Eastern Hill Academic Precinct: 2027 Honours Projects

The Eastern Hill Precinct is located near the Melbourne Museum, St Vincents Hospital and the Royal Victorian Eye and Ear Hospital. We offer a diverse range of basic, clinical and applied research in areas including basic mechanisms of biology and physiology, clinical and community-based epidemiology, clinical neurosciences, cancer, infection and immunity, as well as clinical trials of new therapies and devices. Students can undertake research projects within the University of Melbourne Departments (Medicine, Surgery, Ophthalmology (CERA), Otolaryngology and Medical Bionics), or in one of our affiliated partner institutes such as St Vincents Institute of Medical Research, Centre for Eye Research Australia, Bionics Institute or the in the brand new ACMD facility.

If you'd like to be kept up to date with information about our next planned Honours information session please register your email below and we will contact you with further details as they become available: **Register for 2027 Eastern Hill Honours information session here**

Modelling Macrophage-Mediated Cardiac Inflammation in Friedreich Ataxia Using iPSC-Derived Macrophages

Suitable for: Master of Biomedical Science

Project Location:
St Vincent's Institute of Medical Research

University of Melbourne Enrolling Department:
Medicine (St Vincent's Hospital)

Cardiomyopathy is the leading cause of death in Friedreich ataxia (FRDA), yet the role of innate immune cells in driving cardiac tissue damage remains unexplored. Frataxin deficiency disrupts mitochondrial iron handling and respiratory chain function, two processes central to macrophage metabolic reprogramming during activation. Cardiac macrophages regulate myocardial inflammation and fibrosis, making them a plausible but unstudied contributor to FRDA heart disease.

This project will generate macrophages from FRDA patient iPSC lines and matched controls to assess disease-relevant functional deficits, including inflammatory cytokine output, mitochondrial respiration, iron metabolism, and fibroblast activation capacity. Results will determine whether macrophage dysfunction is a meaningful driver of FRDA cardiomyopathy and identify potential targets for cardiac-focused intervention.

Primary Supervisor: A/Prof Shiang Yong (Max) Lim

Contact: maxlim@unimelb.edu.au

Co-supervisor(s): Dr Jarmon Lees

Unlocking the secrets of heart aging with stem cells

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Cardiovascular disease is the leading cause of age-related death, with conditions such as heart failure being ten times more prevalent in individuals over 75. This project will model human heart aging by generating 3D cardiac tissue derived from induced pluripotent stem cells (iPSCs) and developing an aged 'heart-in-a-dish' model. Using gene editing and introducing aging-associated stressors, this project will aim to identify functional and structural changes in aged cardiomyocytes which will subsequently be used to develop novel therapeutics to mitigate age-related cardiac diseases.

Primary Supervisor: A/Prof Shiang Yong (Max) Lim

Contact: maxlim@unimelb.edu.au

Co-supervisor(s): Dr Sebastian Bass-Stringer

When the heart and kidney fail together: modelling cardiorenal syndrome with human organoids

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Every year, thousands of patients are admitted to hospital with heart failure, only to watch their kidney function deteriorate within days. The reverse is equally true: chronic kidney disease quietly strains the heart until it gives out. This destructive relationship is called cardiorenal syndrome, and it remains one of the hardest problems in cardiovascular medicine to treat, because no human model system has existed to study both organs together.

Using induced pluripotent stem cells (iPSCs) derived from patients, you will grow beating cardiac organoids and kidney organoids in a shared culture environment that allows the two tissues to interact, just as they do in the body. This human cardiorenal co-culture platform will be used to study how injury to one organ drives dysfunction in the other, with the specific disease context, whether hypertensive, diabetic, ischaemic, inflammatory, cardiotoxic, nephrotoxic, or septic, developed in conversation with the student based on their interests.

You will develop skills in stem cell culture, 3D organoid generation, live imaging, and functional assays, working within a team that combines cardiac and kidney biology, omics, and translational medicine.

Primary Supervisor: Dr Jarmon Lees

Contact: jarmon.lees@unimelb.edu.au

Targeting the nucleoli to treat cancer

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

The nucleoli are the site of RNA polymerase I (Pol I) transcription of ribosomal RNA (rRNA) genes and ribosome assembly. The first-in-class inhibitor of Pol I transcription, CX-5461, has shown promising anti-tumour activity in various preclinical cancer models and in Phase I clinical trials in blood and solid cancers. Our work has shown that CX-5461 activates a unique form of stress, termed nucleolar stress, leading to inhibition of cell proliferation with low levels of global DNA damage. CX-5461 has a unique sensitivity profile compared to chemotherapeutics. Thus, we propose that activating nucleolar stress represents a promising new cancer therapy paradigm.

To characterize nucleolar stress pathways, we have performed a whole-genome synthetic lethal RNA interference screen and identified that CX-5461 is synthetic lethal with various DNA repair pathways, highlighting the strong links between nucleolar stress and global DNA replication stress. We have recently completed an innovative arrayed CRISPR-Cas9 screen to identify genes whose deletion induces changes in nucleolar morphology as an indicator of nucleolar stress. We have identified factors involved in ribosome biogenesis, DNA replication, cell cycle and RNA metabolism as mediators of nucleolar stress.

Altogether, our work defines nucleolar stress pathways and highlights harnessing nucleolar stress as a novel cancer therapy approach. This project aims to validate targets identified in our screens as mediators of nucleolar stress and novel cancer therapeutic targets

Primary Supervisor: A/Prof Elaine Sanij **Contact:** esanij@svi.edu.au

Co-supervisor(s): Dr Jian Kang

Define the role of mRNA translation reprogramming in multiple myeloma progression and response to therapy

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Multiple myeloma (MM) is a rare cancer type of white blood cell called plasma cells within the bone marrow. The exceptionally high rate of protein synthesis and the increased processing load, render MM cells particularly susceptible to perturbations in protein homeostasis. The ubiquitin-proteasome system is a key mechanism by which MM cells maintain a balance between protein synthesis and disposing of damaged proteins. The induction of proteotoxic stress by targeting protein degradation with proteasome inhibitors is an effective therapeutic approach. However, resistance to this treatment modality is inevitable. Protein homeostasis also relies on exquisite regulation of mRNA translation and protein synthesis. Many MM genetic drivers have direct impact on mRNA translational activity. Therefore, investigating altered mRNA translational activity in MM cells will provide new understanding of MM oncogenic transformation and disease progression and identify novel therapeutic approaches for treating MM.

Heterozygous deletion of RPL5, a component of the 60S ribosome subunit, has been found in 20-40% of MM patients. Patients with low RPL5 expression level have a worse survival outcome but respond better to the proteasome inhibitor than patients with high RPL5 expression. We hypothesize that translational adaptation mediated by RPL5 deficiency promotes MM progression and affects therapeutic response. This project aims to interrogate the functional impact of RPL5 deficiency in MM cells.

We have established RPL5 deficient MM cell lines by either CRISPR-Cas9 knock-out or inducible shRNA knockdown. Cell proliferation and drug sensitivity will be assessed. As deficiency in RPL5 can alter ribosome composition leading to ribosome heterogeneity, we will isolate 40S and 60S ribosomal subunits and 80S monosomes by sucrose gradient separation and fractionation and the abundance of

ribosomal proteins will be quantified by LC-MS/MS. To determine the effect of RPL5 deficiency on mRNA translation and protein synthesis, we will also perform polysome profiling and proteomics analysis. In addition, the effect of RPL5 deficiency on p53-mediated ribosome biogenesis checkpoint activation will be determined. The findings will provide new insight into mRNA translation reprogramming in MM pathogenesis and provide evidence for RPL5 as a potential biomarker of cancer therapy in MM.

Primary Supervisor: A/Prof Elaine Sanij **Contact:** esanij@svi.edu.au

Co-supervisor(s): Dr Jian Kang

Structural biology of proteins involved in mental illnesses

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

We are focused on understanding the molecular bases of a range of neurodegenerative diseases and to develop much needed treatments. One area of focus is Alzheimer's disease (AD) which is the fourth biggest killer in developed countries. Amyloid precursor protein (APP) plays a central role in the development of AD. Here we will use biophysical and cell biology approaches to probe APP function together with X-ray crystallography at the Australian Synchrotron and cryo electron microscopy to determine the 3D atomic structures of APP and of potential therapeutic antibodies and diabodies bound to parts of APP. The latter project allows us to rationally engineer more potent antibodies and diabodies as treatments for AD. Toxic molecules associated with neurodegenerative diseases are disposed of by the brain's immune cells called microglia. We are investigating the structure and function of key protein receptors found on the surface of microglia cells as a basis for the discovery of drugs to treat a range of neurodegenerative diseases including AD, Lewy Body Disease, Motor Neuron Disease and Parkinson's Disease. Our work is strongly complemented by cell biology approaches to characterise the action of drugs we discover in cell models of disease.

Primary Supervisor: Prof Michael Parker **Contact:** mwp@unimelb.edu.au

Co-supervisor(s): Dr Stefan Hermans, Dr Emma Van Der Westhuizen,

Investigating a novel mechanism for improving beta-cell function in type 2 diabetes

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

We aim to investigate whether pharmacological inhibition of SIKs signalling will enhance ?-cell function and improve glucose homeostasis in type 2 diabetes.

Primary Supervisor: Dr Kim Loh **Contact:** kloh@svi.edu.au

Investigating a novel mechanism for suppressing hepatic steatosis in NAFLD.

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

We aim to investigate whether pharmacological inhibition of SIKs signalling will suppress liver fat accumulation in NAFLD.

Primary Supervisor: Dr Kim Loh

Contact: kloh@svi.edu.au

The impact of cancer therapies on the bone marrow microenvironment

Suitable for: Honours

Project Location: *St. Vincent's Institute of Medical Institute*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

All blood cells are formed from haematopoietic stem and progenitor cells (HSPCs). Cancer therapies cause profound reductions in blood cell counts in a range of patients and can affect treatment outcomes. We have shown that some of these effects are caused by damage to the non-blood cells (bone marrow microenvironment cells) that regulate blood cell production. This project will explore how different HSPC populations and other blood-forming cells communicate with their surrounding bone marrow microenvironment cells and how these change after cancer therapies using in-house single-cell gene expression data. This project is flexible and can involve both bioinformatics and wet lab experiments. The project will be using advanced bioinformatics tools and R programming, wet lab experiments such as advanced immunofluorescence, imaging and cell culture of bone marrow microenvironment cells.

Primary Supervisor: Prof Louise Purton

Contact: lpurton@svi.edu.au

Co-supervisor(s): Dr Gavin Tjin, Dr Sagrika Chugh

Identifying the roles of inflammation in the pathogenesis of myelodysplastic syndromes

Suitable for: Honours

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Myelodysplastic syndromes (MDS) are a heterogeneous group of blood cell cancers that are poorly understood and lack curative treatments. We have developed two different mouse models of MDS by differentially altering the expression of Homeobox a1 (Hoxa1) isoforms in the blood-forming cells. These two models display different levels of disease burden as well as inflammation, providing an oppurtunity to better understand MDS pathogenesis. We have also identified that the JAK/STAT pathway is dysregulated in these mice. Here we will be investigating the interplay between inflammation and JAK/STAT signalling, with a focus on how this influences MDS development. A myriad of cell biology and molecular techniques will be used to profile both myeloid and lymphoid populations. Cell populations

of interest will be futher characterised using next-gen sequencing, providing the oppurtunity for bioinformatics as well.

Primary Supervisor: Prof Louise Purton **Contact:** lpurton@svi.edu.au

Co-supervisor(s): Dr Luban Sobah, Dr Sagrika Chugh

Regulation of blood cell production by endothelial cell-derived retinoic acid receptor gamma

Suitable for: Honours

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

We make billions of blood cells every day. Non-blood cells that form the bone marrow microenvironment are essential in regulating blood cell production. We have deleted one of the vitamin A receptors in endothelial cells in mice and have identified significant blood cell defects in the mice. The blood cell phenotypes are accompanied by increased inflammation and some of the phenotypes are sex-specific. Here we will investigate how deletion of the vitamin A receptor causes inflammation in the mice, and further characterise the inflammation in a range of haematopoietic organs. Cell biology and molecular techniques will be used to profile both myeloid and lymphoid populations. Cell populations of interest will be further characterised using next-gen sequencing, providing the opportunity to learn and apply bioinformatics skills.

Primary Supervisor: Prof Louise Purton **Contact:** lpurton@svi.edu.au

Co-supervisor(s): Dr Luban Sobah, Dr Sagrika Chugh

Development and validation of artificial intelligence approaches for detecting chromosome fragility in rare disease

Suitable for: Honours or Master of Biomedical Science

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Fanconi anaemia (FA) is a rare inherited disorder characterised by defects in DNA repair and marked chromosome instability. FA predisposes to solid cancers, blood cancers and bone marrow failure. Laboratory diagnosis commonly relies on chromosome fragility testing, where peripheral blood lymphocytes are exposed to DNA damaging agents. Cells from individuals with FA display increased chromosome breaks and complex chromosomal abnormalities that can be visualised in metaphase chromosome preparations.

Interpretation of chromosome fragility assays is currently labour-intensive and requires trained personnel to manually identify chromosome breaks and radial figures. Advances in artificial intelligence (AI) and computer vision offer the potential to automate this process, improving diagnostic efficiency and consistency. Our laboratory has developed a prototype AI platform for chromosome fragility detection, but further training and validation are required before clinical deployment.

Project Aims

-Generate high-quality annotations of chromosome fragility images for AI model training.

-Evaluate agreement between human annotators and existing AI predictions.

-Generate new chromosome fragility datasets using cultured cell lines and chromosome breakage assays.

-Assess the performance of AI-assisted scoring compared with conventional manual scoring methods.

-Explore strategies for improving model accuracy through iterative human-in-the-loop training.

Research activities

The student will:

-Learn the principles of chromosome fragility testing and Fanconi anaemia diagnosis.

-Review and classify metaphase chromosome images using a purpose-built annotation platform.

-Label chromosome abnormalities according to predefined categories, including chromosome breaks, chromatid breaks, radial figures, and normal metaphases.

-Analyse annotation consistency between different scorers.

-Culture human cell lines and perform chromosome fragility assays using DNA-damaging agents.

-Prepare metaphase chromosome spreads and generate new image datasets.

-Contribute to retraining and validating AI models using newly generated annotations.

-Perform statistical analyses of model performance, including sensitivity, specificity, and inter-rater agreement.

Skills developed

-Cytogenetics and chromosome fragility testing

-Human cell culture

-Microscopy and image acquisition

-Artificial intelligence and computer vision workflows

-Biomedical image annotation

-Statistical analysis and data visualisation

-Reproducible research practices in R and/or Python

Expected outcomes

The project will contribute to the development of an AI-assisted diagnostic workflow for Fanconi anaemia. Outcomes may include improved training datasets, enhanced model performance, validation of automated chromosome scoring approaches, and potential publication of findings in a peer-reviewed journal.

This project is suitable for:

Students with interests in genetics, molecular biology, bioinformatics, biomedical science, computer vision, or artificial intelligence applied to healthcare. No prior AI experience is required, although familiarity with image analysis and molecular biology, or programming would be advantageous.

Primary Supervisor: A/Prof Wayne Crismani **Contact:** wcrismani@svi.edu.au

CRISPR Blitz: Illuminating Gene Mysteries through Saturation Genome Editing

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

The proposed research student project centers on exploring the potential of saturation genome editing as a powerful tool for understanding gene function and regulation in complex biological systems.

Leveraging the advancements in CRISPR-based technologies, the project aims to systematically introduce diverse and targeted mutations in specific important human genes. By employing high-throughput screening approaches and bioinformatics analyses, the student will comprehensively assess the phenotypic consequences of the introduced mutations, shedding light on essential genetic elements, regulatory networks, and disease-associated genes. This project's outcomes hold tremendous promise for uncovering novel gene interactions, elucidating functional pathways, and providing valuable insights into the genetic basis of various biological processes, thus contributing to the advancement of both fundamental research and therapeutic applications.

Primary Supervisor: A/Prof Wayne Crismani **Contact:** wcrismani@svi.edu.au

Hidden Challenges in Healthcare: Analyzing Diagnostic Delays for Rare and Chronic Diseases

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Fanconi Anaemia (FA) is a rare and chronic genetic disorder. FA is a multisystem disorder with extremely heterogeneous presentation, which makes the diagnosis challenging. FA predisposes to early onset cancers, progressive bone marrow failure, endocrine abnormalities, birth defects and other symptoms. Some patients however, have no symptoms for many decades, but still have the underlying condition. This research project aims to explore national diagnostic data and a small cohort of FA patients from Australia and New Zealand. This study presents a unique opportunity to delve into the intricacies of the disease within this specific geographic region. By meticulously analysing the available data, the study seeks to uncover potential clues in the diagnostic odyssey that may inform future guidelines for diagnostic testing to improve patient outcomes. This exploratory work will lay the groundwork to generate testable hypotheses and encourage collaborations among researchers worldwide to decipher the diverse presentations of Fanconi Anaemia. This project promises to add valuable insights to the current body of knowledge, contributing to improved patient care, genetic counselling, and possibly, paving the way for tailored therapeutic interventions in this chronic and rare disease.

Primary Supervisor: A/Prof Wayne Crismani **Contact:** wcrismani@svi.edu.au

Dissecting the genetics of chromosome fragility

Suitable for: Honours or Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

This project investigates the genetic causes of chromosome breakage and cancer predisposition using traditional cytogenetic techniques, coupled with advanced CRISPR-based gene editing. During this project you will analyse the effect of loss of function of individual Fanconi anemia (FA) genes in a controlled isogenic background, such as hap1 cells and patient-dervied cells. By focusing on each gene as a unique variable, we aim to unravel the specific genetic mechanisms and severity of chromosome instability. You will develop deeper insights into the mechanisms of cancer biology and rare disease.

This study will contribute to a clearer understanding of how genetics impacts genomic integrity and may reveal new avenues for targeted therapies.

Primary Supervisor: A/Prof Wayne Crismani **Contact:** wcrismani@svi.edu.au

Methods for robust comparisons between highly heterogeneous spatial transcriptomics samples

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Spatial transcriptomics technologies offer exciting opportunities for multi-modal investigations of cells and tissue structures. However, spatial transcriptomics samples are highly heterogeneous, making it challenging to make robust comparisons between samples from different individuals or conditions. This project will apply statistical and AI techniques to develop methods and software to enable robust comparisons across spatial transcriptomics samples.

Primary Supervisor: A/Prof Davis McCarthy **Contact:** dmccarthy@svi.edu.au

Graph foundational models for mapping genotype to phenotype

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Understanding how genotype (variation in DNA) relates to phenotype (observed characterestics of an individual) is at the foundation of modern biomedical science. Genome-wide association studies and quantitative trait locus mapping have been successful in linking genetic variation to phenotypes of interest, for example disease status or gene expression in specific tissues and cell types. However, with datasets growing in size and complexity, new approaches are needed. Graph foundation models offer a new way to integrate relationships between observations and data types. This project will explore the use of these methods to develop new approaches to mapping genotype to multi-omics phenotypes in diseases like pulmonary fibrosis.

Primary Supervisor: A/Prof Davis McCarthy **Contact:** dmccarthy@svi.edu.au

Joint gene expression and chromatin accessibility quantitative trait locus mapping in pulmonary fibrosis

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Understanding how genotype (variation in DNA) relates to phenotype (observed charactereistics of an individual) is at the foundation of modern biomedical science. Genome-wide association studies and quantitative trait locus (QTL) mapping have been successful in linking genetic variation to phenotypes of interest, for example disease status or gene expression in specific tissues and cell types. However, QTL mapping has primarily been limited to a single modality (e.g., gene expression) per study. We have single-cell resolution gene expression (RNA-seq) and chromatin accessibility (ATAC-seq) data from the same lung cells for 200 individuals with and without pulmonary fibrosis. This project will be the first to jointly map gene expression and chromatin accessibility QTLs in a solid human tissue, applying new methodological approaches at scale.

Primary Supervisor: A/Prof Davis McCarthy **Contact:** dmccarthy@svi.edu.au

Defining cytokine driven transcriptional and epigenetic programming of T cells in autoimmunity

Suitable for: Honours

Project Location: *St Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Insulin producing beta cells are destroyed by autoreactive T cells in type 1 diabetes. During chronic activation, these autoreactive T cells develop into stem like memory T cells that can give rise to effector T cells capable of killing beta cells. Cytokines that signal through the JAK–STAT pathway play a critical role in driving the differentiation of stem like memory T cells into effector T cells. We have shown that inhibition of the JAK–STAT pathway with a JAK inhibitor protects beta cells from effector T cell–mediated destruction in both mice and humans.

We hypothesise that JAK inhibitors block effector T cell differentiation by dampening cytokine driven epigenetic reprogramming. In this project, we will use transgenic mouse models, gene editing technologies, RNA seq and epigenetic profiling to dissect how individual cytokines shape the epigenetic changes required for effector T cell differentiation. These deep mechanistic insights will ultimately guide the design of more effective combination immunotherapies to prevent type 1 diabetes.

Primary Supervisor: Dr Prerak Trivedi **Contact:** ptrivedi@svi.edu.au

Co-supervisor(s): A/Prof Bala Krishnamurthy, Prof Thomas Kay

Developing an assay for human IL-2

Suitable for: Master of Biomedical Science

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Our work focuses on the immunology of the autoimmune disease type 1 diabetes (T1D). T1D develops when the immune system's T cells destroy the insulin producing beta cells which are found within the islets of Langerhans (aka islets) of the pancreas.

A long-standing goal of the field has been to develop an assay that can measure this T1D-causing autoimmune T-cell response. This has been difficult because the relevant T cells are present at very low frequencies in the peripheral blood – the only tissue routinely available for analysis. We have developed

a suite of whole blood-based assay that can measure different facets of the autoimmune T-cell response against beta-cell antigens in vitro. The common readout of these in vitro assays is the secretion of IL-2 in the plasma.

Our goal is to 'translate' these assays into a blood test that can be used by clinicians. However, the currently available assays for IL-2 are unsuitable for two reasons: they are not licenced for clinical use and they are very expensive. For this reason, we are working on developing an alternative assay for IL-2. Our current challenge is to develop an assay that is suitably sensitive for this application.

The goal of this project is to use a screening approached, developed in the lab, to identify variants that give higher sensitivity to IL-2. This project will give the student and excellent background in immunology, protein engineering and assay development. The project will involve flow cytometry, lentiviral mediated transduction, sequencing, protein structure analysis and conducting IL-2 assays.

The student will be support by the PI, A/Prof Stuart Mannering, postdocs/RAs and PhD students within the Human Immunology Lab. This project will suit a motivated student with an interest in translational human immunology, assay development and protein engineering.

Primary Supervisor: A/Prof Stuart Mannering **Contact:** smannering@svi.edu.au

Co-supervisor(s): Dr Chris Langendorf

Developing a method to produce immunology grade peptides

Suitable for: Master of Biomedical Science

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Our work focuses on the immunology of the autoimmune disease type 1 diabetes (T1D). T1D develops when the immune system's T cells destroy the insulin-producing beta cells which are found within the islets of Langerhans (aka islets) of the pancreas.

A long-standing goal of the field has been to develop an assay that can measure this T1D-causing autoimmune T-cell response. This has been difficult because the relevant T cells are present at very low frequencies in the peripheral blood – the only tissue routinely available for analysis. We have developed a suite of whole blood-based assay that can measure different facets of the autoimmune T-cell response against beta-cell antigens in vitro. Currently, these assays use synthetic peptides to stimulate antigen specific T-cell responses, which are then measured by the secretion of IL-2 into the plasma.

Our goal is to 'translate' these assays into a blood test that can be used by clinicians. We have shown that these assays have great potential for giving scientists and clinicians the tools they need to measure pathogenic and protective immune responses. However, we have also discovered that synthetic peptides are not suitable for this application. Due to the peptide synthesis process, the batch-batch variation in synthetic peptides makes them unsuitable for use in our whole blood assay.

The goal of this project is to develop and optimise and alternative approaches to making peptides that mimic the sequence of beta-cell antigens. This project will give the student and excellent background in immunology, protein chemistry and assay development. The project will involve expression, purification and analysis of peptides using modern protein chemistry techniques. Depending on progress the project may also involve testing new peptides using the whole blood assays.

The student will be support by the PI, A/Prof Stuart Mannering, Dr Chris Langendorf, postdocs/RAs and PhD students within the Human Immunology Lab. This project will suit a motivated student with an interest in translational human immunology, assay development and protein engineering.

Primary Supervisor: A/Prof Stuart Mannering **Contact:** smannering@svi.edu.au

Co-supervisor(s): Dr Chris Langendorf

Bio-engineering tissue engineered blood vessels

Suitable for: Master of Biomedical Science

Project Location: *St Vincent's Institute, ACMD*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

The Vascular Biology group at SVI is developing technologies to assemble tissue engineered branched medium sized blood vessels incorporated into a human skin flap in the laboratory from human induced pluripotent stem cells (hiPSC).

In this particular project we will develop techniques for producing the wall of the blood vessels using various biomaterials and hiPSC-derived vascular smooth muscle cells.

This will involve biomaterials testing, some 3D cell culture, cell viability, and structure/function assessments using microscopy techniques.

Primary Supervisor: Dr Kate Firipis **Contact:** kfiripis@svi.edu.au

Co-supervisor(s): Dr Elizabeth Footner, A/Prof Geraldine Mitchell

How does ageing change bone structure? A chemometric FTIRM (Fourier-transform infrared microspectroscopy) study of human osteons

Suitable for: Honours or Master of Biomedical Science

Project Location: *St. Vincent's Institute of Medical Research*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Osteoporosis is a major public health problem, particularly with as the global population is ageing. Bones become fragile not only because of bone loss, but also because of changes in bone matrix composition, including mineral and collagen. Bone is continuously renewed through remodelling, during which new osteons form and progressively mature as they accumulate calcium and phosphate. Our previous FTIRM (Fourier-transform infrared microspectroscopy) analysis of femoral bone samples shows that the bone produced by older women during remodelling has defects in collagen deposition compared to younger women. However, we focused only on a few known features of the FTIRM spectra, and there is much more to be learned from our large datasets. Taking an unbiased approach to these data may reveal new information about how bone ages. This project will apply chemometric analysis to existing FTIR spectral data from osteons from young and elderly women and men. Using Python-based workflows, the student will perform principal component analysis (PCA) of spectral data to identify molecular signatures of osteon maturation and ageing and, with an unbiased approach, find new information about components of bone structure that change with bone mineralisation and age. This project will improve understanding of how ageing affects bone composition and will provide training in bone infrared microspectroscopy, spectral analysis, chemometric analysis, and data visualisation.

Primary Supervisor: Prof Natalie Sims **Contact:** nsims@svi.edu.au

Co-supervisor(s): Haniyeh Hemmatian

How does Semaphorin 3D control bone formation?

Suitable for: Honours or Master of Biomedical Science

Project Location:

St. Vincent's Institute of Medical Research

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

In long bones such as the bones in the arm or leg, the outer shell of bone, cortical bone, is the main determinant of bone strength. We have found that semaphorin 3D (Sema3D) is highly expressed by mature osteoblasts and osteocytes within the bone matrix. It is also strongly inhibited by treatment with an anabolic (bone forming) stimulus, and regulated in two mouse models with defective cortical bone. This all suggests Sema3D has an important physiological role in controlling bone strength, but this needs to be tested. In this project, you will use cell culture and cell-based assays to investigate the role of Sema3D in osteoblast differentiation, cell metabolism and their ability to produce collagen and deposit mineral.

Primary Supervisor: Prof Natalie Sims

Contact: nsims@svi.edu.au

Co-supervisor(s): Dr Martha Blank

Developing methods to understand the two major types of bone

Suitable for: Honours or Master of Biomedical Science

Project Location:

St. Vincent's Institute of Medical Research

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

Bone strength depends on both bone mass and bone's structural and compositional organisation. There are two major types of bone material, depending on the context in which it is formed. During skeletal development and fracture repair, bone is formed rapidly, with a disorganised collagen network, and is termed "woven bone". This is progressively replaced by highly organised, layered "lamellar bone" which is more mechanically strong. Osteoblasts produce both tissue types, but even though this has been known for many years, the molecular differences between their production processes are unknown. This project will develop laser dissection methods combined with proteomics to isolate bone tissue from distinct woven and lamellar regions and compare their proteome. This will reveal mechanisms that control osteoblast behaviour, and will inform future strategies to improve bone growth and repair.

Primary Supervisor: Prof Natalie Sims

Contact: nsims@svi.edu.au

Co-supervisor(s): Dr Martha Blank

Perspectives and attitudes on gene therapy to treat chronic eye diseases

Suitable for: Honours

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

Gene therapies can now recover vision for people living with inherited eye diseases, but using gene therapy to treat chronic eye conditions, such as glaucoma and age-related macular degeneration, is the next frontier. This project explores the perspectives and attitudes towards gene therapy treatment from the patient (consumer) perspective. It will provide us with valuable insights in our work to develop new

gene therapies to treat chronic eye disease, including gaps in public education and understanding consumer expectations.

Primary Supervisor: Dr Flora Hui **Contact:** fhui@cera.org.au

Co-supervisor(s): Prof Rick Liu, Prof Pete Williams, Dr Myra McGuinness

Optimising ND4 gene therapy for Leber hereditary optic neuropathy using engineered AAV delivery and mitochondrial targeting sequences

Suitable for: Honours or Master of Biomedical Science

Project Location: *Centre for Eye Research Australia*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Leber hereditary optic neuropathy is a severe inherited mitochondrial eye disease that causes rapid and often irreversible vision loss, mainly in young adults. The most common disease-causing mutation affects the mitochondrial ND4 gene, which is essential for normal energy production in retinal ganglion cells, the neurons that connect the eye to the brain. Because ND4 is encoded by mitochondrial DNA, gene therapy requires not only efficient delivery to retinal ganglion cells but also accurate targeting of the therapeutic ND4 protein into mitochondria. Current approaches rely on mitochondrial targeting sequences that have generally been chosen empirically rather than systematically optimised, which may limit treatment efficiency. This project aims to improve ND4 gene therapy by combining an engineered intravitreal AAV vector, AAV2.IvtB, with a panel of candidate mitochondrial targeting sequences selected using mitochondrial import biology and human retinal ganglion cell single-cell RNA sequencing data. Ten candidate MTS-ND4 constructs will be generated and compared against the clinically benchmarked COX10-MTS-ND4 cassette. These constructs will first be screened in vitro for mitochondrial localisation, mitochondrial membrane association and functional rescue potential. The best-performing candidates will then be packaged into AAV2.IvtB and evaluated in vivo for retinal delivery, ND4 expression, safety and therapeutic potential. The expected outcome is a more efficient and clinically translatable ND4 gene therapy platform for LHON, with broader relevance to mitochondrial gene therapy and optic neuropathies.

Primary Supervisor: Dr Jiang-Hui (Sloan) Wang **Contact:** sloan.wang@unimelb.edu.au

Co-supervisor(s): Dr Isabel Lopez Sanchez

Revolutionising eye disease treatment with next-generation gene therapy

Suitable for: Honours or Master of Biomedical Science

Project Location: *Centre for Eye Research Australia*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Current retinal gene therapies using adeno-associated virus vectors are commonly delivered by subretinal injection, an invasive surgical procedure that can be technically demanding and carries risks such as retinal detachment and localised retinal injury. Intravitreal injection offers a safer, simpler and more clinically scalable alternative, but current AAV vectors delivered by this route mainly target the inner retina and show limited ability to reach photoreceptors. A major barrier is the inner limiting membrane, where heparan sulfate can trap AAV particles and restrict deeper retinal penetration. Although engineered vectors such as AAV2.7m8 reduce heparan sulfate binding and improve photoreceptor transduction in mice, their performance remains limited in larger animal and primate models, suggesting that reduced heparan sulfate binding alone is insufficient for efficient and

translatable outer retinal delivery. This project aims to develop next-generation engineered AAV capsids capable of efficient photoreceptor transduction following intravitreal injection. Building on a novel capsid screening platform, we will design and select AAV variants that combine reduced heparan sulfate binding with enhanced affinity for photoreceptor-enriched surface molecules. The central hypothesis is that dual-targeted capsids will overcome key limitations in current retinal gene delivery, including poor retinal penetration, inconsistent tissue targeting and species-specific differences in vector performance. The project will engineer AAV2 capsids with both reduced heparan sulfate binding and improved engagement of photoreceptor-associated surface receptors, then validate the most promising variants in human retinal organoids and in vivo models, including small and large animals. The expected outcome is a safer, more effective and broadly translatable intravitreal AAV platform for treating inherited retinal diseases affecting photoreceptors.

Primary Supervisor: Dr Jiang-Hui (Sloan) Wang **Contact:** sloan.wang@unimelb.edu.au

Co-supervisor(s): Prof Guei-Sheung Liu

Restoring vision in Usher 1B and Stargardt's disease using next-generation gene therapies

Suitable for: Honours or Master of Biomedical Science

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

Inherited retinal diseases are a major cause of progressive vision loss, but many of the genes responsible are too large to fit into a single adeno-associated virus (AAV) vector, the most widely used delivery system for ocular gene therapy. This size limitation has slowed the development of treatments for conditions such as Usher syndrome type 1B, caused by mutations in MYO7A, and Stargardt disease, commonly caused by mutations in ABCA4. Both diseases affect photoreceptors and can lead to severe, irreversible vision impairment. This project aims to develop next-generation AAV-based gene therapies that can restore the function of these large retinal disease genes in vivo. We will design and optimise dual-AAV systems in which each therapeutic gene is split across two vectors and reassembled inside retinal cells. Two complementary reconstitution strategies will be compared: split intein protein trans-splicing, which joins two protein fragments after translation, and ribozyme-mediated mRNA ligation, which joins split RNA transcripts to generate a full-length message. The most promising dual-AAV designs will be evaluated in relevant preclinical models of Usher syndrome type 1B and Stargardt disease, including Myo7a and Abca4 deficiency models. Outcomes will include restoration of full-length protein expression, correction of disease-relevant cellular defects, preservation of photoreceptor structure, and improvement in retinal function. By directly comparing intein- and ribozyme-based approaches, this project will define the strengths, limitations and translational potential of each strategy. The expected outcome is a validated platform for treating large-gene inherited retinal diseases, with direct relevance to future therapies for Usher syndrome, Stargardt disease and other currently untreatable blinding conditions.

Primary Supervisor: Dr Jiang-Hui (Sloan) Wang **Contact:** sloan.wang@unimelb.edu.au

Co-supervisor(s): Prof Lauren Ayton

Exosomes as Drug and Gene Delivery Tools for Retinal Degeneration to Stop Blindness

Suitable for: Honours or Master of Biomedical Science

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

Retinal diseases are a major cause of blindness, with limited therapeutic options. This project aims to revolutionise retinal therapy by harnessing exosomes, naturally occurring extracellular vesicles, as targeted vehicles for drug and gene delivery. Focusing on Macular Telangiectasia Type 2 (MacTel) and Stargardt disease, the project will engineer exosomes to deliver supplemental serine and large therapeutic plasmids encoding retinal-protective genes that exceed viral vector capacity. Using advanced cell and preclinical models, this research will evaluate delivery efficiency and therapeutic efficacy. The outcomes could establish exosomes as a next-generation platform to prevent blindness and restore retinal health. Retinal diseases are a leading cause of blindness, affecting millions of people worldwide and significantly diminishing quality of life. Despite major advances in biomedical research, effective treatments for many retinal degenerative diseases remain limited. This Honours/Masters research project aims to transform retinal disease treatment by developing next-generation exosome and gene therapy approaches for targeted retinal drug delivery. The project will focus on Macular Telangiectasia Type 2 (MacTel), an incurable retinal disease characterised by low serine levels and the accumulation of toxic deoxysphingolipids (deoxySLs), which contribute to progressive retinal degeneration and vision loss. The successful candidate will investigate innovative strategies to engineer extracellular vesicles (exosomes) and gene therapy platforms capable of delivering therapeutic molecules directly to affected retinal cells. A major component of the project will involve developing exosome-based delivery systems for targeted serine supplementation and exploring gene therapy approaches to restore metabolic balance in the retina. The project will also examine how engineered exosomes can serve as non-viral therapeutic carriers, offering potential advantages over conventional viral vector systems in precision medicine.

Primary Supervisor: Dr Sushma Anand

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Co-supervisor(s): Dr Tom Edwards

Development of NMNAT2-targeted small molecules for neuroprotection.

Suitable for: Honours

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

We are pharmacologically targeting NMNAT2, the neuron's regulator of NAD, an essential metabolite that governs neuron health. The project is embedded within a larger drug development project and the key tasks will be primarily in vitro cell work, microscopy, and some bioinformatics/statistics. This project is ideal for a student interested in drug development for neurodegenerative disease.

Key reading:

- https://pubmed.ncbi.nlm.nih.gov/39048544/
- https://pubmed.ncbi.nlm.nih.gov/41982735/

Primary Supervisor: Prof Pete Williams

Contact: pwilliams@cera.org.au

Co-supervisor(s): Dr Flora Hui, Dr Andrea Brancale

Nanoparticle functionalization of NMNAT2-targeted small molecules

Suitable for: Honours

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

As part of a wider collaboration, we are developing new strategies to enable efficient drug delivery. This includes functionalization of small molecules in nanoparticle formulations and encapsulation strategies. The key tasks will be primarily in vitro cell work, assay development, and some chemistry and statistics. This project is ideal for a student with an interest in drug development and chemistry.

Key reading:

- https://pubmed.ncbi.nlm.nih.gov/39048544/
- https://pubmed.ncbi.nlm.nih.gov/41982735/
- https://pubmed.ncbi.nlm.nih.gov/32290273/

Other key personnel:

- Flora Hui (CERA, co-supervisor)
- Alan Nicol (University of Melbourne PhD student)
- Andrea Brancale (UCT Prague, external collaborator)
- Georgios Sotiriou (Stockholm University, external collaborator)

Primary Supervisor: Prof Pete Williams **Contact:** pwilliams@cera.org.au

Co-supervisor(s): Dr Flora Hui, Dr Andrea Brancale

Switchable NMNAT2 gene therapies

Suitable for: Honours

Project Location:

Centre for Eye Research Australia

University of Melbourne Enrolling Department:

Medicine (St Vincent's Hospital)

We are developing NMNAT2 gene therapies that provide neuroprotection. Gene therapy has succeeded in monogenic eye diseases (i.e. replacing an absent or mutated gene). However, there is a barrier to regulatory acceptance for genes targeting common pathways (e.g. 'always on' genes producing a dynamic product such as NAD). We will utilize a 'switchable' gene therapy system, a sophisticated means of regulating protein expression following gene therapy. The key tasks will be primarily in vitro cell work, microscopy, and some statistics. This project is ideal for a student with an interest in cell biology and gene therapy.

Key reading:

- https://pubmed.ncbi.nlm.nih.gov/28209901/
- https://pubmed.ncbi.nlm.nih.gov/39048544/
- https://pubmed.ncbi.nlm.nih.gov/32935224/

Primary Supervisor: Prof Pete Williams **Contact:** pwilliams@cera.org.au

Co-supervisor(s): Dr Flora Hui, Prof Rick Liu

Novel ATP boosting PQQ prodrugs

Suitable for: Honours

Project Location: *Centre for Eye Research Australia*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Pyrroloquinoline quinone (PQQ) is an essential nutrient that plays a critical role in cellular energy metabolism and mitochondrial function. We have demonstrated that PQQ drives ATP synthesis in the CNS and mitigates mitochondrial stress in vivo, and is gero- and metabo- protective in C. elegans. In our original mouse and rat in vivo experiments, neuroprotection was limited to doses close to the known toxicity limits. To address this we are developing new PQQ formulations which include PQQ prodrugs and encapsulation strategies. The key tasks will be primarily in vitro cell work, mitochondrial / metabolic assays, and some microscopy and statistics. This project is ideal for a student with an interest in drug development, chemistry, and mitochondrial biology. Key reading:

Primary Supervisor: Prof Pete Williams **Contact:** pwilliams@cera.org.au

Co-supervisor(s): Dr Isabel Lopez Sanchez, Dr Andrea Brancale

Oxidant signalling in ocular injury and scarring

Suitable for: Honours or Master of Biomedical Science

Project Location: *Centre for Eye Research Australia*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Scarring and fibrosis can occur after eye injury, inflammation or surgery and may contribute to impaired vision. This project will use laboratory based ocular cell models to investigate how wound healing and pro-scarring signals influence cellular stress, cell activation, extracellular matrix production and tissue remodelling. The project will also explore whether selected non-cytotoxic interventions can reduce excessive scarring responses.

The student will gain experience in cell culture, wound healing assays, drug treatment, live cell imaging, fluorescence based cellular stress assays, qPCR, Western blotting, ELISA, immunostaining, high-content fluorescence imaging, microscopy, quantitative image analysis and basic statistical data analysis. Depending on project direction and feasibility, the project may also include 2D/ 3D culture models, protein based analysis of secreted inflammatory fibrotic factors and assessment of tissue responses in relevant preclinical ocular models.

Primary Supervisor: Dr Manisha Shah **Contact:** mshah@cera.org.au

Co-supervisor(s): Dr Greg Dusting

Corneal scarring due to severe microbial keratitis: a retrospective medical records study

Suitable for: Honours

Project Location: *Centre for Eye Research Australia*

University of Melbourne Enrolling Department: *Medicine (St Vincent's Hospital)*

Microbial keratitis (MK) is a leading cause of irreversible blindness worldwide. Severe cases of microbial keratitis result in corneal ulceration, scarring (CS) and permanent vision loss. In Australia, MK leads to a

significant cost to the health care system and individuals. MK CS cases are routinely referred to major eye centres such as the Royal Victorian Eye and Ear Hospital (RVEEH) in Melbourne. Understanding the demographics of patients, common types and geographical distributions of causative organisms, the diagnostic timeline, and the effectiveness of current treatment strategies is essential in informing and developing treatment guidelines for a specific region and patient demographic. Applicant to this program must have completed statistics as their electives in the undergraduate degree, and previous experience in RedCap instrument design, Medicine (MD pathway) and data science would be beneficial. The applicant should have a minimal WAM of 75.

Primary Supervisor: Dr Gink Yang **Contact:** gyang@cera.org.au

Co-supervisor(s): Prof Mark Daniell, A/Prof Elaine Chong