HUDSON
INSTITUTE OF MEDICAL RESEARCH

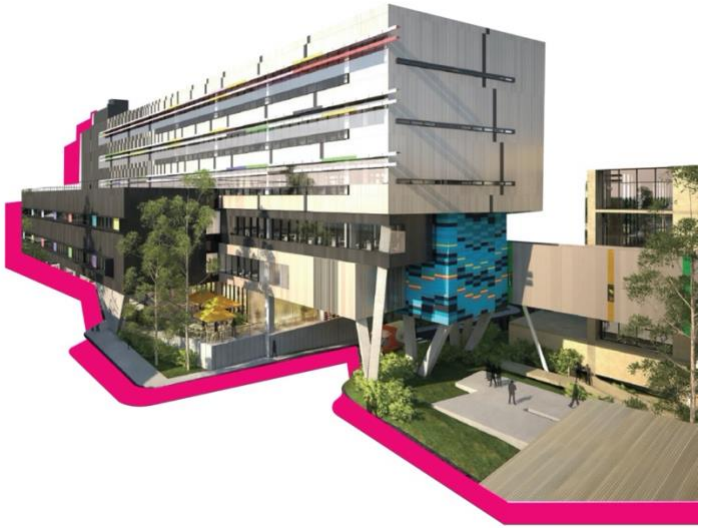
# CENTRE FOR CANCER RESEARCH

## 2021 Student Research Projects

MHTP Monash Health Translation Precinct | MONASH University | HUDSON INSTITUTE OF MEDICAL RESEARCH | Monash Health

# Contents





The Translational Research Facility is connected via a link bridge to Monash Health. The facility provides a crucial link between our scientific discoveries and medical treatments, housing nine world-leading technology platforms and an eight-bed, 21-chair Clinical Trials Centre that support the transition of discoveries from initial Phase I testing through to Phase IV primary health trials.

# Welcome to Hudson Institute

Hudson Institute specialises in discoveries in four areas of medical need

- **Infant and child health**
- **Reproductive health and pregnancy**
- **Inflammation**
- **Cancer**

Our 448 scientists and students focus on laboratory discovery science, plus translational research – taking discoveries to patients and industry for real-world impact.

**296** STAFF

**152** STUDENTS

**50** RESEARCH GROUPS

**283** RESEARCH PUBLICATIONS

## Students at a glance 2019

**58** POSTGRADUATE AND HONOURS STUDENTS COMPLETED

**152** STUDENTS 113 PHD 4 MASTERS 35 HONOURS

**28** STUDENTS WITH MEDICAL TRAINING

We educate and train more than 150 students through our academic affiliation with Monash University. Our postgraduate training is predominantly through the School of Clinical Sciences at Monash Health, part of the Faculty of Medicine, Nursing and Health Sciences at Monash University.

## Our students

- Are exposed to university, institute and hospital research
- Attend national and international conferences
- Publish their research (there were 43 student first author publications in 2019)
- Are mentored by leading supervisors and their teams
- Regularly win prestigious prizes and awards
- Take part in regular networking and learning and development programs.

## All work and no play …

Our students can join in a range of student networking and social events organised by Hudson Institute Student Society (HISS), including being part of the management committee.

## Our precinct

Hudson Institute is a leading Australian medical research institute recognised internationally for discovery science and translational research into infant and child health, reproductive health and pregnancy, inflammation, and cancer.

Our Institute is home to 448 world-class scientists, who push the boundaries of scientific knowledge to answer complex questions about human disease, including prevention and treatment.

We are a founding member of the Monash Health Translation Precinct with partners Monash Health and Monash University. Our close ties with clinicians and industry enable us to translate our discoveries into new preventative approaches, therapies and devices for patients.

Our location at Monash Medical Centre means our research is informed by patient need and our discoveries are rapidly transitioned into practical treatments.

Working alongside clinicians in Melbourne hospitals for more than 50 years, our scientists pioneered IVF and stem cell discoveries and are now leading developments in cell therapies, paediatric cancer and the human microbiome. Our worldwide scientific and medical collaborations provide a foundation for transformative healthcare programs across the globe.

# Centre for Cancer Research

**Location:** Hudson Institute of Medical Research
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**w:** hudson.org.au/research-centre/centre-for-cancer-research/

## Centre Head

**Assoc/Prof Ron Firestein**

Scientists working in the Centre for Cancer Research undertake basic research into the molecular mechanisms underlying the development, growth and metastasis of tumours, as well as the relationship between the innate immune system and cancer. The discovery and development of novel therapies for the treatment of cancers is also an important aspect of the team's work.

**Current key areas of interest include:**

- Links between innate immunity, inflammatory processes and cancer– Role of embryonic signalling pathways in cancer, and the targeting of these pathways with novel therapies
- Cell signalling pathways involved in tumour survival and growth, and the development of monoclonal antibodies to treat glioma and other cancers
- Role of integrin-linked kinase in cell migration and oncogenesis
- Molecular pathways involved in the metastasis of tumours, including colorectal, ovarian, prostate and bladder cancers
- Role of steroid hormones and nuclear receptors in breast cancer development and progression
- Role of peptidase activity on inflammatory signalling and tumour microenvironment in ovarian cancer
- Molecular links between obesity, oestrogens and cancer, and therapies aimed at breaking the linkage
- Role of the microenvironment in tumour progression, chemoresistance and metastasis
- Cancer precision medicine, including childhood brain cancer and solid tumours

## Research Group Heads and Project Supervisors

**Hudson Monash Paediatric Precision Medicine Program (HMPPMP);**
**Cancer Genetics and Functional Genomics**
Research Group Head
Assoc/Prof Ron Firestein

**Developmental and Cancer Biology**
Research Group Head
Dr Jason Cain

**Cancer and Innate Immunity**
Research Group Head
Prof Bryan Williams

**Immunohaematology**
Research Group Head
Dr George Grigoriadis

Research Group Head
Dr Jim Vadolas

**Ovarian Cancer Biomarkers**
Research Group Head
Dr Andrew Stephens

Research Scientist
Dr Maree Bilandzic

**STAT Cancer Biology**
Research Group Head
Dr Daniel Gough

**Functional RNAomics**
Research Group Head
Dr Minni Änkö

**Genetics and Molecular Pathology**
Research Group Head
Asoc/Prof Elizabeth Algar

# Cancer

## Hudson Monash Paediatric Precision Medicine Program (HMPPMP)

### Precision Medicine for Childhood Brain Cancer

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** The Hudson Monash Paediatric Precision Medicine Program marks a significant investment in future clinical management and novel research discovery in childhood cancer.

The program includes:

The development of a living tumour biobank for paediatric solid tumours

At present, very few reliable patient-derived preclinical models are available to researchers. To bridge this gap, our program will establish and bank organoid, cell lines, and xenograft models directly from childhood tumour tissue. The establishment of a living biobank for paediatric solid tumours will provide a critical renewable resource for local, national and international researchers.

The establishment of a functional genomics pipeline

We capitalise on the living biobank tumour samples to integrate genomic data (next generation sequencing) with functional data obtained from high-throughput genetic (Cas9/CRISPR) and results from global pharmacological drug screens.

Translation of genomic data into targeted therapy

The comprehensive molecular analysis of individual patient tumours will help identify both new and existing therapies that can be rapidly implemented in the clinic. This approach will facilitate clinical implications of data from the functional genomics pipeline for individual paediatric patients.

Unique national and global collaborations

The establishment of a living biobank and functional genomic testing for paediatric solid tumours provides a critical resource for local, national and international researchers. Thus, a key element of the program includes national and international stakeholders' involvement to build expertise, share resources and disseminate results that will advance the field of precision medicine for paediatric cancer patients.

**Keywords:** cancer, genetics, paediatrics, brain cancer, CRISPR, drug screens, genomics, personalised medicine, precision therapy

## Cancer Genetics and Functional Genomics

### Understanding cancer resistance to chemotherapy

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** The majority of cancers initially respond very well to standard of care chemotherapeutics but invariably become resistant leading to cancer relapse and patient mortality. This project seeks to identify novel therapeutic targets that will synergise resensitize tumours to chemotherapies in the resistant setting.

**Keywords:** chemotherapy, cancer treatment, drug targets, screen, genetics

### Functional genomic screens to identify new therapeutic targets for bowel cancer

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** Bowel/colon cancer is a major cause of cancer related morbidity worldwide. We will use novel genomic technologies (e.g. CRISPR, shRNAs) to screen the cancer genome in an effort to identify novel therapeutic targets to colon cancer patients.

**Keywords:** genetics, genomics, cancer, screen, personalised medicine

### How can we do a better job detecting cancer in patients? Devising new strategies and technologies using blood based biomarkers

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** Early detection of cancer is a key determinant of patient survival. This project utilises a new class of biomarkers called non-coding RNA (ncRNA) that are differentially expressed in cancer compared to normal tissues. In this project we will determine the value of non-coding RNA in predicting cancer and patient response to cancer therapies.

**Keywords:** genetics, genomics, cancer, diagnostics, non-coding RNA, personalised medicine

## Development of new 3-dimensional models of cancer to model drug resistance and develop new cancer treatment

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** The development of clinically relevant cancer models that recapitulate human cancer is key to both understanding biological mechanisms of cancer growth as well fine tuning therapeutic cancer treatments. In this project, the student will work with both human tissues and animal models to develop 3-dimensional organotypic culture of genetically defined cancer models. Using CRISPR and other technologies we will genetically manipulate these models, and assess the contribution of new targets in mediating cancer growth.

**Keywords:** colon cancer, organoids, models

## Transcriptional regulators as cancer targets: new models and therapeutic approaches

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Assoc/Prof Ron Firestein

**e:** ron.firestein@hudson.org.au

**Project description:** Transcriptional regulators play a key role in activating oncogenic pathways that impinge on tumour growth, invasion and mestasasis. We have recently used CRISPR to generate cancer cell lines with fluorescent and luminescent reporters of key transcriptional pathways in colorectal cancer. In this project, the student will utilise cell biology and molecular biology techniques to dissect the components of the transcriptional machinery in cancer and identify new therapeutic targets.

**Keywords:** genetics, genomics, cancer, oncogenes, transcription

# Developmental and Cancer Biology

## Defining the roles of epigenetic dysregulation in Diffuse Intrinsic Pontine Glioma (DIPG)

**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Jason Cain

**e:** jason.cain@hudson.org.au

**Project description:** Diffuse Intrinsic Pontine Glioma is a highly aggressive cancer that arises in the brainstem of children and is universally fatal. Using next-generation sequencing strategies, significant advancement has been made in understanding the genetic profile of these tumours. Mutations in either of two genes encoding the Histone H3 protein converge on a critical lysine residue resulting in substitution with a methionine residue (K27M) have been described in the vast majority of DIPG patients, suggesting a pathogenic role in this disease. The purpose of this project is to elucidate potential mechanisms of H3K27M tumorigenesis and identify likely therapeutic interventions that could be rapidly progressed into the clinic.

**Keywords:** DIPG, Histone H3, epigenetics, mouse models

## Exploiting Epigenetic Dysregulation in SWI/SNF-Deficient Solid Tumours

**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Jason Cain

**e:** jason.cain@hudson.org.au

**Project description:** Impaired differentiation is a common feature of cancer. We have recently demonstrated the differentiation potential of histone deacetylase inhibitors (HDACi) in paediatric (rhabdoid tumours) and adult (lung adenocarcinoma) solid tumours that are genetically defined by mutations in the SWI/SNF chromatin remodelling complex. Recent genomic studies have shown that mutations in subunits of this complex occur in at least 20% of all cancer. Using preclinical models of SWI/SNF-deficient and intact cancers, the successful candidate will investigate the mechanisms of epigenetic-mediated differentiation and apply these findings to a broader clinical context.

**Keywords:** epigenetics, cancer, peadiatrics, brain, lung

## Immunohaematology

### Deregulation of Key Signalling Molecules in the NF-kB Pathway and their links to Chronic Disease Development

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Dr George Grigoriadis

**e:** george.grigoriadis@monash.edu

**Project description:** Individuals that lack a normal functioning immune system are susceptible to opportunistic infections when challenged by pathogens (e.g viruses and microbes). Treatment with intravenous antibodies can successfully reduce the infectious burden, however a significant number of patients develop non-infectious complications, including autoimmune disease and cancer. We have found the transcription factor called NFkB1 to be a critical regulator of B and T cell function, and deregulation of this factor leads to aberrant lymphoproliferative disease (de Valle et al., 2016). We have examined young and ageing Nfkb1-haploinsufficient mice (Nfkb1+/-) to elucidate the impact of Nfκb1 haploinsufficiency. The Nfkb1+/- mice developed late-onset complications, including splenomegaly, and a multi-organ immune cell infiltrate in target organs. This pathology coincided with multiple aberrant immunological manifestations, including the excessive differentiation of CD4+ T follicular helper cells and the marked expansion of an atypical B cell population characterized by low levels of cell surface CD21 and high expression of the key transcriptional regulator T-bet.

While the above project is ongoing, new and exciting research initiatives have commenced examining the role of NFkB-Inducing Kinase (NIK) – a key kinase that regulates the function of NFkB2. NFkB2 is a related family member of NFkB1, and human mutations in this gene are linked to immunodeficiency, cancer and autoimmune disease. We have generated unique mouse models of NIK by CRISPR/Cas9 technology, and plan to elucidate NIK function in lymphoid and myeloid cell subsets. We anticipate our research findings will lead to important information about these key signaling molecules, how their deregulation is associated with chronic disease development. Future work will consider such molecules as potential diagnostic markers and facilitate the generation novel drug agents.

Projects Aims

1) To examine the role of NFkB1 deregulation in developing B

cells and how this relates to disease pathogenesis;

2) To assess the function of NFkB1 in CD4+ T cells, and understand how the impaired function of NFkB1 impacts on T – B cell collaboration;

3) To determine the roles of NIK in immune cells and chronic disease pathogenesis;

Techniques

Students will gain an understanding of cell signaling, particularly in lymphoid cells; work with unique mouse models; Tissue Culture assays, Flow Cytometry; and gain experience in molecular biology techniques, including CRISPR/Cas9; Real Time PCR; Chromatin Immunoprecipitation (ChIP) and ChIP-sequencing.

**Keywords:** NF-kB

### Harnessing RNA interference in gene therapy vectors for β-thalassaemia

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Dr Jim Vadolas

**e:** jim.vadolas@hudson.org.au

**Project description:** The β-haemoglobin disorders such as β thalassaemia, haemoglobin E (HbE), and sickle cell disease (SCD) are among the most prevalent inherited disorders worldwide. The conditions are the result of mutations in the adult β-globin gene, leading to production of either aberrant or insufficient β-globin protein. Symptoms appear in the first year of life, the period when fetal haemoglobin (HbF) is replaced by the adult form (HbA), leaving the patient dependent upon the mutated adult β-globin gene. Much of the pathology of this disease is due to excess α-globin chains forming toxic insoluble precipitates in erythroid cells resulting in cell death, ineffective erythropoiesis and severe anaemia. Interestingly, restoration of balanced globin protein synthesis through the reduction of α-globin expression can ameliorate the disease phenotype, exemplified by individuals who co-inherit α- and β-thalassaemia. This definitive observation forms the basis of a novel therapeutic strategy for β-thalassaemia, involving not an elimination but a targeted reduction of complementary α-globin chains, to mimic co-inheritance of α- and β thalassaemia. While the benefits of increased β-globin expression in the context of β-thalassaemia are very clear, decreasing α-globin expression has not yet been extensively investigated. This project aims to develop novel gene therapy strategies harnessing RNAi in gene therapy vectors for β-thalassaemia. Initial studies will be conducted in vitro using both cell lines and primary haematopoietic stem cells. Further studies will also be conducted in vivo using our unique humanised β-thalassaemia mouse models and patient-derived cells.

**Keywords:** gene therapy, RNA interferance, anaemia

## Epigenetic modifications of the human β-globin locus: new therapeutic targets for haemoglobin disorders

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Dr Jim Vadolas

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**Project description:** Haemoglobin disorders, such as sickle cell disease and β-thalassaemia are the result of mutations in the adult β-globin gene. When these disorders are co-inherited with hereditary persistence of fetal haemoglobin, (high levels of γ-globin gene expression in adult life) the disease phenotype is much reduced. Understanding the mechanism of γ-globin globin gene regulation through development has been the subject of intense investigation for many years. These studies led to an appreciation of the role of epigenetic modifications such as DNA methylation and histone acetylation in globin gene expression and regulation. Networks of regulatory proteins interact with epigenetic complexes to regulate DNA accessibility and histone modifications, thereby determining appropriate patterns of globin gene expression, giving rise to several developmental stage-specific hemoglobin variants. This study will investigate the potential impact of epigenetic regulators on globin gene expression. Functional genomic screening strategies will be performed using RNA interference (RNAi) or CRISPR/Cas9 genome editing to either suppress or knockout the expression of specific epigenetic regulators in erythroid cells modified to express fluorescent reporter genes under the control of the γ-globin promoter. Further studies will also be conducted in vivo using unique humanised β-thalassaemia mouse models. Positive outcomes of such studies could pave the way for better treatment strategies for sickle cell anaemia and β thalassaemia patients by targeting epigenetic regulators to increase fetal globin expression.

**Keywords:** epigentics, RNA interference, CRISPR/Cas9 genome editing

## Impact of impaired immune function in haemoglobin disorders

**Suitability:** PhD/Doctorate, Masters by Research, Honours

**Project leader:** Dr Jim Vadolas

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**Project description:** Haemoglobin disorders, such as sickle cell disease and β-thalassaemia are the result of mutations in the adult β-globin gene. Patients suffering with the most severe form of the disease require chronic blood transfusion for survival. Ongoing transfusion therapy to counteract anaemia exacerbates iron overload, and necessitates iron chelation therapy. One important clinical feature of these conditions is the increased frequency of infectious complications such as pneumonia and sepsis, which are significantly associated with an increased rate of morbidity and mortality. The increased susceptibility to pathogenic organisms has been attributed to multiple deficiencies affecting both innate and adaptive immune systems. What has become apparent, is that iron overload in chronically anaemic patients contributes to aberrant neutrophil effector functions resulting in increased susceptibility to infection and inflammation-related organ damage. This knowledge, combined with the emergence of novel immunomodulatory function and phenotypes for neutrophils has helped to re-invigorate interest in the field. To further understand the clinical significance of aberrant immune function in β-thalassaemia, we will undertake a comprehensive evaluation of the molecular and cellular mechanisms responsible for aberrant innate immune effector functions in β-thalassaemic mice and β-thalassaemia patients. The work proposed in this project will generate a better understanding of the mechanism underlying aberrant immune functions and provide novel insights into disease progression. Positive outcomes of such studies could pave the way for better treatment strategies for β-thalassaemia and related patients.

**Keywords:** thalassaemia, chronic anemia, immune response, iron overload

# Ovarian Cancer Biomarkers

## Identifying New Drug Targets in Ovarian Cancer Stem-Like Cells

**Suitability:** PhD/Doctorate, Honours

**Project leaders:** Dr Andrew Stephens, Dr Maree Bilandzic

**e:** andrew.n.stephens@hudson.org.au

**Project description:** Ovarian cancers are the most lethal of all gynaecological malignancies, with <30% 5-year survival. Cancer progression requires cells to orchestrate a highly co-ordinated program of attachment, migration and invasion into healthy tissues. We have identified that a specialized subset of stem-like cancer cells, termed “Leader Cells”, control these processes in ovarian tumours. Leader cells are also enriched by chemotherapy and exert immune suppressive effects in vivo. Existing therapies do not kill or inhibit the leader cell population, resulting in their enrichment over time and ultimately leading to a poor prognosis for patients.

We hypothesize that therapies targeting leader cells will synergize effectively with standard chemotherapy to achieve stable, long-term disease regression.

This project will use a combination of molecular, biochemical and precision medicine approaches to investigate molecular pathways and identify “druggable” targets in ovarian cancer leader cells, and develop therapeutic strategies for translation into clinical practice.

**Keywords:** cancer, stem cell, therapeutic, metastasis, ovarian, translation

## Photodynamic Therapy for Cancer Treatment

**Suitability:** PhD/Doctorate, Honours

**Project leaders:** Dr Andrew Stephens, Dr Maree Bilandzic

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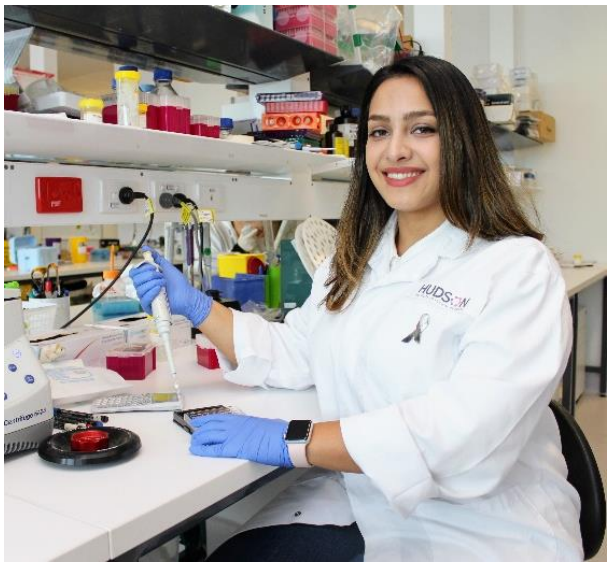
**Project description:** Photodynamic therapy (PDT) involves delivery of a light-sensitising agent into tumours, followed by laser-induced activation and destruction of tumour tissue. This is accompanied by a secondary immune response, resulting in immune-mediated tumour regressesion and in some cases can induce protective immunity.

In collaboration with Invion Ltd and Fotovet Pty Ltd we are developing a new photosensitiser for use in veterinary medicine. This project will generate proof-of-principle for specific veterinary oncology indications, and examine the anti-tumour immune response induced following PDT. This will be sued to initiate veterinary clinical trials, and will also inform human clinical studies.

**Keywords:** photodynamic therapy, cancer, PDT, veterinary, chemoresistance, tumour



# STAT Cancer Biology

## Defining the mechanisms regulating macrophage metabolic reprogramming

**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Daniel Gough

**e:** daniel.gough@hudson.org.au

**Project description:** Detection of microbial components such as lipopolysaccharide (LPS) by Toll-like receptor (TLR)-4 expressed on macrophages induces a robust pro-inflammatory response which has recently been shown to be dependent on metabolic reprogramming. These innate metabolic changes have been compared to the Warburg effect (also known as aerobic glycolysis) described in tumour cells which is required to meet the rapid increase in demand for biosynthetic precursors for lipids, proteins, nucleic acids and the increased energy demand of the inflammatory state. LPS-induced transcription of inflammatory cytokines and chemokines is also dependent on metabolic reprogramming. However, all of these critical studies have been performed on macrophages differentiated ex vivo in media with supra-physiological nutrient levels. Evidence from cancer research shows that traditional cell culture media drastically alters metabolism and skews the outcomes of many studies. However, to date, no studies have been performed on macrophages using physiologically relevant media. Furthermore, no studies on the metabolic reprogramming of primary tissue resident macrophages have been published. This project will address these critical questions and you will gain experience in measurement of mitochondrial activity (seahorse assays), cytokine production (ELISA), transcriptional responses (quantitative real-time PCR and RNA-Sequencing) and metabolomics (mass-spectrometry).

**Keywords:** innate immunology, macrophages, TLR signaling, metabolism

## Defining mechanisms of mitochondrial protein import

**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Daniel Gough

**e:** daniel.gough@hudson.org.au

**Project description:** The JAK-STAT3 signaling pathway is engaged by many cytokines and growth factor stimuli to control diverse biological processes including proliferation, angiogenesis, survival, immune modulation, and metabolism. For over two decades it has been accepted that STAT3-dependent biology is due to its potency as a transcription factor capable of regulating the expression of many hundreds of genes. However, our recent discovery of non-canonical and non-genomic activities of STAT3 from within the mitochondria has expanded this dogma. STAT3 translocates into the mitochondria where it regulates the activity of the electron transport chain and the opening of the mitochondrial permeability transition pore. These have broad consequences including cell survival, the production of reactive oxygen species and ATP in both normal tissue and under pathological conditions. Indeed, loss of mitochondrial STAT3 activity blocks tumour formation by mutated Ras oncogenes. However, the mechanism that controls STAT3's import into the mitochondria remain completely unknown. This project will take advantage of the cell biology and biochemical tools established in my laboratory to address this question which has implications for mitochondrial and cancer biology.

**Keywords:** STAT3, mitochondria, protein trafficking, metabolism, biochemistry

## Functional genomic screening to identify novel approaches to overcome drug resistance in Small Cell Lung Cancer

**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Daniel Gough

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**Project description:** Small cell lung cancer is an aggressive and highly metastatic disease that represents around 15% of all lung cancer patients. The majority of patients (70%) present in the clinic with advanced disease that has spread beyond the lung. The treatment options available to these patients are limited to platinum-based chemotherapy. This is effective in the majority of patients, however almost all will rapidly relapse with platinum resistant disease. There is no effective second line therapies which has meant these patients have an appalling overall survival rate of 2-5% which has not improved over the past three decades. Therefore there is an urgent and unmet need to understand the mechanisms of platinum resistance and how to overcome it to provide meaningful improvements in patient outcomes. My laboratory has developed panels of platinum resistant small cell lung cancer cell lines and genetically engineered mouse models. In this project we will use CRISPR/Cas9 technology to perform unbiased pooled screening (whole genome or draggable targets) to identify mechanisms of resistance which will be interrogated in vitro and in vivo.

**Keywords:** Small Cell Lung Cancer, Metastasis, Mouse models of cancer

## Targeting purine and pyrimidine synthesis to treat Small Cell Lung Cancer

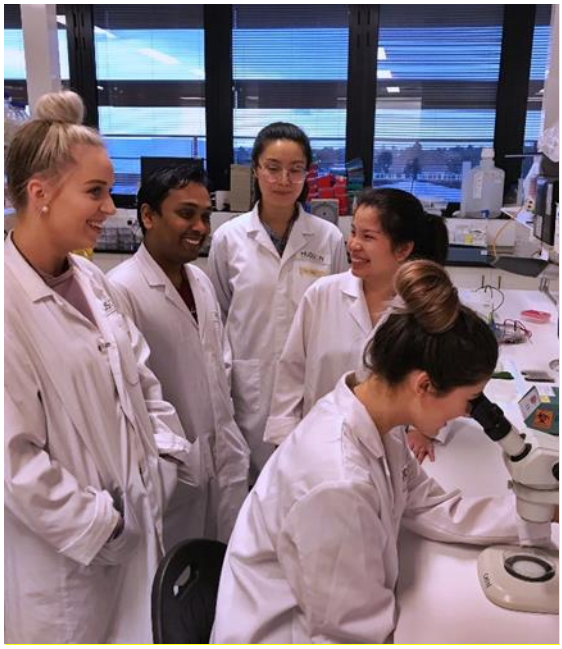
**Suitability:** PhD/Doctorate, Honours

**Project leader:** Dr Daniel Gough

**e:** daniel.gough@hudson.org.au

**Project description:** Small cell lung cancer is an aggressive and highly metastatic disease that represents around 15% of all lung cancer patients. The majority of patients (70%) present in the clinic with advanced disease that has spread beyond the lung. The treatment options available to these patients are limited to platinum-based chemotherapy. This is effective in the majority of patients, however almost all will rapidly relapse with platinum resistant disease. There is no effective second line therapies which has meant these patients have an appalling overall survival rate of 2-5% which has not improved over the past three decades. We have developed mouse models of platinum-resistant small cell lung cancer and performed extensive RNA-sequencing and metabolomics analysis on the primary tumour tissue from these animals which has revealed a dramatic increase in purine and pyrimidine synthesis. Importantly we have shown that inhibitors of these pathways kill small cell lung cancer cell lines. This project will take advantage of our mouse models of small cell lung to investigate the efficacy of these agents in vitro and in vivo as well as their capacity to kill primary or metastatic tumours or both.

**Keywords:** Small Cell Lung Cancer, therapy, mouse models of cancer



# Functional RNAomics

## Discovering the role of miRNA processing in cancer

**Suitability:** PhD/Doctorate, Masters by Research, Honours, Short Projects

**Project leader:** Dr Minni Änkö

**e:** minni.anko@hudson.org.au

**Project description:** Previous studies suggest that overexpression of an RNA binding protein called SRSF3 is required for cancer cell growth and survival, however the underlying molecular mechanisms remain unclear. We have discovered a novel gene expression signature that in associated with SRSF3 expression both in normal highly proliferating cells such as embryonic stem cells and cancer cells. We have mechanistically shown that SRSR3 directly regulates the production of defined set of small noncoding RNAs, microRNAs, that are central for this so-called ‘Oncomir-1 gene expression signature’. This project investigates how SRSF3 and potentially together other RNA binding proteins regulate the production of oncogenic miRNAs, wiht the focus on colorectal cancer.

**Keywords:** RNA binding protein, cancer, oncogene, gene expression, Australian Regenerative Medicine Institute

# Contact our supervisors

**Students are encouraged to contact supervisors to discuss projects, arrange a time to visit the lab and view our facilities. Simply email the supervisor to arrange a time.**

**STEP 1:** Find a project that you are interested in.

**STEP 2**: Email the supervisor: *"I am interested in your student project. Could I please arrange a time to visit you in your lab?"*

All the information you need to enrol is on Hudson Institute's website, or the project supervisor can help you enrol.

**w:** hudson.org.au/students/courses-available/

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