

Honours Projects on offer in the Charles Perkins Centre Hub 2021

Research Group Leader	Department/School	Research Area
Associate Professor Corinne Caillaud	School of Medical Sciences	Biomedical Informatics and Digital Health
Associate Professor Mathias Francois	Centenary Institute of Cancer Medicine & Cell Biology	David Richmond Laboratory for Cardiovascular Development: Gene Regulation and Editing Program
Professor David James	School of Life and Environmental Sciences	Metabolism and Biological Sciences
Dr Melkam Kebede	School of Life and Environmental Sciences	Islet Biology and Metabolism
Dr Mark Larance	School of Life and Environmental Sciences	Biochemistry, proteomics, intermittent fasting, metabolism
Professor Greg Neely	School of Life and Environmental Sciences	Dr John and Anne Chong Lab for Functional Genomics
Dr Samantha Rowebotham	Menzies Centre for Health Policy, Sydney School of Public Health	Citizen science approaches with the Australian Prevention Partnership Centre

ASSOCIATE PROFESSOR CORINNE CAILLAUD

Discipline of Biomedical Informatics and Digital Health
School of Medical Sciences, Faculty of Medicine and Health
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[Academic profile](#)

Two projects related to obesity prevention in adolescents in the Australia-Pacific region.

1. The first one is related to better understanding nutrition and physical activity patterns in various environments and their relation to health outcomes and physical fitness.
2. The second one is related to preventing obesity in young adolescents through digital health intervention – in particular in refining our existing iEngage program through engagement and co-design with users.

ASSOCIATE PROFESSOR MATHIAS FRANCOIS

Group Leader, Medical Research Institutes - Centenary Institute of Cancer Medicine & Cell Biology and The School of Life and Environmental Sciences, Faculty of Science
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[Academic Profile](#)

The David Richmond (DR) program for cardio-vascular development welcomes only a limited number of Honours / PhD candidates to ensure high quality supervision is provided to the student. Usually student work on their own project but embedded in a team with a post doc and research assistant. The DR laboratory is physically located at the CPC and therefore benefits from a great scientific environment from both the Centenary Institute and the CPC.

Project #1

The primary objective of this project is to develop a research study with general and specific in vitro techniques in stem cells and in vivo approaches in early stage mouse embryo to study the molecular basis of cell fate decision during embryogenesis.

This will work take advantage of cutting edge approaches based on single molecule approaches to study the role of different components of the transcriptional machinery in stem cells. Two types of complementary approaches will be used in parallel either based on live imaging methods or on fixed cells with super resolution microscopy. Further the work will be complemented by genomic and transcriptomic approaches to correlate changes in gene output with molecular activity imaged in a cell.

Project #2

The primary objective of this project is to develop a research study with general and specific in vivo techniques in mouse or zebrafish model system to study the molecular and cellular biology of vascular development during embryogenesis.

The biological question is centred around the molecular control of cell fate during lymphatic endothelial cell specification by a novel transcriptional effector. The work will involve wet and dry lab approach to understand how this new gene modulates the program of lymphatic endothelial cell differentiation on a genome wide scale. Techniques used will cover a broad range of skills from phenotyping vascular networks using confocal microscopy to gene editing with crispr/cas9 and genomics and transcriptomics approaches.

THE JAMES LABORATORY

Professor David James

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[Academic profile](#)

1. Genetics of Healthy Ageing

Supervisor: David James

By exploiting the vast genetic landscape of an outbred mouse population we aim to explore the molecular cause of a range of diseases that limit healthy ageing in humans. This includes cardiovascular disease, bone function, diabetes, liver disease and insulin resistance. All of these disorders occur in these mice with different frequencies and are thus amenable to genetic mapping.

2. Insulin Mediated Regulation of Lipolysis

Supervisors: David James and Jacqueline Stoeckli

Insulin, a hormone that is released after a meal, regulates many aspects of metabolism including a process called lipolysis that involves the release of fatty acids into the circulation. Insulin suppresses the release of fatty acids from the fat tissue and while dysregulation of this process can markedly impact whole body metabolism, it is not well understood how insulin regulates this process. Here we will shed light on the mechanism by which insulin regulates lipolysis.

3. Molecular Mechanism of Insulin Resistance

Supervisor: David James

Insulin resistance is a major physiological problem that is associated with an inability of insulin to regulate glucose and lipid metabolism. We now know that metabolism is central to many diseases and how it is regulated in health and disease is a major question.

4. Role of Protein Phosphorylation in Cellular Function

Supervisors: David James and Sean Humphrey

Using advances in mass spectrometry-based proteomics this project aims to uncover how phosphorylation affects the function of proteins and cells in both healthy and diseased states.

5. Dissecting the architecture of the Insulin Signaling Pathway

Supervisors: David James and James Burchfield

The aim of this pathway is to understand how the insulin signalling pathway regulates metabolic homeostasis.

KEBEDE ISLET BIOLOGY AND METABOLISM LAB

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A major feature in the pathogenesis of type 2 diabetes (T2D) is the loss of pancreatic β -cell function. This manifests mainly as a reduction in glucose-stimulated insulin secretion. The molecular mechanisms that control β -cell failure during the progression to T2D remain poorly understood. Our research interest is to understand the mechanisms of β -cell failure in the pathogenesis of T2D. The current projects in the lab focus on understanding the mechanisms behind insulin biogenesis, maturation, stability and targeting for secretion.

1: Role of Golgi proteins on insulin secretory granule biogenesis.

2: Role of cytosolic adaptor proteins on insulin secretory granule biogenesis.

3: Proteomics of insulin secretory granules.

DR MARK LARANCE

CINSW Future Research Leader Fellow

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[Academic Profile](#)

1) Systems biology view of the intermittent fasting response in mice and humans

Intermittent fasting is an effective intervention for the treatment of metabolic disease. But how the proteome in each tissue is reprogrammed by this dietary intervention is currently unknown. Our goal is to use state-of-the-art proteomic analysis to uncover the complex interaction between organ systems that leads to the beneficial effects of intermittent fasting.

2) Characterisation of erusiolin a novel putative hormone

Using our SPEA methodology and unbiased mass spectrometry-based proteomics has allowed us to identify several new putative hormones in human plasma. Erusiolin is among these, which we hypothesise plays a role in appetite regulation. Our goal is to characterise the role of this hormone in mammalian physiology using human clinical trial samples, CRISPR knock-out mice, peptide injection experiments and bioinformatic analysis.

PROFESSOR GREG NEELY

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[Academic Profile](#)

1. Functional Genomics of SARS-CoV2 infection

In this project we are using new unbiased functional genomics techniques to map out human factors required for SARS-CoV2 infections. This project uses CRISPR genome editing, flow cytometry, microscopy, molecular biology and the results of our efforts are tested with live SARS-CoV2 infections through a collaboration. We are working both with modified human cell lines and human stem cell derived tissues.

2. Mechanisms of actions for deadly toxins and venoms

We use whole genome CRISPR genome editing to identify the mechanisms of action for medically relevant drugs, environmental toxins, and deadly venoms. The overall goal of these activities are to define new mechanisms of action, attribute function for uncharacterized human genes, and identify methods to mitigate negative outcomes from toxin or venom exposure. We have generated a new antidote for the box jellyfish sting, and now we are continuing this work identifying the major mechanisms of action and methods to block the most deadly snake venoms in the world. This project will involve CRISPR genome editing and molecular biology, human cell culture including stem cell derived tissues, and animal work, and will help develop new broadly active venom antidotes to help millions of people bitten each year globally.

3. A New cell death gene

We have evaluated all human genes for a role in resistance to 27 commonly used chemotherapies and have identified the new gene *RDD1* (*Required for Drug-induced Death 1*) which controls resistance to at least 7 chemotherapy agents. Importantly, *RDD1* expression is reduced in a wide range of cancers (breast, colorectal, lung, ovarian, gastric, liver, kidney, sarcoma), and *RDD1* levels can predict chemotherapy responses and overall patient survival. We know that *RDD1* plays a role in cancer cell death somehow, but since we only recently found this gene, we don't know the mechanisms involved and are actively investigating this. This project will use CRISPR genome editing, flow cytometry, microscopy, molecular biology, and transgenic mice to investigate how *RDD1* works in health and disease. Overall this project can teach us more about how human cells live and die, will help us enhance the potency of existing chemotherapies or make new more targeted anti-cancer drugs.

4. Human stem cell and organoid biology

Mouse genetics made a major impact on our ability to treat human disease in the 20th century, however major advances in 21st century medicine will be driven by human genetics and stem cell biology. Over the last 10 years there has been a revolution in our ability to make and genetically change human stem cells. We can now generate most human organs (called organoids) in a dish, and can use CRISPR to change the genetic code and learn more about how our genes contribute to disease. Moreover, we can combine these technologies with high throughput drug screening to find new medicines that we know will work in the human system. We are applying these technologies to human brain development, the human pain system, muscular dystrophy or wasting, and heart function.

5. New pain therapies

Our goal is to develop new ways to treat pain that target the underlying cause and not just to treat the symptoms. For this we need a better basic understanding of what is driving chronic pain including back pain, accidental injury, sciatica, cancer pain, shingles, and arthritis. To this end, we use new genome editing (CRISPR) and genetic techniques to find genes and pathways that are necessary and sufficient to drive pain diseases, and we study these new factors using fruit flies, mice, and human pain neurons grown from stem cells. We also apply high throughput drug screening to these systems to accelerate the chances of helping the ~70% of chronic pain patients that are currently not helped by existing drugs.

DR SAMANTHA ROWBOTHAM, PHD, MRES, BSC (HONS)

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I lead a program of work focused around [citizen science approaches](#) with the Australian Prevention Partnership Centre. If this is an area you are interested in then we could put something together. Here is a [paper](#) that introduces this area that you might find useful.