RESEARCHER PROFILES AND PROJECTS
AT THE UNIVERSITY OF QUEENSLAND DIAMANTINA INSTITUTE

2018/2019
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
- Immunotherapy
- Genomic Medicine
- Skin and Skin Cancer
- Immunity and Inflammation
STUDENT RESEARCH PROJECTS

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
https://di.uq.edu.au/study/undergraduate

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

WINTER RESEARCH PROJECTS
For further information visit:
https://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:

HONOURS PROGRAM
UQDI hosts honours students enrolled through other schools within the Faculties of Science or Medicine at The University of Queensland, 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:
https://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:
https://medicine-program.uq.edu.au/research/research-your-medical-degree

RESEARCH HIGHER DEGREES
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: https://medicine.uq.edu.au/future-students#qt-study-foundation-tabs-4
ASSOCIATE PROFESSOR ANTJE BLUMENTHAL

Research Field
Innate Immunity and Infectious Diseases.

Research Synopsis
With antimicrobial 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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PROFESSOR RICCARDO DOLCETTI

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.

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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.
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.
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.

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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.
DR STEPHEN MATTAROLLO

Research Field
Immunology and Immunotherapy in Blood Cancers.

Research Synopsis
We fundamentally investigate the interactions between blood cancers (leukaemias/ lymphomas) and the immune system in order to develop immunotherapy strategies that will be most effective for achieving durable clinical responses and improving patient outcomes.

We are developing a range of therapeutic cancer vaccines in mice which aims to stimulate a specific immune response targeting the tumors to halt the growth and spread of the cancer.

We are also investigating how external ‘modifiable’ factors such as chronic psychological stress impacts upon immune system function and how this subsequently affects both cancer progression and responses to cancer therapies. The goal of this research is to identify the consequences of chronic stress and neural pathways on immune function to provide evidence for treatment approaches that aim to minimise impact of stress on this disease.

Research Projects
• NKT cell-targeting therapeutic vaccines for treatment of B cell lymphoma and AML.
• Immunometabolic changes in response to blood cancer environment and impact on anti-tumor immunity.
• Chronic stress (beta-adrenergic signalling) and impact on immune function in cancer and responses to immunotherapy.
• Repurposing chemotherapy for immunomodulation to boost immunotherapeutic approaches.
DR JOHAN MEDINA

Research Field
HLA-G/H2Bl role in the inflammatory process that affects liver regeneration;
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 HELMUT SCHAIDER

Research Field
Understanding the epigenetic mechanisms of stress induced drug tolerance in cancer.

Research Synopsis
Cancer cells exposed to stressors like drugs, hypoxia or nutrient starvation undergo a generic transition in to slow cycling drug tolerant cells.

An in vitro model of this transition from parental cells to multi-drug tolerant cells was established in the lab.

The transition is characterised by epigenetic changes, in particular a distinct pattern of histone modifications.

Studies focus on epigenetic modifiers, which drive these histone modifications.

Experiments employ molecular techniques to determine epigenetic changes, the in vitro model of drug tolerance and findings are tested in xenograft mouse models.

Research Projects
• How can early drug tolerance be prevented to re-sensitise cancer cells to targeted therapies.
• Identify new targets, which prevent histone modifications and the transition into permanent resistance.

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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.
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?

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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.
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 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.

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PROFESSOR JOHN UPHAM

Research Field
Immune dysregulation in asthma.
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 key immune cells such as antigen presenting 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.
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.
• Inhibitory antibodies in Gram-negative sepsis.

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