and testing of novel hypotheses in complex-traits genetics.

Research Projects
- Development of cloud computing platforms and web applications for genetics research. E.g. Complex-Traits Genetics Virtual Lab (https://genoma.io)
- Development of methods and computational tools to integrate and mine hundreds of databases containing genomic data
Dr Jatin Patel

Research Field
Vascular stem cell biology and tissue regeneration

Research Synopsis
My group is delineating the cell biology and function of tissue resident vascular stem cells and their role in tissue regeneration during homeostasis and disease such as cancer.

Research Projects
• Assessing the role of endovascular progenitors in aorta regeneration during homeostasis
• Blocking vasculogenesis in melanoma
• The role of endothelial to mesenchymal transition in skin fibrosis and wound healing

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Dr Fiona Simpson

Research Field
Cancer immunotherapy

Research Synopsis
The laboratory is developing adjuvant / combination therapy to improve efficacy of treatment for monoclonal antibody therapy and to decrease innate and acquired resistance. Consequently the laboratory also has cell biological projects on immune cell trafficking, proteins involved in biogenesis of the immunological synapse and monitoring of immune responses during therapy and tumour regression.

Research Projects
• Combination therapies to improve monoclonal antibody therapy outcomes
• Cell biological mechanisms of biogenesis of the immune synapse
Research Field
Leukaemia; haematopoietic stem cells

Research Synopsis
Our laboratory is interested in self-renewal, a defining property of haematopoietic stem cells (HSCs); it allows a cell to divide without differentiation, meaning that it is essentially immortal.

Mechanisms controlling self-renewal are co-opted or inappropriately maintained in leukaemia; it is therefore also a defining property of leukaemia stem cells. When leukaemia is driven into remission by chemotherapy, the stem cells are the cells that survive and initiate relapse, which is then generally non-responsive to further therapy.

Targeting self-renewal may therefore improve relapse-free survival. One way in which we do this is to study the role of the HSC niche (or microenvironment) in self-renewal. The niche is comprised of multiple cell types (osteoblasts, megakaryocytes, endothelial cells), and the composition of the niche changes in leukaemia as the leukemic cells “remodel” the niche to conditions favourable to harbouring leukemic stem cells over healthy HSCs.

We use in vivo and in vitro models, multi-colour flow cytometry and high-end imaging technologies to drive our research. Targeting stem cells is the next frontier in therapeutics, and the specific interactions of these cells with the remodelled niche are attractive targets because of their accessibility and disease specificity.

Research Projects
- Novel cell-cell interactors in the myelodysplastic stem cell niche
- Homeobox gene regulation in haematopoiesis
- Eph-ephrin interactions in leukaemia: defending the niche
- Cell competition as a tumour suppressive mechanism in leukaemia
Research Field
Clinical Sciences - dermatology

Research Synopsis
Melanoma incidence in Australia continues to increase, affecting almost 14,000 Australians per year and resulting in over 1,800 deaths annually. Mortality risk from melanoma increases monotonically with tumour thickness, and earlier detection improves treatment outcomes. Direct healthcare costs for new melanoma cases in Australia have now reached $200 million per year, a 7-fold increase from $30 million in 2008, and the costs of therapies for advanced melanoma treatment are extraordinarily high at -$150,000 per person. These escalating healthcare costs, high incidence and mortality rates, demonstrate a strong need to develop and employ effective and cost-efficient early detection strategies. There is broad clinical consensus that improved melanoma outcomes will be achieved most effectively by targeting appropriate surveillance strategies to those most at risk. Current guidelines for high risk individuals recommend full skin examination with dermoscopy supported by total body photography, however there are currently no structured approaches or recommendations on how to achieve this.

Our partnership will evaluate the integration of a 3D teledermatology network into a high risk screening pathway for the early detection of melanoma in a single clinical setting. The technical, clinical and health service outcomes will be used to inform a framework for state-wide, and eventually national implementation, with the aim of detecting melanoma earlier and at a lower cost to patients and the health care system.

Research Projects
• Photo damage assessment of skin using 3D total body imaging
• Analysis of naevi and/or skin lesion burden associated with body site using 3D total body photography
• Comparison of white vs cross polarized light on 3D total body imaging
Dr Mitchell Stark

Research Field
Melanoma/skin cancer genomics and biomarker discovery

Research Synopsis
My research group is based within the Dermatology Research Centre at UQDI and our overall theme is to identifying biomarkers for the early detection of melanoma and skin cancers. By preventing melanoma/skin cancer formation in its earliest stages, we can effectively put the brakes on and halt the formation of metastatic disease. At the other end of the spectrum, late-stage melanoma patients are currently being treated with effective therapies but unfortunately this doesn’t apply to everybody. By investigating the clinical utility of predictive and prognostic ‘liquid biopsy’ biomarkers, we aim to improve the overall efficacy of current therapies.

Together with our biomarker discovery, we are also currently creating a “pre-cancer” atlas of over-lapping genomic data (exome, RNA-seq, methylation) from skin and naevi to identify novel mechanisms for melanoma development which may provide avenues for potential therapeutic intervention.

Research Projects
• Melanoma and Naevi genomics and transcriptomics
• MicroRNA analysis of the progression of early skin lesions toward SCC
• Predictive and prognostic biomarkers for melanoma brain metastasis
• Functional validation of molecular pathways involved in Seborrhoeic Keratosis development
Associate Professor Ray Steptoe

Research Field
Understanding the mechanisms and requirements of peripheral T-cell tolerance

Research Synopsis
Peripheral T-cell tolerance crucially limits the development of immune-mediated diseases such as type 1 diabetes and allergies.

The research performed is directed at determining how the immune system controls T-cell responses and studies focus on the role antigen-presenting cells play in this process and how this might be exploited for therapeutic benefit.

Experimental studies employ a range of genetically-modified transgenic and gene-deficient mice to explore what the requirements for T-cell are and the molecular mechanisms that contribute.

Research Projects
• Gene expression profiling in peripheral tolerance induction
• Turning-off T-cell responses that underlie autoimmune diabetes
• Therapy of allergic airway inflammation using gene therapy
• Does B-cell lymphoma evade immune attack by inducing T-cell tolerance?
Professor Michael Stowasser

Research Field
Pathogenesis (including genetics), diagnosis and management of hypertension, with an emphasis on secondary endocrine forms

Research Synopsis
The Endocrine Hypertension Research Centre conducts research into all forms of human hypertension, with particular expertise in endocrine varieties, especially primary aldosteronism (PA), renovascular hypertension, pheochromocytoma and the syndrome of familial hypertension and hyperkalemia (Gordon’s syndrome, named after the Centre’s founder). Its demonstration 20 years ago that PA is ten times more common than previously thought led to the identification of thousands of patients in whom hypertension has been cured or markedly improved following surgical or specific medical treatment. The centre has made major contributions to improving diagnosis and management of PA, from screening to confirmatory testing (recently designing and validating the highly reliable yet streamlined seated saline suppression test) to differentiating surgically curable unilateral adrenal forms from bilateral forms (treated medically). It also described a new familial variety, and helped elucidate its genetic basis (Nature Genetics, 2018). A recently formed international collaboration with five other research groups in Europe and USA is exploring how dietary potassium regulates blood pressure.

Research Projects
• Improving methods to detect and diagnose primary aldosteronism (PA) and its subtypes
• Exploring genotype/phenotype correlations in patients with aldosterone-producing adenomas
• Identifying genetic mutations responsible for PA
• Exploring renal molecular pathways by which potassium regulates blood pressure
• The role of the mineralocorticoid receptor in regulating brown fat and metabolic status

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Associate Professor Rick Sturm

Research Field
Human pigmentation genetics, naevi and melanoma

Research Synopsis
The overall goal of my research group is to combine population genetic studies of human pigmentation with basic discoveries in the molecular and cellular biology of melanocyte cells that are responsible for skin, hair and eye colour.

We are also conducting a study of germline and somatic mutations in genes associated with total body mole count, and in skin biopsies and cultured naevus cells.

This information will be used to understand individual risk of developing melanoma and to design a clinical management program for preventative screening of melanoma.

This will allow a personalised assessment of risk incorporating individual genotype and phenotypic host risk factors together with regular total body screening of dermoscopic patterns of naevi.

Research Projects
• Genetics of human pigmentation traits including comparing individuals of high and low mole number, and looking at genes controlling mole morphology, melanogenesis, tanning, freckling and iris pigmentation

• Cell biology of human pigmentation through characterisation of primary cultures of human melanocytes alone or together with keratinocytes to assay function of genes and examine the UV induced tanning response

• Whole exome sequence and bioinformatic analysis of patients at high risk of melanoma and cell culture of melanocytic lesions
Research Field
Antigen-specific immunotherapy of autoimmune disease

Research Synopsis
We have developed nanoparticle-based immunotherapy for antigen-specific prevention and treatment of autoimmune disease.

To understand the T cell response to autoantigens in autoimmune diseases of skin, thyroid, salivary glands, joints and pancreatic islets we are isolating and characterizing the T cell receptors of antigen-specific cells and T cell clones.

We are then developing tests to identify those cells in patient blood, so that suitable individuals can be identified and cells can be monitored after treatment.

Research Projects
• TCR analysis of autoreactive T cells
Professor John Upham

Research Field
Immune dysregulation in asthma and host defence against respiratory viruses

Research Synopsis
Our program of translational research is focussed on the study of immune function and dysfunction in asthma, and host defence against respiratory viruses, especially human rhinoviruses.

We are interested in the mechanisms leading to excessive airway inflammation in asthma, and why people with asthma are unusually susceptible to asthma attacks during respiratory viral infections.

Our aim is to discover new therapeutic targets in severe asthma.

Research Projects
• The function of antigen presenting cells, innate lymphoid cells and NK cells
• The role of polarising cytokines such as IL-33, IL-25 and TSLP in altering host defence against viruses
• How macrolide antibiotics alter immune function
• How dietary fibre and the gut microbiome alter immune function in chronic lung disease
Dr Haolu Wang

Research Field
Mesenchymal stem cells, liver diseases, liver cancer

Research Synopsis
Mesenchymal stem cells (MSCs) show homing in injured, inflamed or ischemic liver as well as liver cancer, together with adhesion to the liver sinusoidal endothelium (engraftment) mediated through CD29 and CD44. Until now, MSCs have been used as a therapy for liver diseases in 55 clinical trials (searching results from clinicaltrial.gov). The extent of cell engraftment and function has been shown to be related to the dosing route and number of hepatocyte affected.

We are generating functional normal liver cells and liver cancer cells using in vitro 3D cell culture platform, and studying the interaction and crosstalk between cancer cells, MSCs, MSC-derived liver cells, and liver cells. We are also investigating the in vivo functional integration of human MSC-derived liver cells into mouse livers and assessing if these cells can be used as therapeutics against liver diseases. In complementary studies, we are studying the seeding and migrating process of cancer cells in the liver.

Research Projects
• Generation of functional liver cells from mesenchymal stem cells for cell therapy
• Disarming the cancer cells form seeding and migrating to the liver
Dr James Wells

Research Field
Tumour immunology

Research Synopsis
Our group has 2 major areas of focus.

(1) Immune system recognition and destruction of squamous skin cancers.

We are investigating the mechanisms through which immune cells destroy tumours. Our goal is to determine how immune cells destroy tumours using animal models, so that we can correlate this information to patients in order to highlight appropriate points and strategies for immunotherapy.

(2) Tumor behavior that permits squamous skin cancers to evade host immunity.

Using genetically-linked regressor and progressor tumours, we are seeking to understand how a tumour modifies the immune system in order to become established. Our goal is to understand the key early immunological events that allow tumours to evade the immune system.

Research Projects
• Assessing mechanisms of immune-control for their role in mediating tumor regression
• Defining how tumours harness the immune system in order to establish themselves

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Dr Timothy Wells

Research Field
Host-pathogen interactions in chronic lung disease

Research Synopsis
Our laboratory focuses on the interactions between bacterial pathogens and the host immune response during chronic lung infections such as bronchiectasis and cystic fibrosis.

Although antibody usually protects against infection, our laboratory has identified a specific type of ‘inhibitory antibody’ that actually protects colonising bacteria from immune killing.

Patients with this ‘inhibitory antibody’ were found to have worse lung function.

We aim to understand both the bacterial causes and the induction of the immunological response that leads to inhibition of bacterial killing.

We also have a keen interest in studying inhibitory antibodies in the context of the whole lung microbiome in patients by using a mixture of molecular microbiology, immunology and genomic approaches.

Research Projects
• The impact of inhibitory antibodies on the human microbiota
• Antibody-mediated inhibition of phagocytosis
For more information, please contact

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