The University Of Queensland
AUSTRALIA

CREATE CHANGE

Researcher profiles and projects

Diamantina Institute

2021/2022

Diamantina Institute

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

Cancer

Genomic medicine

Immunity and Inflammation

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*

Professor Gabrielle Belz

Research Field

Transcriptional regulation of immune cell development and memory formation in pathogen defence and mucosal immunity

Research Synopsis

Our work aims to understand how the immune system responds to infections including viruses, bacteria and parasites.

We are investigating how different types of immune cells develop, and what factors influences their decision to become one type of immune cell or another to mediate long term immune protection.

Understanding how the body deals with pathogens will give clues about how to enhance protective immunity. Our goal is to discover new therapies that boost our immune system to protect against infection.

Research Projects

- Identifying novel functions of innate lymphoid cells and NK cells in immune protection
- Unravelling the microbome-epithelial-immune interface protecting mucosal surfaces
- Elucidating the mechanisms responsible for the generation of protective immunity in response to lung and gastrointestinal pathogens

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Dr Anne-Sophie Bergot

Research Field

Immunology and pathogenesis of Spondyloarthropathies

Research Synopsis

Spondyloarthropathies (SpA) are progressive and chronic diseases with limited treatment option, affecting 1-3% of the population. SpA consist of several clinically and genetically related rheumatic conditions, such as Ankylosing Spondylitis (AS). Extra-articular inflammation is also common with numerous cases of inflammatory bowel diseases (IBD) such as Crohn's disease (CD) or Ulcerative colitis (UC). We are using a mouse model of SpA, called SKG, that recapitulates human SpA. We are trying to understand the role of the gut microbiome as a trigger for gut and joint inflammation. We work with germ-free or SPF mice.

Research Projects

- Analysis of CD4 CD8 double positive T cells in the gut
- Analysis of monocolonised SKG and BALB/c for gut and joint disease
- Deciphering the role for IL-24 in SKG and BALB/c mice

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Associate Professor Antje Blumenthal

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

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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

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Dr Janin Chandra

Research Field

Immunobiology of antigen-presenting cells in health and disease

Research Synopsis

Immunotherapy aims to correct a mal-functioning 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

- Characterising the diversity of dendritic cells in steady state and disease
- Defining and optimising 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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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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Professor Ian Frazer

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

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Dr Fernando S. F. Guimaraes

Research Field

NK cell biology and immunotherapy

Research Synopsis

Natural killer (NK) cells can recognise and respond to tumour cells through a broad range of inhibitory and activating receptors. The regulation of these responses emerges from the integrated balance of activating and inhibitory signals at the NK cell-tumour interface, which help NK-cells discriminate between altered target cells (cancer or pathogen-infected cells) and healthy cells. However, both cancer cells and pathogens can still evade NK cells' detection and killing action. My research focus is to develop effective therapies that maximise NK cell responses—an emerging field with great potential for applications in the clinical management of disseminated cancer and sepsis prevention. For example, my work has uncovered that members of the Transforming Growth Factor (TGF) beta superfamily are potent inhibitory checkpoints of NK cells function. Their presence within the tumour microenvironment and infection sites can lead to tumour immunity and sepsis, respectively. This knowledge is opening a new paradigm for developing cancer and infection immunotherapy approaches. My vision is to build from this discovery and other advances in the field to generate a novel pipeline of cell immunotherapies both "targeting" NK-cells and "based on" NK-cells to increase NK-cells function against cancer (e.g., anti-metastatic function) and sepsis.

Research Projects

- Developing and tailoring NK cell-based cancer immunotherapies
- Deciphering regulatory signalling pathways in NK cells
- Elucidating the role of NK cells in inflammatory disorders

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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

- Modulating phenotypic melanoma heterogeneity and lymphocyte infiltration to improve both targeted and immune therapy
- The role of microtubule-dependent 'mechanosensing' in melanoma plasticity, invasion and therapy
- Defining molecular signatures that orchestrate tumor subpopulations in melanoma models mimicking tumor microenvironment and drug tolerance
- Induction of endoplasmic reticulum stress to potentiate immunogenic cell death to improve melanoma therapy
- Generating mathematical models of 4D multicellular melanoma spheroids (joint project with Professor Matthew Simpson, QUT)

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Associate Prof Emma Hamilton-Williams

Research Field

Immunology and pathogenesis of type 1 diabetes

Research Synopsis

Type 1 diabetes is an autoimmune disease with no cure. Our laboratory focuses on investigating the immune defects leading the destruction the insulin producing cells of the pancreas and type 1 diabetes and studying immunotherapeutic strategies to correct these defects. We also study environmental drivers that may trigger the autoimmune process, with a focus on the role of the gut microbiota and how the microbiota may be manipulated to prevent disease.

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 immunotherapy in type 1 diabetes.

Our goal is to restore tolerance in autoreactive islet-specific T cells. We are using multi-dimensional profiling of antigen-specific T cells to optimise our immunotherapy strategy.

(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 function in type 1 diabetes alter the islet immune response.

We are using germ-free mice colonised with human derived microbiota to study how changes in the gut flora of patients may modify the immune response and lead to disease. We are also using human cohort and intervention studies with a multi-omic analysis approach to understand how the host and microbiota interact in the lead-up to disease onset.

Research Projects

- Host-microbiota interactions in the pathogenesis of type 1 diabetes: wet lab and dry lab (bioinformatics based) projects available
- 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 vascularisation 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.

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Dr Snehlata Kumari

Research Field

Immunomodulatory signalling mechanisms regulating inflammation

Research Synopsis

Our work is focused on elucidating immuno-modulatory signalling mechanisms regulating inflammation to develop new therapeutic strategies for inflammatory skin diseases and cancer. The skin forms immunological, mechanical and structural barrier to protect the organisms from external challenges. Active communication between soluble factors and cells in the skin, such as epithelia, stromal and immune cells are crucial to maintain skin homeostasis. We have previously shown that NF-kappaB, cytokine and cell death signalling pathways are crucial in regulating inflammation. We aim to deciphering novel signalling pathways and mechanisms in immune and non-immune cells in regulating skin inflammation and cancer. The project provides excellent exciting opportunity to students to learn and engage in techniques in Immunology, Molecular Biology, Cell Biology and Genetics including microscopy, CRISPR/Cas9-mediated genetic engineering, flow cytometry as well as in vitro and in vivo models.

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Dr Xiaowen Liang

Research Field

Liver cancer

Research Synopsis

Liver cancer is the fastest increasing cancer with the 4th highest cancer mortality rate worldwide. Despite significant advances in the treatment of liver cancer, response rates of current treatments are still low. Our projects aim to investigate and understand the role of tumour self-seeding and tumour microenvironments (hepatic stellate cells) in liver cancer progression and chemoresistance. The success of these studies will identify a new cell population within primary tumour with prognostic and therapeutic potential and provide new strategies to improve the response to current treatments and prevent the relapse of liver cancer.

Research Projects

- Therapeutic targeting of tumour self-seeded cells in liver cancer
- Investigating the mechanism of chemotherapy-induced hepatic stellate cell activation in liver cancer

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Dr Aideen McInerney-Leo

Research Field

Translating genomics into clinical practice

Research Synopsis

I am a clinician-academic whose interactions with patients have shaped my research questions and fuelled my enthusiasm for the importance of clinical research. I trained as a genetic counsellor and my research now focuses on the integration of genomics into clinical care. My research program has had three primary themes: evaluating the psychosocial impact of genetic conditions and/or genetic testing; evaluating genetics education preferences for patients and healthcare providers; and using next-generation sequencing to increase diagnostic yield for rare disorders.

Research Projects

- Exploring whether genetic fatalism affects sun-related health behaviours in high-risk individuals following genetic testing
- Evaluating the efficacy of videos to promote informed consent for genetic testing
- Mainstreaming Genetic Testing for Melanoma into Dermatology Practice.X

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Dr Ahmed Mehdi

Research Field

Genomic medicine, Computational Immunology, Bioinformatics and COVID-19 biomarkers

Research Synopsis

The novel coronavirus disease-2019 (COVID-19) is a recently emerged human pathogenic disease and announced as a pandemic by the WHO. A number of genomic, proteomics and cellular markers have been uncovered that correlate with disease onset. The COVID-19 symptoms can vary from modest, mild to severe respiratory distress syndrome. The factors that trigger COVID-19 patients to get severe disease are largely unknown, but are believed to be a combination of prior health conditions and some immune system dysregulation. Our vision is that a better understanding of COVID-19 progression mechanisms can be established by integrating the huge resource of the heterogeneous data that is currently being generated in COVID-19 research.

In this research project the student(s) will learn the process of performing Biostatistics and Bioinformatics approaches towards predictive COVID-19 markers. A search strategy has been already established for the identification of studies of interest. They will use and learn R programming language, linear and/or probabilistic modelling.

Research Projects

- Prediction models of severe onset of COVID-19
- Developing connectivity maps of COVID-19 disease

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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 characterise 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 Abbas Shafiee

Research Field

Stem cell biology and regenerative medicine

Research Synopsis

Using innovative technologies, including 3D printing, stem cell biology, organoid technology, tissue engineering, and advanced three-dimensional *in vitro* and *in vivo* models, we aim to develop new therapies to improve tissue regeneration.

Research Projects

Research Project (1): *Skin Organoid for Human Skin Development and Reconstructive Surgery*

The application of stem cells to derive functional skin is a research area of great interest. Recent studies showed success in generating some types of skin cells from human pluripotent stem cells. However, creating fully functional skin organ is still an unmet challenge in the field. Organoids are 3D cell structures that have been used to recapitulate the anatomy and physiology of the respective organs. In our team, we aim to develop protocols for generating human pluripotent derived skin organoids to recapitulate human skin organs. The human skin organoids generated in the current study could be utilised as an important platform to study human skin development, disease modelling, and reconstructive surgeries. This project involves advanced imaging technologies, cell and molecular biology assays, three-dimensional in vitro models, and in vivo studies.

Research Project (2): *Stem cells for Wound Healing*

Despite considerable research on the potential of stem cell-based therapies in enhancing wound closure, their potential in reducing scarring is limited. We aim to combine 3D printing technology and stem cell therapy to develop new therapies for skin wounds. Therefore, using 3D printing we develop biomimetically designed constructs with a critically mechanical characteristic and seed them with stem cells and investigate their regenerative potential. This project involves using novel 3D printing methods, and cell and molecular biology assays.

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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

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Dr Chris Slape

Research Field

Leukaemia; pre-leukaemia, stem cells

Research Synopsis

Pre-leukaemia is any abnormal haematopoietic state which precedes leukaemia. In some cases (eg. myelodysplastic syndrome), it is clinically apparent. In other cases (eg. T cell leukaemia), patients do not present until acute leukaemia is apparent, and the pre-leukaemic phase can be considered a missed opportunity for therapy.

One of the features of many pre-leukaemic states is, paradoxically, a deficiency of cell numbers in certain stem cell and progenitor cell populations. In our models, we have found that restoration of these cell numbers, by various manipulations, mitigates or abolishes progression to full leukaemia. Our current aims are centred on understanding the mechanisms by which this occurs, and identifying ways to exploit this finding for therapeutic implementation.

We use in vivo and in vitro models, multi-colour flow cytometry, single cell RNA sequencing and imaging technologies to drive our research. All projects have flexible scope and can accommodate the diverse interests of students.

Research Projects

- T cell pre-leukaemia detection in humans
- Eph-ephrin interactions in pre-leukaemia
- Cell competition as a tumour suppressor mechanism
- Therapeutic progenitor restoration in pre-leukemic mice
- Imaging analysis of deficient and restored progenitor populations

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Professor H. Peter Soyer

Research Field

Early detection of melanoma

Research Synopsis

Professor Soyer is an internationally renowned academic dermatologist with over 30 years experience in the field with special expertise in preventative dermatooncology, dermatopathology and dermatologic imaging. His main research focus is skin cancer (both melanoma and keratinocyte skin cancer), with a particular interest in early detection strategies and expanding the concept and applications of teledermatology and teledermoscopy. He is Chief Investigator of the CRE for the Study of Naevi was awarded an NHMRC Partnership Grant to implement an innovative 3D teledermatology network for the early detection of melanoma in high risk individuals. He was awarded a MRFF Practitioner Fellowship, Next Generation Clinical Researchers Program. Most recently he obtained funding from the Australian Cancer Research Foundation (ACRF) to establish the Australian Centre of Excellence in Melanoma Imaging & Diagnosis (ACEMID). ACRF ACEMID will enable establishment of 15 3D total body imaging systems, linked by a telemedicine network, across Australia's east coast, and facilitate research in the early detection of melanoma.

Research Projects

- Australian Cancer Research Foundation (ACRF) Australian Centre of Excellence in Melanoma Imaging and Diagnosis (ACEMID)
- NHMRC Collaborative European Union grant: Intelligent total body scanner for early detection of melanoma
- Automated Objective deep phenotype for melanoma risk factors from 3D total body imaging
- Validation of AI software for lesion diagnosis and change detection

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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

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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

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Professor Ranjeny Thomas

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 characterising 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

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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

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Professor Brandon Wainwright

Research Field

Developing new therapies for paediatric brain cancer

Research Synopsis

Brain cancer is the most common cause of cancer-related death in children. Since the establishment of core radiotherapy and chemotherapy approaches around 25 years ago overall survival has not improved at all despite many clinical trials. Additionally, for those children who survive they commonly suffer serious long term side effects of the treatment itself. Therefore there is an urgent need for better treatments to improve survival, and to discover approaches to both prevent and treat the side effects of therapy.

The Wainwright laboratory discovered the first gene known to cause brain cancer in children. Since that time we have focused on defining the cells of origin of the disease, the genetic pathways that lead to tumour growth and metastasis and the development and testing of new therapies. Our approaches include cell biology, developmental neurobiology, genetics/genomics/bioinformatics and, increasingly, immunotherapies. We have strong and active clinical linkages locally, nationally and internationally and a number of projects that are either in the clinic, or will be in the next 12 months.

Research Projects

- Manipulating the inflammatory response to reduce the side effects of chemotherapy and radiotherapy
- The discovery of genes which influence the response of medulloblastoma to radiotherapy
- Factors which regulate the blood-brain barrier and therapeutic effectiveness in brain cancer
- Attacking cell cycle regulation and the cytoskeleton in medulloblastoma – the molecular basis of the response and drug resistance
- A liquid biopsy approach to monitoring molecular basis of therapeutic response and relapse in brain tumour patients

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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) medicated 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

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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
- Antibody-mediated enhancement of inflammation

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Professor Di Yu

Research Field

T-cell Immunology and Immunotherapy

Research Synopsis

Dr Di Yu is a leading immunologist with a major research focus on the function of T cell subsets in autoimmune diseases, infection and cancer. His research utilises mouse models to dissect immune mechanisms, analytic approaches to monitor individuals' immune features and clincial trials to modulate immune respsonses. He published in top-tier journals including Nature, Nature Immunology, Nature Medicine and Immunity and is a Clarivate Highly Cited Researcher (2019).

Research Projects

- The regulation of T cell-B cell interaction in vaccination and autoimmune diseases
- Protective and pathogenic function of cytotoxic T cells in infection and cancer
- Cytokine-based immunotherapy
- Using machine learning to understand the human immune system

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