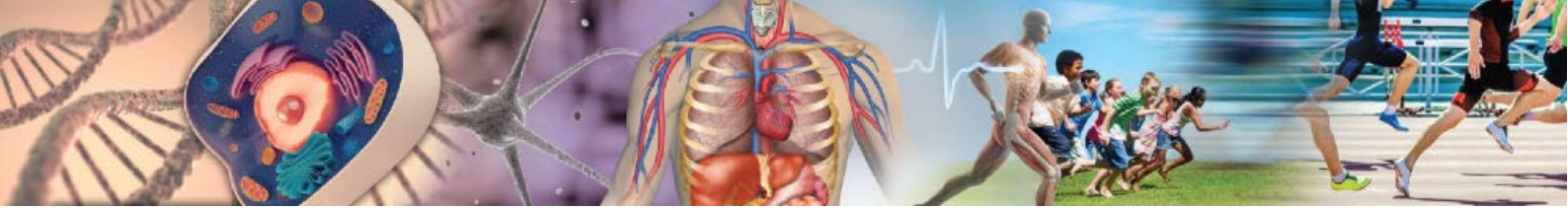

THE UNIVERSITY OF WESTERN AUSTRALIA

School of Human Sciences

HONOURS/MASTERS RESEARCH PROJECTS

2024

ANATOMY, PHYSIOLOGY & HUMAN BIOLOGY

NEUROSCIENCE

SPORT SCIENCE, EXERCISE AND HEALTH

Contents

Tips for Choosing an Honours project

Supervisor and Topic

Supervision

The role of the supervisor is to advise, guide and provide constructive feedback to the student through the processes of choosing a realistic topic, designing a project, doing the research, and interpreting the findings and writing the dissertation.

Things to do before deciding on a supervisor:

- Talk with a few prospective supervisors about their research interests and prospective topics, as well as their styles of supervision and what they expect of their students; and
- Talk with your prospective supervisors' current and former Honours and postgraduate students about their experiences.
- Things to discuss and negotiate with your supervisor very early in the program:
- The regularity, timing and format of your meetings;
- The type and level of assistance that you would like, and your supervisor is prepared to give, with respect to choosing a topic and setting goals; finding appropriate literature; collecting the data and information; analysing and interpreting your findings; planning the dissertation; and writing and reviewing the dissertation.

Choosing a Topic

Before deciding on a topic, it is usually a good idea to first identify one or more prospective supervisors according to the criteria above. Then, in consultation with your prospective supervisor/s, identify some possible topics and projects according to the following criteria:

- Choose an area that is sufficiently interesting to you to maintain your enthusiasm for a year-long project;
- Choose a topic in which you can identify questions to be answered or gaps to be filled in the current knowledge; and
- Find a project that is realistic for you to complete within the time allocated for your research and dissertation.

Honours – in the Health Department

Honours in the Health Department

THE UNIVERSITY OF WESTERN AUSTRALIA

In 2024, there is an opportunity for three students to conduct their Honours project within the health department. The *"Honours in the Health Department"* scheme is suitable for students who are interested in research, but see themselves pursing employment outside of academia.

General details

- Projects advertised late November
- Expression of interest
- Selection process in early December
- Support provided by a supervisor from the Health Department and an internal supervisor within the School of Human Sciences

For further information, please contact Peter Noble peter.noble@uwa.edu.au
Jeremy Smith jeremy.smith@uwa.edu.au

Government of **Western Australia**
Department of **Health**

Information for Honours Applicants

In an Honours year, the learning emphasis is on completing an original research project. Projects are guided by academic staff who are internationally recognised in their specific fields of research. Students acquire the specialized skills required to complete their particular research project, and also develop generic research skills such as analytical and problem-solving abilities, and a variety of communication skills. These are not only vital for future success in research but stand graduates in good stead whatever career they may subsequently pursue. Throughout the year, students also work in close collaboration with a like-minded peer group and professional university staff.

Honours are available in the following disciplines:

- Anatomy and Human Biology
- Physiology
- Neuroscience
- Sport Science, Exercise and Health

Essential qualifications

For Honours: An appropriate undergraduate degree with a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major, from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Enrolment must be full time.

Scholarships Available

DR MARGARET LOMAN-HALL HONOURS SCHOLARSHIP (APHB)

Scholarships are funded by a bequest from Dr Margaret Loman-Hall for the purpose of encouraging eligible students to undertake a Bachelor of Science (Honours) or Bachelor of Philosophy (Honours) in the Department of Anatomy, Physiology & Human Biology), School of Human Sciences.

Each Scholarship is valued at $7500 and comprises:

- $6000 during the honours enrolment as a stipend
- $1500 during the honours enrolment as research costs allowance payable to the student's supervisor.

THE FRANK PYKE MEMORIAL SCHOLARSHIP (SSEH)

A stipend of $5000 is available to assist an Honours student, (who has demonstrated academic excellence and other outstanding achievements, abilities, leadership or community involvement in sport or exercise related activities) to complete a Bachelor of Science (Honours) degree course in SSEH at UWA.

THE HIGH PERFORMANCE SPORT RESEARCH CENTRE (HPSRC) AD-HOC HONOURS SCHOLARSHIP

These scholarships will provide selected UWA honours students with research project funds and a small personal stipend ($3,000) in order to conduct an honours-level research project that aligns with the research focus areas of the HPSRC. In a collaborative effort between service providers from the Western Australian Institute of Sport (WAIS) and academic staff from the University of Western Australia (UWA), the honours research project should have a focus on the daily training environment and/or the performance outcomes of WAIS athletes and sport programs.

THE "KIDDO" HONOURS SCHOLARSHIP

The Kiddo $5000 Honours Scholarship is open for students eligible to undertake a BSc (Honours) course in 2024. The aim of this scholarship is to encourage and assist a meritorious student to undertake an honours course with a thesis related to the Kiddo program, www.kiddo.edu.au within the School of Human Sciences in 2024 The stipend of $5000 is expected to contribute to the student's living expenses. Successful applicant/s will be selected based on their academic performance. Prior experience in the Kiddo program will be considered favourably.
Email amanda.derbyshire@uwa.edu.au to register your interest.

EXERCISE AS CARDIOVASCULAR AND CEREBROVASCULAR MEDICINE- RESEARCH SCHOLARSHIPS

The Cardiovascular Research Group is a world leading team of experts who use state-of-the-art techniques to address clinically relevant questions pertaining to the impacts of exercise on human cardiovascular and cerebro-vascular health and disease. Our team is offering a 2024 Honours scholarship to assist a meritorious student to undertake an honours course in 2024 with a thesis related to cardiovascular or cerebrovascular health in the School of Human Sciences (Exercise and Sport Science) at the University of Western Australia.

Brief Overview of APHB Honours Units (2024)

Unit	Unit name	Tasks	Final Honours Mark %
Semester 1			
APHB4001 6 Points	Scientific Communication Part 1	Project Plan, Research Proposal, Proposal Seminar	12.5
HMSC5004 6 points	Research Methods	Conceptual Examination of the Research Process	12.5
HMSC5005 6 Points	Data Analysis	Statistics and Data Analysis Modules	12.5
APHP/NEUR5514 6 Points	Honours Dissertation Part 1	Dissertation (AC Assessment Continuing)	AC
Semester 2			
APHB4008 6 Points	Scientific Communication Part 2	Final Seminar, Student Viva	12.5
APHB/NEUR5515 6 Points	Honours Dissertation Part 2	Dissertation	AC
APHB/NEUR5516 6 Points	Honours Dissertation Part 3	Dissertation	AC
APHB/NEUR5517 6 Points	Honours Dissertation Part 4	Dissertation	50

Students who complete this Honours degree will be eligible for up to 24 points credit if they then go on to study the Master of Biomedical Sciences or other Master degrees. Students who have competed Honours will therefore have completed the units APHB/NEUR 5514,5515,5516,5517 which form the Dissertation part of the Coursework and Dissertation pathway of a Master degree. Note that no credit will be offered to students who take the Master of Clinical Audiology.

Brief Overview of SSEH Honours Units (2024)

Unit	Unit name	Tasks	Final Honours Mark %
Semester 1			
HMSC5004 6 Points	Research Methods	Conceptual Examination of the Research Process	12.5
HMSC5005 6 points	Data Analysis	Statistics and Data Analysis Modules	12. 5
SSEH4711 6 Points	Honours Dissertation Part 1	Dissertation (AC Assessment Continuing)	AC
SSEH4712 6 Points	Honours Dissertation Part 2	Dissertation	AC
SSEH4644 or SSEH4654* or SSEH4664 or SSEH4633	Advanced Exercise Physiology Advanced Motor Control Exercise and Health Psychology Advanced Biomechanical Methods	Advanced Knowledge in a Select Sub-discipline Area * Semester 2 unit	12.5
Semester 2			
SCIE4481 6 Points	Good, Bogus and Corrupted Science	Distinguish Genuine Scientific Findings from Spurious Ones	12.5
SSEH4713 6 Points	Honours Dissertation Part 3	Dissertation	AC
SSEH4714 6 Points	Honours Dissertation Part 4	Dissertation	50

Honours in Sport Science, Exercise and Health provides you with interdisciplinary research skills and advanced knowledge in a select sub-discipline area (exercise physiology/biochemistry, biomechanics, motor development, exercise and health psychology or activity promotion). The honours specialisation provides an ideal background for continuance to a PhD or other professional-based research degrees.

You will gain a greater depth of knowledge in your area of specialisation, while also developing research skills. You will learn (1) to plan, administer testing, analyse and present data both in written and oral formats; (2) prepare a written manuscript for peer-reviewed publications; (3) independent time and work management skills and the ability to develop leadership potential; (4) advanced computer skills; and (5) problem-solving and organisational skills.

Honours in the Health Department

Cancer Exercise and Health Literary Program

UWA Contact:
Associate Professor Peter Noble

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Government of **Western Australia**
Department of **Health**

Health Networks Division

Exercise has been demonstrated to reduce cancer treatment side-effects and improve quality of life and wellbeing for cancer patients and survivors. To support Western Australian cancer survivors, the Cancer Network will commission a service by an external provider for the delivery of a cancer exercise and health literacy program for cancer survivors.

To ensure that the service requirements are informed by evidence-based practice, and to support the delivery of the program, the Cancer Network requires a literature review on cancer exercise and health literacy programs for cancer survivors. There is the opportunity for an Honours student to undertake this literature review to identify best practice approaches and provide recommendations for the department. If time permits, there is also the opportunity for the student to assist the Cancer Network in preparing a report with key findings and recommendations from the literature review.

Project Objectives: To identify best practice approaches for exercise and health literacy programs and initiatives for cancer survivors via a literature review.

Project Outcomes: A literature review on cancer exercise and health literacy programs for cancer survivors.

Embedding Equity across Future Health Research and Innovation (FHRI) Fund Programs and Initiatives (P&Is) to promote equitable health outcomes for WA.

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Government of **Western Australia**
Department of **Health**

Deputy Director General Division

The Future Health Research and Innovation (FHRI) Fund provides a secure source of funding to drive health and medical research, innovation and commercialisation and through these activities, improve the health and prosperity of all Western Australians. It also provides an opportunity to diversify the economy, create jobs, improve the sustainability of the health system and position WA as a leader in research and innovation.

Once fully operational the FHRI Fund will provide more than $50 million annually to the WA health and medical research and innovation sector and disbursements are guided by the FHRI Fund Strategy and Priority Goals. The WA Department of Health (DoH), Office of Medical Research and Innovation (OMRI) develops Programs and Initiative (P&Is) that contribute to achieving one or more Priority Goal and the Advisory Council provides a recommendation to the Minister for Medical Research regarding whether these P&Is should be approved.

The FHRI Fund Funding Principles have been determined by the Advisory Council to guide the design and implementation of P&Is as well as the application assessment and award process. The funding principles can be accessed on the FHRI Fund website with the following tenth principle approved by the Advisory Council on 17 November 2022 after consideration of a discussion paper that focuses on specific challenges and barriers in relation to Aboriginal health equity, gender equity and career progression in the health and medical research sector and how these might be addressed through the introduction of the following 'equity' funding principle:

Equitable Outcomes

Support equitable outcomes by considering the structures of bias, disadvantage and inequity in Australian society stemming from dimensions such as Aboriginal or Torres Strait Islander status, gender identity, career stage, race, ethnicity, language, religion and disability or a combination of all or any of these. Ensure that strategies to promote equity are considered, and incorporated where appropriate, into the design and implementation of funding programs.

Health and medical research and innovation are key to achieving gains in health equity through improved understanding of health and wellbeing trends for specific groups, assessing the impact of policies, programs and services and finding new ways to prevent and treat disease and illness. Therefore, the development of FHRI Fund P&Is that are designed, implemented and evaluated in line with evidence based, best practice approaches to health equity are vital to ensure excellence in health and medical research and innovation that benefits all Western Australians.

While a number of measures already exist to address equity in FHRI Fund P&Is, a systematic review of equity indicators across past FHRI Fund P&Is is required for an analysis of past performance as well as the implementation of recommendations (short-term and long-term) and indicators to ensure that equity is embedded across all FHRI Fund P&Is and can continue to be monitored and assessed in terms of performance and outcomes.

Major Project Objectives include:

- Develop project plan to map out key milestones and deliverables against timeframes
- Undertake an environmental scan of policies, practices and initiatives used by relevant funding agencies both nationally and internationally to address equity in health and medical research and innovation funding, with specific reference to Aboriginal health equity and gender equity, but also looking at other groups in which equity considerations are important such as people with poor mental health, people with disabilities, refugees, people from culturally and linguistically diverse backgrounds, people with low socioeconomic status and people living outside major cities.
- Undertake a review and analysis of equity indicators across past FHRI Fund P&Is
- Prepare a consultation plan and undertake consultation with targeted stakeholders
- Prepare draft Gender Equity and draft Aboriginal Health Equity policies for the FHRI Fund
- Develop short-term and long-term recommendations to further embed the equity principle across all FHRI Fund P&Is and achieve more equitable funding and health outcomes.
- Develop a set of performance indicators that will allow OMRI to monitor and evaluate FHRI Fund success in achieving equitable funding and health outcomes for the WA community.

Assessing the impact of COVID-19 restrictions and lockdowns on adolescent and/or childhood immunisation rates in Western Australia.

UWA Contact:
Associate Professor Peter Noble

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Government of **Western Australia**
Department of **Health**

Communicable Disease Control Directorate,
Public and Aboriginal Health Division

Western Australia (WA) closed its state and international borders from 1 April 2020 and did not reopen until 18 February 2022. During the border closure, the state eliminated community transmission of COVID-19, with a range of restriction measures. These included regional border restrictions, lockdowns, hotel quarantine for visitors to the state and gathering restrictions amongst other measures. Following the border reopening in May 2022, WA however experienced sharply rising infection cases which were amongst the highest per capita cases seen anywhere in the world throughout the pandemic. The increasing number of cases, and identification of close contacts with, also contributed to school closures and home isolation for positive cases and their families.

Worldwide reports suggest that routine immunisation rates have declined. The pandemic impacted healthcare services and resources were re-directed to leading to disruption of routine immunisation services. Data from Victoria, Australia published in 2021 however did not find that lockdown restrictions affected childhood immunisation rates, although human papillomavirus dose 1 vaccination of adolescents did decline during the first but not the second epidemic wave.

Adolescent and childhood immunisation coverage in WA has however declined since 2021. While residents of WA were able to live free from COVID-19 in 2020 and 2021 when the rest of the world was experiencing mass infections, there were disruptions in 2022 following border reopening's which impacted access to healthcare providers. This project therefore aims to determine if the COVID-19 pandemic contributed to a decline in routine immunisation in WA.

Project Objectives: To assess the direct impact of rising COVID-19 infections following the state border reopening on immunisation rates in adolescents in the school-based immunisation program and/or childhood immunisation coverage.

Project Outcomes: The student will use data from the Australian Immunisation Register will be extracted from 1 January 2019 to 31 December 2023 for adolescents in the Year 7 and Year 10 school program to undertake this project. If a two-semester project is selected, data on children from 12 months to 5 years will also be extracted. The timeline of major events such as border closures, lockdowns, peaks in COVID-19 cases in WA will be tracked and number of immunisations recorded in the days following these events will be analysed.

Investigating factors for low influenza vaccination uptake in primary school aged children.

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Associate Professor Peter Noble

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Government of **Western Australia**
Department of **Health**

Communicable Disease Control Directorate,
Public and Aboriginal Health Division

Disease notification data sourced from the Western Australian Notifiable Infectious Diseases Database (WANIDD) shows that in the 2023 influenza season so far, the highest number of Influenza notifications have occurred in the 5-to-9-year age group. Annual vaccination is the most important measure to prevent influenza and its complications. It is recommended for all people aged ≥6 months and over. Since 2020, WA primary school aged children have had access to free influenza vaccinations. Despite this, influenza vaccination coverage has been the lowest in this age cohort at less than 20% this year, with national data showing similar findings.

Apart from preventing severe influenza disease, primary school-aged children drive influenza transmission in the community. Increasing vaccination rates in this cohort will have the added benefit of reducing the spread of influenza to the wider community. To increase vaccination coverage in this cohort, understanding into factors leading to the lower vaccination uptake is needed in order to inform effective campaigns and programs.

Project Objectives: To identify factors contributing to low influenza vaccinations in primary school-aged children in WA.

Project Outcomes: The student will use data on influenza vaccinations in children aged 5 years to 11 years living in WA extracted from the Australian Immunisation Register from 1 March 23 to 1 October 23 for this project. Associations between potential factors such as residential area, previous vaccination status, vaccination status of the parent/guardian, and vaccination provider type will be determined. If a two-semester project is selected, a survey will be designed for administration to a random sample of parents of vaccinated and un-vaccinated children to understand the reasons for vaccinating or not vaccinating their child.

Student Research Projects

The Auditory Laboratory

Associate Professor Helmy Mulders

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@theAuditoryLab

Deafness and other hearing disorders such as tinnitus are among the most common forms of sensory impairment with profound consequences for the individual and society. Hearing loss can affect quality of life including mental health and cognition. In our laboratory we work with animal models to investigate neural mechanisms of tinnitus, effects of hearing loss on cognition and the effects of fibrosis on the effectiveness of cochlear implants.

Project: Relationship between hearing loss and spatial memory

Human studies have demonstrated a strong association between hearing loss and cognitive decline. It has been suggested that changes in central auditory processing following hearing loss are associated with high incidence of cognitive decline and Alzheimer's disease. We have previously investigated cognition (spatial learning and memory via Morris water Maze) in young and old guinea pigs with and without hearing loss. We now want to investigate Amyloid beta and Tau accumulation in the brains of these animals. This project will involve using a freezing microtome to cut sections, histology and immunohistochemistry.

Project is suitable for: Honours, Masters, PhD

Supervisors: Dr Kristin Barry and A/Prof Helmy Mulders

Project: Modelling and regulating extracellular matrix deposition in the inner ear

Fibrosis in the inner ear can occur following cochlear implant surgery and as a complication of infection. This can result in the formation of a fibrotic barrier between the electrode and the target neurons, causing loss of residual hearing and function of the implant. In this study we will examine the efficacy of the anti-fibrotic drugs in regulating extracellular matrix protein deposition by inner ear fibroblasts. Dose response curves will be performed and effects on TGFB-induced smad2/3 and p38 pathway activation will be confirmed by western blot. The effects of drug treatment on inner ear fibroblast cell proliferation, differentiation and ECM protein deposition by inner ear fibroblasts confirmed using in vitro assays.

Project is suitable for: Honours, Masters

Supervisors: A/Prof Cecilia Prêle and A/Prof Helmy Mulders

Project: Investigation into the potential of anti-fibrotic drugs as treatment for cochlear fibrosis

Cochlear implants, the gold standard treatment for profound hearing loss, are as yet the most successful sensory prosthesis, however there is considerable variation in outcomes for patients. One of the factors may be fibrosis in the cochlea caused by the insertion of the implant. In this project we will investigate the potential of a novel anti-fibrotic drug as a treatment using in vitro techniques and an in vivo animal model.

Project is suitable for: Honours, Masters

Supervisors: A/Prof Cecilia Prêle and A/Prof Helmy Mulders

Cancer and Cancer Targeted Therapies

Associate Professor Pilar Blancafort

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Each project will take place in the Cancer Epigenetics Laboratory at the Harry Perkins institute of Medical Research.

Project 1. Engineering the cancer epigenome and targeting metastatic behaviour using epigenetic editing tools.

With Dr. Charlene Waryah

Cancer is one of the major causes of death in Australia. For decades, the origin of cancer was attributed to genetic mutations, deletions and copy number amplifications. Recent advances have illuminated the aberrant epigenetic landscape which not only contributes but, in some cases, drives cancer development and progression. Epigenetic marks are heritable covalent modifications in the DNA or associated proteins. Epigenetic modifications provide the mechanisms by which a cell "knows" and "remembers" which genetic information to read and which to ignore. Epigenetic modifications include DNA methylation and modifications in the proteins that the DNA is wrapped around. Unlike genetic mutations, epigenetic modifications are reversible, and this can be used to restore the normal state of gene expression in the cancer. Our laboratory develops novel epigenome-targeted therapies to reverse the abnormal epigenetic modifications frequently observed in cancer. In this proposal, we aim to reverse the epigenetic modifications of key cancer drivers using the CRISPR/dCas9 system. We propose the development novel and more selective technologies able to stably suppress the genes that cause cancer spread.

Project is suitable for Honours, Masters, PhD

Supervisor: A/Prof Pilar Blancafort

Essential qualifications

For Honours: An appropriate undergraduate degree with a biological science, cell biology and basic molecular biology emphasis, and a minimum weighted average of 65% in the level 3 subjects that comprise the relevant major from an approved institution. Applicants will be assessed on a case-by-case basis.

For Masters or PhD: An appropriate Honours degree with a biological, cellular and basic molecular biology science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable Skills/Experience

Knowledge of statistics, cell biology, basic biochemistry and cell biology

Project 2. Development of a novel strategy using engineered peptides to selectively sensitise metastatic breast cancers to chemotherapy agents.

With Dr. Edina Wang

The goal of this study is to develop innovative targeted treatments for triple negative breast cancers (TNBCs). TNBCs are responsible for the majority of breast cancer deaths in Australia and throughout the world. These cancers do not express oestrogen receptor alpha, progesterone receptor and epidermal growth factor receptor 2, which are common targets exploited in the clinic.

They belong to the basal-like subtype breast cancer, which accounts for 15% of all breast cancers. In the metastatic setting, they are highly resistant to chemotherapy. DNA-damaging agents used in chemotherapy that lack target specificity, cause wide range adverse effects. Thus, there is an urgent need to develop novel, more specific and targeted molecular approaches to treating this lethal disease.

As a cutting-edge therapy for TNBCs, we propose the generation of interference peptides (iPeps), which are synthetic peptides engineered from oncogenic transcription factors overexpressed in these breast cancers. The iPeps carry cell penetration and nuclear localization sequences that allow the peptide to be rapidly internalized across the cell and nuclear membranes. In addition, the iPeps are designed with residues essential for protein-protein interactions and DNA-binding derived from the endogenous oncogenic transcription factor. The iPeps then compete with the endogenous transcription factor by sequestering the binding partners necessary for transcriptional and DNA-binding activities.

Furthermore, we will use this highly innovative approach to physically link the iPep with small molecules like Doxorubicin and pro-drugs like platinum IV, to localize them specifically in the nucleus of the cancer cells. We hypothesize that the iPeps will serve as “guides” for the chemotherapeutic drugs, directing them precisely into the nucleus to induce DNA damage. These iPeps will increase the selectivity and the kinetics of the small molecule’s uptake, as well as decrease the dose of the small molecule required for anti-cancer efficacy, thus lowering chemotherapy toxicity. This strategy will be employed in both TNBC cell lines and several aggressive breast cancer animal models, and eventually be adapted to patients to help eliminate the mortality associated with metastatic breast cancer, particularly for these triple negative breast cancers.

Supervisor: A/Prof Pilar Blancafort

Essential qualifications

For Masters or PhD: An appropriate Honours degree with a biological, cellular and basic molecular biology science emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable Skills/Experience

Knowledge of statistics, cell biology, basic biochemistry and cell biology

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Gene regulation in development and disease

Associate Professor Archa Fox

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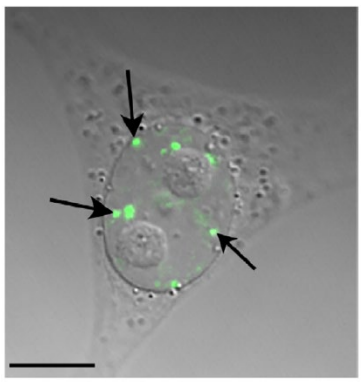
Project: How changing paraspeckles influences cell health and response to stress

Most human cells have the potential to build paraspeckles in their nuclei, however generally they have small/less abundant paraspeckles under normal growth conditions. In contrast, when cells are stressed through a variety of signals such as serum starvation, oxidative stress, pH imbalance, mitochondrial stress, heat shock and proteotoxicity, cells increase transcription of NEAT1 and thereby increase the abundance of paraspeckles. One challenge in studying the downstream roles of paraspeckles in response to these stressors has been separating the effects of the stressor from the effects of paraspeckles. To overcome this, we have developed a method of transiently increasing paraspeckle abundance without stressing the cell first: through delivery of antisense oligonucleotides that bind the nascent NEAT1 transcript.



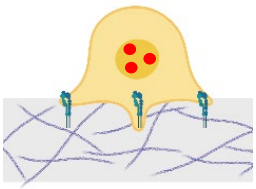
In this project you will characterise this new tool to boost paraspeckles in a variety of cell and disease models. You will culture cells, deliver the antisense oligos and then track cell health and characteristics in a variety of assays. You will also experiment with ways of labelling the cells that have taken up the oligos.

This project would suit someone with an interest in cell biology, cell culture and cellular models of disease

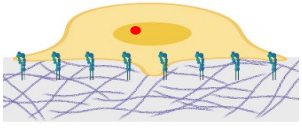
References: McCluggage and Fox (2021) Paraspeckle nuclear condensates: Global sensors of cell stress? Bioessays. 43 (5) 2000245

Project: Investigating how the cell nucleus responds to mechanical insults

Cells need to navigate and adapt to different environments within the body. There is growing appreciation that the rigid cell nucleus has to respond to the external environment that a cell experiences. The nucleus can respond to environmental cues by altering gene expression in the cell.

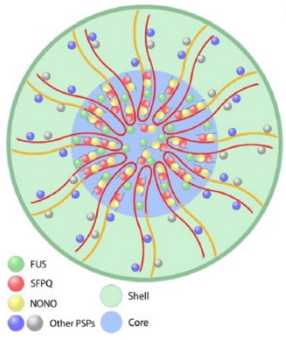


In this project you will investigate nuclear organisation, primarily focusing on paraspeckle nuclear bodies, within a variety of cells that experience different external environments. You will culture cells in different conditions and monitor how the nuclear responds. You will also assess the impact of increasing paraspeckles on cell responses to different environments. This work is critical for understanding and eventually targeting diseases such as cancer, where metastasis involves cells experiencing, and surviving, under extreme confinement.



This project would suit someone with an interest in cell biology, mechanobiology, and cellular models of disease.

Project: Studying the molecular glue that holds paraspeckles together



Paraspeckles are subnuclear RNA-protein granules that regulate gene expression in many contexts, particularly under stress conditions. We are interested in studying the underlying properties of the forces that hold paraspeckles together. They are interesting structures, as they are not enclosed in a membrane – so how do molecules get targeted there, and how are these molecules held there? It is important to understand these processes as many of the molecules found within paraspeckles are also found in pathological toxic aggregates in neurodegenerative disorders, such as motor neuron disease. We need to understand the way these molecules functionally aggregate into structures such as paraspeckles, in order to figure out why they pathologically aggregate in neurodegeneration.

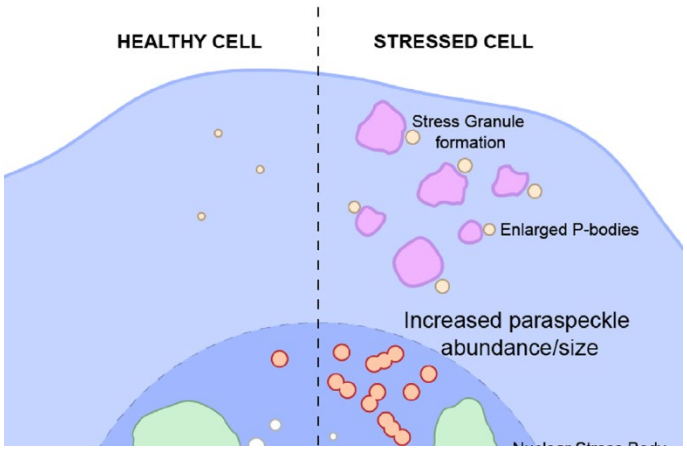
In this project you will use different molecular biology techniques to create mutations in key amino acids within different paraspeckle proteins, and then transfect fluorescent protein fusions of these constructs into cultured cells to examine their paraspeckle localisation. You will use fluorescent in situ hybridisation against the paraspeckle marker NEAT1 to detect paraspeckles. You will also work in vitro to study the biophysical properties of these proteins, in collaboration with Professor Charlie Bond.

This project will yield important insights into the nature of the functional aggregation of MND-associated proteins into paraspeckles.

This project would suit someone with an interest in molecular cell biology and biochemistry.

Project: A biomarker for physiological stress in large animals

It is well known that many different stressors influence cellular responses and physiological outcome. Paraspeckles are subnuclear bodies that regulate gene expression in many cellular contexts, and particularly in response to cellular stress. Paraspeckles are a cellular structure that is built on a long noncoding RNA molecule, called NEAT1 (nuclear paraspeckle assembly transcript 1).



Loss of NEAT1 in mice results in an inadequate reaction to physiological stress manifested as hyperlocomotion and panic escape response. Our preliminary work has shown NEAT1 is expressed in sheep peripheral tissues and blood samples. However, the physiological role of NEAT1 and paraspeckles in the central nervous system in response to physiological stresses is still poorly understood. In this project we will use a variety of samples from large animals (sheep and pigs) that have been subject to different stressful scenarios. We will use these samples to investigate the role of NEAT1 and paraspeckles in different physiological settings. In addition, we also hope to develop a novel biomarker in blood samples with real-time, quantitative measures of animal brain function that can inform a lifetime index of animal welfare and stress state.

This project would suit someone with an interest in physiology and cell biology.

Cardiovascular Electrophysiology - Ion Channels in Heart Muscle

Professor Livia Hool

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Currently, cardiovascular disease accounts for 32 % of all deaths in Australia. This is a staggering proportion and continues to exceed death from all cancers combined (30%) and from road deaths (4%). A number of the deaths in the cardiovascular group are due to arrhythmia or disturbances in the electrical activity in the heart.

The normal electrical activity in the heart is controlled by the movement of ions through specialised channels in the membranes of cardiac cells. The autonomic nervous system plays an essential role in regulating cardiac function and many of its effects are mediated via sympathetic neurotransmitters that regulate the activity of these ion channels.

Certain pathophysiological conditions contribute to arrhythmias such as hypoxia and oxidative stress. Under these conditions there is a reduction in blood flow to the muscle in the heart resulting in a reduction in available oxygen and reactive oxygen species production. This is then followed by an increase in generation of reactive oxygen species. There is increased sympathetic drive and the heart has a greater vulnerability to sudden cardiac death. Understanding how cardiac ion channels are regulated under these conditions is crucial to understanding the ionic mechanisms involved in the triggering of ischemic arrhythmias. In addition an increase in reactive oxygen species can contribute to the development of cardiac hypertrophy (enlarged heart) and cardiac failure. We have good evidence that an early mechanism involves increased calcium influx through the L-type calcium channel.

The laboratory uses molecular biology techniques for expression and purification of ion channel protein and biochemical techniques for assay of generation of reactive oxygen species and cell viability. The method that will be used to study membrane currents is the patch-clamp technique. This technique is an extremely powerful method for studying the electrophysiological properties of biological membranes and its contribution to the advancement of research was justly recognised with the awarding of the Nobel Prize in Physiology or Medicine in 1991 to its developers Erwin Neher and Bert Sakmann. The technique can be used to study ion channels either at a whole-cell level or at the level of a single channel. In addition, since the intracellular composition of the cell can be controlled, this can be exploited to determine any second messengers involved. Patch-clamp technique is also used in the laboratory in conjunction with fluorescent dyes to record changes in intracellular calcium, reactive oxygen species generation and mitochondrial function.

Project 1. How does the L-type calcium channel regulate mitochondrial function in pathology where actin filaments are disrupted?

(Collaboration with Prof Christine Seidman, Harvard University and Prof Chris Semsarian, Sydney University)

Mitochondrial respiration is abnormal in hearts where actin or cytoskeletal proteins are disrupted and it is not understood why. This project follows from data generated by previous students in the lab. We have evidence that the L-type calcium channel can regulate mitochondrial function via the actin cytoskeleton. The project involves the use of patch clamp technique to study L-type calcium channel currents in mouse myocytes isolated from hearts of mice with disease involving disruption in cytoskeletal proteins and fluorescent detection of changes in mitochondrial membrane potential, NADH and superoxide production after activation of the channel.

Alterations in expression of proteins in mdx mouse hearts that co-immunoprecipitate with the channel (assessed by Mass Spec) will be identified using immunoblot analysis.

Project 2. How does oxidative stress alter the sensitivity of the L-type calcium channel to isoproterenol? What effect does this have on the action potential?

(Collaboration with Professor Yoram Rudy, University of Washington, St Louis, Missouri, USA)

This question seeks to understand how arrhythmias occur during ischemia/reperfusion in the heart (after a heart attack). Isoproterenol is a beta- adrenergic agonist (and mimics the effects of catecholamines such as adrenaline in the heart). This project will use patch clamp technique to study the effect of oxidative stress and isoproterenol on L- type calcium channel currents in addition to K and Na channel currents and record changes in action potentials. Information gained from patch-clamp studies are incorporated into the Rudy-Luo model. Changes in action potential configuration are modelled and the relative risk of arrhythmia is determined.

Supervisor: Prof Livia Hool

Cell/Molecular Biology and Genetics

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High-resolution analysis of the human immune response to HIV: implications for cure research and vaccine design

Summary: More than 35 million people worldwide are infected with HIV including >22,000 Australians. Anti-HIV therapy can reduce mortality associated with infection but treatment does not provide a cure, is life-long and remains a substantial financial burden in Australia and worldwide. The main impediment to cure is the enormous diversity of HIV. A significant proportion of this variation is due to mutations in the HIV genome that allow the virus to escape from our immune response (viral adaptation). In this study, we will utilize our unique ability to analyze the host's immune response at the single cell level to examine viral adaptation during the critical acute phase of infection. Understanding viral adaptation will aid in the rational design of vaccine candidates for either preventative or therapeutic strategies.

Scientific Background and Rationale: The prototypic anti-viral immune response requires the actions of an array of naïve $CD4^+$ and $CD8^+$ T cells which, upon antigen-stimulation, differentiate into a highly specific population of "best–fit" clonotypes with an optimal T cell receptor (TCR) repertoire for clearance of virally infected targets and anti-viral memory. In the case of highly mutable viruses such as HIV, this process is subverted prominently by an extreme capacity for viral escape from $CD8^+$ T cells. The extent of $CD8^+$ escape, or more broadly adaptation, to immune responses, in founder/transmitting viruses or vaccine immunogens influences the subsequent quality of immunological control (1).

However, this mechanism alone is not sufficient to explain immune failure in HIV infection. It has been established that effective $CD4^+$ T cell responses are necessary for quality $CD8^+$ T cell responses (2, 3). We have characterised mutations in HIV sequences, which suggest that HIV can actually adapt to $CD4^+$ T cell responses. This is a novel form of adaptation, which may operate in early infection, and have critical long-lasting effects on subsequent antibody and $CD8^+$ T cell responses. Furthermore, while functional studies have shown examples of viral mutations causing disruption of antigen presentation leading to loss of antigen recognition, these 'classical' mechanisms represent only one strategy of adaptation. We have previously shown that the adapted viral strain can still be recognised by the host's T cells in many instances (4, 5) and these T cells can exhibit greater functional avidity to the cognate peptide than T cells that target the non-adapted form (6).

We **hypothesise** that viral adaptation to T cell pressure, rather than leading to 'classical' escape, may result in the selection of a narrow, high avidity, TCR repertoire that ultimately is less effective at viral control, perhaps because of viral exhaustion. We can now address this issue using our established single cell analysis approach. Understanding how the TCR diversity of a maturing immune response can be altered or exploited by a pathogen is a fundamental question for many acute and chronic pathogens for which natural, vaccine or cell therapy-based immunity is not currently effective or available.

The link between TCR repertoire changes and effector functions at the single clonotype and global response levels is also a fundamental question for anti-viral immunity.

Significance: The mechanisms of viral adaptation to T cell responses **are fundamental concepts for host-pathogen interaction** and have important clinical implications. The cumulative burden of providing immediate and life-long anti-retroviral therapy (ART) to all individuals with HIV infection is significant, and the HIV incidence and prevalence continues to increase in Australia every year since 1999 despite good ART coverage (7). Harnessing immunological clearance as an alternative to 'drugs for life' could reduce this health and economic burden, as well as advance the global research efforts for HIV eradication. Improved therapeutic vaccines could ideally be combined with anti-latency strategies as a potential synergy in Australian research, with resulting benefits for global health.

Current immunogen design approaches do not solve the problem of viral adaptation nor do they consider how to overcome viral adaptation to $CD4^+$ T cell responses in ensuring sustained $CD8^+$ and antibody responses for vaccine memory.

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The role of NKT cells in the outcome of liver transplantation in a murine model

Organ transplantation is the final treatment option for many patients with end-stage diseases. Despite improvements in short-term outcomes, long-term organ survival has remained poor for the past two decades. This is primarily due to chronic rejection, caused by a long-term, uncontrolled immune response against the transplanted organ. Understanding this damaging immune response is vital to improving outcomes for organ transplant patients.

We have an established liver transplantation model in mice which can be manipulated to tolerate or reject the transplanted liver depending on the genetic mismatch between the donor and recipient mice. Preliminary data in our model indicates that a specific type of immune cell, called a natural killer T (NKT) cell, could be vital in controlling the survival of the transplanted liver. NKT cells are multi-functional immune cells that recognise and react to a broad range of activating signals in different ways.

There is evidence that immune cells that are contained within the transplanted liver are necessary for it to be tolerated by the recipient. By transplanting livers which have or which lack NKT cells we can assess their importance for successful transplantation. By transplanting normal livers into recipients which have or which lack NKT cells, we can assess if transplant success is dependent on recipient NKT cells.

The health of the transplants will be assessed by measuring levels of liver tissue damage and cytokines in the blood, and by characterisation of the immune response in the graft and peripheral lymphoid organs using flow cytometry. Ultimately, we aim to use this model to discover potential new targets to enable tolerance to transplanted solid organs and consequently reducing the need for life-long immunosuppression and the associated adverse side effects.

Supervisors: A/Prof Silvana Gaudieri, Prof Michaela Lucas and Dr Amy Prosser (Perkins)

Desirable Skills/Experience: Background in immunology would be preferred.

Comparative Physiology of Adaptation

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Prof Shane Maloney


Dr Dominique Blache

Our group is interested in the physiological mechanisms whereby animal species (including humans) adapt to environmental stressors. We focus mainly on thermal and osmotic stress, but exercise, inanition (starvation), and infection are also studied, and recently the operation of circadian clocks and their role in physiological function (with Dr Peter Mark). Most experimental work is at systems level, but organ and molecular levels are also studied. Our long-term aim is to identify specific adaptations that allow animals to survive and reproduce in challenging environments, and to identify how "homeostasis" handles the trade-offs when simultaneous challenges are presented to an organism. Prospective Honours students with a background in General Systems Physiology, Exercise Physiology, Applied Animal Physiology, or Comparative Physiology are encouraged to apply. Depending on the project chosen a background in Cell Physiology could be an advantage.

Students will be exposed to a range of approaches and techniques including (in non-human animals) recovery anaesthesia and surgery, implantation of physiological recording equipment, blood sampling for hormone measurement, and husbandry techniques for various species. In human research we use state of the art equipment to record physiological parameters in ambulatory subjects, including core and skin temperature transmitters, ambulatory blood pressure recording equipment, laser Doppler skin blood flow techniques, and infra-red thermography for surface temperature measurement.

Project 1: Biomarkers of positive animal welfare state

The viability of the animal production industries is dependent on their ability to demonstrate to the broader community that the welfare of production animals is being rigorously assessed using indicators that reflect the animals' positive experience. New methods for the assessment of animal welfare are needed to match the new and future standards for welfare. Over the last 5-10 years, the definition of animal welfare has included the concept that animals should experience a "life worth of living" and therefore the next generation of biomarkers for animal welfare need to reflect a positive welfare state and a positive mental status. The project aims to screen biomarkers that have been linked to positive emotion, or positive perception of a situation, by humans and other laboratory animals.

The candidate will run animal experiments using sheep exposed to known positive, neutral, and negative situations. The emotional state of the animal will be measured at different time points using established behavioural tests.

Biological samples, primarily blood and also less invasive samples such as saliva, will be collected to measure a suite of potential novel markers of positive experiential state. The tools to measure these new biomarkers will be developed and further validated under field conditions on farm.

Supervisors: Dr Dominique Blache (SAgE), Prof Shane Maloney, Prof Alan Tilbrook (Uni of Queensland)

Project 2. The role of episodic ultradian events of temperature in preparedness in humans

Biological rhythms are characterized as infradian (> 24 hours), circadian (~24 hours), or ultradian (~4 hours). Ultradian rhythms are often dismissed as noise within the circadian rhythm, but growing evidence suggests that ultradian events may be centrally regulated, like circadian rhythms. Spikes in brain temperature precede locomotive and foraging activity, and ultradian rhythms in core body temperature have been hypothesized to play a role in mental alertness. Evolutionarily speaking, ultradian rhythms may underlie the preparedness of an organism to respond to external stimuli, such as during hunting or predation. The aim of this project is to establish the nature of the relationship between mental alertness and ultradian rhythms of core body temperature in humans. You will record and analyze motor data in response to transcranial magnetic stimuli that are given at various stages of naturally occurring ultradian events characterised using telemetric (real-time) measures of body temperature.

Supervisors: Dr Dominique Blache (SAgE), Prof Shane Maloney, A/Prof Jennifer Rodger (SBS)

Project 3. Relative importance of different Zeitgebers in the control of rhythmicity and survival in the *Drosophila*

Circadian rhythms refer to endogenous biological processes that fluctuate over a 24-hour period, allowing organisms to anticipate predictable physiological challenges that occur during the day/night cycle. Research in chronobiology increasingly indicates that robust circadian rhythms (i.e., rhythms with large amplitudes) are linked to improved metabolic health and longevity. Zeitgebers refer to resetting cues that synchronize and set the timing of circadian rhythms. Temperature appears to be a potent zeitgeber for circadian rhythms and may directly drive clock gene expression; therefore, it is possible that an increased amplitude of clock gene expression, driven by an increased amplitude of temperature cycles, could have a positive effect on longevity. In laboratory mammals, it is a challenge to demonstrate a direct relationship because of the difficulties of manipulating their body temperature. However, we can drive circadian gene expression in *Drosophila melanogaster*, a well-established model organism for genetics and circadian biology, by manipulating ambient temperature, which is impossible to do in mammals. Recently, we demonstrated that flies exposed to cycling ambient temperatures live significantly longer compared to flies housed at constant temperature.

The project aims to investigate the effect of constant or cycling ambient temperatures on circadian gene expression and lifespan. Sub-projects may include investigations into the interaction of temperature with various other known zeitgebers, including light, noise, and diet, and investigate their effects on clock gene expression, lifespan, activity, feeding/mating behaviour, and physiology. Results from this project may shed light onto the role of circadian rhythms and various zeitgebers on the process of ageing.

Supervisors: Prof Shane Maloney, Dr Dominique Blache (SAgE), Dr Grace Goh

Project 4. Nerve conduction velocity, ion pump activity, and the cardiac pacemaker during cooling in the cane toad (*Rhinella marina*)

In Australia, cane toads (*Rhinella marina*) are classified as pests. Since their introduction into Queensland in 1930, their numbers have reached around 200 million. To try to limit the population, many thousands of toads are killed annually using a variety of methods. Toads are also killed for university teaching and research. Gradual cooling then freezing has been a common method for humane killing, but is now deemed unacceptable by some authorities. The aim of the project is to measure the activity of various components of the nociceptive pathway at different temperatures. You will make measures using a PowerLab, similar to the practicals you did in PHYL2002, to elucidate the Q10 for nervous activity in toads. Your results will help to determine whether cane toads have the necessary physiology to detect pain when they are frozen.

Supervisors: Prof Shane Maloney, Dr Dominique Blache (SAgE)

Project 5. Impact of ultradian patterns of body temperature on lifespan and reproduction in *Drosophila*

Metabolic processes control the flow of energy and protein in the body, helping to maintain biological function. One function central to metabolism in mammals and birds is the regulation of body temperature. Research in chronobiology increasingly indicates that robust circadian rhythms (i.e., rhythms with large amplitudes) are linked to improved metabolic health and longevity. In addition to the circadian rhythm of body temperature, there exist very short episodic increases in temperature (also called episodic ultradian events). An inverse relationship between the amplitude of circadian rhythm and the number of episodic ultradian events has been described in a number of all homeotherm species. The role and the mechanism controlling the interaction between circadian and ultradian rhythms has never been studied simply because, in homeotherm, it is impossible to dissociate or manipulate them independently. Drosophila is a perfect model to investigate the role of body temperature on biological function. However, the body temperature of *Drosophila melanogaster*, a small body size heterotherm, can be easily manipulated with changing ambient temperatures.

The project aims to investigate the relative role of both the circadian and the ultradain rhythm of body temperature on lifespan reproductive function and associated gene expression.

Supervisors: Dr Dominique Blache (SAgE), Dr Kelsey Pool (SAgE], Prof Shane Maloney

Project 6. Orbital tissue relationships to intraocular and intracranial pressure.

The orbit represents the contents of the bony orbit in mammals and all vertebrates. The eye sits within the orbit, insulated by loose fat and fibrous tissue which performs a delicate and complex role. This role is necessary to insulate the eye from sudden movements, shockwaves and to form a steady base to allow rotational eye movements without translation of the eye in any particular direction (in order to keep ones visual world stable). Several diseases can affect the orbit and they do this principally by adding tissue either through tumour growth or inflammatory tissues which have a bulk or mass effect upon the orbital tissue compressing the optic nerve or muscles or distorting the eyeball itself.

Our work will mimic tumour growth by implanting balloon catheters within the orbits of pigs whilst we measure the intraocular, intraorbital and intracranial (cerebrospinal fluid pressure) pressures.

The technical setup is complex but one will learn a great deal about ocular and orbital pressure physiology through this work. One core hypothesis will be that the orbital tissue pressure is evenly distributed with relatively little tissue buffering within the orbit.

The orbital pressure is likely to impinge directly upon the cerebrospinal fluid compartment that exists around the optic nerve right up to the eyeball itself and hence have a direct effect upon that pressure compartment. New methods to directly measure the cerebrospinal fluid pressure around the optic nerve will be used. We will also be apply photoplethysmographic techniques to develop methods to non-invasively measure the pressure in orbital tissue. Depending upon your interests, some of these core aims can be built into a prospective PhD.

Supervisors: Prof Shane Maloney, Prof Bill Morgan [Lion's Eye Institute]

Project 7. Photoplethysmography estimation of cerebrospinal fluid pressure and its utility in measuring aspects of retinal vascular disease.

Most of our attention in relation to blood vessel physiology concerns blood flow, pressure differentials, and resistance in classical physical terms. However, there is recent, exciting new understanding of how pulse waves are transmitted along blood vessels and how pulse wave transmission can be influenced by vascular compliance and resistance in particular. The translation of an intravascular pressure pulse wave to blood vessel wall pulsation involves local compliance and vascular stiffness. All of these factors are involved in significant blinding diseases such as glaucoma, diabetic retinopathy, retinal vascular diseases, and also raised intracranial hypertension. We have developed a photoplethysmographic technique that maps the retinal vascular pulsation characteristics (amplitudes and timing). We have only just begun tapping into how this technique can be applied to diseases as well as using it to understand basic physiology of the retinal vessels. How the retinal vessel (in particular vein) wall pulse wave attenuates (the rate of pulse amplitude reduction with distance along vessel) is thought to change with alterations in vessel compliance and resistance. Several diseases are key exemplars causing change in those parameters, namely diabetes with diabetic retinopathy, long standing systemic hypertension and retinal vein occlusion. Diabetic retinopathy and vein occlusion cause approximately 12% of blindness which is clearly a devastating problem.

There is a great need to identify patients at risk of going blind with these diseases and this technology shows great potential. It requires much deeper physiological understanding for its application.

This project would be for someone interested in characterising normal pulse wave attenuation characteristics and in the diseases mentioned, along with exploring the role of timing characteristics including pulse wave transmission in normality and disease. It is most likely that much deeper understanding of vascular physiology including pulse wave transmission characteristics will be derived through this work which will have as yet unknown applications and ramifications. It is almost certain that some of the applications will be very relevant to the monitoring and treatment of the diseases mentioned.

Supervisors: Prof Shane Maloney, Prof Bill Morgan [Lion's Eye Institute]

Project 8: Is there a clock in the sheep stomach? Or chronobiology and rumen function

Circadian rhythms refer to endogenous biological processes that fluctuate over a 24-hour period, allowing organisms to anticipate predictable physiological challenges that occur during the day/night cycle. Research in chronobiology increasingly indicates that robust circadian rhythms (i.e., rhythms with large amplitudes) are linked to improved metabolic health and longevity. Zeitgebers refer to resetting cues that synchronize and set the timing of circadian rhythms. Temperature appears to be a potent zeitgeber for circadian rhythms and may directly drive clock gene expression; therefore, it is possible that an increased amplitude of clock gene expression, driven by an increased amplitude of temperature cycles, could have a positive effect on longevity. The microbial population that is present in the rumen is crucial for digestion of a forage diet, and that population is naturally exposed to the circadian rhythms of temperature of the sheep. Amazingly, so far all experiments done using either artificial rumen or culture of rumen fluid in-vitro have been done at constant temperature.

This project aims to explore the role of circadian rhythms of temperature in the rumen on the activity and survival of the microbial population.

Supervisors: Dr Dominique Blache [SAgE], Prof Phil Vercoe [SAgE], Prof Shane Maloney

Ecology and Evolution

Associate Professor Cyril Grueter

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Project 1: Primate behavioural ecology research:

- Comparative study on aspects of primate socioecology (using literature data)
- Observational research on primate behaviour/cognition at the Perth Zoo

Project 2: Human behavioural ecology

Example: Questionnaire-based, experimental, and observational research on social behaviour/organisation, mate choice and cooperation in humans

Desirable Skills/Experience

Basic knowledge of statistics (especially regression analyses) would be desirable.

Biological Anthroplogy

Associate Professor Debra Judge

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Project:

- For **highly motivated** students there is potential to undertake field studies of family well-being in East Timor involving questions of family structure, ecology, social networks and child growth. Some language study before commencing will be required and only students with records of high achievement in appropriate units will be considered.

Essential qualifications

For Masters or PhD: An appropriate honours degree with a human biology, zoology or anthropology emphasis or equivalent research experience from an approved institution. Applicants will be assessed on a case-by-case basis.

Desirable skills/experience

Knowledge of basic statistical analyses is helpful but can be learned during the project. Ability to learn a further language is a requirement for some international research projects.

Neuroscience

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A/Prof Stuart Hodgetts

Emeritus Prof Alan Harvey

Cell and tissue transplantation, pharmacotherapy, gene therapy and the repair of central nervous tissue damaged after injury.

The research by the neuroscience groups in Anatomy, Physiology and Human Biology has a particular emphasis on cell and tissue transplantation, gene therapy, bioengineering, in vivo reprogramming, pharmacotherapy, photobiomodulation, and the repair of central nervous tissue damaged after injury. Ways are being tested for preventing nerve cells from dying after injury and promoting plasticity and the regenerative growth of damaged axons. The potential for replacing compromised cells with new healthy cells, including stem cells, is also under investigation. Studies are mostly carried out in the spinal cord.

Supervisor: A/Prof. Stuart Hodgetts

Other supervisors: Emeritus Prof Alan Harvey

Desirable skills/experience

Neuroscience emphasis. Cellular and molecular biology knowledge would be helpful

The role of kisspeptin in energy expenditure in the mouse

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Recent data from our laboratory demonstrate no effect of central kisspeptin treatment on accumulative food intake. Despite this, neuroanatomical links have been established between kisspeptin cells and appetite regulating neurons expressing neuropeptide Y (NPY) and Pro-opiomelanocortin (POMC). Moreover, kisspeptin results in the activation of NPY cells in the hypothalamus. Electrophysiological data also suggests kisspeptin regulates the activity of NPY, and also POMC neurons. Taken together, these data strongly suggest kisspeptin has effects on energy expenditure.

Experiments will be conducted to measure the effect of kisspeptin and the absence of kisspeptin signalling in mice on energy Expenditure.GPR54 (Kiss1r) knock-out mice or their wild-type littermates will be challenged with a high fat diet for 12 weeks. Mice will then be tested on indices of energy balance including:

- Measurement of whole body energy metabolism (using metabolic cages for indirect calorimetetry
- Assessment of whole body glucose metabolism (using intraperitoneal glucose and insulin tolerance tests)
- Assessment of body composition (Using dual energy X-ray absorptiomentry DEXA)
- Assessment of neuropeptide systems involved in energy metabolism (using in situ hybridisation).

Results from these experiments will shed light on the known link between the reproductive system and metabolism and will, potentially, offer novel therapeutic alternatives for the treatment of obesity and related metabolic disorders.

The role of kisspeptin in implantation and placentation

Kisspeptin, the neuropeptide product of the Kiss1 gene, is synthesized by neurons within the hypothalamus and is critical for the release of gonadotrophin-releasing hormone (GnRH) and fertility. In humans, kisspeptin secretion into the peripheral circulation increases dramatically (approximately ten-thousand-fold) during pregnancy and declines precipitously at term, indicating a placental origin. The placenta is known to express KISS1 and kisspeptin receptor (KISS1R) mRNA and it appears to be localized to the trophoblast compartment. We aim to determine the expression of Kiss1 mRNA in the mouse placenta and examine the effect of reduced kisspeptin signalling (using a kisspeptin receptor knock-out mouse) on feto-placental growth.

Experiments will be conducted to measure feto-placental growth in an Kiss1r KO model.

Kiss1rKO mice or their wild-type littermates will be examined at day 14 and 18 of pregnancy.

We will examine:

- Fetal weight
- Placental weight and morphology
- Assessment of key placental genes (using RT-PCR)
- The effect of kisspeptin and the absence of kisspeptin signalling in mice on placental histology

Results from these experiments will shed light on the function of kisspeptin in the placenta and will, potentially, offer novel therapeutic alternatives for the treatment of placental insufficiency and/or pre-eclampsia.

Supervisors Dr Jeremy Smith and A/Prof Caitlin Wyrwoll

Fetal/Neonatal Anatomy, Physiology and Biology

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Innate Defence Regulator Peptides to Modulate Postnatal Inflammatory Response

Inflammation and infection are the key drivers of adverse neurodevelopmental outcomes and increased morbidity and mortality in preterm infants. New immunomodulatory therapies that target inflammation and infection may improve preterm infant outcomes. Innate defence regulators (IDR) are synthetic derivatives of host defence peptides, which have antimicrobial and immunomodulatory actions. IDR-1018 is a highly promising IDR with demonstrated immunomodulatory and neuroprotective efficacy in newborn mice, and antimicrobial activity against gram-positive and gram-negative bacteria. Newborn lambs were ventilated for 48 hours in 2021 prior to euthanasia and tissue collection. Lambs received IDR-1018 via either an enteral or intravenous route, or placebo control.

This project offers Honours or HDR students opportunities for investigating the impact of IDR-1018 on postnatal inflammatory response in the lung +/- liver of tissues collected during this study. Students will have the opportunity to be involved in some similar postnatal lamb studies in 2024 so that they also develop an appreciation of the nature of the management of the 2022 lambs.

Principal Supervisor: Prof Jane Pillow

Additional supervisors will be involved depending on the student interests and organ system to be studied.

Desirable skills/experience

Preparedness to work with large animals including surgery and post-mortem tissue collection. Evidence of successful teamwork and personal organizational skills. Strong work ethic, & commitment to excellence.

Effects of environmental stressors on pregnancy and subsequent development

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Early life environment is a powerful determinant of adult health outcomes. Each year, Dr Wyrwoll offers a range of research projects that address this topic. Broadly, these environmental stressors encompass issues such as malnutrition, physiological stressors arising from climate change, drug use, and models of glucocorticoid exposure. Projects can range from working with animals models, to computer modelling, to cell based projects, to analysis of human health datasets. Please contact Caitlin directly for more information.

Specific projects for 2024 include:

Nitrate contamination of drinking water and pregnancy complications

Water quality parameters that do not conform with drinking water guidelines are well documented in regional Western Australian communities (Water Corporation Annual Report, 2019-2020, Western Australian Auditor General, 2020-2021). Recent research in the Goldfields found higher than expected prevalence of risk factors for type-2 diabetes and renal disease in both Aboriginal and non-Aboriginal children (Jeffries-Stokes et al., 2020). This elevated risk, independent of ethnicity, was attributed to water quality, specifically nitrate contamination. It is now emerging that the negative impact of nitrate contamination of drinking water on child health also extends to adverse effects in pregnancy.

Nitrate contamination of groundwater is prevalent in numerous small towns (including Cue, Meekatharra, Mount Magnet, New Norica, Sandstone, Yaalgoo, Laverton, Leonora, Menzies and Wiluna) and remote communities in the Goldfields, Pilbara, Kimberley and Mid-West of WA. All pregnant women and children who drink the water are at risk of adverse health effects. While guidelines have been established for "safe" thresholds of nitrate contamination, the guidelines are based on limited information. Currently, a guideline of 50 mg/L and above for nitrate in drinking water has been established as unsafe for bottle-fed infants under 3 months as it causes methaemoglobinaemia (insufficient blood oxygen). Adults (including pregnant women) and children over 3 months are recommended to be able to consume nitrate concentrations up to 100 mg/L without adverse effect. However, this guideline for safe levels of nitrate in drinking water may be incorrect. There has been no research that has conclusively shown that 100 mg/L of nitrate is safe to drink in pregnancy. Concerningly, recent epidemiological studies show that nitrate concentrations of 50 mg/L, and even lower, in drinking water may associate with preterm birth, fetal growth restriction and nervous system birth defects (Coffman et al., 2021, Sherris et al., 2021, Stayner et al., 2022). There is also evidence to suggest child respiratory function may also be affected (Gupta et al. 2000). There is a substantial gap in knowledge of what levels of nitrate are safe to consume.

There is currently no biological evidence to support the recommended guidelines for consumption of nitrate in drinking water during pregnancy. Using a rat model of pregnancy, we will establish whether contamination of drinking water with nitrate elicits adverse effects. Time-mated rats will be allocated to relevant concentrations of nitrate in drinking water. Key outcomes for this project include preclinical ultrasound, placental function, and fetal development assessments.

Supervisors: A/Prof Caitlin Wyrwoll & Mx. Leaf Kardol.

Reproductive and Developmental Biology

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The major interests of our group centre on the importance of circadian biology in relation to placental function, maternal adaptation to pregnancy, and developmental programming. Current studies are focussed on the impact of maternal obesity, omega-3 fatty acids and glucocorticoid excess on pregnancy outcome (from the perspective of both the mother and the developing fetus).

Projects are suitable for Honours, Masters by Research, PhD

Project 1: Developmental origins of health and disease (DOHAD)

Studies in relation to DOHAD focus on the effects of fetal glucocorticoid excess on the adult phenotype, particularly in relation to programming of adult-onset diseases such as hypertension, diabetes and obesity. The capacity of postnatal diets to either exacerbate (e.g. by a high fat diet) or rescue (e.g. dietary fish oil) adverse outcomes is an important focus of this work.

Tissue banks have been collected from a large scale glucocorticoid programming study and these are available for analysis. Tissues including heart, kidney and adrenal gland have been collected at 6 months of age from control and programmed offspring raised on standard, high fat or high fat/high omega-3 diets. They have been collected at four time points across a 24 hour period, enabling circadian profiling of gene expression and tissue function to be layered into the analysis.

Supervisors: Dr Peter Mark (Chief), with Em Prof Brendan Waddell

Project 2: Circadian rhythms in the spiny mouse placenta

Circadian biology underpins all major metabolic processes to appropriately align physiology of the organism with behaviour. Altricial (immature at birth) organisms, such as the rat and mouse, have minimal circadian variation in placental function, possibly to supply the fetus with constant nutrition during the relatively brief period of fetal growth. Precocial (relatively mature at birth) organisms are often born with metabolic rhythmicity (e.g. in liver function) which may be driven by exposure to peaks and troughs in substrate supply from the placenta.

This project aims to determine whether placentas from the precocial spiny mouse exhibit distinct circadian rhythmicity in their function in association with fetal liver rhythmicity. Samples have been collected from pregnant spiny mice in collaboration with Dr Hayley Dickinson, The Ritchie Centre at The Hudson Institute, Victoria. Placental expression of clock genes and nutrient transporters will be determined at various stages throughout gestation to determine the timing of onset for placental rhythmicity.

Supervisors: Dr Peter Mark (Chief), with Em Prof Brendan Waddell and Dr Hayley Dickinson, Monash University

Project 3: Maternal circadian adaptation to pregnancy

Pregnancy is one of the greatest physiological and metabolic challenges the body is confronted with. Maternal metabolism exhibits a predominantly anabolic phase during the first half of gestation, to lay down sufficient nutrients in maternal metabolic tissues (e.g., liver and adipose tissue) to meet the high energetic demands of the developing fetus later in gestation, via catabolism of the stored nutrients.

In addition, many metabolic pathways exhibit circadian rhythmicity in their activity, so they can optimise their performance to appropriate times of day e.g. food consumption during the day and fasting overnight.

Tissues have been collected at 4 hourly timepoints across 24 hours from non-pregnant mice and during mouse pregnancy (days 6, 10, 14 and 18 of pregnancy; term =19 days). Metabolic pathways and their circadian rhythmicity in these tissues will be interrogated through quantitative PCR and Western blot analysis to identify how liver and adipose tissue change during this metabolic adaptation to pregnancy.

Supervisors: Dr Peter Mark (Chief), with Em Prof Brendan Waddell

Project 4: Maternal obesity disrupts circadian adaptation to pregnancy and fetal and placental development.

Obesity during pregnancy is associated with numerous adverse outcomes including preeclampsia, gestational diabetes, fetal overgrowth and somewhat counter-intuitively, some mothers exhibit fetal growth restriction. In obese pregnancies complicated by fetal growth restriction, placental dysfunction is considered a likely cause of the reduced fetal growth. This placental dysfunction may eventuate, in part, through maladaptation of maternal circadian rhythmicity in metabolic processes.

Female rats were fed cafeteria items (e.g., meat pies, biscuits, chocolate cake) for eight weeks prior to mating, and through pregnancy. By the time of mating, the CAF-fed rats were ~25% heavier than control rats, fed only normal chow. Maternal metabolic tissues (liver and adipose tissue), placental tissue and fetal liver were collected at 4 hourly intervals across days 15-16 and 21-22 of gestation (term = 23 days). These tissues show marked changes in circadian expression of clock genes following consumption of the CAF diet, with the amplitude of the rhythm frequently reduced. Further investigation in alterations in metabolic pathways will identify other genes that are dysregulated in maternal obesity.

Supervisors: Dr Peter Mark (Chief), with Em Prof Brendan Waddell

Project 5: Pathways to infertility: mechanisms of action of phyto-oestrogens

Background: *Trifolium subterraneum* clover has historically been used as a pasture throughout Western Australian sheep farms, due to its palatability to livestock and low maintenance requirements. However, in the 1930s and 40s, reproductive anomalies in flocks grazing *Trifolium subterraneum* clover were linked to the presence of phytoestrogens. Phytoestrogens are non-steroidal, naturally occurring phytochemicals produced in plants, partly in response to stress. Phytoestrogens are functionally and structurally similar to oestrogens, particularly 17β-oestradiol, found in mammals including sheep. Phytoestrogens act as a mixed agonist/antagonist of oestrogen action, suppressing the hypogonadal-pituitary axis and competing for oestrogen receptors, ERα and ERβ.

In sheep ingesting oestrogenic clover, the cervix loses the ability to respond to oestrogen, thus failing to produce the viscoelastic mucous necessary for fertilisation. However, some sheep are not affected by the ingestion of oestrogenic clover.

The molecular basis of the resistance to phyto-oestrogen exposure is not understood. This project aims to compare the expression of oestrogen receptors ERα and ERβ and related intracellular mechanisms in ewes exposed to phyto-oestrogens, that were either successful or unsuccessful in the production of a lamb.

Supervisors: Dr Peter Mark, Dr Dominique Blache, A/Prof Caitlin Wyrwoll

Reproductive Biology

Associate Professor Kathy Sanders

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Lifestyle and psychosocial factors influencing human fecundity and fertility (database and survey studies)

- The impact and interaction of age, nutrition, and stress on male and female reproductive processes (database, survey and lab based projects possible).
- Issues surrounding the use of donated gametes and embryos in assisted reproductive technology (survey based and qualitative type projects possible).

For students interested in assisted reproductive technology (ART), opportunities exist for collaborative projects in the above areas with Dr Peter Burton at Concept Fertility Centre. Laboratory based projects focus on the impact of ART procedures on sperm biology and clinical outcomes.

Students are encouraged to contact Kathy Sanders to discuss any other topics on Reproductive Biology they may wish to pursue.

Supervisor: A/Prof Kathy Sanders

Airway Physiological Research Laboratory

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Professor Alan James

Mr John Elliott

Mr Michael Hackmann

The Airway Physiological Research Laboratory in the School of Human Sciences, in collaboration with clinicians and scientists at Sir Charles Gairdner Hospital, has a long-standing interest in the control and function of conducting bronchi. The trachea, bronchi and other airways conduct air into and out of the lung. During an asthma attack, contraction of airway smooth muscle narrows the conducting bronchi and obstructs airflow. Airway obstruction also occurs in several other respiratory diseases including chronic obstructive pulmonary disease (COPD), chronic bronchitis and emphysema. We perform *in vivo* and *in vitro* experiments on human and animal models with a broad focus of understanding the detailed mechanisms involved in the control of airway diameter and airway obstruction.

Project 1: Pharmacological ablation of the airway smooth muscle layer as a new treatment for asthma

One of the primary pathologies of asthma is increased airway smooth muscle thickness which contributes in no small part to disease severity; yet this structural abnormality has never seriously been used as a specific drug target. It has been well established that the airway smooth muscle layer is in a state of ongoing proliferation and apoptosis. Shifting the balance in favour of apoptosis (inhibiting proliferation or upregulating apoptosis) is a logical intervention to reduce airway smooth muscle thickness. Under biomechanically relevant cell culture conditions, this study will trial 'hypotrophic/anti-proliferative agents' and attempt to pharmacologically degrade the airway smooth muscle layer, forming a basis for a new therapy in the treatment of asthma.

Supervisors: A/Prof Peter Noble, Dr Kimberley Wang, Dr Yu Suk Choi

Project 2: Quantification of airway-associated adipose tissue by polarisation-sensitive optical coherence tomography

We have recently used *ex vivo* human tissue to demonstrate airway-associated adipose tissue as a contributing factor in co-morbid asthma and obesity. For a respiratory physician, fat infiltration of the airway wall was not previously a consideration and certainly not one to guide treatment. What we are in fact seeing is a fatty invasion of the airway wall and therefore an immediate shift in the constituent properties, analogous to airway remodelling (structural modification) that is believed to play a fundamental role in the manifestation of breathing difficulties in asthma. How do we diagnostically assess airway-associated adipose tissue in patients? We are developing polarisation-sensitive optical coherence tomography (PS-OCT) as a non-invasive diagnostic tool for the assessment of airway-associated adipose tissue in patients. The present study will validate measurements of airway-associated adipose tissue using PS-OCT in pig bronchial segments by comparing them with histological measurements.

Supervisors: A/Prof Peter Noble, Dr Alvenia Cairncross, Mr Michael Hackmann

Project 3: Electrical impedance tomography for the assessment of lung disease

Electrical impedance tomography (EIT) is a safe, non-invasive, cheap and portable technology that constructs maps of lung ventilation from surface electrodes positioned around the chest. The underlying principle of EIT is that electrical impedance increases in proportion to lung inflation such that the degree of lung aeration during breathing can be tracked from changes in impedance. EIT has the potential to characterise ventilation heterogeneity which is typically increased in respiratory disease. The present project will determine whether EIT is a useful diagnostic approach in patients with asthma, chronic obstructive pulmonary disease, interstitial lung disease, cystic fibrosis and non-cystic fibrosis bronchiectasis.

Supervisors: A/Prof Peter Noble, A/Prof John Blakey, Dr Alvenia Cairncross

Project 4: Feasibility of remote spirometry in the management of respiratory outpatients

In Australia, respiratory disease affects 31% of the population and is the sixth leading contributor to health burden. Diagnosis and ongoing management of respiratory disease is reliant on routine non-invasive spirometry which measures exhaled gas volumes over time. Although in-clinic spirometry is highly valuable and is still the gold standard of lung function testing, it is not easily or readily accessible for all patients and there are health-related risks. The COVID-19 pandemic in particular, has highlighted a new demand for remote spirometry testing due to lockdowns and associated restrictions, preventing patients from attending regular appointments. Smartphone-connected home spirometers are being developed to overcome the burden associated with in-clinic spirometry, allowing lung function testing to be conducted from the patient's home. The present study will assess the quality of remote spirometry data from patients with asthma, chronic obstructive pulmonary disease, interstitial lung disease and non-cystic fibrosis bronchiectasis.

Supervisors: A/Prof Peter Noble, A/Prof John Blakey, Dr Alvenia Cairncross

Project 5: Characterising structural properties of kangaroo airways

Comparative physiological studies using animal models provide an opportunity to better understand the relationship between airway structure and function. The present study will focus on the kangaroo airway. In preliminary findings, we have identified a thickened basement membrane, at the level and beyond that which is observed in patients with asthma. We also observed infiltration of eosinophils, which led us to conclude that kangaroos are an innate model of allergic airway disease. The present study will further characterise basement membrane thickness in relation to inflammation with the hope of revealing phenomena relevant to human asthma.

Supervisors: A/Prof Peter Noble, Dr Kimberley Wang, Mr John Elliot

Project 6: Application of the Airway Disease Biobank to advance our understanding of respiratory disease

The Airway Disease Biobank is a Western Australian resource compromising airway samples from > 350 subjects with and without respiratory disease. Using histological and stereological techniques to examine human tissue, the Biobank has advanced our understanding of asthma and chronic obstructive disease. In particularly, the fundamental role of airway smooth muscle remodelling in determining disease severity has been revealed through decades of publications utilising Biobank tissue. Yearly projects are run for students who enjoy histology and are keen to generate clinically relevant data. Projects are custom-designed to student interest. An emerging question is whether sarcoidosis is also a disease where airway disorder is produced by thickening of the airway smooth muscle layer.

Supervisors: A/Prof Peter Noble, Mr John Elliot

Project 7: Intrauterine growth restriction and asthma development

Studies have shown that restricted fetal growth in the womb may be linked to the development of asthma in childhood and adulthood. The reason for this association is not clear but we believe that restricted growth may alter the normal development of airway and lung tissue leading to impaired function and symptoms of wheeze, chest tightness and cough. Using an established *in utero* growth restricted mouse model, this project aims to determine if growth restriction is accompanied by a change in airway structure that is analogous to what is observed in asthma.

Supervisors: Dr Kimberley Wang, A/Prof Peter Noble

Evaluating skeletal muscle performance in mouse models of disease and superior athleticism

Associate Professor Tony Bakker

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Skeletal muscle comprises up to 40% of a human's body mass and is crucial for everyday actions such as breathing, moving and swallowing. When skeletal muscles do not function properly they can cause severe diseases, such as muscular dystrophy and congenital myopathy. An emerging skeletal muscle disease associated with ageing is sarcopenia, which is tightly linked to osteoporosis and falls in the elderly.

Having the ability to study animal models is often crucial for medical researchers to better understand biology, and to then devise and evaluate potential therapies for disease. Even if certain experiments can be performed in tissue culture, ultimately studies require an animal model to be the test-bed to allow appropriate and thorough evaluation.

We have previously successfully studied the skeletal muscle physiology of a range of mouse models. We currently have a range of mouse lines that have skeletal muscles that are either impaired or superior in function. For those that are impaired, where mice have an inability to exercise normally, the aim is to understand why this impairment exists, and whether the application of possible treatments is efficacious. In those mouse lines with skeletal muscles that are performing better than expected (eg. mice show an exceptionally high capacity to exercise), we would like to unravel the underlying mechanisms responsible. Once uncovered, activation of these mechanisms could be used in the future to prevent or treat skeletal muscle diseases such as muscular dystrophy.

In addition to skeletal muscle physiology techniques, students would have the opportunity to include other techniques used to phenotype mice in their tailored Honours project.

These include genetics and molecular biology, tissue biopsy and histology, immunostaining, various types of microscopy, protein and RNA extraction, voluntary running wheel analysis, and magnetic resonance imaging.

Please contact us to discuss the possible projects on offer if you are inspired to try to better understand skeletal muscle diseases and to develop therapies for them. If you choose such a project, you would use a range of exciting techniques with well-established, respected and friendly medical researchers at the School of Anatomy, Physiology and Human Biology, and at the Harry Perkins Institute of Medical Research.

Supervisor: A/Prof Tony Bakker

Can blocking skeletal muscle stretch-activated Ca^{2+} channels prevent ventilation-induced diaphragm skeletal muscle damage.

Preterm babies are often unable to breathe on their own due to the immaturity of the respiratory system, and require an extended period of mechanical ventilation. While essential for survival, this intervention is thought to lead to damage of the developing respiratory muscles, which can significantly extended the requirement for ventilation and also contribute to respiratory failure.

We have recently shown that diaphragm muscle from preterm lambs is more susceptible to stretch-induced muscle damage than diaphragm muscle from lambs born after the normal gestation period. Skeletal muscle fibres contain specialised stretch-activated Ca^{2+} channels, which are thought to play a role in muscle development and growth. However when they are inappropriately or over activated, muscle damage can result through intracellular Ca^{2+} overload and activation of Ca^{2+}-activated proteases and the release of reactive oxygen species.

Stretch-activated Ca^{2+} channels can be blocked by the antibiotic streptomycin, and this drug has been used to prevent stretch-induced muscle damage in animal models of Duchenne muscular dystrophy (Zhang *et al.*, 2012). We hypothesise that stretch of the diaphragm during artificial ventilation activates stretch-activated Ca^{2+} channels leading to muscle damage and dysfunction.

Aims of the study:

Aim 1. To compare the effects of passive stretch and lengthening (eccentric) contractions on force output in diaphragm preparations from young (3 weeks old) and mature mice (8 weeks) using a muscle test system. These experiments will determine whether young mice are more susceptible to stretch induced diaphragm damage.

Aim 2. To investigate the ability of streptomycin to prevent stretch-induced muscle damage in diaphragm preparations from young and mature mice.

Aim 3. To determine whether mechanical ventilation results in diaphragm muscle damage using a mouse artificial ventilation model.

Aim 4. To examine whether any ventilation-induced diaphragm damage can be prevented in mice by pre-exposure to streptomycin.

The results of this study could provide new strategies to prevent ventilator-induced diaphragm dysfunction in premature babies.

References: Zhang BT, Whitehead NP, Gervasio OL, Reardon TF, Vale M, Fatkin D, Dietrich A, Yeung EW & Allen DG. (2012). Pathways of Ca(2)(+) entry and cytoskeletal damage following eccentric contractions in mouse skeletal muscle. *J Appl Physiol (1985)* **112,** 2077-2086.

Supervisor: A/Prof Tony Bakker

Skeletal Muscle Physiology

Dr Tom Lea

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I am a skeletal muscle physiologist with an interest in the interplay between skeletal muscle disease and skeletal muscle function. My research largely focuses on understanding the mechanisms of muscle damage and dysfunction in Duchenne muscular dystrophy to identify novel drug targets. I employ several physiological techniques in my research including *ex vivo* muscle testing, fluorescent Ca^{2+} imaging and isolated single muscle cell experimentation to elucidate the mechanisms of muscle dysfunction in disease states.

Some sample projects are listed here which are available in 2024. I also have other projects potentially available if you are interested to discuss further. Please feel free to email me if you are interested in a potential honours project!

The Effects of Hypochlorous Acid on Ca^{2+} Signalling in Slow-Twitch Soleus Muscle: Implications for the pathophysiology of Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a fatal X-linked disease characterised by severe muscle wasting. The mechanisms of DMD remain complex and not well understood but seem to involve the complex interaction between chronic inflammation, oxidative stress and impaired Ca^{2+} signalling. Our research has found that the potent endogenous oxidant, hypochlorous acid (HOCl) may form a link between these factors [1].

The pathophysiology of DMD is further complicated by the fact that fast-twitch muscles are preferentially affected compared to slow-twitch muscles [2]. We already have some preliminary results indicating that HOCl has a comparatively greater effect on fast-twitch muscles compared to slow-twitch muscles further implicating HOCl in the pathophysiology of Duchenne muscular dystrophy. The mechanistic reasons for these differential effects are largely unknown. This project will build onto these preliminary results by investigating the effects of HOCl on Ca^{2+} signalling proteins in slow-twitch soleus muscle isolated from mice using *ex vivo* whole muscle testing.

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1. Lea TA. (2023). The Effects of Hypochlorous Acid on Skeletal Muscle Function: Implications for the Pathophysiology of Duchenne Muscular Dystrophy. [Doctoral Thesis, The University of Western Australia].
2. Webster C, Silberstein L, Hays AP & Blau HM. (1988). Fast muscle fibers are preferentially affected in Duchenne muscular dystrophy. Cell 52, 503-513.

Supervisor: Dr Tom Lea **Co-supervisors:** A/Prof Tony Bakker, Ms Irene Tsioutsias

Impacts of hypochlorous acid on slow-twitch and fast-twitch muscles of dysferlin-deficient BLAJ mice

Dysferlinopathy is a form of muscular dystrophy caused by a gene mutation that results in lack of the membrane-associated protein dysferlin. Symptoms typically manifest in young adults and are characterised by progressive wasting of skeletal muscles in the limbs and limb-girdle (e.g., quadriceps and psoas), inflammation, accumulation of lipid droplets in slow-twitch myofibres, and later replacement of myofibres by adipocytes (fat) [1]; however, the exact mechanistic link between these features remains unknown. Protein thiol oxidation is also elevated with increased lipofuscin in some muscles from young dysferlin-deficient mice [2]) suggesting an early involvement of reactive oxygen species such as the thiol oxidant hypochlorous acid. In addition, we have previously shown subtle but different effects of dysferlin deficiency on the function of slow- and fast-twitch muscles [3, 4].
This exciting project will investigate these findings further by studying the effects of hypochlorous acid on the function of slow-twitch (soleus) and fast-twitch (extensor digitorum longus) muscles isolated from dysferlin-deficient mice.
These techniques are well established in the Skeletal Muscle Lab [5] and are being used by several students. This project is part of a team doing intensive research into dysferlinopathy [1, 3, 4] and other muscular dystrophies.

References

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2. Terrill JR, Radley-Crabb HG, Iwasaki T, Lemckert FA, Arthur PG & Grounds MD. (2013). Oxidative stress and pathology in muscular dystrophies: focus on protein thiol oxidation and dysferlinopathies. *The FEBS Journal* 280, 4149-4164.
3. Lloyd EM, Xu HY, Murphy RM, Grounds MD & Pinniger GJ. (2019). Dysferlin-deficiency has greater impact on function of slow muscles, compared with fast, in aged BLAJ mice. *PLoS One* 14, e0214908.
4. Lloyd EM, Pinniger GJ, Grounds MD & Murphy RM. (2023). Dysferlin deficiency results in myofiber-type specific differences in abundances of calcium-handling and glycogen metabolism proteins. *Int J Mol Sci* 24, 76.
5. Lea TA. (2023). The Effects of Hypochlorous Acid on Skeletal Muscle Function: Implications for the Pathophysiology of Duchenne Muscular Dystrophy. [Doctoral Thesis, The University of Western Australia].

Supervisors: Dr Tom Lea, Dr Erin M Lloyd, Emeritus Professor Miranda D Grounds.

Investigating the Effects of Endogenous Oxidants on Skeletal Muscle Contractile Filaments in Different Activation States

The contractile filaments of skeletal muscles are a complex network of proteins including myosin, actin, troponin C, tropomyosin, titin and nebulin among others. These proteins are dynamic and exist in different conformational states depending on the degree of activation of the contractile apparatus. Importantly, if a protein is in a different conformational state, different amino acid residues may be exposed. This is important when considering the effects of oxidants on the contractile filaments as the effects of oxidants may be different at different degrees of activation of the contractile filaments. Much previous research has focused on the effects of oxidants specifically on the contractile filaments at rest, but little is understood of the differential effects of endogenously relevant oxidants such as HOCl on the contractile filaments at different levels of activation [1, 2, 3, 4].

This exciting project will investigate the effects of hypochlorous acid and other oxidants on isolated single muscle cells at different activation states. These results will be important for understanding the effects of oxidants on the contractile filaments in disease states such as Duchenne muscular dystrophy.

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2. Lafoux, A., A. Divet, P. Gervier and C. Huchet-Cadiou (2010). "Diaphragm tension reduced in dystrophic mice by oxidant, hypochlorous acid." Can J Physiol Pharmacol 88(2): 130 - 40.
3. Lamb, G., Posterino, G. (2003). Effects of oxidation and reduction on contractile function in skeletal muscle fibres of the rat. Physiol J, 546, 149 - 63.
4. Plant, D., Lynch,G. & Williams, D. (2000). Hydrogen peroxide Modulates Ca^{2}+-Activation of Single permeabilized Fibres from Fast- and Slow-twitch Skeletal Muscles of Rats. J Muscle Res Cell Motil, 21, 747 - 52.

Supervisor: Dr Tom Lea **Co-supervisors:** A/Prof Tony Bakker, Ms Irene Tsioutsias

Investigating the Effectiveness of Antioxidant Treatments for Hydrogen Peroxide-Induced Muscle Dysfunction

Increased endogenous emission of hydrogen peroxide has been associated with muscle disease pathologies including hypoxia-reperfusion injury, muscular dystrophies, and other inflammatory disorders. We have some preliminary data indicating that hydrogen peroxide adversely affects skeletal muscle function in isolated extensor digitorum longus muscles. It is currently unknown if these effects of hydrogen peroxide on isolated muscle function are reversible with an antioxidant such as dithiothreitol or N-acetyl cysteine [1, 2, 3]. This project will hence involve dosing isolated whole muscles exposed to hydrogen peroxide with antioxidant compounds to see if the effects of hydrogen peroxide on whole muscle function can be ameliorated.

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2. Eley D, Korecky B & Fliss H. (1989). Dithiothreitol restores contractile function to oxidant-injured cardiac muscle. Am J Physiol 4, H1321 - 1325.
3. Whitehead, N., Pham, C., Gervasio, O. & Allen, D. (2008). N-acetylcysteine ameliorates skeletal muscle pathophysiology in mdx mice. J Physiol, 586, 2003 - 14.

Supervisor: Dr Tom Lea **Co-supervisors:** A/Prof Tony Bakker, Ms Irene Tsioutsias

The Effects of Glucocorticoid Treatment on Ca^{2+} signalling in Dystrophic Mice

The current gold-standard treatment for Duchenne muscular dystrophy is glucocorticoid treatment [1]. Treatment of DMD patients with glucocorticoids can improve muscle function and delay the progression of DMD. The exact mechanisms behind this are proposed to be due to the anti-inflammatory properties of glucocorticoids but some parts of this mechanism remain unclear. Some of the beneficial effects of glucocorticoid treatment in DMD may be due to direct acute effects on Ca^{2+} signalling in skeletal muscle rather than just solely anti-inflammatory effects. Glucocorticoids have been found to directly influence Ca^{2+} signalling in neurons but it is unclear if glucocorticoids can also exert similar effects in skeletal muscle [2]. In this project, you will fluorescently measure intracellular Ca^{2+} levels in isolated skeletal muscle cells from dystrophic mice treated with glucocorticoids.

1. Manzur, A., Kuntzer, T, Pike, M. & Swan, A. (2008). Glucocorticoid corticosteroids for Duchenne muscular dystrophy. Cochrane Database Syst Rev, 1, CD003725.
2. Suwanjang, W., Holmstrom, K., Chetsawang, B. & Abramov, A. (2013). Glucocorticoids reduce intracellular calcium concentration and protects neurons against glutamate toxicity. Cell Calcium, 53 (4) 256 – 63.

Supervisor: Dr Tom Lea **Co-supervisors:** A/Prof Tony Bakker, Ms Irene Tsioutsias

Skeletal Muscles: normal, ageing and diseased

Emeritus Professor Miranda Grounds

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The research of the Grounds laboratory is dedicated to all aspect of skeletal muscle biology, mainly using *in vivo* pre-clinical animal studies, with a recent focus on loss of muscle mass during normal ageing, and on basic research and development of therapies for muscular dystrophies: specifically, the severe childhood disease Duchenne Muscular Dystrophy (current collaboration with Peter Arthur at UWA) and the adult onset Limb Girdle Muscular Dystrophy type 2B (due to dysferlin-deficiency). One defined Honours project for 2023 is indicated below, but several others will emerge later in 2022 (depending on new data and potential funding). We are happy to discuss projects with students related to their specific interests**.**

Project: Adverse effects of glucocorticoids in dysferlin deficient mice: focus on immune cells.

This research builds upon our investigations into the molecular basis for the dystropathology in dysferlinopathies (Grounds et al, 2014. PMID: 24685690) and relates to our recent papers using dysferlin-deficient BLAJ mice describing novel alteration in muscle lipid metabolism and lipidomics (Haynes et al, 2019. PMID: 31203232) and different effects on function of slow and fast myofibres (Lloyd et al, 2019. PMID: 30970035). There is a strong inflammatory response associated with dysferlinopathies and for the last few years we have been conducting intensive studies into altered immune response in these BLAJ mice, with much new data generated (Jackaman et al, unpublished data). This research involves many collaborators.

One interesting feature of this disease is that the use of gluccorticoids (GCs - very widely used anti-inflammatory drugs) has unexpected adverse effects in patients with dysferlinopathy with loss of muscle function. This contrasts with benefits of GCs in many other muscle disorders including Duchenne muscular dystrophy. We have already conducted 2 studies in BLAJ mice (young and old), using the GC Dexamethasone. This project builds upon our unpublished data, with a new focus on monitoring the impact of GCs on the immune response in BLAJ mice.

Project is suitable for: Honours, PhD

Supervisors: Prof Miranda D Grounds and Dr Erin Lloyd (UWA), with Dr Connie Jackaman (Curtin University)

Stem Cell Mechanobiology

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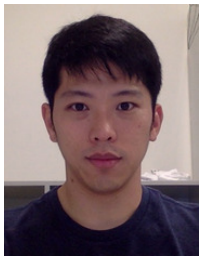

Choi lab's focus is on controlling cell behaviour by providing various microenvironments. The fate of cells was thought to be primarily dictated by biochemical signals including cytokines and growth factors for decades, however, more recent data suggested cells also responded to their microenvironments including neighbouring cells and extracellular matrices (ECMs). Previously, we showed that stem cells from fat (adipose-derived stem cells – ASCs) were able to feel/sense and respond (mechanosense) to matrices mimicked stiffness of brain, skeletal muscle, and bone and committed to those tissue lineages, respectively. Intracellularly, stem cells transduce these biophysical/mechanical signals into biochemical signals from cell membrane to nucleus and this process is called mechanotransduction. Our group aims to study how mechanical cues (especially stiffness) control stem cells (and other cells e.g. cancer cells) by focusing on 3 areas: 1) investigating intracellular mechanisms how (stem) cells respond to ECM mechanical cues, 2) developing bio-inspired ECM (2D and 3D biomaterials) as platforms to control (stem) cell fate, 3) programming (stem) cells to be used in (stem) cell therapy, tissue engineering and regenerative medicine.

Project 1. Mechanosensing-driven cancer cell screening on high-throughput stiffness gradient hydrogel.

With Drs. Andrew Holle and Jennifer Young at National University of Singapore / Mechanobiology Institute

The stiffness (one of the mechanical properties of tissue) is known to be involved with epithelial to mesenchymal transition (EMT) which is the initial step for metastasis responsible for most of the deaths related to breast cancer in Australia and worldwide. However, our understandings of how cells in breast tissue interact with their healthy vs. cancerous microenvironment are very limited. In this project, MCF10A (healthy epithelial cells) will be tested on stiffness linear gradient hydrogel ranging from 1 to 10kPa (covering healthy and cancerous stiffness) to screen the interaction between cells and their mechanical environment at a single cell level. MCF7 (cancerous but not metastatic) and MDA231 (metastatic cancer) cells will also be studied on gradient platforms to study the effect of environmental stiffness on cancer migration/invasion. Findings from this project may open new opportunities to treat cancer patients as 'mechanotherapy' in near future.

Project 2. Role of YAP/TAZ in stem cell mechanotransduction, differentiation, and migration in 3D

With Dr. Henry Park at Yonsei University

There are several pathways and key signaling molecules suggested in mechanotransduction. Most of suggested pathways involve focal adhesion with extracellular binding of integrin to ECM protein as a starting point and intracellular interaction of beta unit of integrin to actin-myosin through focal adhesion kinase (FAK), talin, and vinculin binding. Intracellular forces generated by different matrix stiffness will decide localization (cytoplasmic vs. nucleic) of YAP/TAZ (transcriptional coactivator in Hippo pathway), which will control transcriptional level as a final step. Bone marrow-derived stem cells exhibited cytoplasmic localization of YAP/TAZ on soft hydrogel (fat-like stiffness) but YAP/TAZ was localized in nuclei on stiffer hydrogel (bone-like stiffness). Differentiations into fat and bone lineages were also observed and YAP/TAZ overexpression or knockdown cells altered mechanical induction (no bone differentiation on bone-like stiffness when YAP/TAZ knock-downed).

Most studies with YAP/TAZ assumed it as a downstream of mechanosensing but more recent results (YAP/TAZ changes integrin expression profile in cancer research) suggest that YAP/TAZ may have a feedback effect on 'feeling' or YAP/TAZ act as upstream of 'feeling' as well.

In this project, we aim to investigate the effect of YAP/TAZ on mechanosensing (once considered as upstream of YAP/TAZ) in the context of intracellular force generation (direct response from extracellular stiffness), migration, and differentiation.

Project 3. Mechanotransduction driven cardiac differentiation of stem cells in 3D

With Professor Adam Engler at the University of California, San Diego (UCSD)

The human heart, a mechanically dynamic tissue, pumps out ~5L of blood/ minute. At the tissue level, its mechanical function has been widely studied, but little is known at the cellular level about how cardiac muscle cells mechanically coordinate their beating with neighboring cells or how mechanical extracellular stimuli dictate cardiac muscle cell behavior. One cardiac muscle cell *in vivo* may make three principal connections with its surroundings (i) cell-ECM adhesion via integrin-mediated focal adhesion, (ii) cell-cell adhesion via N-cadherin, and (iii) cell-cell gap junction with ion channels including the calcium channel. In disease models, in particular, not only biochemical signaling changes but also the mechanical environment alters the cell's behavior via these 3 main connections. For example after myocardial infarction (MI), excessive deposition of collagen causes greater ECM stiffness, which may alter focal adhesion complex / actinin (i.e. the Z-band – an important structure bearing contractile forces) and disrupt cytoskeletal structure resulting in loss of contraction and alteration of cell-cell interaction via N-cadherin. This project aims to address how these 3 main connections (N-cadherin, focal adhesion, and gap junction) control the cardiomyocyte's function in disease. Three specific aims address 1) the effects of ECM stiffness on cardiomyocyte function; cell-ECM mechanotransduction, 2) mechanosensitivity of cardiomyocyte via N-cadherin; cell-cell mechanotransduction, and 3) ion handling capacity, especially calcium which is the main driving force for cardiomyocyte contraction, examining different cell-cell / cell-ECM situations.

Supervisor: A/Prof Yu Suk Choi

Exercise Physiology and Biochemistry

Professor Peter Peeling

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T: +61 8 6488 2363

Peter's research program is centred around delivering evidence-based, innovative solutions to performance-driven questions generated in conjunction with the service provision team at the WA Institute of Sport (WAIS). Research projects aligned with WAIS are developed in collaboration with the performance science staff at the institute. Successful students will be embedded within a WAIS sports program, providing research support to applied sports science projects.

Current areas of research priority include:

- Enhancing athlete performance in competition
- Enriching our understanding of athlete development and adaptation
- Augmenting the daily training environment
- Generating new knowledge in performance health
- Leveraging sports data, technology and engineering

If you are interested in an honours project embedded at the WA Institute of Sport, please reach out to Peter on the above contact details for more information.

Associate Professor Olivier Girard

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https://www.oliviergirard.com/training-under-environmental-stress

If you have a passion for exploring the limits of human performance and implementing innovative interventions, come and have a chat!

My research identifies, quantifies and explains mechanisms responsible for fatigue during high-intensity intermittent exercises performed by team- or racket-sport athletes under challenging environmental conditions (i.e. heat stress or hypoxia).
Several projects also shed light on the neuro-mechanical determinants of team-sport performance, with a special focus on (repeated) sprinting mechanics and underpinning neuromuscular factors.
Current research is focussed on therapeutic use of hypoxia to improve cardio-metabolic health of 'at risk' patients and improve exercise tolerance in load-compromised individuals (injured athletes).

Four main research areas:

1. Training under environmental stress (altitude, heat)
2. Exercising in hypoxic and/or hot conditions
3. Neuro-mechanical adjustments to exhaustive running
4. Racket sports

Key words: Neuromuscular fatigue, repeated-sprint ability, hypoxia, altitude training, heat stress, sprinting mechanics, cardio-metabolic health, team and racket sports.

This year, several applied projects (working directly with athletes) are proposed and include:

- **Energy requirements and physical demands (lower limb activity) in racket sports (tennis and new formats such as padel etc)**
- **Training load monitoring, fatigue and recovery practices in team and racket sports**
- **Repeated sprint training in hypoxia and altitude training**
- **Heat acclimation (high performance sport) and heat tolerance (occupational settings such as mining industry)**
- **Exercise with blood flow restriction**

This list is certainly not exhaustive and if you have some burning real world (practical) questions that need to be answered working with your athletes or patients, please reach out!

Associate Professor Karen Wallman

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We have a proposed honours project working with the WA police in order to determine physical attributes required by police who work with the canine squad, and for police who work in the mounted section (riding horses).

Officers who work in the canine squad need to be able to lift their dog over fences, carry their dog if need be, and have good physical fitness to keep up with their dog.

Police in the mounted section need to be able to sit comfortably for many hours in the saddle, often wearing heavy uniform.

These projects will be about determining the physical attributes that officers in each squad need to be able to successfully perform their duties.

You would be working with myself, Dr Grant Landers and Prof Tim Ackland.

Email Karen if interested: karen.wallman@uwa.edu.au

Professor Paul Fournier

E: paul.fournier@uwa.edu.au
T: +61 8 6488 1356

Sport performance research

- Effect of breakfast skipping on exercise and cognitive performance. *Co-supervisor: Troy Visser*
- Effect of breakfast skipping combined with exercise on cognitive function and driving performance on a driving simulator. *Co-supervisor: Troy Visser, Brendan Lay*
- Effect of bicarbonate loading as a means to oppose the appetite suppression and nausea that occur after sprinting
- Effect of carbohydrate intake as a means to oppose the appetite suppression and nausea that occur after sprinting
- Effect of carbohydrate intake post-sprinting as a means to speed up recovery of sprint performance capacity

Nutrition Science

- Effect of ingesting protein to oppose the oxidative stress and other ill effects that are associated with breakfast skipping. *Co-supervisors: Prof Peter Arthur*
- Effect of dietary state and time of day on the oxidative stress that is caused by carbohydrate ingestion. *Co-supervisor: Prof Peter Arthur*

Exercise and type 1 diabetes

- Effect of under-water cycling in cold water on blood glucose in people with type 1 diabetes. *Co-supervisor: Prof Shane Maloney*
- Effect of high temperature and body hydration level on blood glucose response to exercise in people with type 1 diabetes. *Co-supervisor: Prof Shane Maloney*
- Localised skin cooling as a means to prevent exercise-mediated hypoglycaemia in type 1 diabetes. *Co-supervisor*: *Prof Shane Maloney*
- Effect of high blood glucose level on cognitive function and driving performance in type 1 diabetes. *Co-supervisor: Prof Brendan Lay*
- Effect of simulated high altitude on the hyperglycaemia associated with high intensity exercise in type 1 diabetes. *Co-supervisor: Prof Shane Maloney*

Senior Lecturer Grant Landers

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Projects for 2024 **assess the demands of human performance** to improve our understanding and allow suitable modifications be recommended to enhance performance in a variety of sport and exercise settings.

Open water swimming

- Determining the energy cost of swimming in waves (using the uwa wave flume).
- Determining the optimal feeding strategy during the Rotto Channel Swim.

Triathlon

- Should barefoot running be an important part of a triathletes training program?
- Do brick sessions improve the transitions from one discipline to the next in triathlon?

WA Police

- Exploring the physical demands of police officers working in the canine or mounted sections and determine appropriate minimum standards for inclusion.

Athlete Monitoring

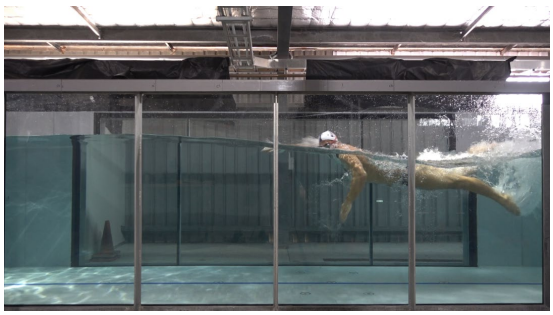
- Changes in perceived training distress before and after physical activity.

Body composition

- Does aquatic exercise affect the subsequent measurement of adipose tissue via ultrasound?
- The Bone, Muscle, and Balance (BOMB) study: Feasibility of a Community-based High Intensity Resistance and Impact Training Program for Older Adults.

Physical Activity & Inclusion

- Does wearing a chest binder affect physical function during exercise?



Cardiovascular Exercise Science Group

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Jaye Lewis
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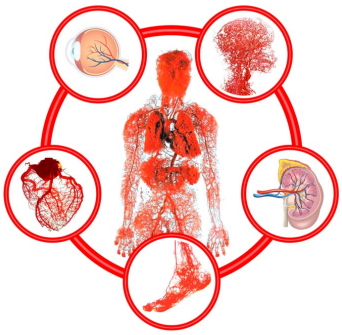
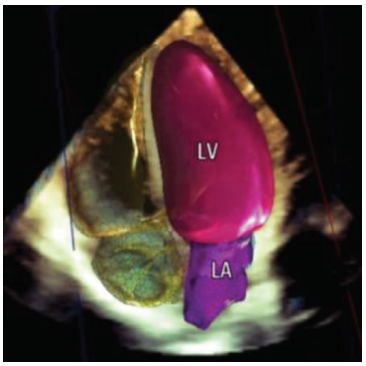
WHO WE ARE We are a dedicated team of researchers and clinicians working at the forefront of cardiovascular disease prevention and management to optimise human health and wellbeing.

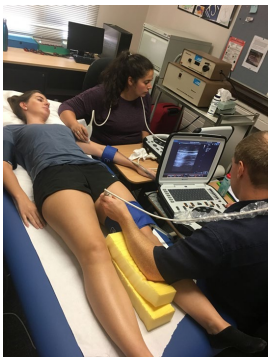
OUR VISION is to keep people healthier for longer by decreasing the progression and impact of cardiovascular diseases.

Come and have a chat to us if you are considering doing Honours – no strings attached, and we even make great coffee… You may not have seen us much in your journey through Sport Science to date, because we live more in our (purpose built) lab than the lecture theatres, but our Cardiovascular Exercise Science group is a friendly and supportive research team, led by Danny Green and Louise Naylor. Our team produces world-leading research that aims to make a difference to the health of all people, whether they are healthy or have a cardiovascular disease. We have plenty of openings for new students and would love to have you join our team.

We have excellent links with all of the major Perth hospitals, and close ties with universities and other research groups in the UK, USA, Canada, the Netherlands and interstate, so you can make some great contacts. You will get experience with some great new technologies, including echocardiography, OCT and ultrasound. We will teach you to look inside arteries in the brain and limbs, and see what happens when people exercise (or don't). You will be supported every step of the way, from your research proposal, through developing your technical skills, to writing your thesis and presenting at conferences – maybe even publishing a paper or two.







Some links to our research projects and talks:

Heart Failure Study

Preventia (exercise for dementia prevention)

Cardiovascular risk factor gap

Testosterone and exercise

Tailoring Exercise Prescription

Professor Green's profile

The Biozone team

We work across a lot of areas, with athletes and 'couch potatoes'; kids and adults; sick people and well people, so there will be a lot of options open to you. However, we generally like to explore these broad questions:

- **How does exercise work?**
- **How can we use exercise to prevent disease and improve people's quality of life?**

Here are some of our latest research questions:

- Defence Force research - what does exercising in the heat do to your blood vessels?
- Responder or non-responder to exercise: nature or nurture. Why do some people have a great response to exercise while others don't?
- Testosterone, exercise or both? A new direction for ageing men.
- The cost of being sedentary – what does prolonged sitting do to your brain?
- What can twins teach us about exercise?
- Childhood origins of adult disease – what's the impact of exercise?
- How does exercise stack up for improving obesity, diabetes, Metabolic Syndrome, and heart disease, and what difference can it make to outcomes for heart failure patients or survivors of childhood cancer?
- Use it or lose it – what's the effect of inactivity on small or large arteries? (Hint: it's not good.)
- Cardiac response to exercise – what is 'Athlete's heart' and is it good or bad?
- The exercise paradox – why does exercise *acutely* increase cardiovascular risk but reduce it in the longer term?

Motor Control & Exercise Rehabilitation

Dr Siobhan Reid

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T: +61 8 6488 8781

Our research broadly seeks to understand neurodevelopmental disability and motor impairment particularly in paediatrics, with the aim of developing targeted interventions to improve functional outcomes for children and their families. We have many collaborative opportunities to work with clinical teams at **Perth Children's Hospital** and **Telethon Kids Institute** as well as community research partnerships with **Special Olympics Australia**.

Some of the projects we have on offer in 2024 include:

Special Olympic Athletes: Health & Wellbeing

Working in partnership with Special Olympics Australia, TKI and UWA, this project aims to understand the impact of being involved with Sport on the health and wellbeing of Athletes with Intellectual Disabilities.

Understanding Physical activity engagement in children with Disabilities

The benefits of physical activity are very well established, however children and families impacted by disability experience many barriers to participation in exercise. This project involves collaboration with the Disability Research team at Telethon Kids Institute to develop a tool to assess children's participation and engagement in physical activity.

Paediatric Exercise Programs

There are many opportunities to investigate the outcomes of children and their family's following participation in our paediatric exercise programs, Minigym, Unigym and *iFit.* If you want your research to have real impact for children and families – come and chat…

Dr Brendan Lay

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Project: Visual Perceptual Skill and Anterior Cruciate Ligament (ACL) Injury Risk

At UWA, we have a long history of investigating the Biomechanics of ACL injury risk when performing sidestepping manoeuvres. We know that the injurious loads carried by the ACL increase greatly when an individual has little time to organise a sidestep, therefore, more recently we have been investigating the visual perceptual skill and its role in giving an individual more time to plan a safe sidestep. We have also been investigating whether perceptual training (such as Above-Real-Time training) can improve an individual's capability to sidestep safely.

***Collaborator(s)**: Prof Jacqueline Alderson*

Project: Effect of diabetes on eye tracking and reaction time.

It is well established that diabetic individuals have a higher incidence of fall and are more prone to car accidents. Our goal is to elucidate some of the mechanisms involved.

***Collaborator(s):** Prof. Paul Fournier*

Project: Visual perceptual expertise and movement assessment.

We are currently undertaking a series of experiments assessing the capability of parents, teachers, coaches and other movement experts to assess various motor skills including Fundamental Movement Skills (FMS) and swimming technique. A key question we are asking is what do expert see (perceive) that novices don't? For these experiments, we utilise the eye-tracker and a verbal report protocol.

Collaborator(s): A*/Prof Rebecca Braham, Prof Michael Rosenberg (FMS) & Dr Nat Benjanuvatra (swimming)*

Project: Equipment scaling in a range of Children's Sport.

Up until very recently there has been no scientific rationale for the different sized (smaller. shorter, lighter) equipment that is used in junior sports. Tennis Australia has recently led the world into the effects of equipment scaling on motor skill acquisition and performance and we are extending this research to other sports. A key question here is what are the effects of systematically manipulating equipment and playing area on the acquisition of sport specific motor skills in children?

***Collaborator(s):** Dr Machar Reid (Tennis Australia)*

Dr Nat Benjanuvatra

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T: +61 8 6488 2437

Understanding asymmetry and its impact on function and performance

Asymmetry refers to the inherent and often subtle differences in motor control and movement patterns between the left and right sides of the body. Understanding the influence of asymmetry can have direct implication on performance and musculoskeletal health of the individual. This research theme is about trying to understand asymmetry and seeks to explore questions such as: How do asymmetries develop, and to what extent are they modifiable through training and interventions? What are the potential benefits and detriments of asymmetry in specific sports and activities? How can we leverage our understanding of asymmetry to design individualised training and rehabilitation programs?

Post-Activation Performance Enhancement

Post-Activation Performance Enhancement (PAPE) is a phenomenon where a short bout of high-intensity exercise can temporarily boost a subsequent athletic performance. While this phenomenon is generally accepted, the mechanisms behind PAPE is not well understood. It is also unclear what activity types (i.e. (absolute strength, power and speed, endurance) benefit most from PAPE and what is the optimal PAPE protocols for different sports.

Aquatic Sport/Exercise & Strength Training Research

If you have a keen interest in understanding the science behind strength training or aquatic sports like swimming, surfing, or surf lifesaving, let's discuss potential research projects.

Health Behaviour and Performance Psychology

Professor Ben Jackson

E: ben.jackson@uwa.edu.au
T: +61 8 6488 4625

Any students with an interest in the psychology behind sport, exercise, physical activity, or other health issues (e.g., diet), please contact Ben for a chat. Similarly, Ben is also involved in the coordination and evaluation of several exercise, weight loss, and physical/mental health promotion programs – with a range of supportive community partners and agencies. If you are interested in learning more about any of these opportunities, and discussing projects that suit your particular interests, you are encouraged to speak with Ben

Dr Timothy Budden & Professor Ben Jackson

E: timothy.budden@uwa.edu.au

E: ben.jackson@uwa.edu.au

Dr Timothy Budden

Prof Ben Jackson

PSYCHOLOGY OF ACTIVE, HEALTHY LIVING GROUP (PAHL)

"Our group focuses on applying psychological research to solve health problems. We work with a variety of populations and contexts. If students are interested in working on a specific health problem, we are happy to explore Honours project options. Otherwise, current projects we would like to work on include:

1. What role does competition play in men's weight loss?

This project would offer opportunities to conduct qualitative and / or quantitative research.

2. How do we promote creative movement and wellbeing?

This project would be exploratory in nature. We would like to investigate the perspectives and experiences of a range of movement practitioners who support creativity in movement (and, often, with the explicit objective of promoting well-being). This project would offer opportunities to conduct qualitative research and inform intervention development.

3. How do habitual exercisers describe their relationship with exercise?

We would like to explore how people use language to describe activities like exercise. This project would involve using LIWC-22, a software designed to analyse language. This project would be quantitative in nature.

Importantly, we would encourage students to contribute to and refine any of the projects outlined above. Alternatively, we also encourage students to bring their own ideas, and we can help identify a feasible and engaging project topic."

Professor Michael Rosenberg

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TECHNOLOGY BASED SPORT SCIENCE AND HEALTH

Technological advances in the measurement of physical activity have created new opportunities to understand and influence how people engage in regular physical activity. Our research group has been involved in the development of several innovative technologies that have the potential to significantly improve the health of the population. If you have an interest in technology and its use in novel ways the following research opportunities might be of interest to you. We are always happy to discuss these and other research opportunities.

Study 1: The use of RFID technology to determine the effect of a simple experiment.

Remote Frequency Identification (RFID) technology provides accurate information on whether a person is inside or outside an established boundary (Such as their house). The RFID system can also tell the amount of time a person spends within the boundary in certain locations (lounge room). We have developed the first available ad-hoc RFID system to determine the length of time people spend in a boundary and the amount of energy expended.

For an honours project we are interested in understanding the impact of simple household modifications to the way screen based activities, such as Fixed and portable screen use influences family sedentary behaviours. For example, does removing screen use before sunset influence activity levels and where people locate within their house, or outside? There is surprisingly little objective evidence to help answer these questions, as until now the technology has been unavailable.

Study 2: FITBIT (tracking of children's physical activity)

Advances in relatively inexpensive user-friendly wearable activity trackers like the Fitbit® mean it is now realistic to continuously measure movement patterns of children over several months, without considerable participant burden. This level of data offers previously unavailable insights into daily, weekly, monthly and seasonal variations in physical activity (PA). Children's PA and sedentary behaviours influence a range of health, social and academic outcomes and children's development in the early years may influence the development of disease in later life. To date, patterns of PA have either relied on self-report surveys, or objective monitoring over at most two-weeks at any one time. *Therefore, we propose to measure PA continuously over a six month period to develop the most comprehensive description of children's PA to date. If you want to be involved in internationally leading research around children's physical activity, please come and discuss this topic with us.*

Study 3: Music based motor control development.

The link between music and physical movement is both entrained and observable in neurological development. There is perhaps no stronger behaviour to unite humans than coordinated rhythmic movement. This is because humans have the capacity to become entrained with one another or an external stimulus. Entrainment is a powerful adaptive process that indicates a mutual perceptual and social experience from the sharing in time and space of music and rhythm. Evidence of the benefits of music entrainment in the development of motor control in children and in rehabilitation is plentiful. Recent advances in wearable sensor technology have transformed rhythmic entrainment into a self-sustaining biofeedback mechanism.

We have developed the first music based rhythmic entrainment mobile phone app that incorporates Bluetooth enabled wearable sensors to provide real time feedback. This breakthrough technology uses a range of Bluetooth enabled accelerometers, Stretch Sense material and force place sensors in socks to entrain the user to move rhythmically. It is like learning to dance or run with wearable sensors that give you feedback on how to achieve this goal.

We are looking for interested students to conduct a range of experience with this new technology on typically developing children, children with delayed coordination, and children undergoing rehabilitation.

Study 4: Classification of movement during active video gaming

For several years we have been capturing children's movement during active video game play. Our research team has developed software to classify fundamental movement skills of children to parse game play data and count the number of movements children perform within a 15 minute game play situation. The advancement of this system requires several experiments using the Vicon System to match movements captured by our system and the gold-standard Vicon System. If you are interested in this study, or any research related to the health impact of active video gaming please speak with us.

KIDDO – Improve your Move (www.kiddo.edu.au)

Potential supervisors:

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T: +61 8 6488 5609

Dr Ashleigh Thornton
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Prof Ben Jackson
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A/Prof Hayley Christian
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Dr Brodie Ward
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Amanda Derbyshire
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KIDDO is offering a **$5000 Honours scholarship** to encourage and assist a student to undertake an Honours course with a thesis related to the KIDDO program.

KIDDO is predominantly an online physical literacy program run in Primary Schools and Early Childhood Education and Care Centres in Western Australia that has been developed and implemented since 2014 by the UWA School of Human Sciences.

KIDDO received Healthway and Lotterywest funding (2021-2023) to expand the program and embed it within all Early Childhood Education and Care services in Western Australia in collaboration with the Department of Education and the Department of Sport and Recreation. With 70% of WA Primary Schools using KIDDO and over 10,000 members from Australia and internationally KIDDO can provide extensive research opportunities across many different areas of interest. KIDDO is working towards equipping all children with the skills and confidence to be active for life. To find out more see our website: www.kiddo.edu.au

KIDDO has opportunities for students to work with existing data or collect new data and undertake projects across the following research topics:

1. Are children ready to move when they start school? Describe the current prevalence of children's FMS before they start Year 1
2. Does participating in KIDDO lead to increased overall physical activity levels?
3. Gender differences in skill acquisition and development
4. Feasibility of the KIDDO assessment in schools
5. Developing culturally appropriate resources and training for physical literacy
6. Effect of a weekly tailored email on educators provision of physical activity
7. Can children's mental health and wellbeing be improved as part of an 8 week physical activity program
8. Does a child's physical literacy differ by socioeconomic status?
9. Mapping movement skill proficiency across metropolitan and rural areas
10. Evaluating the implementation of KIDDO in an Early Childhood Care setting

Risk Perception in Children's Sport

We are partnering with Kidsafe to investigate the risk perception from a parental and coaches perspective of injury in sport. There is the potential to complete projects in a variety of areas around this core topic. If you are interested in injury surveillance, prevention and children in sport, then please come and speak to us.

Potential supervisors:

A/Prof Hayley Christian
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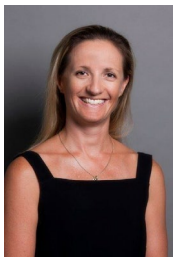

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Dr Ashleigh Thornton
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Ms Clover Maitland
WA Dept of Sport & Recreation

The PLAYCE Study: Play Spaces & Environments for Children's Physical Activity and Health

Background: There is growing interest in environmental interventions targeted at increasing children's physical activity because of their potential reach and impact on the health and well-being of future generations. In the last decade there has been a 20% increase in the number of 0-4 year olds in WA with 63% of WA's 2-3 year olds attending some type of child care. The childcare setting is where children spend a considerable portion of their time, thus it is an important setting in which children should have the opportunity to accumulate physical activity and other forms of unstructured physical play to facilitate their health and development.

Outline: The PLAYCE (Places Spaces & Environments for Children's Physical Activity) program of research investigates the influence of the physical, social and policy environment on young children's physical activity, sedentary behaviour, eating behaviour, weight status, sun exposure and development across different behaviour settings (childcare, home and the neighbourhood). PLAYCE aims to provide information on how best to create healthy environments for young children and families to enable them to lead healthy and fulfilling lives. A range of PLAYCE research projects are available.

Some of these include: 'Professional development programs to improve young children's fundamental movement skills'; Professional development programs to increase young children's time spent in outdoor-nature based play'; 'Evaluate the effect of childcare care centre outdoor space upgrades on children's and educators physical activity'; 'Using GPS to understand where and how young children move around their home and neighbourhood'; 'Qualitative research with children, parents, staff and key stake holders in the childcare setting'. Students are welcome to arrange a time to meet and discuss potential research topics.

Suitable for Honours/12 or 24 point Masters dissertation or project/Masters by Research thesis/PhD or able to be tailored to any of these.

How does contact with nature facilitate young children's health and development?

***Background**:* Contact with nature (plants and animals) is associated with children developing a sense of identity, autonomy, psychological resilience, self-regulation, gross motor skills and learning healthy behaviours. However, while the pathways through which contact with nature facilitates child health and development have been examined in older children, studies to date have not examined the effect of nature contact on young children's health and development.

Outline: This project will involve collaboration with industry partner Nature Play WA. The project will evaluate the impact of Nature Play WA's education program aimed at providing early childhood education and care staff with the knowledge and skills to create nature play spaces within the childcare setting. The student will conduct a literature review on the effects of nature contact on young children's health and development. The student will undertake a follow-up survey of early childhood education and care staff to ask them about changes to their childcare centre (e.g., changes to the outdoor physical environment, program content, care and teaching practices) post taking part in the Nature Play WA program. Visits to childcare centres to objectively assess changes to the childcare environment and its effect on young children's health and development can also be done.

Supervisors: Asst/Prof Hayley Christian, Prof Michael Rosenberg, A/Prof Leanne Lester

Benefits of Family Dog Ownership for Children's Physical Activity and Health

Background: Physical inactivity and rising levels of overweight and obesity are a public health concern. Dog ownership is associated with higher levels of physical activity in adults but few studies have examined the physical, social and emotional health benefits associated with dog ownership in children.
Outline: The aim of this study will be to examine the association between dog ownership and physical activity, sedentary behaviour and overweight/obesity in children. The relationship between family dog ownership and dog-facilitated physical activity from active play with a family dog or walking with a dog will be examined for different child age groups (e.g., early years, primary school and adolescents). The influence of socio-demographic, social and physical environment factors on these relationships will be considered. There is scope for qualitative research with parents and children on the motivators and barriers to dog walking and dog-centred play as well as intervention research to determine strategies for improving the child health benefits of family dog ownership.

Supervisors*:* Asst/Prof Hayley Christian, Prof Michael Rosenberg

Physical Activity Intervention Targeting Dog Owners

***Background**:* There is growing awareness about the importance of dog ownership to physical and emotional human health. Almost half of all Australian households own a dog. Dog owners do more walking and are more physically active compared with non-owners. Importantly, dog walking has been shown to be a potentially viable strategy for increasing the proportion of the community who are sufficiently active for health benefit.

***Outline**:* This project will involve intervention research to examine the potential of dog walking to contribute to owners' overall level of physical activity and increase the proportion of people who meet the recommended level of physical activity. There is scope for interventions targeting adults and or children. The project is likely to have significant implications for health promotion policy and practice and will involve working closely with industry partners.

Supervisors: Asst/Prof Hayley Christian, Prof Michael Rosenberg, Ms Clover Maitland

WA Department of Sport and Recreation Projects

Supervisors: Asst/Prof Hayley Christian, Dr Ashleigh Thornton, Prof Michael Rosenberg, Ms Clover Maitland, WA Department of Sport and Recreation

These projects are in collaboration with the WA Department of Sport and Recreation and align with the Department's Strategic Directions 6 (2016-2021).

Understanding the role of informal social networks in facilitating accessible low-cost physical activity options.

What role do informal social networks play as barriers and or motivators for physical activity behaviour? How do these informal social networks function across different life stages (e.g., new parent, retiree, married no children etc)?

What are the factors associated with participation in sport and recreation at various life stages?

Interests and motivations for participating in sport and recreation evolve and change, as do barriers to participation, and people are likely over the course of their lives, to be involved in a range of activities and challenges.

What intervention strategies would encourage children's participation in physical activity, with a focus on fundamental movement skills? In Australia, we face the most inactive generation of all time.

This project focuses on strategies for encouraging physical activity in children through targeting those not currently enrolled in sporting clubs but who would like to participate.

Clinical Exercise Physiology

Dr Jay Ebert

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Dr Ebert is currently involved in a range of research projects, largely focused in the fields of musculoskeletal and orthopaedic rehabilitation, and pertinent to the improvement of current clinical practice. These areas of research are varied and, while a number of smaller student research projects may be available, the primary areas of research include:

- Anterior cruciate ligament (ACL) and multi-ligament knee injury, surgical reconstruction methods, improving rehabilitation and return to activity/sport pathways.
- Lateral hip pain, including hip abductor pathology (tendinopathy and gluteal tendon tears), surgical intervention and rehabilitation.
- Hip pathology, including the investigation of conservative management, as well as improving outcomes after arthroscopic hip surgery.
- Proximal hamstring tendon injuries: improving surgical, rehabilitation and return to activity/sport pathways.
- Knee and hip osteoarthritis and joint replacement surgery.
- Shoulder injury, rehabilitation and return to sport.

UWA Mental Health & Exercise Research Group

E: mhex@uwa.edu.au

W: https://www.uwa.edu.au/Projects/Exercise-as-therapy-in-mental-health-disorders

Collaborators include Telethon Kids Institute; Perth Children's Hospital; Fremantle Hospital Mental Health Services; The Auditory Laboratory (UWA); Psychology of Healthy, Active Living Group; Thriving in Motion; and more!

Broadly, we explore the role of exercise in the management of physical and mental health outcomes for those living with, or at risk of, mental ill health. Whilst exercise is broadly acknowledged as beneficial for humans across multiple domains, an understanding of how best to facilitate positive outcomes, support individuals and embed exercise within care pathways is yet to be established.

Our research team including academic and clinical staff, along with current research students, and a whole stack of research and community collaborators depending on the project.

Here are some of our current research projects:

- Move your mind: exercise to support the physical and mental health outcomes of individuals living with severe mental illness (in partnership with Fremantle Hospital Mental Health Service); PhD Candidate – Caleb McMahen)
- Gender, Health, Eating + Exercise (GHEEX) (in partnership with Thriving in Motion; Research Officer – Kai Schweizer)
- "What if every day was game day?": Physical and psychological thriving in occupations with recurring trauma (PhD Candidate – Sally Edmondson)
- Physical Activity for Health in Trans + Non-Binary Young People (in partnership with Gender Diversity Service at Perth Children's Hospital; PhD Candidate – Felicity Austin)
- Sport for children in out-of-home care (in partnership with Telethon Kids Institute; PhD Candidate – Aaron Simpson)
- Functioning in Children and Adolescents with Chronic Pain (in partnership with Perth Children's Hospital)
- Auditory Cued Exercise Therapy for Children with Auditory Processing Disorder (in partnership with The Auditory Lab UWA)
- Physical activity to support youth transitioning through WA mental health services (PhD Candidate – Ben Kramer)

Honours/Masters projects available for 2024:

Physical activity for young people in alternate education pathways

Supervisors: Ben Jackson, Aaron Simpson, Felicity Austin + Bonnie Furzer

Collaborators: Thriving in Motion, community based alternate education facilities

Many young people experience adverse situations which may increase their likelihood of developing mental health concerns. One at-risk group is young people in alternate education pathways. These pathways allow young people with behavioural and emotional difficulties or mental health concerns to complete their secondary education with additional supports in place. Physical activity and exercise can be a useful preventative tool for at-risk young people, however they often engage differently with exercise programs compared to young people in mainstream schooling.

The aim of this study is to examine the barriers and challenges in engaging young people in alternate education pathways with physical activity, and to explore how we can provide a physical activity program tailored to their unique needs and experiences.

With the support of your supervisory team, you will consult with stakeholders who provide services or support within alternate education pathways, through a survey and qualitative interviews. Informed by stakeholder experiences, your research will inform the development and provision of future physical activity programmes within this population.

Does wearing a chest binder impact physical function during exercise? (GHEEX)

Supervisors + Team: Bonnie Furzer (she/her), Grant Landers (he/him), Brett Buist (he/him), Ben Kramer (he/him), Kai Schweizer (they/he), Felicity Austin (she/her)

Collaborators: Thriving in Motion, Telethon Kids Institute

The term *trans* refers to an individual whose gender identity and sex assigned at birth are incongruent. This includes non-binary, gender questioning, and other diverse gender identities. Chest binding is the practice of compressing breast tissue to create the appearance and sensation of a flat chest. This is a very common practice amongst trans people registered female at birth. Binding is beneficial to the mental health of trans people by assisting to alleviate gender dysphoria and affirm their experienced gender.

As a population, trans people engage in lower levels of physical activity compared to their cisgender peers impacting negatively on short- and long-term health. Global trans organisations provide the advice that exercise should not be undertaken in a chest binder due to concerns around safety, with reduces trans people's willingness to exercise or play sports. Additionally, binding advice as a barrier to employment in roles where any physical tasks are required.
Despite these recommendations there is currently no research exploring the impact of chest binders on physical function during physical activity.

Objective(s)
Our aim is to compare the impact of wearing a chest binder on physical function (e.g., lung function, cardiorespiratory performance, skin temperature) and physical perception (e.g., perceived effort, comfort and breathlessness) during aerobic and resistance exercise tasks.

Hypothesis

The wearing of a chest binder will not limit physiological function or performance, however the changes in perception from wearing a compressive garment on the trunk would be altered and may lead participants to perceive greater restrictions or limitations to exercise capacity.

Get in touch to chat about either of these specific projects, and/or if there is something in our list of projects underway that particularly interests you come have a chat and there might be additional project opportunities!

UWA Exercise & Performance Centre + Collaborators

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The UWA Exercise and Performance Centre (EPC) is a community-based exercise physiology clinic based within the School of Human Sciences. The mission of the UWA EPC is to provide a gold standard education and clinical exercise physiology facility which directly engages the community and contributes to the development of the industry and the exercise physiology knowledge base.

Honours/Masters projects available for 2024:

The Bone, Muscle, and Balance (BOMB) study: Feasibility of a Community-based High Intensity Resistance and Impact Training Program for Older Adults.

Supervisors: Brett Buist, Ben Kramer, Grant Landers + Bonnie Furzer (in collaboration with the EPC Team)

In 2019-2020, injurious falls have accounted for 224,000 hospitalisations, with the vast majority of these occurring in older adults (65+years). A number of age-related changes in our body's physiology are known to predispose adults to higher risk of injurious falls including declines in balance and musculoskeletal function. Participation in high intensity resistance and impact training has been shown to result in improvements in bone mineral density. However, this study aims to examine the feasibility of such an intervention in a community setting, as well as the impact that this form of training may have on rates of injurious falls and measures of balance.

Skills: You will acquire training on a range of different areas including power, strength and balance assessments; body composition scanning; exercise delivery; service coordination and evaluation; qualitative and quantitative research methods.