MONASH University | ARMI AUSTRALIAN REGENERATIVE MEDICINE INSTITUTE

STUDENT RESEARCH PROJECTS 2024


ARMI
AUSTRIAN REGENERATIVE MEDICINE INSTITUTE

Research at ARMI is structured along five integrated Discovery Pipelines that allow research groups to explore specific aspects of the regenerative process.

HEART AND MUSCLE DEVELOPMENT AND REGENERATION

Cardiovascular diseases are the number one cause of death globally: more people die annually from CVDs than from any other cause. An estimated 17.9 million people died from CVDs in 2016, representing 31% of all global deaths. Of these deaths, 85% are due to heart attack and stroke.

ARMI researchers are studying animals with highly sophisticated and specific tissue regenerative qualities, to develop cures for heart disease and other muscular disorders including dystrophies that can be translated to the patient bed-side.

IMMUNITY AND REGENERATION

Soon after birth, our own immune systems mature and we lose our capacity to respond to damage with scar free healing. ARMI scientists are exploring the relationships between immunity and regeneration in the animal kingdom to enhance tissue repair in patients with wounds or degenerative diseases.

STEM CELLS AND REGENERATION

Stem cells are integral to the development of tissues in the embryo and persist in adults as essential building blocks for our bodies. ARMI studies embryonic stem cells as a window on the mechanisms of human development, and as an essential part of the tool kit of regenerative medicine.

ARMI has devised methods for growing stem cells that can be used to repair damaged tissue, investigate particular diseases, test drug candidates for therapeutic safety and effectiveness, and develop ways to enhance the intrinsic mechanisms of stem-mediated repair. ARMI is able to offer IP on specific stem cells for culturing and scale up and models that allow testing of stem cell potency.

NEURAL REGENERATION

Unlocking the regenerative potential in the central nervous system so it can be harnessed to treat neurodegenerative disorders.

ARMI scientists are tackling the fundamental obstacles in neural repair for diseases such as multiple sclerosis and Alzheimer's, by uncovering neural regenerative potential across the animal kingdom.

ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

ARMI is exploring a number of innovative techniques to enhance function and form that is lost as a consequence of ageing and degenerative diseases.

These techniques explore various aspects of tissue engineering including organoid and organ on a chip technology, bioactive biomaterials and biointerfaces that simulate the cellular microenvironment at the micro and nanoscale, functional biomaterials and synthetic and biological matrices for tissue engineering and transplant development.

DRIVING REGENERATIVE SCIENCE

ARMI was established in 2006 to deliver on this medical research field's promising work of harnessing the healing power of stem cells to unlock the body's own potential to heal and regenerate damaged organs or tissues caused by disease, injury or genetic conditions.

A research institute of Monash University's Faculty of Medicine, Nursing and Health Sciences, ARMI is located at one of the world's largest regenerative medicine and stem cell research centres at Clayton in Victoria, Australia.

The Institute was established through a joint venture between Monash University and the Victorian State Government with additional funding from the Australian Federal Government. ARMI today acts as a focus for public engagement in regenerative medicine and is the source of advice for policymakers.

The Institute builds on Monash University's existing strengths in biomedical research, and the work of the University's pioneers in IVF and stem cells, to attract global regenerative science leaders and a new generation of young and creative researchers; to inspire and lead discoveries and developments in this exciting new therapeutic field.

ARMI's science focuses on delivering the next generation of discoveries in regenerative medicine. The Institute is actively engaged in the emerging area of systems biology, or "systems medicine" – the study of biological components, be it molecules, cells, organisms or entire species – which views the dynamic systems of the human body as an integrated whole, incorporating biomedical, physiological, and environment interactions that sustain life.

This research takes a new approach to clinical problems.

Some species in the animal kingdom have high regenerative potential. ARMI researchers are learning about this ability for self-repair in order to develop new therapies for conditions such as heart disease, muscular dystrophy, diabetes, multiple sclerosis, Alzheimer's Disease, brain injury and autoimmune disorders.

The Institute is one of the largest regenerative medicine and stem cell research organisations in the world and Australia's only research institute specialising in regeneration and stem cells; with a broad program across five overlapping key research streams:

- neural regeneration
- stem cells, cancer and regeneration
- heart and muscle development and regeneration
- immunity and regeneration
- organ engineering and synthetic biology

The Institute trains the next generation of research and clinical scientists.

Most ARMI researchers are based at Monash University's Clayton campus with some having joint appointments with other Monash academic department or the CSIRO. Some of the Institute's research is undertaken through participation in national initiatives including Stem Cells Australia and the EMBL Australia Partner Laboratory.

OUR RESEARCH TEAMS

HEART AND MUSCLE DEVELOPMENT AND REGENERATION

CURRIE GROUP

The Currie group is curious about the biological mechanisms of the Zebrafish, a fresh water fish that is native to South East Asia. Zebrafish are used in scientific research to understand human genetics and the biological processes of human diseases.

The Currie group use zebrafish embryos to learn about muscle cell types. In particular, they are interested in how specific muscle cell types are determined within the developing embryo, how they grow and how they regenerate after injury, to provide insights into muscle wasting and other diseases including the dystrophies.

MCGLINN GROUP

The McGlinn Group is interested in how genes influence the pattern mechanisms of the vertebrate skeleton. Pattern formation refers to how particular cells develop into final cell types.

The group use the limb bud and axial skeleton as points of study because it helps them understand broader developmental processes. A greater level of comprehension into the limb bud and axial skeleton will allow the group to provide insight into how genetic hierarchies govern how the vertebrate skeleton is formed. This work has developed an understanding of how to grow and shape different tissue for therapeutic benefit.

DEL MONTE NIETO GROUP

The del Monte-Nieto group is interested in the study of the molecular mechanisms and developmental processes orchestrating normal heart development in embryos by integrating all the cellular and non-cellular components involved.

The lab aims to apply multidisciplinary approaches including mathematical modeling and bioengineering to developmental biology studies in order to generate in silico and in vitro models to confirm our biological results and formulate new hypothesis. The group aims to apply multidisciplinary approaches including mathematical modeling and bioengineering to developmental biology studies in order to generate in silico and in vitro models to confirm our biological results and formulate new hypothese to design novel therapies for heart disease.

CHOW GROUP

The Chow group is interested in the study of heart valve development, disease, and regeneration. The lab develops novel micromanipulation methods to perturb mechanical forces in the zebrafish heart and combines these methods with computational modelling, live imaging, and genetics to uncover the role of mechanical signals caused by heartbeat and blood flow on heart valve biology.

EYNON GROUP

The Eynon Group is interested in the study of epigenetics and other molecules associated with healthy aging and exercise. The group investigates the role of epigenetics in ageing and exercise adaptations, as well as sex differences in response to exercise. The lab uses a combination of wet-lab and bioinformatics analyses, with a particular focus on ‘omics’ datasets including DNA methylation, transcriptomics and proteomics.

IMMUNITY AND REGENERATION

LIESCHKE GROUP

The Lieschke group studies the haemopoietic system and leukocytes.The haemopoietic system is a collection of organs and tissues (bone marrow, spleen, lymph nodes etc.) responsible for the production of blood in the body.

Leukocytes (white blood cells) are the keys cells involved for counteracting foreign substances and disease. They also play a major role in determining whether tissue repairs and regenerates rather than scars after injury. The group's increased understanding of the role of the leucocytes when the immune system is compromised, eg as in leukemias has helped identify potential target molecules.

MARTINO GROUP

Dr Mikaël Martino and his group focusses on the immune regulations of stem cells and regeneration, seeking to design regenerative medicine strategies integrating a control of the immune system.

Compounds that can accelerate regenerative processes in a wide range of tissues and organs are being identified and evaluated.

STEM CELLS AND REGENERATION

NAGY GROUP

The Nagy Group is focused on combining knowledge of developmental biology, stem cells and genetic engineering to create successful therapeutics for regenerative medicine applications.

The group's research program also aims to tackle several major challenges facing the translation of cell therapies to the clinic, such as generating and improving the effectiveness of therapeutic cells and eliminating risks of tumorigenesis.

NILSSON GROUP

The Nilsson Group is currently involved in a number of research projects that focus on understanding haemopoietic stem cells (HSC). Haemopoietic stem cells are responsible for the production of blood and immune cells.

The main objective of the group's research is to characterise the microenvironment in which blood stem cells reside. They also look at blood stems cells at a cellular and molecular level, as well as analysing how they create new blood cells.

This can be used to treat a range of blood diseases including leukemia.

ZENKER GROUP

The Zenker group seeks to understand how a cell's structure and function is regulated by the continuous re-organization of the microtubule network. Live imaging is used to discover the spatio-temporal accuracy of the microtubule dynamics in animal models of developmental and stem cell biology. Understanding the formation of the first stem cells in embryos is leading to insights into how these cells can be harnessed for therapeutic benefit.

NEURAL REGENERATION

KASLIN GROUP

The Kaslin group is interested in cellular plasticity, which is the ability of cells to take on characteristics of other cells in the body. But rather than study the process throughout the entire body, the group are focused in understanding the molecular and cellular mechanisms that control this process in the intact or injured vertebrate brain.

Understanding the process of cellular plasticity is essential to the development of successful therapies to promote neural regeneration.

NILLEGODA GROUP

The Nillegoda group is probing attractive new proteostasis-based directions for future therapeutic interventions that could potentially slow and/or reverse neurodegeneration and are applicable for a broad range of disorders from Alzheimer's disease to Multiple sclerosis.

ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

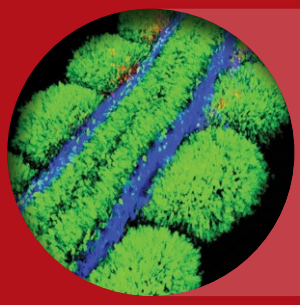
ROSSELLO-DIEZ GROUP

The Roselló-Díez group studies the signals that operate within the bones and between them and other tissues/organs during development and regeneration. At the local level, they study phenomena such as compensatory proliferation in response to biochemical and mechanical changes in the cell vicinity. At the systemic level, they are exploring the role of the vascular and nervous systems in the bidirectional communication between the bones and the rest of the body. The group has devleoped insights into growth regulation in the developing body enabling the design of therapeutics for situations where tissue growth and organ repair is perturbed.

ROMAN GROUP

The Roman Group is investigating how cells communicate to establish organ architecture and function. We use the skeletal muscle cell as a model to study cell-cell interactions by focusing on specialized regions such as the neuromuscular junction or the stem cell niche. Combining microscopy, tissue engineering and spatial genomics, we can monitor intercellular signals with high spatiotemporal resolution during development or homeostasis and observe how these are affected in diseases and ageing. The lab aims to identify fundamental principles of intercellular communication as well as translational discoveries to improve muscle disorders and ageing.

ARMI DISCOVERY PIPELINES

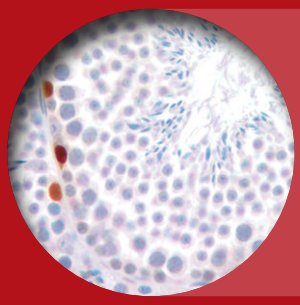


HEART AND MUSCLE DEVELOPMENT AND REGENERATION

Currie	www.armi.org.au/research-leadership/currie-group
McGlinn	www.armi.org.au/research-leadership/mcglinn-group
del Monte Nieto	www.armi.org.au/research-leadership/del-monte-nieto-group
Chow	www.armi.org.au/our-groups/chow-group
Eynon	www.armi.org.au/our-groups/eynon-group

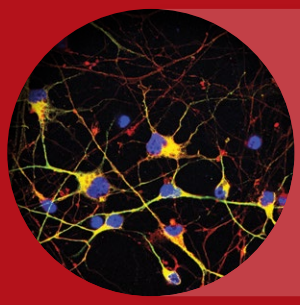
IMMUNITY AND REGENERATION

Lieschke	www.armi.org.au/research-leadership/lieschke-group
Martino	www.armi.org.au/research-leadership/martino-group



STEM CELLS AND REGENERATION

Nagy	www.armi.org.au/research-leadership/nagy-group
Nilsson	www.armi.org.au/research-leadership/nilsson-group
Zenker	www.armi.org.au/research-leadership/zenker-group



NEURAL REGENERATION

Kaslin	www.armi.org.au/research-leadership/kaslin-group
Nillegoda	www.armi.org.au/research-leadership/nillegoda-group

ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

Rossello-Diez	www.armi.org.au/research-leadership/rossello-diez-group
Roman	www.armi.org.au/our-groups/roman-group

WHY STUDY AT ARMI?

- Our Higher Degree by Research (HDR) and Honours programs attract talented students from Australia and abroad.
- Our students reflect ARMI's international perspective with students from Malaysia, Singapore, The Netherlands, Mexico, Iran and Sri Lanka.
- The highly collaborative, interdisciplinary nature of the ARMI research program exposes students to cutting edge science in our laboratories.
- Students are supported to engage in career building opportunities in Australia and overseas.

ARMI'S VISION IS FOR TODAY'S STUDENTS TO BE TRAINED TO AN EXCEPTIONALLY HIGH STANDARD, TO BE THE NEXT GENERATION OF SCIENTIFIC LEADERS.

HOW TO APPLY FOR HONOURS AT ARMI

Students from the following fields of study are encouraged to apply to do an Honours project at ARMI Biomedical Sciences:

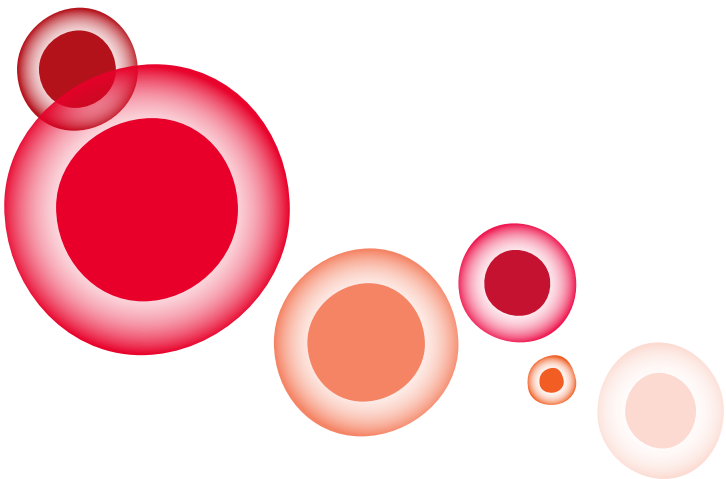
- Science
- Medical Science
- Health Science
- Engineering
- Pharmacy.

The next step is to contact the Group Leaders to discuss the project further.

Current projects are listed below in this booklet or to suggest your concept for a project, please contact one of our research group leaders. All are happy to meet with potential honours students.

Once you and your supervisor have agreed on a project:

1. **Your supervisor will need to fill out an ARMI Honours EOI undertaking to be your supervisor and stating the name of the project.**
2. **Prepare a copy of your transcript highlighting the subjects you wish to be considered for entry.**
3. **Submit completed ARMI Honours EOI, Faculty and transcript to the ARMI Honours Coordinator for approval.**
4. **Complete the relevant faculty's online application form**
   BMS Students: https://www.monash.edu/discovery-institute/honours
   Science Students: www.monash.edu/science/current-students/science-honours/



ELIGIBILITY CRITERIA FOR HONOURS

Completion of a Bachelor's degree in either Science or Biomedical Science.

If you are a BSc student, you need an average of at least 70% in four relevant third year units.

BMS students need an average of at least 70% across BMS3021, BMS3042 and the two highest level 3 electives.

How to apply:

BMS students must enrol directly through the Med Faculty for BMS Hons.

An application form can be found at: https://www.monash.edu/discovery-institute/honours

BMS Honours Students must enrol for the following units:

- BMS4100 Biomedical science research project
- BMS4200 Advanced studies in biomedical science.

BSc students enrol through the Science Faculty for BSc Hons.

Application details can be found at: http://www.monash.edu/science/current-students/science-honours

BSc Honours Students must enrol for the following Regenerative medicine units:

- MIS4100 Regenerative medicine research project (36 points)
- MIS4200 Advanced studies in regenerative medicine (12 points).

RESEARCH GROUPS
HEART AND MUSCLE DEVELOPMENT AND REGENERATION

CURRIE GROUP

Research Themes:

- Dissecting molecular mechanisms that act to pattern the vertebrate embryo
- Discovering how specific muscle cell types are determined within the developing embryo
- Discovering how different muscle cell types have evolved
- Determining how muscle types cells grow and regenerate after injury
- Large-scale mutagenesis of the zebrafish genome to produce different classes of mutations which disrupt gene function.

Project title	**Understanding the mechanisms regulating sarcopenia using zebrafish**
Project summary	Sarcopenia, the age-related decline in muscle mass and function, places a great burden on the health care system. Despite this, very little is known about the molecular pathways that drive this process. This project will therefore elucidate the mechanisms that regulates sarcopenia, focusing on the muscle stem cell niche.
Main techniques	Using the advantages of the zebrafish model system combined with live imaging and confocal microscopy, immunofluorescence, CRISPR/Cas9 genome editing, genetic and physiology techniques
Group leader	Prof Peter Currie
Supervisor	Avnika Ruparelia

DEL MONTE-NIETO GROUP

Research Themes:

- To study the molecular mechanisms and developmental processes controlling heart development.
- To understand the molecular and cellular etiology of Congenital Heart Disease.
- To study ECM composition/patterning during heart development, adulthood and disease/injury models.
- To develop computational models for the different developmental processes in the heart.
- To apply the knowledge generated from developmental biology to improve heart regeneration, organ-on-a-chip technologies and tissue engineering.

Project title	**Study of the EndMT process during cardiac valve development**
Project summary	The project aims to investigate in detail the process of EndMT taking place during cardiac valve formation in the developing embryo. We will identify the specific cells activating this process, the cellular behaviours controlling this process, the molecular regulation activated in the cells undergoing EndMT and how the surrounding cells maintain the integrity of the endocardial layer.
Main techniques	Embryo dissection, tissue embedding in paraffin and microtome sectioning, histological staining, immunofluorescence and in situ hybridization in wholemount samples and sections, qPCR, 3D and 4D light-sheet/two-photon microscopy imaging, 3D reconstructions and 2D and 3D image quantification.
Group leader	Dr Gonzalo del Monte Nieto
Supervisor	Dr Gonzalo del Monte Nieto

Project title	**Study of the process of atrial development**
Project summary	The project aims to investigate the process by which the atrial chambers form during embryonic development. We will apply the new notions described in our recent study (del Monte-Nieto et al., Nature 2018) on ventricular chamber development to determine the cellular behaviours, ECM dynamics and molecular regulation controlling atrial development.
Main techniques	Embryo dissection, tissue embedding in paraffin and microtome sectioning, histological staining, immunofluorescence and in situ hybridization in wholemount samples and sections, qPCR, 3D and 4D light-sheet/two-photon microscopy imaging, 3D reconstructions and 2D and 3D image quantification.
Group leader	Dr Gonzalo del Monte Nieto
Supervisor	Dr Gonzalo del Monte Nieto

RESEARCH GROUPS
HEART AND MUSCLE DEVELOPMENT AND REGENERATION

MCGLINN GROUP

Research Themes:

- microRNA control of Hox gene networks
- Genomic/epigenomic regulation of axis elongation and vertebral patterning
- Formation and patterning of spinal cord circuitry
- Evolutionary acquisition of microRNAs shapes developmental networks

Project title	**Using ES cells to model formation of the vertebral column and spinal cord**
Project summary	Our lab is interested in understanding how early progenitor cells of the embryo make lineage choices between neural and mesodermal cell fate. We use mouse genetics, combined with in vitro ES cell differentiation protocols, to understand gene networks and regulatory mechanisms that guide this process.
Main techniques	ES cell differentiation Quantitative PCR Immunofluorescence
Group leader	A/Prof Edwina McGlinn
Supervisor	A/Prof Edwina McGlinn

Project title	**Signals controlling formation of the head and face**
Project summary	The formation of the head and face is a tightly regulated process, with gene defects and environmental insults both contributing to craniofacial defects. We have established a mouse model of craniofacial malformation that shows cleft lip and cleft palate upon inhibition of the retinoic acid pathway. Strikingly, removing the *Gdf11* gene in this context is able to rescue these craniofacial defects. We are investigating the mechanisms underlying this genetic interaction, with the aim of harnessing this observation for therapeutical purposes.
Main techniques	Mouse genetics, micro computed tomography (µCT), light-sheet microscopy, *in situ* hybridisation, embryonic stem cell and neural crest cell cultures, RNA sequencing.
Group leader	Associate Professor Edwina McGlinn
Supervisor	Dr Jan Manent

Project title	**microRNA control of developmental haematopoiesis**
Project summary	Developmental haematopoiesis, the process by which all blood cell types arise in the vertebrate embryo and are maintained throughout adult life, is a tightly regulated process. We have uncovered a novel and important role for a specific microRNA family in developmental haematopoiesis. We are using state of the art mouse genetics, microscopy, flow cytometry and in vitro stem cell differentiation techniques to characterise the function of this microRNA family, with the ultimate goal to harness this discovery for therapeutical purposes.
Main techniques	Mouse genetics, flow cytometry, confocal and light-sheet microscopy, embryonic and hematopoietic stem cell cultures, RNA sequencing.
Group leader	Associate Professor Edwina McGlinn
Supervisor	Dr Jan Manent

CHOW GROUP

Research Themes:

- Heart valve development, disease, and regeneration
- Mechanobiology
- Cell-based therapies (endothelial progenitor cells)

Project title	**The role of mechanical forces on heart valve development**
Project summary	The embryonic heart beats even as it is forming. Using the zebrafish as an animal model, this project aims to determine how mechanical forces due to heart beat and blood flow affect the ability of cell clusters to separate from each together and form heart valves.
Main techniques	Micromanipulation, microscopy, zebrafish husbandry
Group leader	Renee Chow
Supervisor	Renee Chow

Project title	**What's sex got to do with it?**
Project summary	Males and females have different clinical presentations of heart valve disease, as well as different responses to treatment. This project aims to develop a humanized zebrafish model of heart valve disease and to determine if sex hormones could affect the ability of endothelial progenitor cells to repair heart valves.
Main techniques	Culturing cells from human blood, ultrasound imaging of adult fish hearts, making transgenic zebrafish lines.
Group leader	Renee Chow
Supervisor	Renee Chow

Project title	**The role of Nfatc1 on heart valve development**
Project summary	This project aims to develop a novel zebrafish transgenic line to temporally control Nfatc1 activity and use it determine how Nfatc1 activity impacts gene expression and cell migration during heart valve development.
Main techniques	Zebrafish husbandry, microscopy, making transgenic zebrafish lines, molecular and cell biology.
Group leader	Renee Chow
Supervisor	Renee Chow

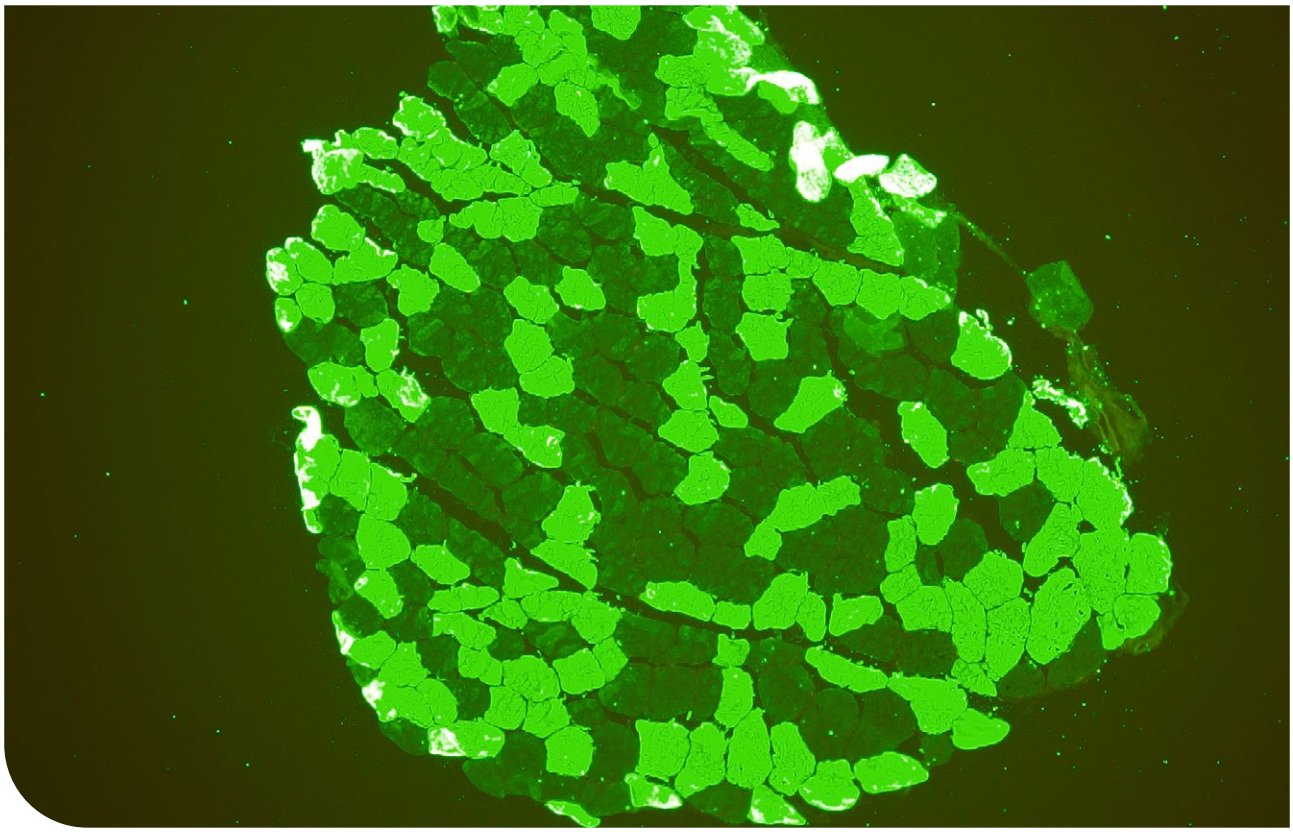
RESEARCH GROUPS
HEART AND MUSCLE DEVELOPMENT AND REGENERATION

EYNON GROUP

Research Themes:

- Epigenetics and adaptation to exercise in health and disease
- Epigenetics, Gene and Proteins expression and aging
- Exercise and muscle physiology

Project title	**Uncovering molecules associated with healthy ageing and exercise responses**
Project summary	This project aims to uncover sex-specific molecular marks that either predict or mediate healthy ageing and exercise responses in muscle.
Main techniques	Human exercise trials to measure fitness outcomes (VO_2 max and strength) and molecular outcomes via analysis of blood and muscle samples. Techniques used for molecular analysis include muscle cross-sectional area and fibre type using immuno-histochemistry, preparation and analysis of 'omics' datasets including methylation, transcriptomics and proteomics. In addition, we use Bioinformatics techniques for data analyses.
Group leader	Professor Nir Eynon
Supervisors	Professor Nir Eynon Dr Megan Taylor



RESEARCH GROUPS
IMMUNITY AND REGENERATION

LIESCHKE GROUP

Research Themes:

- Discovery of genes critical for white blood cell development
- How the inflammatory response is regulated
- How modulating the inflammatory white blood cells might tip the outcome to favour regeneration rather than scarring
- Investigating how white blood cells keep out and contain micro-organisms.

MARTINO GROUP

Research Themes:

- Dissecting how the innate immune system affects tissue-resident/transplanted stem cells and growth factors activities.
- Understanding the immune modulations of stem cells and regeneration by T lymphocytes.
- Developing effective systems for delivering stem cells and cytokines/growth factors, using biomaterials and protein engineering.

Project title	**Engineering myeloid cell-targeting cytokines to improve tissue regeneration**
Project summary	The goal of this project is to engineer immunomodulatory cytokines with therapeutic potential to specifically target myeloid cells (e.g. neutrophils, monocytes, macrophages) within injured tissues in order to promote a pro-regenerative immune microenvironment. These therapeutic protein candidates will be recombinantly produced in the laboratory and tested *in vitro* using cell culture methods to verify their activity, as well as *in vivo* using mouse skin and/or muscle injury models to assess their overall capacity to promote tissue regeneration. This novel approach has the potential to create powerful immune-centric regenerative therapies and may form the foundation of a future PhD project.
Main techniques	Protein engineering; recombinant protein production; cell culture; mouse injury models.
Group leader	A/Prof. Mikaël Martino
Supervisors	A/Prof. Mikaël Martino Dr Julien Legrand

RESEARCH GROUPS
STEM CELLS AND REGENERATION

NILSSON GROUP

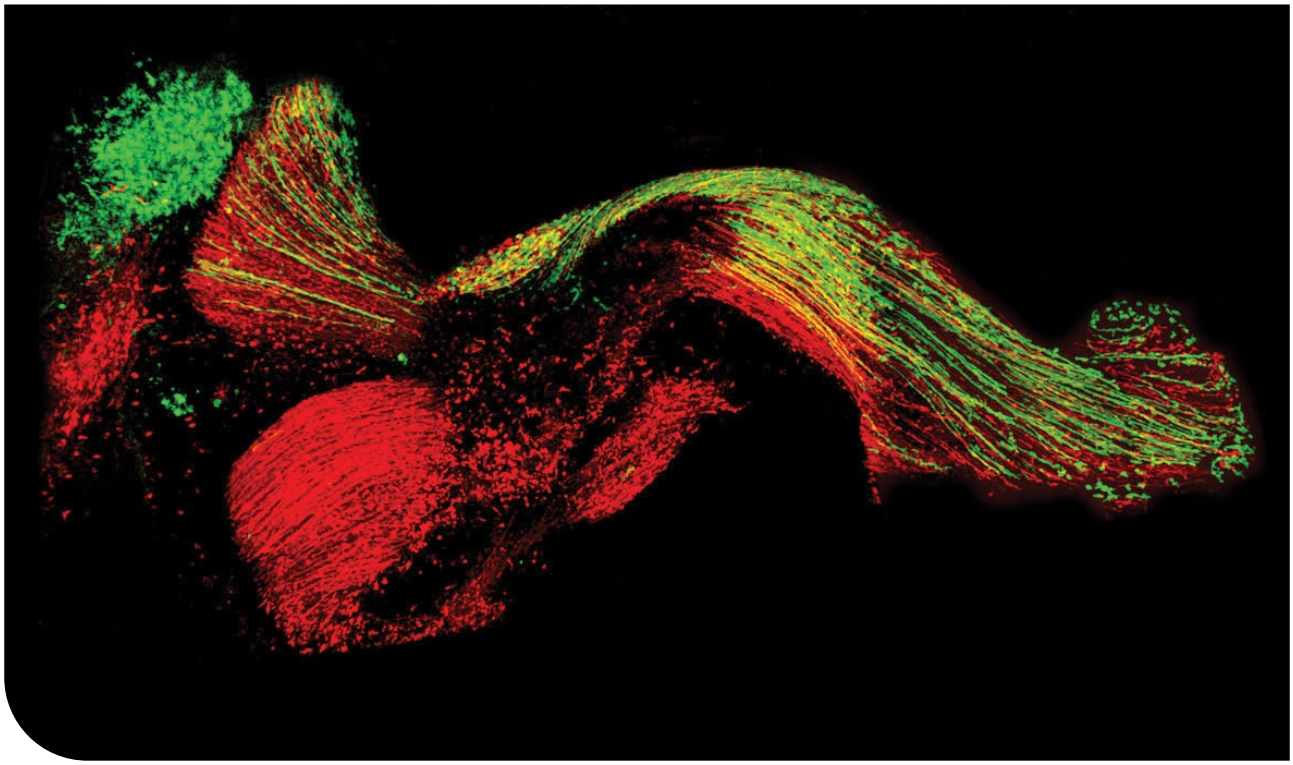
Research Themes:

- Understanding the role of the endosteal niche in the regulation and function of haemopoietic stem cells
- Characterising the role of megakaryocytes in the endosteal niche and haemopoietic stem cell regulation
- Isolating bone marrow sinusoidal endothelial cells and characterising their role and potential
- Understanding the role of key extracellular matrix molecules in the adult bone marrow microenvironment in foetal haemopoietic development
- Design and synthesis of novel haemopoietic stem cell mobilisation agents
- Characterising adult cells that have been directly differentiated into hemopoietic stem cells.
- Functionally assessing embryonic stem cell subpopulations whose differentiation has been directed towards hemopoietic stem cells.

NAGY GROUP

Research Themes:

- Transferring and establishing our patented safety and immune “cloaking” technologies in non-human primate pluripotent stem cells
- Developing protocols to differentiate pluripotent stem cells into therapeutic cell types
- Combining cell and gene therapy to target key cytokines involved in central nervous system autoimmunity
- Functional validation of cells engineered with our immune “cloaking” system
- Testing designer cells in pre-clinical models of stroke and multiple sclerosis

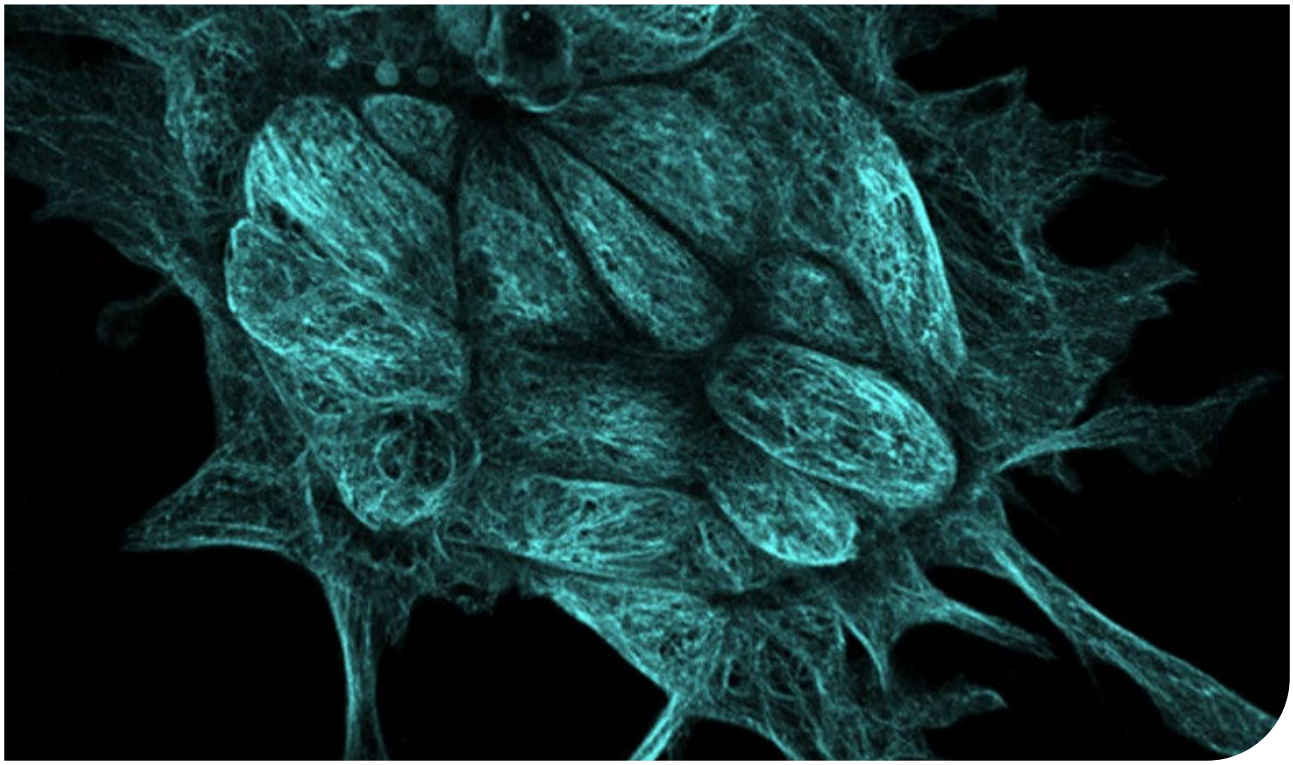


ZENKER GROUP

Research Themes:

- The establishment of new methods to visualize and manipulate the microtubule dynamics in complex 3D model systems
- To determine how the microtubule architecture regulates early embryonic development
- To uncover the role of the inner skeleton in stem cell plasticity

Project title	**Visualising microtubule remodelling in pluripotent cells**
Project summary	Pluripotent cells hold an incomparable potential for regenerative medicine by being able to be transformed into any cell type the adult body is made of. They can be found in the early mammalian embryo or be produced in a dish as induced pluripotent stem cells (iPSCs). The overall aim of this project is to unravel how the architecture of the microtubule cytoskeleton regulates pluripotency and the subsequent differentiation processes of such cells. To address this question, the inner skeleton of pluripotent cells in the living mouse embryo or human iPSCs will be fluorescently labelled. The real-time changes of the microtubule network will be imaged as the pluripotent cells start to differentiate in the developing embryo or *in vitro*. The specific aims are to determine the origin, speed and directionality of microtubule growth and the functional consequences in pluripotent versus differentiated cells.
Main techniques	Live imaging, cloning, cell culture, mouse embryo handling, computational image analysis.
Group leader	Jennifer Zenker
Supervisor	Jennifer Zenker



RESEARCH GROUPS
NEURAL REGENERATION

KASLIN GROUP

Research Themes:

- Understanding the molecular and cellular mechanisms that control cellular plasticity in the intact and injured vertebrate brain
- How neuronal stem cell niches arise and are being maintained, using high-resolution in vivo imaging, novel genetic tools and cellular reprogramming
- Using high-throughput methods to get a comprehensive understanding of the genetic networks that regulate cellular plasticity during homeostasis and regeneration.

Project title	**Evolution of spinal cord regeneration in vertebrates**
Project summary	In this project we aim to define how the ability to regenerate axons and neurons originated during evolution. In particular, we aim to identify the ground plan by using elasmobranch models (sharks).
Main techniques	Vertebrate models (fish, sharks and avian). Diverse imaging techniques, cloning, in situ hybridisation, immunohistochemistry, genetic tools.
Group leader	Dr Jan Kaslin
Supervisors	Dr Mitra Amiri Dr Frank Tulenko

Project title	**Architectural transcription factors in controlling metabolism and neural stem cells**
Project summary	In this project we examine how architectural transcription factors control neural stem cells during development and after injury. The architectural transcription factor expression is induced after tissue injury and is pivotal in stem cell control.
Main techniques	Zebrafish model. Diverse imaging techniques, genetic tools and molecular techniques. In vitro models and biochemical assays.
Group leaders	Dr Jan Kaslin Dr Minni Anko (Hudson)
Supervisor	Dr Jan Kaslin

Project title	**Inflammatory control of neurogenesis in the intact and injured brain**
Project summary	In this project we examine how immune cell and glia interaction control neural stem cells during homeostasis and after injury
Main techniques	Zebrafish model. Diverse imaging techniques, genetic tools and molecular techniques. In vitro models.
Group leaders	Jan Kaslin Minni Anko (Hudson)
Supervisor	Dr Jan Kaslin

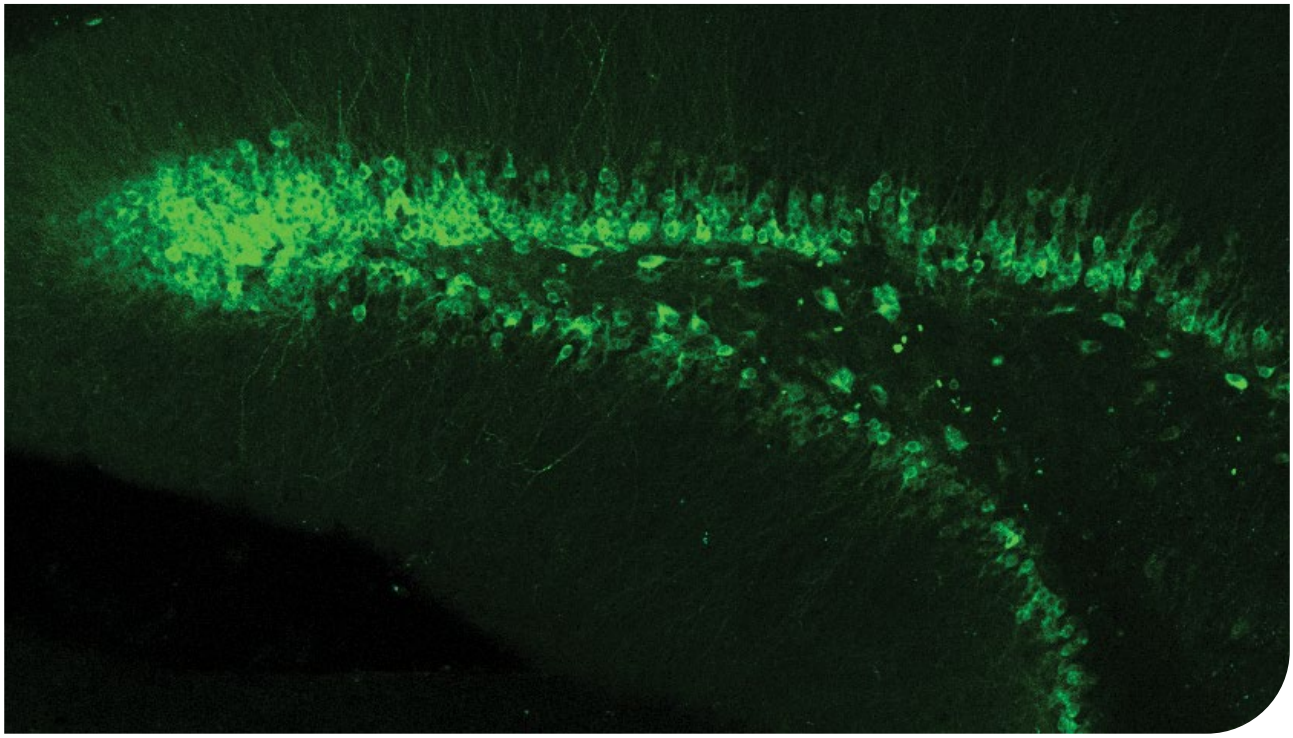
KASLIN GROUP CONT.

Project title	**Investigating genetic components of cerebral palsy**
Project summary	In order to elucidate the so far relatively unknown genetic background of cerebral palsy, this project plans to use zebrafish (danio rerio) and methods like CRISPR/Cas to rapidly screen the previously identified candidate genes for their involvement in the disease. This should help to recognise and understand the underlying molecular pathways, which in return hopefully provides opportunities for prevention and treatment in the future.
Main techniques	CRSIPR/Cas9 genome editing, molecular cloning, behavioural analysis, diverse imaging techniques.
Group leaders	Jan Kaslin Michael Fahey
Supervisor	Dr Samuel Crossman

NILLEGODA GROUP

Research Themes:

- Characterizing the poorly understood role of protein disaggregases in protein conformational diseases in humans
- Dissecting novel regulators of protein disaggregation
- Exploring the J-domain protein (Hsp40)-Hsp70 chaperone networks vital for aggregate clearance in human cells
- Developing methods for capturing molecular dynamics of distinct Hsp70 chaperone machineries in vivo



RESEARCH GROUPS
ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

ROSELLO-DIEZ GROUP

Research Themes:

- Characterising the local cell-autonomous and nonautonomous responses to an injury, including the production and role of alarm signal(s) and the response of stem/progenitor cells
- Dissecting the inter-organ communication mechanisms that lead to systemic growth effects upon local injury, with a focus on the role of the vascular and nervous systems
- Exploring the impact of the discovered injury response pathways on the buffering of developmental noise (random perturbations during normal development)
- Exploiting the discovered injury response pathways for the treatment of animal models of dwarfism and fracture repair

Project title	**Generating rat-mouse chimeras to study limb growth regulation**
Project summary	To determine the control of limb size by intrinsic and extrinsic factors, we plan to generate chimeras in which the limbs are generated from rat pluripotent stem cells injected into mouse embryos that cannot generate the limbs. Anatomical and molecular features of these limbs will be determined and compared with those of normal rat and mouse limbs, to identify key gene regulatory networks that could be used to manipulate limb size in commercial and clinical applications.
Main techniques	Mouse and rat timed mating and embryo collection and dissection, culture of rat embryonic stem cells, histology, immunofluorescence on tissue sections, image analysis.
Group leader	Dr Alberto Roselló-Díez
Supervisors	Dr Alberto Rosello-Diez Xinli Qu

Project title	**Characterising a transient but highly reparative cartilage progenitor in perinatal mice**
Project summary	Long bones grow by forming a cartilage template that provides a scaffold to be replaced by mineralised bone. We have recently identified a cartilage progenitor population that gets mostly extinguished around birth during normal mouse growth, but that expands and lingers for a longer time in response to cartilage injury. We are characterising the origin and role of these progenitors in normal growth and in several models of injury, using single-cell RNA-seq and sophisticated genomics and genetic models
Main techniques	Mouse timed mating and embryo collection, PCR genotyping, flow cytometry, single-cell preparation, bioinformatics analysis.
Group leader	Dr Alberto Roselló-Díez
Supervisors	Dr Alberto Rosello-Diez Ehsan Razmara Shani Amarasinghe

ROMAN GROUP

Research Themes:

- Skeletal muscle cell biology, regeneration, and repair.
- Tissue bioengineering of skeletal muscle organs using iPSCs and microfabrication.
- Intra- and intercellular communication from cell behaviour to genomic response.

Project title	**Performing exercise in a dish to study muscle injuries**
Project summary	Movement is natural to us. From slowly crawling out of bed to the occasional dash to catch the bus, our muscles are hardwired to mechanically comply to our command. It is therefore easy to overlook the extent of the stress and strain they endure as a biological system. And despite an architecture geared for contraction, our muscles are prone to ripping and tearing. In this project, we will mimic the damage that occurs during exercise in in vitro muscle cultures using optogenetics. By reproducing injuries in a dish, we will strip all the barriers separating us from the cells we are observing. This will allow us to monitor how cells repair their damage with unprecedented spatial and temporal resolution. We will first assess how cells change their behavior after damage using a panel of cell biology and microscopy tools. We will also identify which repair genes are upregulated and determine when and where they are expressed using sequencing and imaged-based spatial genomic techniques. The ultimate objective is to find a master regulator of the repair transcriptional program which we can then modulate to preserve muscle function. We will then be able to improve muscle health in myopathies, after exercise and during aging but other outcomes could also surface for in vitro meat production or preserving muscle in space flight.
Main techniques	Tissue engineering, RNA-sequencing, microscopy, cell biology and spatial transcriptomics.
Group leader	William Roman
Supervisor	William Roman

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