





MONASH MEDICINE, NURSING AND HEALTH SCIENCES

Honours Program in Anatomy & Developmental Biology

The Honours program in Anatomy and Developmental Biology is an excellent opportunity for students to undertake research in one of the Department's key research areas. By enrolling in Honours, students will increase employment opportunities, develop research skills and critical thinking, learn to work collaboratively in a team and develop new discoveries in biomedical science.

STRUCTURE OF HONOURS COURSE

The course is divided into two units

- 1. BMS4100/BMH4100 = 75% of overall course mark
- 2. BMS4200BMH4200 = 25% of overall course mark

BMS4100/BMH4100 – Biomedicine research project

Synopsis

Students will undertake a supervised research project of a publishable standard. Students will research literature relevant to their topic, carry out a research project and present the results of their study in both written and oral form.

Outcomes

On completion of this unit, students will be able to:

- 1. Critically review the scientific literature that underpins the area of the research project;
- 2. Undertake a supervised research project and contribute to project design and management;
- 3. Apply appropriate laboratory techniques, research methodologies and data analysis methods to collect, interpret and report research findings;
- 4. Effectively present research and findings orally showing a firm grasp of the area;
- 5. Analyse research undertaken in the context of the discipline area and report findings in an extended written report.

BMS4200/BMH4200 - Advanced studies in biomedicine

Students will develop analytic abilities and critical thinking skills in specific areas of Biomedical Science. Each module within the unit will include common coursework activities and a common assessment regime.

Outcomes

On completion of this unit, students will be able to:

- 1. Critically review scientific literature in the discipline area of research;
- 2. Apply knowledge of current methodologies and concepts to appraise scientific literature in the discipline area;
- 3. Apply analytical and data analysis techniques relevant to the discipline area of research;
- 4. Effectively communicate concepts in the discipline area of research both in writing and orally.

Course Components – BMS Students

BMS4100 (75%) - Biomedicine research project		
Components	Assessment (%)	
Literature Review & Project Outline	10	
Seminar 1	Pass/Fail	
Thesis	80	
Seminar 2	10	
Thesis Review	*Contributes to thesis mark	
Total	100	

BMS4200 (25%) - Biomedicine research project		
Components	Assessment (%)	
Written Critical Review Exam	30	
Journal Club presentation	40	
Biostatistics Module	30	
Total	100	

Course Components – Science Students

BMH4100 (75%) - Biomedicine research project		
Components	Assessment (%)	
Literature Review & Project Outline	10	
Seminar 1	Pass/Fail	
Thesis	80	
Seminar 2	10	
Thesis Review	*Contributes to thesis mark	
Total	100	

BMH4200 (25%) - Biomedicine research project		
Components	Assessment (%)	
Written Critical Review Exam	30	
Journal Club presentation	30	
Biostatistics Module	40	
Total	100	

How do I apply?

There is a 3-step application process for entry into Honours in Anatomy and Developmental Biology:

- 1. Discuss the projects of interest with the potential supervisors by appointment.
- 2. Submission of a project application signed by the supervisors to the Honours Convenors (adb-honoursteaching@monash.edu)
- 3. Formal application to the Faculty. The application form can be downloaded from the Monash Biomedicine Discovery Institute website: https://www.monash.edu/discovery-institute/honours/so-how-do-i-apply

The closing date for Bachelor of Biomedical Science and the Faculty of Science applications is usually mid-November.

Entry criteria

Bachelor of Science (Honours)

Bachelor of Science students wishing to undertake an Honours degree in the School of Biomedical Science (SOBS) have increased flexibility to complete an Honours degree in the Department of Anatomy and Developmental Biology. **Any major** in the School of Biomedical Science will allow students to undertake an Honours degree within the Department of Anatomy and Developmental Biology.

A distinction grade average (70%) in 24 points of relevant 3rd year units, of which normally 18 points are developmental biology or biochemistry, human pathology, immunology, microbiology, pharmacology and physiology units. In addition to the requirements listed above, students must meet the entry requirements for the Science Honours program relevant to their course of enrolment. Enrolment in an Honours project is subject to approval of the supervisor and the Honours Convenor.

Bachelor of Biomedical Science (Honours)

An average of 70% or higher in at least 24 points at 3rd year (including 12 points in Biomedical Science core units).

If you have a query regarding eligibility, please submit an enquiry online via ask.monash or call 1800 MONASH (1800 666 274).

Key research areas

The Department of Anatomy & Developmental Biology at Monash University is very active in a variety of research areas. It boasts several of the world's leading research scientists in the field of developmental biology and anatomy. Our expertise extends from the genetic and molecular regulation of embryo and foetal development, to stem cell patterning, the anatomy of the adult body and human evolution.

Major areas of research include:

Research Group/Laboratory	Research Area	BDI Program
Prof Helen Abud	Epithelial regeneration	Development & Stem
Abud Laboratory		Cells; Cancer; Immunity
Dr Justin Adams	Integrated morphology and	Development & Stem
Adams Laboratory	palaeontology	Cells
Dr Senthil Arumugam	Cellular physiology	Development & Stem
Arumugam Laboratory		Cells; Neuroscience
Prof John Bertram	Kidney development,	Development & Stem
Bertram Laboratory	programming and disease	Cells; Cardiovascular
	research group	Disease
Prof John Carroll	Oocyte and embryo	Development & Stem
Carroll Laboratory	development	Cells; Cancer;
		Metabolism, Diabetes &
		Obesity
Dr Alex Combes	Development and disease	Development & Stem
Combes Laboratory		Cells; Cancer
Dr Lochlan Fennell	Aging and cancer	Cancer; Development &
		Stem Cells
Assoc Prof Luca Fiorenza	Palaeodiet research	Development & Stem
Fiorenza Laboratory		Cells
Dr David Gonsalvez	Neuroglial development and	Development & Stem
Gonsalvez Laboratory	repair	Cells; Neuroscience
Prof Kieran Harvey	Organogenesis and cancer	Development & Stem
Harvey Laboratory		Cells; Cancer
Assoc Prof Tracy Heng	Stem cells and translational	Immunity; Development
Heng Laboratory	immunology	& Stem Cells
Dr Chantal Hoppe	Engaging students in learning	Education focussed
A D CW 1 H	0 111	D 1
Assoc Prof Karla Hutt	Ovarian biology	Development & Stem
Hutt Laboratory	NT: 1 ' 11'	Cells
Dr Thierry Jarde	Niche signalling, regeneration	Cancer
Jarde Laboratory	and cancer	Company Dec 1
Dr Mitchell Lawrence	Prostate cancer research	Cancer; Development &
Lawrence Group	Harlth and familiar a familiar	Stem Cells
Assoc Prof Michelle Lazarus	Health professions education	Education focussed
Lazarus Research Group	research	Davidamment % Stars
Assoc Prof Daniela Loessner	3D cancer modelling	Development & Stem
Loessner Laboratory Dr. Logon Maggay	Mambalaay, oota zaay 9-	Cells Dayslamment & Stom
Dr Jason Massey	Morphology, ontogeny &	Development & Stem
Massey Laboratory	evolution	Cells

Dr Olga Panagiotopoulou	Moving morphology &	Development & Stem
Panagiotopoulou Laboratory	functional mechanics	Cells
Prof Roger Pocock	Brain development,	Development & Stem
Pocock Laboratory	neuroplasticity and stem cells	Cells; Neuroscience;
		Metabolism, Diabetes &
		Obesity
Prof José Polo	Epigenetics and reprogramming	Development & Stem
Polo Laboratory		Cells; Cancer,
		Cardiovascular Disease
Prof Gail Risbridger	Prostate cancer research	Cancer; Development &
Prostate Cancer Research Group		Stem Cells
Assoc Prof Craig Smith	Comparative development and	Development & Stem
Smith Laboratory	evo-devo	Cells
Prof Ian Smyth	Kidney development and disease	Development & Stem
Smyth Laboratory		Cells; Metabolism,
		Diabetes & Obesity
Dr Amy Winship	Ovarian biology	Development & Stem
Winship Group		Cells; Immunity
Prof Zhicheng Xiao	Neurodegeneration and	Neuroscience;
Xiao Laboratory	regeneration	Development & Stem
		Cells; Immunity

CONTACTS IN THE DEPARTMENT



Associate Professor Tracy Heng
Principal Honours Convenor
Department of Anatomy and Developmental Biology
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Email: tracy.heng@monash.edu



Associate Professor Craig Smith
Honours Co-Convenor
Department of Anatomy and Developmental Biology
Building 76, Level 3, Room 355

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MONASH BIOMEDICINE DISCOVERY INSTITUTE School of Biomedical Sciences

ABOUT THE MONASH BIOMEDICINE DISCOVERY INSTITUTE

(encompassing the School of Biomedical Sciences)

WHO WE ARE

- An institute with the scale and scope to tackle major research questions
- 120+ internationally-renowned research teams committed to addressing global health priorities

WHAT WE DO

- Discovery research to accelerate our ability to prevent, diagnose and treat disease
- Innovate through national and international collaborations and partnerships with researchers, health precincts and industry



700RESEARCHERS



120+
RESEARCH GROUPS



700+
PUBLICATIONS PER YEAR



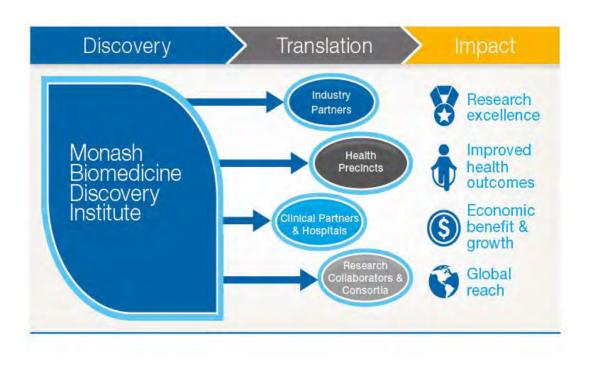
ANNUAL RESEARCH INCOME











MONASH BIOMEDICINE DISCOVERY INSTITUTE School of Biomedical Sciences

With more than 120 internationally-renowned research teams, the Monash Biomedicine Discovery Institute (BDI) is one of the largest and highest-quality biomedical research institutes in Australia. Monash BDI works with national and international collaborators on global health priority areas, including cancer, cardiovascular disease, development and stem cells, infection and immunity, metabolism, diabetes and obesity, and neuroscience.

Our discoveries accelerate the ability to prevent, diagnose and treat disease by leveraging our strong partnerships with researchers, health precincts and industry, together with our access to unparalleled, world-leading research infrastructure.

The Monash BDI encompasses the <u>School of Biomedical Sciences</u>, and is part of Monash's Faculty of Medicine, Nursing and Health Sciences. The School of Biomedical Sciences delivers biomedical sciences education to more than 2,000 undergraduate students and 300 postgraduate students.

Based at Monash's Clayton campus, the Monash BDI is structured to include seven health-focused discovery programs and five discipline-specific departments. This allows for the cross-pollination of ideas needed to tackle the big questions in biomedical research – it is at the intersection of these global health issues that truly innovative discoveries will be made.

DISCOVERY PROGRAMS

- Cancer
- Cardiovascular Disease
- Development & Stem Cells
- <u>Infection</u>
- Immunity
- Metabolism, Diabetes & Obesity
- Neuroscience

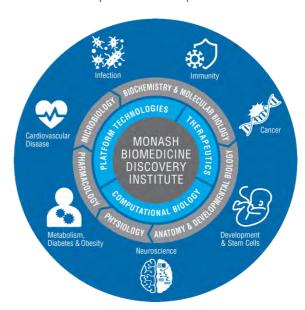
DEPARTMENTS

- Anatomy & Developmental Biology
- Biochemistry & Molecular Biology
- Microbiology
- Pharmacology
- Physiology

CENTRES

Centre for Human Anatomy Education

RESEARCH | EDUCATION | ENGAGEMENT



Stem Cells and Cancer (Abud Lab)



https://www.monash.edu/discovery-institute/abud-lab

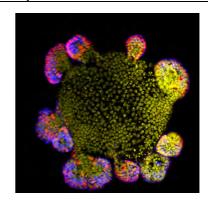
Project Title	Impact of inflammation on intestinal stem cells		
BDI Discovery Program	Development and Ster	n Cells	_
Main Supervisor	Prof Helen Abud	Helen.abud@monash.edu	03 990 29113
	Dr Diana Micati	diana.micati@monash.edu	
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background

Inflammatory bowel disease (IBD) is a multifactorial disease that results in epithelial damage. Intestinal epithelium regeneration is driven by stem cells which can easily be disrupted following injury. This project investigates how inflammatory signals in IBD affect the stem cells and their ability to repair the intestine.

Project aim/s

This project aims to understand the impact of environmental signals on intestinal stem cell function in IBD.



Techniques

This project will involve the use of patient-derived small intestinal organoid cultures to mimic the IBD microenvironment. A range of techniques, including immunofluorescence, single cell and bulk RNA Sequencing, gene editing, and drug assays, will be employed.

Stem Cells and Cancer (Abud Lab)



https://www.monash.edu/discovery-institute/abud-lab

Project Title	Utilising patient-derived organoids for pre-clinical studies in colorectal cancer		
BDI Discovery Program	Development and Ste	em Cells	
Main Supervisor	Dr Rebekah Engel	rebekah.engel@monash.edu	99029196
Other Supervisors	Prof Helen Abud	helen.abud@monash.edu	99029113
	Dr Horace Chen	Horace.chan@monash.edu	99054780
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background

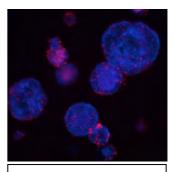
Colorectal cancer is one of the leading causes of cancer-related deaths worldwide. Patients diagnosed with colorectal cancer often experience different clinical outcomes and drug responses, even when controlled for similar pre-operative features, tumour stage and pathological characteristics.

Project aim/s:

This project aims to investigate factors that influence a patient's ability to respond to treatment and determine how we might overcome treatment resistance to improve outcomes for patients.

Techniques to be utilised:

This project will involve a range of techniques including working with human colorectal tumours, patient-derived organoid cell culture, CRISPR/Cas9 genome editing in organoids, drug sensitivity assays and immunohistochemistry.



Human colorectal cancer organoids stained with Hoechst (blue) and propidium iodide (red) to mark live and dead cells, respectively.

Stem Cells and Cancer (Abud Lab)



https://www.monash.edu/discovery-institute/abud-lab

Project Title	Development of the regulation of intestinal epithelial cells		
BDI Discovery Program	Development and Ster	n Cells	
Main Supervisor	Dr Sonja McKeown	Sonja.mckeown@monash.edu	9905 0202
Other Supervisors	Prof Helen Abud	Helen.abud@monash.edu	99029113
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background

The growth and differentiation of the intestinal epithelium can be affected by signals from the enteric nervous system. This can alter the functioning of the gut in different conditions, such as stroke, gastrointestinal cancer and inflammatory bowel disease.

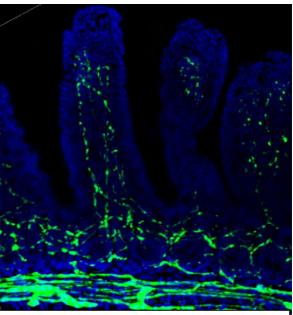
Currently, there is little known about when these interactions begin to occur during post-natal development, and when the epithelium is able to respond to signals from the nervous system.

Project aims:

This project aims to investigate the time during development when the mouse gastrointestinal epithelium becomes capable of responding to signals from the nervous system.

Techniques

This project will use a variety of techniques, including isolation and culture of epithelial stem cells in organoids, qPCR, immunofluorescence and confocal microscopy.



Confocal image showing the extent of neuronal fibres (green) innervating the gastrointestinal mucosa in an adult mouse.

Integrated Morphology and Palaeontology (Adams Lab)



https://www.monash.edu/discovery-institute/adams-lab

Project Title	What's the Deal with the Devil?		
BDI Discovery Program	Development and Stem Ce	ells	
Main Supervisor	A/Prof JW Adams	justin.adams@monash.edu	03 9902 4280
Other Supervisors	A/Prof A Evans	alistair.evans@monash.edu	03 9905 3110
Location	C154 (10 Chancellor's Wall	k, Clayton Campus)	

Background:

The Tasmanian Devil is the last living large carnivorous marsupial in Australia, and extremely unique in their adaptations relative to other living marsupials. Unfortunately, Devil populations are currently at extreme risk due to Devil Facial Tumour Disease (DFTD), which is decimating Tasmanian populations – and leading to significant human intervention to save the species from extinction. These efforts are complicated by the lack of basic biological data about Devils in the literature.



Project aim/s:

In this project, we will take advanced imaging data from contrast-enhanced CT and the Australian Synchrotron to develop a structural model of Tasmanian Devil anatomy – from muscuoloskeletal to neurovascular. An imaging-based approach to build virtual histology and anatomy will fill in critical data on how this species is adapted to their carnivorous lifestyle – and provided essential data on how DFTD impacts various organ systems in the species.

Techniques to be utilised:

This project will utilise techniques applicable to a range of comparative anatomy and modern biological studies including advanced imaging-based reconstruction of organs, 3D morphometrics, 3D data processing and 3D printing, and statistical analysis of shape. Equally this project will develop fundamentally essential data on Devil anatomy that feeds into a variety of disciplines – from evolutionary biology to veterinary management.

Integrated Morphology and Palaeontology (Adams Lab)

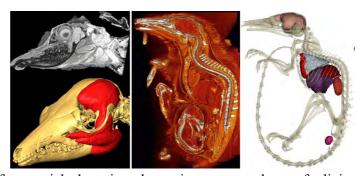


https://www.monash.edu/discovery-institute/adams-lab

Project Title	Australian Marsupials in Arid Habitats: Past Adaptations & Future Survival		
BDI Discovery Program	Development and Stem	ı Cells	
Main Supervisor	A/Prof JW Adams	justin.adams@monash.edu	03 9902 4280
Other Supervisors	A/Prof A Evans	alistair.evans@monash.edu	03 9905 3110
Location	C154 (10 Chancellor's Walk, Clayton Campus)		

Background:

Many different radiations of Australian marsupials have adapted to live in dry environments across the continent. While some of the major biological and physiological ways that marsupials have achieved success in arid ecosystems – from dry grasslands to true deserts – have been studied in common marsupials species, the range and diversity of marsupial adaptations remains unknown. This is not



only a gap in our scientific understanding of marsupial adaptations, but an important study area for living marsupial conservation in changing climates.

Project aim/s:

In this project, we will use advanced imaging methods at the Australian Synchrotron and Monash Biomedical Imaging to unlock the first anatomical data from key organs and organ systems ever obtained from vulnerable, endangered and extinct marsupial species. When placed in a comparative framework we will explore how marsupials have adapted their body systems (from kidneys to lungs to circulatory systems) to occupy hot and dry habitats. In doing so we will also explore many species' anatomy for the first time – from pig-footed bandicoots to greater and lesser bilbies.

Techniques to be utilised:

This project will utilise techniques applicable to a range of comparative anatomy and modern biological studies including medical imaging-based reconstruction of organs from Synchrotron, CT and MRI data, 3D morphometrics, 3D data processing and 3D printing, and statistical analysis of shape. Equally this project will develop new methods and approaches to quantify adaptive structures that reflect form-function relationships across larger datasets and diversity of living and extinct marsupial species.

Development and Disease (Combes Lab)

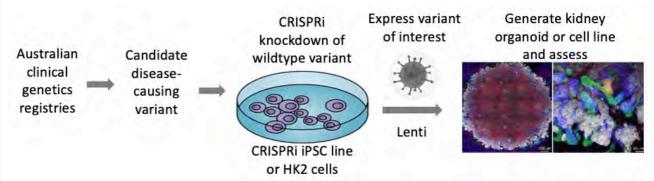


https://www.monash.edu/discovery-institute/combes-lab

Project Title	Stem cell models of inherited kidney disease	
BDI Discovery Program	Development and Stem Cells	
Main Supervisor	Dr Alex Combes <u>alex.combes@monash.edu</u> 99056219	
Other Supervisors		
Location	Level 3, 19 Innovation Walk, Clayton Campus	

Background: Chronic kidney disease is estimated to affect 13% of the global population and half of all adults over the age of 70, with end-stage patients requiring a kidney transplant or life-long dialysis. Human experimental models of genetic and environmental drivers of kidney disease are required to study disease mechanisms and test new therapeutic strategies. We are part of a multidisciplinary project involving clinicians, bioinformaticians and disease modelling experts to improve the capacity to predict and validate new candidate genetic variants (mutations) associated with inherited human disease.

Project Aims: This project aims to experimentally test candidate disease-causing mutations in human kidney cell lines and stem cell-derived kidney organoids.



Techniques:

- Cell culture: immortalized cell lines, human induced pluripotent stem cells (iPSCs)
- Generation and culture of iPSC-derived human kidney organoids
- Gene knock-down with CRISPR interference (CRISPRi)
- Overexpression of candidate disease causing variants with lentiviral vectors
- Gene and protein expression assays (qPCR, Western Blot)
- Immunofluorescence and microscopy

Aging and Cancer (Fennell Lab)



https://research.monash.edu/en/persons/lochlan-fennell

Project Title	Oncogenic Aging – Uncovering the conduits between aging and colorectal cancer		
BDI Discovery Program	Cancer		
Main Supervisor	Dr Lochlan Fennell	lochlan.fennell@monash.edu	99051033
Other Supervisors		-	
Location	Clayton Campus		

Background

Aging and neoplasia are two diametrically opposing biological processes. Aging is characterised by cells exiting the cell cycle and cancer by an overwhelming increase in cell turnover and immortality. Yet there exists a clear link between advanced age and cancer development. Aging is the strongest risk factor for colorectal cancer, yet we know very little about how the aging process predisposes to bowel cancer.

We have previously shown that reversing certain ageassociated alterations in the normal intestinal epithelium can reduce the capacity for oncogenes, such as *Braf*, to transform the cell (Figure 1).

Aim

In this project, we will aim to establish how responses to oncogenic stimuli differ in aged and young intestinal epithelial cells. These data will inform on why the aged epithelium is at risk of cancer initiation.

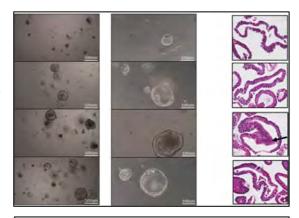


Figure 1: Organotypic assay demonstrating the effects of reversing age-associated DNA methylation on the capacity for BRAF mutation to induce transformation (Top row).

Techniques

This project will use 3D organoid models and novel RNAseq and proteomics approaches to evaluate differences in how aged and young epithelial cells respond to oncogenic mutations. Identifying these differences is crucial for designing preventive interventions aimed at reducing cancer predisposition with age. This project will comprise of both wet and dry lab components. Students can expect to gain experience in stem cell modelling and organoid culture, computational biology, and classical cell and molecular biology techniques.

Paleodiet Research (Fiorenza Lab)

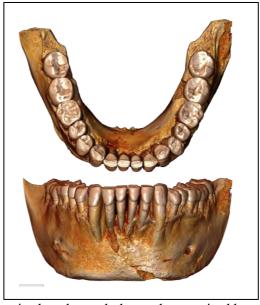


https://www.monash.edu/discovery-institute/fiorenza-lab; www.palaeodiet.org

Project Title	Form, function and wear of Neanderthal teeth			
BDI Discovery Program	Development and Stem Cells			
Main Supervisor	Luca Fiorenza	luca.fiorenza@monash.edu	03 990 59809	
Other Supervisors				
Location	Building 13C, Clayto	Building 13C, Clayton Campus		

Background:

Size and shape variation of molar crowns in humans play an important role for testing phylogenetic hypotheses and for better understanding how species adapted to their environment. Recent studies have shown that Neanderthal dental morphology is characterised by distinctive traits with a marked expression and high frequency, differing from those of modern humans. This Honours project will examine molar functional morphology of important fossil specimens of Neanderthals and modern humans using a multidisciplinary approach that integrates dental topographic methods with tooth wear and enamel thickness analyses derived from high-resolution 3D digital models of teeth.



Project aim/s:

This Honours project aims to understand if Neanderthal cranio-dental morphology, characterised by an overall robusticity with a forwardly projecting face and extensive anterior dental wear, was truly adapted to resist powerful bite forces.

Specifically, the Honours project has three key aims:

- To reconstruct the relationship between occlusal wear and tooth architecture during masticatory function:
- To compare the masticatory efficiency in Neanderthals and modern humans;
- To understand how diet and cultural habits in past human species influenced tooth morphology and enamel thickness variation.

Techniques to be utilised:

The Honours project will be based on a multidisciplinary approach that include advanced 3D computer methods, dental anthropology, biomechanics, functional morphology, palaeontology and statistics. This approach may also have wide future applications in orthodontics, where the relationship between facial morphology, occlusion and tooth morphology is still not well understood.

Paleodiet Research (Fiorenza Lab)



https://www.monash.edu/discovery-institute/fiorenza-lab; www.palaeodiet.org

Project Title	Masticatory efficiency of modern human teeth: a biomechanical study		
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Luca Fiorenza	luca.fiorenza@monash.edu	03 990 59809
Other Supervisors	Jing Fu	jing.fu@monash.edu	
Location	Building 13C, Clayton Campus		

Background:

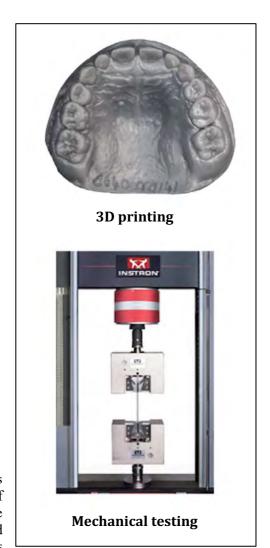
Dental enamel is the hardest and most mineralised tissue found in vertebrates. It plays two fundamental roles: first, it enhances resistance to fracture from biting hard objects. Second, it prolongs tooth lifetime from wear. However, tooth wear is an inevitable process, a process caused by chemical and/or mechanical factors associated with the mastication of food, which changes tooth shape, affects function and that compromises structural integrity. Should we consider tooth wear as an adverse, destructive process, or should we consider it as an inevitable adaptation to make our teeth more efficient? Should we prevent or reduce the destruction of tooth substance, or should we actually facilitate it to prolong the life of our dentition?

Project aim/s:

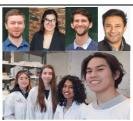
In this project we will investigate if modern human teeth remain functionally efficient for fracturing foods despite wear. We will obtain experimental data of chewing efficiency through mechanical testing that will employ 3D printed teeth and food items. For this study we will use 3D digital models of the dentition of Australian Aboriginal children of the Yuendumu Reserve (Northern Territory), who were annually observed between 1951 and 1971.

Techniques to be utilised:

This is an interdisciplinary project between the Departments of Anatomy and Developmental Biology and Department of Mechanical and Aerospace Engineering. The project will be based on dental anatomy, CAD modelling, 3D printing and biomechanics. The methods may have potential applications in biomedicine and orthodontics.



Neuroglial Development and Repair (Gonsalvez Lab)



https://research.monash.edu/en/persons/david-gonsalvez

Project Title	Using engineered human cortex to better understand the brains insulation		
BDI Discovery Program	Neuroscience; Development and Stem Cells		
Main Supervisor	David Gonsalvez david.gonsalvez@monash.edu 9902 0946		
Other Supervisors	(TBA)		
Location	Level 5 Building 75 Innovation Walk, Monash University Clayton Campus		

Background:

About 50% of your brain volume is accounted for by white matter, which is made up of axons (your brains the electrical wires) and oligodendrocytes (the cells that electrically insulate these axons). It is often underappreciated that white matter is highly plastic, in fact your capacity learning some complex motor tasks depends on this white matter plasticity. Surprisingly, we still know relatively little about oligodendrocyte biology; how are proteins are distributed thought the insulating material (called myelin), or how oligodendrocytes change their insulating material, myelin, in response to experience/neural activity. One limitation to studying the human brain has been access to human neural tissue. Our team now has the capacity to make human brain tissue from induced pluripotent stem cells, importantly these brain organoids can be patterned to different parts of the CNS (Figure 1). Using this new technology, ask the questions like how are proteins distributed throughout the white matter of human oligodendrocytes from different cortical regions? Or how experience or neural activity change the composition of proteins in the brains electrical insulating material?

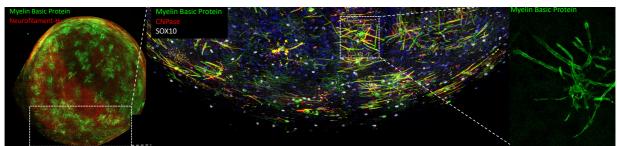


Figure 1: Human iPSC derived CNS organoid (with oligodendrocytes expressing myelin basic protein)

Project aim/s:

To determine if myelin basic protein is organised distinctly in human oligodendrocytes derived from different parts of the developing human cortex.

Techniques to be utilised:

Chemical tissue expansion (or expansion microscopy) will be used on human iPSC derived brain organoids to enable us to optically resolve beyond the limits of light microscopy. Immunofluorescence and advanced microscopy techniques (spinning disc, light sheet, widefield and confocal microscopy) will then be used to image and identify, for the first time, the 3D localisation of key proteins in human myelin.

Organogenesis and Cancer (Harvey Lab)



https://www.monash.edu/discovery-institute/harvey-lab/home

Project Title	Watching the Hippo pathway in real time in growing organs	
BDI Discovery Program	Development and Stem Cells; Cancer	
Main Supervisor	Kieran Harvey	kieran.harvey@monash.edu
Other Supervisors	Samuel Manning	sam.manning@monash.edu
Location	Level 3, 19 Innovation Walk, Clayton Campus	

Background

A new frontier in biomedical research will involve watching individual proteins work in real time, in living organs. Traditionally, researchers have drawn conclusions about gene function using indirect techniques that only allow us to infer what a gene normally does, without actually watching it work. For example, we create organisms that lack a particular gene and determine whether something goes wrong. If the loss of gene X causes organs to overgrow then we assume that gene X normally limits organ size. This has been an extraordinarily powerful approach for interrogating gene function but it cannot substitute the ability to watch gene products executing their function in real time, which allows determination of exactly when, where and how they work.



A *Drosophila* eye with a **Hippo pathway** mutation. These eyes grow in an uncontrollable fashion.

Project aim/s

We will investigate the role of the Hippo tumour suppressor pathway in organ growth by watching, for the first time, its activity, in growing organs, in real time. This will provide novel insights into normal organ growth and pathogenic organ growth in diseases such as cancer.

We aim to observe Hippo pathway activity in real time in the following situations:

- a) When organs are actively growing
- b) When organs stop growing
- c) In regions of organs that are subject to mechanical compression
- d) Throughout the cell cycle

Techniques

You will be taught an array of techniques including ex vivo organ culture, live multi-photon microscopy, image analysis and *Drosophila* genetics.

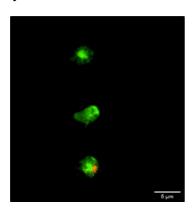
Stem Cells and Translational Immunology (Heng Lab)



https://www.monash.edu/discovery-institute/heng-lab

Project Title	Immune interactions in stem cell therapy			
BDI Discovery Program	Immunity; Development and Stem Cells			
Main Supervisor	A/Prof Tracy Heng	tracy.heng@monash.edu	99050629	
Other Supervisors	Dr Natalie Payne	natalie.payne@monash.edu		
	Dr Andrew Freeman	andrew.freeman@monash.edu		
Location	Level 3, 15 Innovation	Level 3, 15 Innovation Walk, Clayton Campus		

Background: Multipotent mesenchymal stromal cells (MSCs) are fibroblastic precursor cells that have the stem cell-like ability to differentiate into a variety of cell types. Studies have shown that MSCs are also endowed with anti-inflammatory and tissue reparative properties, sparking interest in their potential use in cell therapy. It is generally thought that MSCs secrete soluble factors that dampen inflammation and repair damaged tissue. We recently challenged this dogma by demonstrating that MSCs infused into the blood undergo cell death and are rapidly engulfed by macrophages and cleared from the body (Pang *et al.*, 2021, Nature Communications). Our data indicate a pivotal role for macrophages in MSC therapy, but it remains unclear how macrophages are reprogrammed by MSCs to become anti-inflammatory.



Human induced pluripotent stem cell-derived macrophage (green) engulfing human apoptotic mesenchymal stromal cell (red).

Project aim/s: This project aims to elucidate how the innate and adaptive immune responses to viable and dying MSCs impact therapeutic efficacy. The findings will have broad implications for the future development of MSC-based therapies.

Techniques to be utilised: This project will utilise techniques applicable to both immunology and stem cell research, including stem and immune cell isolation, tissue culture, flow cytometry, immunoassays, stem cell differentiation, fluorescence microscopy, *in vivo* disease models.

Reference: Pang SHM, D'Rozario J, Mendonca S, Bhuvan T, Payne NL, Zheng D, Barugahare A, Powell D, Rautela J, Huntington N, Dewson G, Huang DCS, Gray DHD, **Heng TSP** (2021). Mesenchymal stromal cell apoptosis is required for their therapeutic function. *Nature Communications* 12, 6495. doi: 10.1038/s41467-021-26834-3.

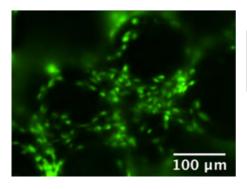
Stem Cells and Translational Immunology (Heng Lab)



https://www.monash.edu/discovery-institute/heng-lab

P	roject Title	Biological considerations in stem cell manufacturing		
В	DI Discovery Program	Immunity; Development and Stem Cells		
M	Iain Supervisor	A/Prof Tracy Heng	tracy.heng@monash.edu	99050629
O	ther Supervisors	Prof Laurence Meagher <u>laurence.meagher@monash.edu</u>		
L	ocation	Level 3, 15 Innovation Walk and New Horizons, 20 Research Way		

Background: Cell-based therapeutics have made advances in recent years. One of the most clinically studied products in regenerative medicine is mesenchymal stromal cells (MSCs). MSCs have stem cell-like properties and the ability to modulate immune cell function, making them valuable for the treatment of a wide array of inflammatory and degenerative disease conditions. However, MSC therapy requires large numbers of cells to be generated via scale-up manufacturing methods (e.g. propagation on microcarriers in stirred-tank bioreactors). Such manufacturing methods are not tailored for MSC expansion and may alter their biological function and, consequently, clinical effectiveness. The successful translation of cell therapy to the clinic requires an understanding of how up-scaling therapeutic cell production affects their biological properties and immunomodulatory function.



3D culture of mesenchymal stromal cells (green) on microcarriers in a bioreactor.

Project aim/s: The project aims to investigate changes in the biological function of MSCs generated from commercial scale-up processes (e.g. on microcarriers in bioreactors), compared to conventional planar culture systems.

Techniques to be utilised: This project will utilise techniques applicable to stem cells, immunology and biomanufacturing: 2D and 3D cell culture, bioreactor systems, flow cytometry, immunoassays, stem cell differentiation, fluorescence microscopy.

Reference: Cherian D, Bhuvan T, Meagher L, Heng TSP (2020). Biological Considerations in Scaling Up Therapeutic Cell Manufacturing. *Frontiers in Pharmacology* 11:654. doi: 10.3389/fphar.2020.00654.

Niche Signalling, Regeneration and Cancer (Jardé Lab)

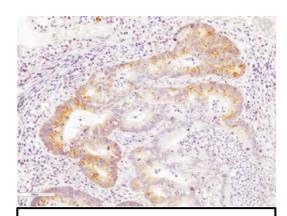


https://research.monash.edu/en/persons/thierry-jarde

Project Title	Characterising the function of Neuregulin 1 in colorectal cancer		
BDI Discovery Program	Cancer		
Main Supervisor	Dr Thierry Jardé	Thierry.jarde@monash.edu	03 990 29208
Other Supervisors	Prof Helen Abud	Helen.abud@monash.edu	03 990 29113
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background

Colorectal cancer is the third most common cancer in Australia and affects thousands of Australians each year. Colorectal tumours are heterogeneous and can be driven by a population of cancer stem cells that self-renew, proliferate and fuel the tumour by continuously giving rise to new cancer cells. Accumulating evidence suggest that the function of CRC stem cells is defined by the microenvironment (or the niche) they reside in. Our unpublished preliminary data show that the growth factor Neuregulin 1 is expressed by niche cells and its receptors are found on putative colorectal stem cells.



Immunohistochemical identification of putative cancer stem cells (brown staining) in a colorectal tumour.

Project aim/s

This project aims to characterise the cellular and molecular mechanisms underlying Neuregulin 1 action in colorectal cancer.

Techniques

The localisation of Neuregulin 1 in specific subsets of niche cells will be investigated by coimmunofluorescence. The molecular function of Neuregulin 1 will be assessed using colorectal cancer organoids and RNA sequencing.

Niche Signalling, Regeneration and Cancer (Jardé Lab)



https://research.monash.edu/en/persons/thierry-jarde

Project Title	Investigating cellular interactions in breast cancer			
BDI Discovery Program	Cancer			
Main Supervisor	Dr Thierry Jardé	Thierry.jarde@monash.edu	03 990 29208	
Other Supervisors	Dr Dilys Leung	Dilys.leung@monash.edu		
	Prof Gary Richardson	Gary.Richardson@monash.edu		
Location	Level 3, 19 Innovation	Level 3, 19 Innovation Walk, Clayton Campus		

Background

The local microenvironment (or niche) plays an important role in regulating the cellular function of breast cancer cells. Cancerassociated fibroblasts are one of the most abundant components of the tumour microenvironment and are suggested to fuel the tumour by producing essential proliferative signals. A knowledge of both the key proliferative signals and how they are delivered to breast cancer cells has the potential to provide new targeted therapeutic strategies.

Project aim/s

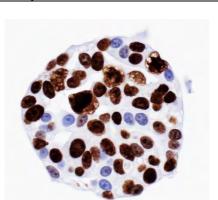
This project aims to characterise the cellular interactions between breast cancer cells and their associated fibroblasts.

Techniques

characterised by RNA sequencing.

The cross-talk between breast cancer cells and niche cells will be evaluated by using co-cultures of breast cancer organoids and primary fibroblasts. The identity of niche-derived ligands and activated signalling pathways will be

organoid.



Immunohistochemical detection of proliferative cells (brown staining) in a breast cancer

Prostate Cancer Research (Lawrence Lab)



https://www.monash.edu/discovery-institute/lawrence-group

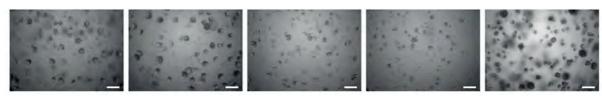
Project Title	Using hormones to treat cancer		
BDI Discovery Program	Cancer		
Main Supervisor	Dr Mitchell Lawrence	mitchell.lawrence@monash.edu	9902 9558
Other Supervisors	A/Prof Renea Taylor	renea.taylor@monash.edu	
	Prof Gail Risbridger	gail.risbridger@monash.edu	
Location	Level 3, 19 Innovation W	Level 3, 19 Innovation Walk, Clayton Campus	

Background: Patients with aggressive prostate cancer usually receive drugs that block hormones. The first clinical trial of this treatment was in 1941. Despite 80 years of progress, and potent new drugs, these treatments are only temporarily effective. Patients develop drug-resistant tumours that are even more aggressive. The current drugs can also be expensive and produce side-effects that reduce quality of life.

Aims: To address these challenges, our goal is to develop a safe, effective and inexpensive new treatment for prostate cancer known as "Bipolar Androgen Therapy" (BAT). BAT differs from current treatments because it overstimulates hormone activity rather than blocking it. Clinical trials of BAT in Australia and the United States are producing promising results.

Techniques: Our plan is to use BAT as the backbone of new combination treatments – combining it with other drugs to control prostate cancer cells for longer.

This raises the question: what is the best drug to combine with BAT? To resolve this question, we are using patient-derived models (xenografts and organoids) to screen different combination treatments. To validate the efficacy of these treatments we use 3D cell culture, microscopy, histology, and quantitative PCR.



(Phase microscope images of different organoid models of prostate cancer)

Prostate Cancer Research (Lawrence Lab)



https://www.monash.edu/discovery-institute/lawrence-group

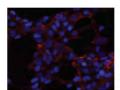
Project Title	Investigating the progression of neuroendocrine prostate cancer		
BDI Discovery Program	Cancer		
Main Supervisor	Dr Mitchell Lawrence	mitchell.lawrence@monash.edu	9902 9558
Other Supervisors	A/Prof Renea Taylor	renea.taylor@monash.edu	
	Prof Gail Risbridger	gail.risbridger@monash.edu	
Location	Level 3, 19 Innovation Walk, Clayton Campus		

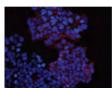
Background: Prostate-specific membrane antigen (PSMA) is a protein on the surface of prostate cancer cells. It can be used as a beacon to specifically detect prostate cancer cells in patients with PET imaging. PSMA can also be used to specifically target prostate cancer cells with radioactive particles.

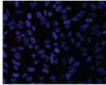
Unfortunately, some tumours do not have enough PSMA. This makes these tumours harder to detect. It also leads to patients being excluded from treatments that target PSMA.

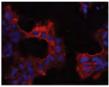
Aims: We are repurposing drugs that boost PSMA levels in cancer cells. To progress this idea into the clinic, we will determine the best way to use these drugs and the types of prostate cancer that are most responsive to them.

Techniques: We will use patient-derived models (xenografts and organoids) to identify the most effective way at boosting PSMA expression across different types of prostate cancer. This involves 3D cell culture, microscopy, flow cytometry and histology.









(Fluorescent microscope images of prostate cancer cells with varying levels of PSMA expression)

Health Professions Education Research (Lazarus Research Group)



https://research.monash.edu/en/persons/michelle-lazarus

Project Title	Exploring Representation in Anatomy Education Resources		
Main Supervisor	A/Prof Michelle Lazarus	michelle.lazarus@monash.edu	9905 0732
Other Supervisors	Dr Asiel Yair Adan	asielyair.adansanchez@unimelb.edu.au	8344 7276
·	Sanchez		
Location	Clayton Campus		

Background:

Future healthcare providers treat a wide variety of patients who vary in gender, skin tone, body habitus, socio-economic status etc. Despite this, anatomy education resources often portray limited demographic



representations in their images. This study will explore anatomy education resources to identify which demographics are represented in current material, and make recommendations for the field. The goal of this work is to develop an evidence-based "call to action" for Anatomy publishers to help bring representation to the sector.

Project aim:

- 1. Develop an evidence-based evaluation rubric for assessing representation in anatomy textbooks
- 2. Identify key anatomical education texts and resources for evaluation.

Techniques to be used:

- 1. Survey design
- 2. Systematic reviews
- 3. Qualitative analysis
- 4. Quantitative analysis

MORPHOLOGY, ONTOGENY, AND EVOLUTION (Massey Lab)



https://research.monash.edu/en/persons/jason-massey

Project Title	Does diet and elevat populations?	ion reliably predict mandibular	shape in gorilla
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Jason Massey	jason.massey@monash.edu	990 29111
Other Supervisors	Justin Adams	justin.adams@monash.edu	990 24280
Location	Building 13C (10 Chancellor's Walk, Clayton Campus)		

Background: Gorillas live across a vast range of altitudes spanning from sea level to about 4,000m. This range places individual populations in very different ecological zones. The extreme differences in elevation and access to fruit resources between western lowland and mountain gorillas is often cited as the reason for variation in behavioural ecology and skeletal morphology.

The mandible's primary function is eating. Therefore, it provides an honest signal of dietary variation. The effects of diet on mandibular morphology have been



well studied, but it is unknown whether gorillas as a whole have altered one or two aspects of the mandible in response to changes in diet or if each species can independently adopt population-specific morphology. Additionally, it is unknown what effects elevation has on skeletal morphology independent of dietary differences.

Project aims: This honours project will seek to answer:

- 1. What aspects of the mandible are most responsive to changes in diet?
- 2. Is the pattern of mandibular variation similar across all populations of gorillas?
- 3. Is there variation in the mandible due to elevation that is not accounted for by diet?

Techniques: This project will utilise techniques applicable to a range of comparative anatomy and biological/biomedical studies including training in mandibular anatomy, measurement of 3D specimens, and common statistical methods.

Moving Morphology & Functional Mechanics Lab





https://www.monash.edu/discovery-institute/panagiotopoulou-lab

Project Title	Feeding mechanics and bite force performance in white sharks during development				
Main Supervisor	Dr Olga Panagiotopoulou	Dr Olga Panagiotopoulou olga.panagiotopoulou@monash.edu 9905 0262			
Other Supervisors	Dr David Reser	david.reser@monash.edu	9902 7393		
•	A/Prof Charlie Huveneers	charlie.huveneers@flinders.edu.au			
Location	10 Chancellors Walk, Level 1, Room C142				

Background:

Sharks are essential top predators in marine ecosystems that are ecologically, economically, and culturally important. Their predatory success relies upon the unique anatomy of their jaws, which produce extremely



high bite forces while withstanding damaging tissue stresses.

Large sharks, such as the white shark, alter their diets during development, with young individuals predominantly pursuing fish, while adults preferentially target large, more energy-dense prey. This preference requires extreme bite force capacity, which develops during ontogeny from juveniles to full-size adults (4–6 metre length).

It is currently unknown whether the increase in bite force is due to increases in head size and muscles, or whether additional maturational factors are

involved. To better understand bite force scaling within and between species during ontogeny and its implications for the ecological role of large sharks, in-depth studies on jaw feeding mechanics are required.

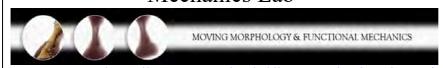
Project Aims

To study the biomechanical function of white shark jaws during growth.

Techniques

Cadaveric dissections, muscle physiological cross-sectional area analyses, optical microscopy, cryoelectron microscopy, 3D virtual reconstruction of CT scans and synchrotron data, finite element modelling, and theoretical mathematical models.

Moving Morphology & Functional Mechanics Lab





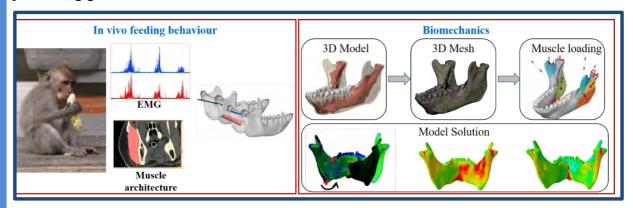
https://www.monash.edu/discovery-institute/panagiotopoulou-lab/home

Project Title	Feeding mechanics and mandible shape in non-human primates during ontogeny		
Main Supervisor	Dr Olga Panagiotopoulou	olga.panagiotopoulou@monash.edu	9905 0262
Other Supervisors	A/ Prof Luca Fiorenza	luca.fiorenza@monash.edu	990 59809
Location	10 Chancellors Walk, Level 1, Room C142, Clayton Campus		

Background:

Lower jaw (mandible) shape has yet to yield definitive information on hominid diet, due to our poor understanding on primate jaw biomechanics during development. While current thinking attributes mandible shape to functional adaptation to food consistency (what we eat) our lab's work suggests a different hypothesis: that, rather than food consistency per se, primate jaws are shaped by the interaction between the developing teeth and feeding behaviour (how they eat). Testing this hypothesis is hampered by almost complete lack of knowledge about how individual feeding behaviour changes jaw structure during development.

We have recently published a novel multi-pronged approach integrating in vivo experiments and bioengineering, which proposes to provide the missing piece in understanding the function of the jaw during growth.



Project Aims

To study the biomechanical function of the macaque jaw during growth.

Techniques

Cadaveric dissections, muscle physiological cross-sectional area analyses, optical microscopy, cryo-electron microscopy, 3D virtual reconstruction of CT scans, finite element modelling, and theoretical mathematical models.

Moving Morphology & Functional Mechanics Lab



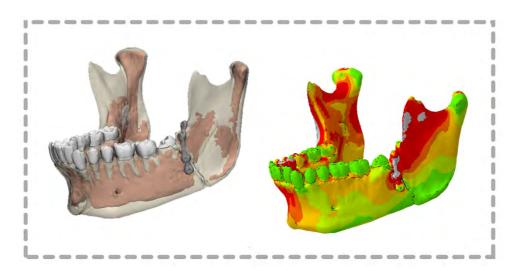


https://www.monash.edu/discovery-institute/panagiotopoulou-lab/home

Project Title	Jaw Fracture Repair and Biomechanics of Chewing			
Main Supervisor	Dr Olga Panagiotopoulou <u>olga.panagiotopoulou@monash.edu</u> 9905 0262			
Other Supervisors				
Location	10 Chancellors Walk, Level	1, Room C142, Clayton Campus		

Background:

Mandible (lower-jaw) fractures account for ~30-40% of all instances of maxillofacial trauma and can occur due to a variety of incidents (e.g. assault, oropharyngeal/congenital disorders, cancer, vehicular accidents, sporting accidents or falls). Current treatment aimed at restoring mandibular function and aesthetics by immobilizing the fracture with fixation mini-plates and screws is not free of morbidity. Approximately 10–30% of mandibular fracture patients experience postoperative complications, such as mal-union (bone segments not fusing properly), malocclusion (tooth misalignment), infection, and joint dysfunction. Moreover, there is no consensus on the optimal surgical interventions for certain types of mandible fracture. We propose that a significant cause of post-surgical complication is the appearance of strain environments in the fracture zone and around the implants, which are not conductive to healing.



Project Aims:

To study the biomechanical function of the jaw during a complete chewing cycle in healthy controls and post fracture fixation.

Techniques:

3D virtual reconstruction of CT scans, 3D implant design, Dynamic Finite Element Modelling, Theoretical mathematical models.

Brain Development, Neuroplasticity and Stem Cells (Pocock Lab)



https://www.monash.edu/discovery-institute/pocock-lab

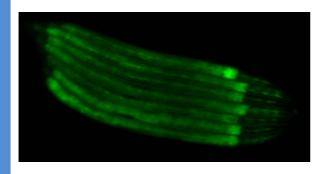
Project Title	Neuronal Regulation of Mitochondrial Health	
BDI Discovery Program	Development and Stem Cells	
Main Supervisor	Prof. Roger Pocock <u>roger.pocock@monash.edu</u> 99050658	
Other Supervisors	Rebecca Cornell	
Location	15 Innovation Walk, Clayton Campus	

Background: Mitochondrial damage is a hallmark of obesity, diabetes and cardiovascular disease. Cells combat mitochondrial damage by triggering protective stress responses to prevent a breakdown in metabolic homeostasis. **Recent evidence demonstrate that the nervous system can regulate stress responses in distal tissues.**

In unpublished work, we discovered that neuropeptide signalling from two sensory neurons regulate the mitochondrial stress response in distal fat storage cells. This project will use state-of-the-art genetic and imaging tools dissect how the brain controls mitochondrial stress.

Project Aims: In this project, you will work with experienced scientists to identify molecular mechanisms through which the brain controls mitochondrial stress responses in distal tissues. Based on our preliminary data we believe that we have discovered a new means of controlling systemic mitochondrial stress, which may be useful in therapies for multiple diseases.

Techniques to be utilised: This project will utilise techniques in genetics, *in vivo* neurodevelopmental dissection, molecular biology (CRISPR), biochemistry, microscopy.



Animal transgenically expressing green fluorescent protein to enable visualisation of mitochondrial stress.

Brain Development, Neuroplasticity and Stem Cells (Pocock Lab)



https://www.monash.edu/discovery-institute/pocock-lab

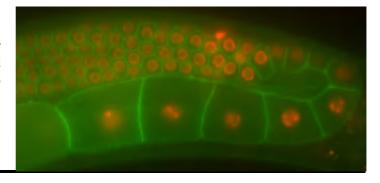
Project Title	Transcriptional control of stem cell development	
BDI Discovery Program	Development and Stem Cells	
Main Supervisor Other Supervisors	Prof. Roger Pocock <u>roger.pocock@monash.edu</u> Dr Wei Cao	
Location	15 Innovation Walk, Clayton Campus	

Background: Human infertility affects up to 186 million individuals globally and 15% of Australian reproductive age couples. At the most fundamental level, fertility requires faithful generation of oocytes and sperm from germ cells. Knowledge of how germ cells develop is thus critical for understanding infertility, optimizing assisted reproduction, and identifying contraceptive targets. However, comprehensive understanding of the molecular components governing germ cell development is lacking. **Our research uses innovative imaging and molecular tools to map the germline regulatory landscape.** We have identified multiple novel fertility factors using this approach.

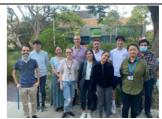
Project Aims: In this project, you will work with an experienced team to dissect the molecular function of a novel fertility factor.

Techniques to be utilised: This project will utilise techniques in genetics, *in vivo* germ cell analysis, confocal microscopy, biochemistry and CRISPR-Cas9.

Image of the *Caenorhabditis elegans* germline highlighting germ cell nuclei (red) and cell membranes (green).



Brain Development, Neuroplasticity and Stem Cells (Pocock Lab)



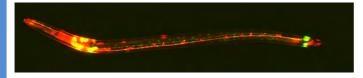
https://www.monash.edu/discovery-institute/pocock-lab

Project Title	How do you make a brain?	
BDI Discovery Program	Development and Stem Cells	
Main Supervisor	Prof. Roger Pocock <u>roger.pocock@monash.edu</u>	
Other Supervisors	Dr Pedro Moreira	
Location	15 Innovation Walk, Clayton Campus	

Background: Neurons in the human brain communicate with each other through ~850,000 kilometres of cables. These cables are called axons, and they are guided to their correct positions during development by an array of cell-surface and secreted molecules. **We have identified a class of lipids that promote axon guidance and prevent axon degeneration across multiple generations.**

Project Aims: In this project, you will join a team to investigate how lipids control axon development and health, which may be useful in therapies for brain disorders.

Techniques to be utilised: This project will utilise techniques in genetics, *in vivo* neuroanatomy dissection, molecular biology (CRISPR), biochemistry, microscopy.



Animal transgenically expressing fluorescent proteins to enable visualisation of the nervous system.

Epigenetics and Reprogramming (Polo Lab)



https://www.monash.edu/discovery-institute/polo-lab

Project Title	Molecular characterisation of human Blastoids		
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Prof. Jose Polo	jose.polo@monash.edu	9905 0005
Other Supervisors	Dr. Sue Mei Lim	sue.lim@monash.edu	9905 0096
Location	Level 3 South, 15 Innovation Walk (Building 75), Clayton Campus		

Background:

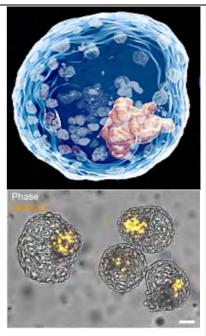
Mammalian embryogenesis commences with the totipotent zygote, progressing through developmental stages such as the morula, followed by the formation of a blastocyst. As the embryo undergoes implantation, the cells of the epiblast (EPI) lineage within the blastocyst develop into the embryo proper and amnion. Meanwhile, cells originating from the trophectoderm (TE), and primitive endoderm (PE) contribute to the formation of the placenta and yolk sac, respectively. Through *in vitro* isolation and culture, epiblast cells have been found to give rise to human embryonic stem cells (hESCs). Alternatively, adult cells can be reprogrammed into human-induced pluripotent stem cells (hiPSCs) via

transcription factor-mediated reprogramming. These pluripotent cells, cultured *in vitro*, have the remarkable ability to differentiate into all cell types present in the body. Consequently, they hold immense potential for disease modelling, and drug screening, as well as gaining deeper insights into the molecular mechanisms of various diseases, embryo development, and organogenesis.

During our investigation into reprogramming intermediates, our lab discovered that the aggregated intermediate cells could form blastocyst-like structures, termed induced blastoids (iBlastoids). Human iBlastoids represent a unique and experimentally tractable system to model and interrogate the complex cellular and molecular interactions that occur during early human embryogenesis. The application of iBlastoids as an *in vitro* model of human blastocysts holds the potential to facilitate research on early human development, explore the effects of gene mutations and toxins during early embryogenesis, and contribute to the advancement of novel therapies associated with assisted reproductive technologies.

Project aims:

In this project, we will investigate iBlastoids and their role in several *in vitro* aspects of early human development, with the following specific aims:



iBlastoids (top and bottom) derived from human dermal fibroblast cells.

- Aim 1. To generate and characterise the molecular properties of iBlastoids.
- Aim 2. To derive and study different blastoid stem cell types from iBlastoids.

Techniques:

This project will use a number of different human cell types, including somatic and pluripotent stem cells, with a combination of different molecular, biochemical, microscopy, cellular techniques and genome-wide approaches (RNA-seq, SC-RNA-seq, etc.) to dissect the mechanisms and dynamics of iBlastoid formation.

Comparative Development and Evo-Devo (Smith Lab)



https://www.monash.edu/discovery-institute/smith-lab

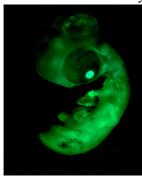
Project Title	Genetic regulation of gonadal development in the avian model			
BDI Discovery Program	Development and Stem Cells			
Main Supervisor	Craig Smith	Craig.Smith@monash.edu	Ph:9905 0203	
Other Supervisors	Andrew Major	Andrew.Major@monash.edu		
Location	Level 3, 15 Innovation	Level 3, 15 Innovation Walk, Clayton Campus		

Background: Sex determination is inherently fascinating to lay people and scientists alike. Those studying sex determination largely focus on the embryonic gonads. Embryonic gonads are unique because they have a developmental choice: testis or ovary formation. Our lab studies how this choice is executed at the molecular genetic level. We use the chicken embryo as a model due to the ease of experimental manipulation (embryonic development occurs in the egg outside the maternal body). We recently conducted a single cell RNA-seq study and identified novel expression of the *OSR1* transcription factor gene in the embryonic chicken gonad. See image below; Whole mount *in situ* hybridisation for *OSR1* mRNA (purple stain) in the gonads of a female embryonic day 10.5 chicken urogenital system). Image at right shows unilateral electroporation of GFP into left embryonic gonad.

Project aims: This project will explore the role of *OSR1* in the gonad, using gene over-expression and knockdown approaches in the chicken model.

Techniques: Methods used will centre around experimental developmental biology; PCR, RT-PCR, gene cloning, *in situ* hybridisation, immunofluorescence and organ culture. We will also use *in ovo* (in the egg) electroporation to deliver genes (over-expression) or short hairpin RNAs (for knockdown) into embryonic gonads. We will then examine gonads for the effects of *OSR1* manipulation. We will examine expression of validated markers of ovarian and testicular development, using immunofluorescence, *in situ* hybridisation and qRT-PCR. ChIP-seq may also be conducted, to identify direct transcriptional targets of OSR1. OSRI in other contexts is a transcriptional inhibitor.

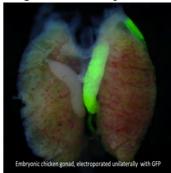
GFP in a chicken embryo



OSR1 mRNA expression



GFP gonadal electroporation



Comparative Development and Evo-Devo (Smith Lab)



https://www.monash.edu/discovery-institute/smith-lab

Project Title	Limbs with zinc finger	rs!	
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Craig Smith	Craig.Smith@monash.edu	Ph:9905 0203
Other Supervisors	Andrew Major	Andrew.Major@monash.edu	
Location	Level 3, 15 Innovation	Walk, Clayton Campus	

Background: Our lab uses the chicken embryo to model developmental processes. Advantages of this model include its accessibility (developing outside the maternal body in shelled eggs) and ease of experimental manipulation - viruses expressing genes or knockdown constructs can be injected into early embryos and effects assessed one week later. In particular, we study gonadal development and limb morphogenesis. This project will focus analysis of a novel gene zinc finger gene, *ZNF385B*, expressed in the limb bud. This gene is expressed in a critical signaling centre, the Apical Ectodermal Ridge (AER). (see image 1 below). A previous independent study identified *Znf385b* as a candidate gene mutated in mice with limb deformities, but further work has not been reported.

Project aims: This project will explore the role of *ZNF385B* in the limb bud, using gene over-expression and knockdown approaches in the chicken model. Effects upon limb bud growth and patterning will be explored.

Techniques: Methods used will centre around experimental developmental biology; PCR, RT-PCR, gene cloning, *in situ* hybridisation, immunofluorescence and organ culture. We will also use *in ovo* (in the egg) electroporation to deliver genes (over-expression) or short hairpin RNAs (for knockdown) into embryonic limb buds (see Fig 2 below). We will then examine limb buds for the effects of *ZNF385B* manipulation. We will examine expression of markers of limb growth and development, using immunofluorescence, *in situ* hybridisation and qRT-PCR. ChIP-seq may also be conducted, to identify direct transcriptional targets of ZNF385B.





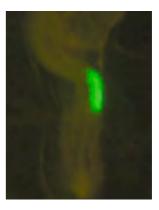


Fig 1. ZNF385B mRNA in a chicken embryo (somites and AER, arrows)

Fig 2. Electroporation of GFP into limb bud

Kidney Development and Disease (Smyth Lab)



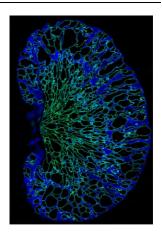
https://www.monash.edu/discovery-institute/smyth-lab

Project Title	Single cell discovery framework for cell programming		
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Ian Smyth ian.smyth@monash.edu 99055169		
Other Supervisors			
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background: This project is focussed on examining the development of Polycystic Kidney Disease (PKD) — one of the commonest inherited conditions and one which often leads to kidney failure requiring transplant. There is no cure for this disease.

Aims: This project will study how cysts develop in the kidney and explore a new pathway which we have discovered that is central to cyst formation and which we hope to target with a new class of drugs aimed at preventing the disease.

Techniques: You will use mouse and cell-based models of genetic deletion and pharmacological inhibition to study how PKD arises and the role key proteins play in its initiation and progression.



Kidney Development and Disease (Smyth Lab)



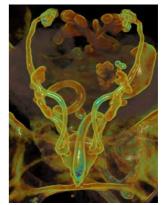
https://www.monash.edu/discovery-institute/smyth-lab

Project Title	Characterising novel genes which cause congenital kidney disease		
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Ian Smyth ian.smyth@monash.edu 99055169		
Other Supervisors			
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background: Our group is involved in an Australia-wide program which aims to identify novel genes in patients with kidney disease. These individuals will have their genomes sequenced to identify potential new disease-causing variants in known and novel genes.

Aims: This project Aims to demonstrate that specific genetic lesions identified in patients with kidney disease are causative, and to understand how the protein involved regulates normal kidney development

Techniques: We will use CRISPR/Cas9 genome engineering approaches to model disease causing mutations in mice. By characterising these models by histology and other approaches, honours students will have a unique



opportunity to establish how novel disease genes function in the kidney, how their protein products regulate cell biology and how their mutation leads to congenital renal malformations.

Kidney Development and Disease (Smyth Lab)



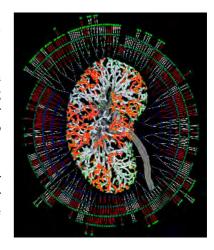
https://www.monash.edu/discovery-institute/smyth-lab

Project Title	How does maternal health impact fetal kidney development?		
BDI Discovery Program	Development and Stem Cells		
Main Supervisor	Ian Smyth	ian.smyth@monash.edu	99055169
Other Supervisors			
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background: Increasing evidence indicates that the fetal environment can significantly affect the development of the kidney.

Aims: This project examines how maternal alcohol consumption affects fetal kidney development. By modelling binge drinking behaviour, you will study the effects of alcohol on the progenitor cells which contribute to the formation of nephrons and begin to understand the anatomical and molecular impacts of this drug.

Techniques: We will use mouse models to examine the cellular impact of alcohol exposure on the developing kidney and molecular techniques to examine how this alters DNA methylation, gene expression and epigenetic change at the level of the single cell.



Prostate Cancer Research Program



https://www.monash.edu/discovery-institute/ prostate-cancer-research-group

Project Title	Identifying new treatments for drug-resistant cancer		
BDI Discovery Program	Cancer		
Main Supervisor	A/Prof Renea Taylor <u>renea.taylor@monash.edu</u> 9902 9558		
Other Supervisors	Prof Gail Risbridger <u>gail.risbridger@monash.edu</u>		
	Dr Mitchell Lawrence <u>mitchell.lawrence@monash.edu</u>		
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background: Over the last decade, new treatments have extended the survival of men with advanced prostate cancer. Unfortunately, patients eventually develop resistance to all current treatments. Therefore, effective new therapies are needed for drug-resistant cancers.

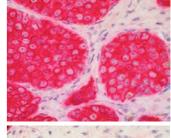
Our group is tackling this challenge in a new way - by growing tumours from different patients in the lab. Using this novel technique, we can compare how tumours respond to novel treatments. Our results

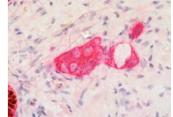
are already showing that some tumours are more sensitive than others to specific treatments. These exciting results are helping us prioritise drugs for further clinical validation.

Aims: In this project, we will test the response of different patients' tumours to novel drugs targeting the epigenome and DNA damage repair. Subsequently, we will identify molecular features that distinguish between sensitive and resistant tumours. These important results will provide new insight into better treatments for tumours that have failed current therapies.

Techniques: This project will use techniques a range of techniques including organoid cell culture, patient-derived xenografts, immunohistochemistry and pathology.

(Image: Patient prostate cancer cells stained in pink before drug treatment (top) and after drug treatment (bottom)).





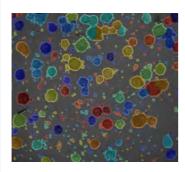
Prostate Cancer Research Program



https://www.monash.edu/discovery-institute/ prostate-cancer-research-group

Project Title	Investigating the progression of neuroendocrine prostate cancer		
BDI Discovery Program	Cancer		
Main Supervisor	A/Prof Renea Taylor <u>renea.taylor@monash.edu</u> 9902 9558		
Other Supervisors	Prof Gail Risbridger <u>gail.risbridger@monash.edu</u>		
	Dr Mitchell Lawrence <u>mitchell.lawrence@monash.edu</u>		
Location	Level 3, 19 Innovation Walk, Clayton Campus		

Background: Prostate cancer is the most commonly diagnosed cancer in Victoria. As most prostate tumours rely on androgen hormones for growth, the most common therapies for metastatic prostate cancer are drugs which inhibit androgen signalling. However, some patients develop neuroendocrine prostate tumours, which are highly aggressive and resistant to androgen inhibitors. Currently, there is limited understanding of how neuroendocrine tumours emerge in patients, and therapeutic options are limited.



Aims: The goal of this project is to use patient-derived models, including xenografts and organoids, of neuroendocrine prostate cancer to study disease progression and test effective therapeutic strategies.

Techniques: The project will involve a variety of techniques including working with human tumours, tissue culture of organoids and immunohistochemistry.

(Image analysis of prostate cancer organoids in 3D culture)



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Disclaimer: The information in this report was correct at the time of publication. Monash University reserves the right to alter this information should the need arise.

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