



STUDENT RESEARCH PROJECTS 2022





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

	<p>HEART AND MUSCLE DEVELOPMENT AND REGENERATION</p> <p>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.</p> <p>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.</p>
	<p>IMMUNITY AND REGENERATION</p> <p>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.</p>
	<p>STEM CELLS AND REGENERATION</p> <p>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.</p> <p>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.</p>
	<p>NEURAL REGENERATION</p> <p>Unlocking the regenerative potential in the central nervous system so it can be harnessed to treat neurodegenerative disorders.</p> <p>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.</p>
	<p>ORGAN ENGINEERING AND SYNTHETIC BIOLOGY</p> <p>ARMI is exploring a number of innovative techniques to enhance function and form that is lost as a consequence of ageing and degenerative diseases.</p> <p>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.</p>

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.

"Young researchers like to try new things and tend to 'push the envelope' in research. This can lead to greater discoveries and innovation."

Prof James Bourne, Head of the Bourne Research Group, ARMI.

OUR RESEARCH TEAMS



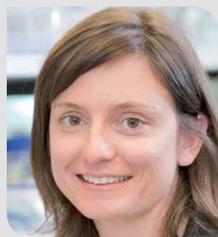
HEART AND MUSCLE DEVELOPMENT AND REGENERATION



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 McGlenn 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.



RAMIALISON GROUP

The Ramialison group is studying development and disease. They are a multidisciplinary team of computational and molecular biologists who specialise in genomics. They conduct their research using new genomic technology and the zebrafish as a model organism.

The group focuses on applying systems biology (the study of biological components, be it molecules, cells, organisms or entire species) to reconstruct the cardiac gene regulatory networks and to work out not only what leads to proper heart formation, but what are the causes of congenital heart disease.



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 hypothesis to design novel therapies for heart disease.

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 key 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 leukocytes 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



LASLETT GROUP

The Laslett group investigate the biology of human pluripotent stem cell lines, including embryonic stem cells (hESC) and human iPS cells.

Further comprehension of human pluripotent stem cell lines will lead to the development of tools and novel cell lines that will be required for the safe use of these cell types in future cell-based industries.

Andrew Laslett and his group are employed by CSIRO and hold adjunct appointments with ARMI.



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.



POLO GROUP

The Polo group is interested in the transcriptional and epigenetic mechanisms that govern cell identity and cell fate, in particular pluripotency and the reprogramming of somatic cells into induced pluripotent stem (iPS) cells and other mature cell types.

Being able to reprogram any specific mature cell into a pluripotent state and then back into any other particular cell gives the group a unique tool to study the molecular and cellular events that permit the conversion of one cell type to another.

This knowledge allows for development of therapies for specific tissue and organs from stem cells.



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



BOURNE GROUP

The Bourne group have garnered an international reputation for being at the forefront of visual neuroscience with a particular emphasis on development, plasticity and repair following injury. The main focus of the group is to study the development and maturation of the cerebral cortex in primates and other mammals. The group explore, at a cellular and system level, how the brain processes the environment, which is rich with visual information.



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.



MERSON GROUP

The Merson group studies the interaction between neurons and glial cells in the central nervous system. A primary focus is understanding the mechanisms that regulate myelination of axons by oligodendrocytes, particularly in response to myelin loss as occurs in multiple sclerosis (MS). The group adopts cutting-edge approaches to identify new therapeutic targets to treat MS. Our core objectives are to optimise myelin regeneration to restore neuronal function rapidly and prevent progressive neurological decline.



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



JANOVJAK GROUP

The Janovjak group combines synthetic biology and physiology to understand and manipulate the behavior of cells in health and disease. By applying physical actuators, such as light or sound, the Group aims to target cells in situ with spatial precision (for instance, selected cells in a tissue or organism) and with temporal precision (for instance, at selected stages during development).

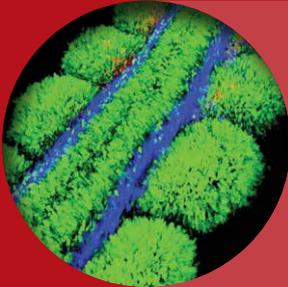
The team is focused on the development of molecular tools for the precise activation or inhibition of cellular signaling pathways and on the application of these tools to tune the balance of cell growth and cell death in animal models.



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 developed insights into growth regulation in the developing body enabling the design of therapeutics for situations where tissue growth and organ repair is perturbed.

ARMI DISCOVERY PIPELINES



HEART AND MUSCLE DEVELOPMENT AND REGENERATION

**Currie
McGlinn
Ramialison
del Monte Nieto**

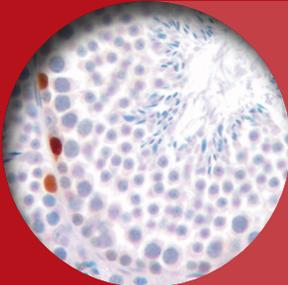
www.armi.org.au/research-leadership/currie-group
www.armi.org.au/research-leadership/mcglinn-group
www.armi.org.au/research-leadership/ramialison-group
www.armi.org.au/research-leadership/del-monte-nieto-group



IMMUNITY AND REGENERATION

**Lieschke
Martino**

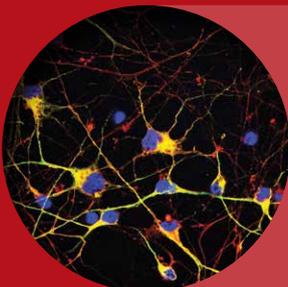
www.armi.org.au/research-leadership/lieschke-group
www.armi.org.au/research-leadership/martino-group



STEM CELLS AND REGENERATION

**Laslett
Nagy
Nilsson
Polo
Zenker**

www.armi.org.au/research-leadership/laslett-group
www.armi.org.au/research-leadership/nagy-group
www.armi.org.au/research-leadership/nilsson-group
www.armi.org.au/research-leadership/polo-group
www.armi.org.au/research-leadership/zenker-group



NEURAL REGENERATION

**Bourne
Kaslin
Merson
Nillegoda**

www.armi.org.au/research-leadership/bourne-group
www.armi.org.au/research-leadership/kaslin-group
www.armi.org.au/research-leadership/merson-group
www.armi.org.au/research-leadership/nillegoda-group



ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

**Janovjak
Rossello-Diez**

www.armi.org.au/research-leadership/janovjak-group
www.armi.org.au/research-leadership/rossello-diez-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:

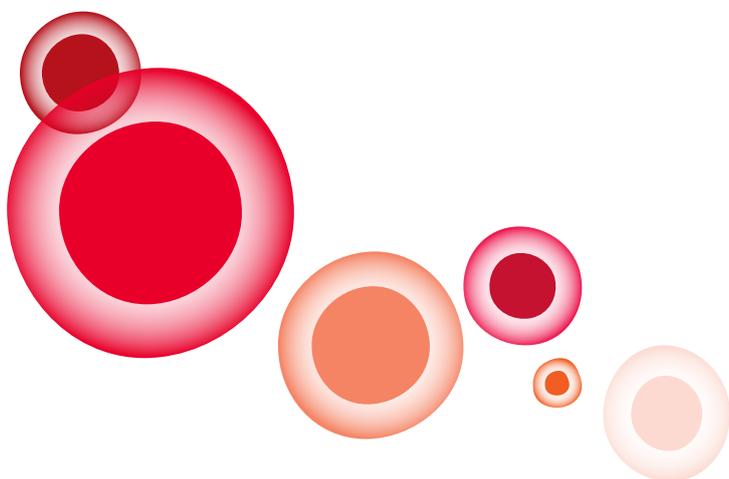
- Science
- Medical Science
- Health Science
- Engineering
- Pharmacy.

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

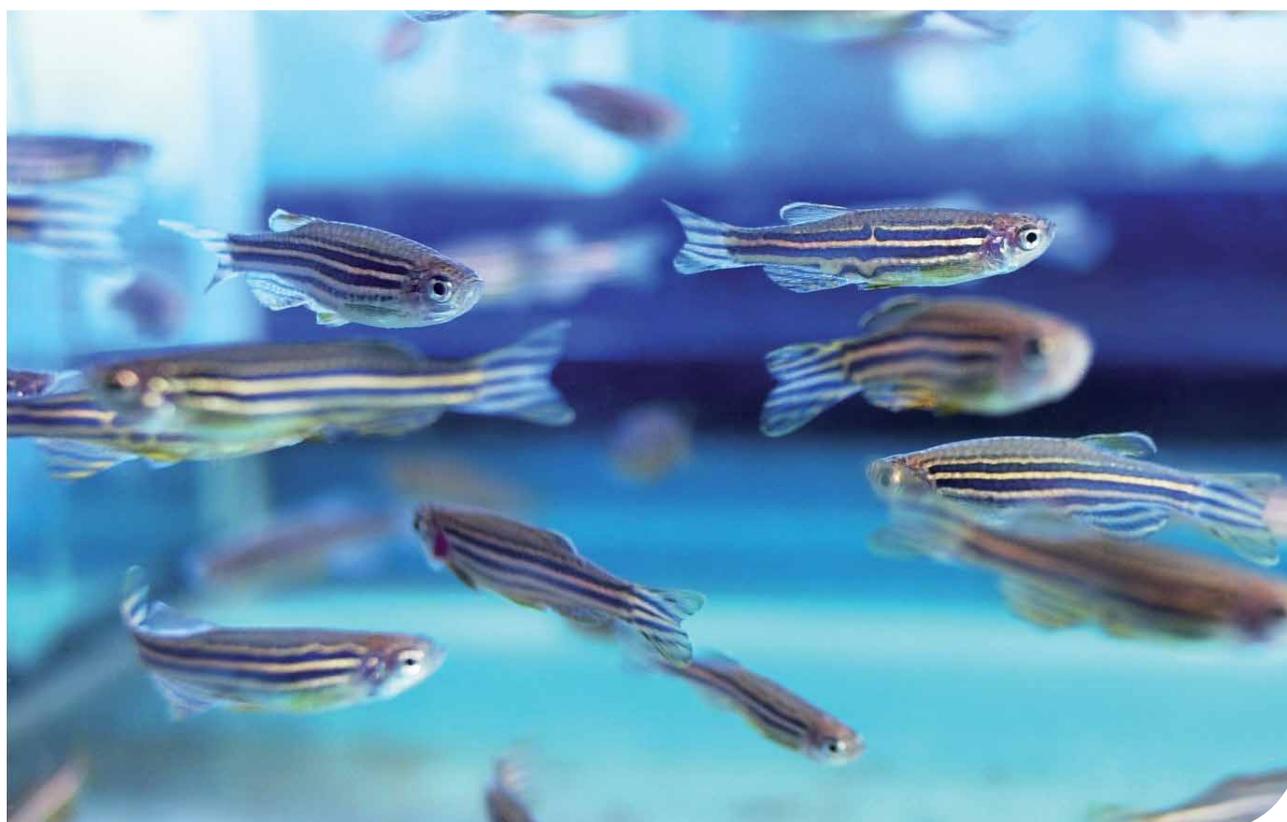
HEART AND MUSCLE DEVELOPMENT AND REGENERATION

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



RESEARCH GROUPS

HEART AND MUSCLE DEVELOPMENT AND REGENERATION

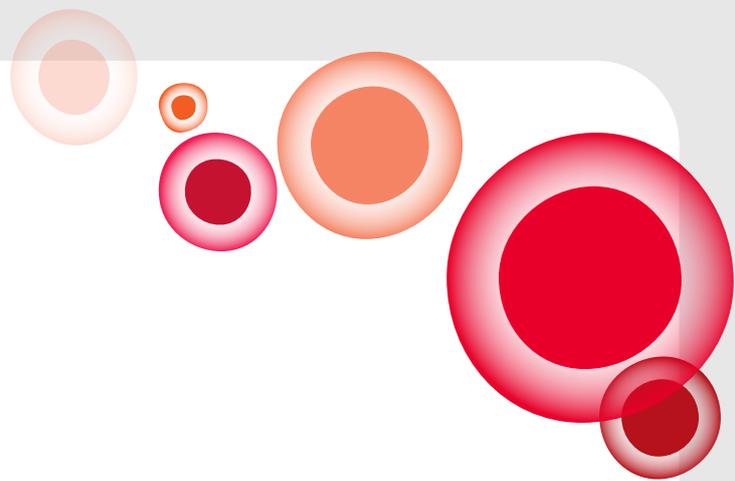
DEL MONTE-NIETO GROUP

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	Endocardial Sprouting during Cardiac Valve Formation
Project summary	The project aims to determine if the same cell decisions leading to the normal formation of blood vessels control the process of Endothelial to Mesenchymal Transition (EndMT) during cardiac valve formation in developing embryos. This project will improve our understanding of the formation of these essential structural components of the heart which allow efficient pumping of the blood during heart contraction. Better understanding of the way the cardiac valves form in the embryo will generate important insights to identify the causes leading congenital and adult heart disease associated to the cardiac valves.
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 importance of the phenotypic onset stage to characterize heart phenotypes in mutant embryos
Project summary	The project aims to investigate the importance of identifying the phenotypic onset stage for morphological and molecular characterization of the cardiac defects associated to aberrant gene function. The phenotypic onset stage is the earliest stage when cardiac defects can be detected by morphological characterization. This is an important notion recently described (del Monte-Nieto et al., Nature 2018) that suggest that the morphological and molecular changes directly associated to gene mutations can be misinterpreted if not characterized at the phenotypic onset stage due to secondary defects associated to the viability of the embryo, secondary pathway dysregulation or hypoxia. The project will characterize these secondary factors and determine their impact on cardiac phenotype interpretation.
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



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 <i>Gdf11</i> 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 therapeutic purposes.
Main techniques	Mouse genetics, micro computed tomography (μ CT), light-sheet microscopy, <i>in situ</i> 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 therapeutic 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

RESEARCH GROUPS

HEART AND MUSCLE DEVELOPMENT AND REGENERATION

RAMIALISON GROUP

Research Themes:

- Dissecting cardiac gene regulatory networks in healthy and diseased hearts
- Combining 'wet' and 'dry' lab: Using bioinformatics to decipher the regulatory code of vertebrate heart development
- Investigating the mechanisms of heart development and evolution
- Identifying candidates for human congenital heart diseases
- Role of ubiquitous transcription factor (compensation?) in heart disease

Project title	Evolution of cardiac enhancers: a comparative genomics approach to identify cis-regulatory elements driving heart evolution
Project summary	The mammalian heart is a complex organ composed of 4 chambers. However, while developing, the heart starts as a single tube which then separates into two chambers that are further divided into the final 4 chambers. This process is reminiscent of how the heart has evolved (1 chamber in flies, 2 chambers in fish, 3 chambers in amphibians and 4 in mammals). This project aims to identify similarities and differences in cardiac regulatory regions across these different species, that can explain these transitions during development and evolution.
Main techniques	Bioinformatics (sequence comparison, motif searching).
Group leader	Dr Mirana Ramialison
Supervisor	Dr Mirana Ramialison



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 of a T cell-recruiting hydrogel to promote tissue regeneration
Project summary	The goal of this project is to engineer a biomaterial hydrogel (based on fibrin) with molecules (e.g. cytokines) able to induce regeneration by mobilizing pro-regenerative T cells at a site of tissue injury. Using molecular cloning and rational protein engineering methods, cytokines will be engineered and recombinantly produced, in order to be incorporated into the hydrogel. Then, the ability of the newly created hydrogel to recruit T cells will be assessed in vitro and in vivo. Ultimately, the hydrogel system will be tested in mouse models of tissue regeneration such as skin, bone, and muscle defects. The output of this project will be integrated into a larger project aiming at reprogramming the immune system (immunoengineering) to stimulate tissue regeneration. This type of approach has the potential of being the next generation of regenerative therapies and this Master project could evolve into a PhD project.
Main techniques	Molecular cloning; protein engineering
Group leader	Assoc Prof Mikael Martino
Supervisor	Assoc Prof Mikael Martino

RESEARCH GROUPS

STEM CELLS AND REGENERATION

POLO GROUP

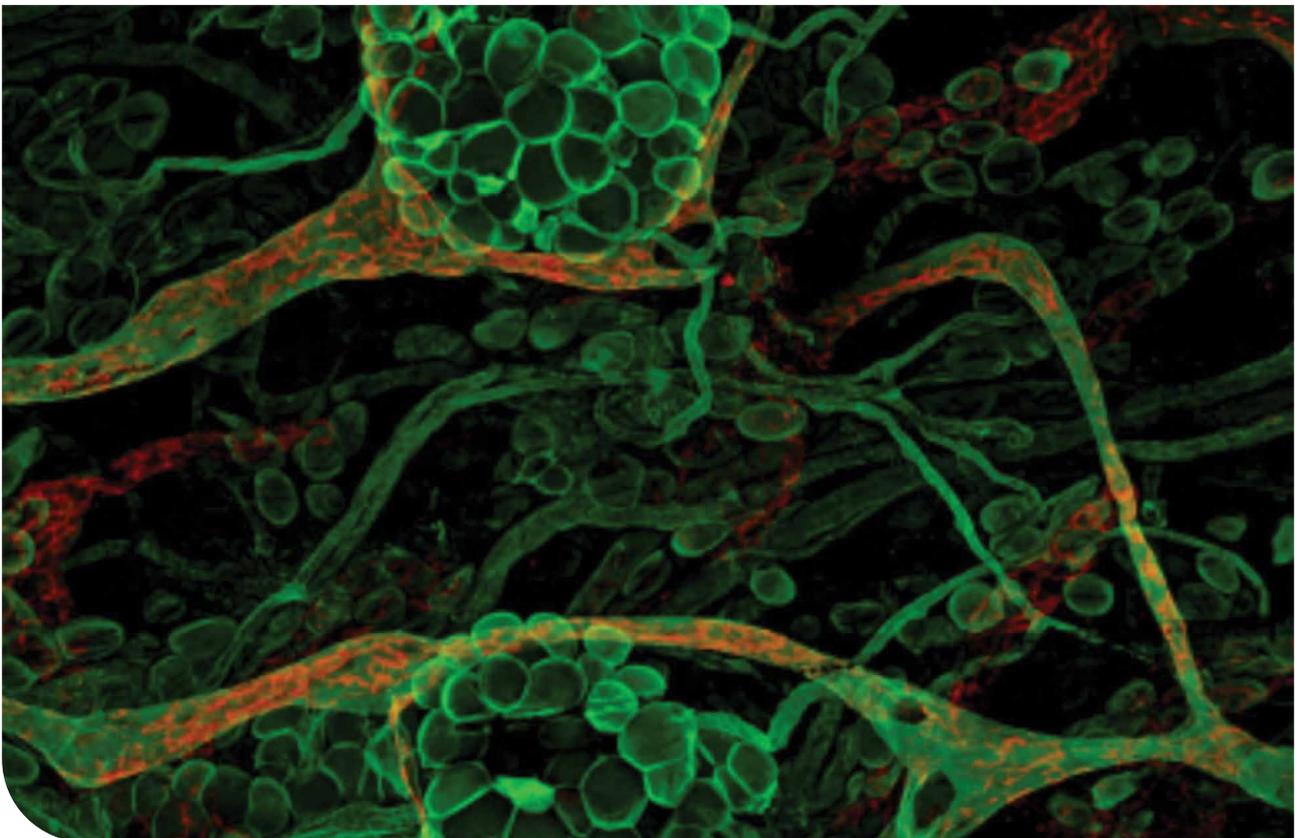
Research Themes:

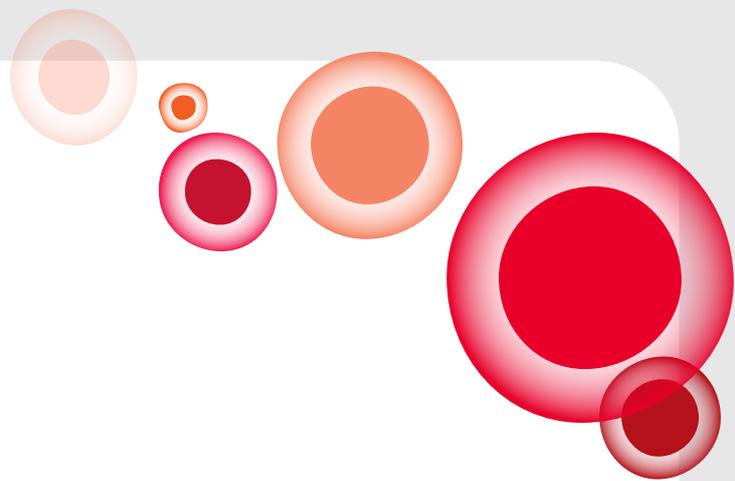
- The kinetics and universality of the epigenetic and genomic changes occurring during reprogramming
- The composition and assembly kinetics of transcriptional regulation complexes at pluripotency genes
- How the cell of origin influences the in vitro and in vivo plasticity potential of cells generated during the reprogramming process
- The epigenetics changes occurring in adult stem cells as a consequence of changes in their environment.

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.





LASLETT GROUP

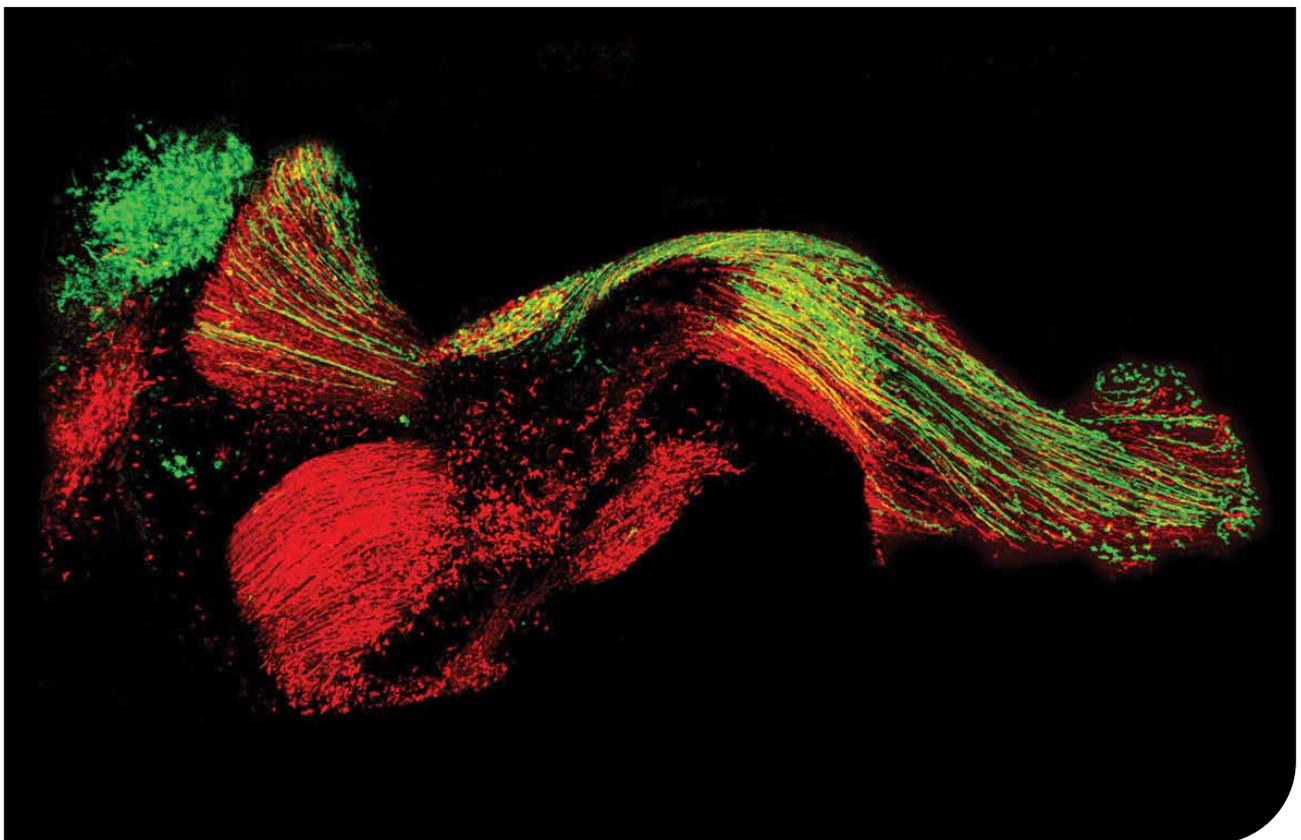
Research Themes:

- The production and characterisation of monoclonal antibodies that detect live human pluripotent stem cells
- Functional uses for monoclonal antibodies that detect live human pluripotent stem cells
- The development of “disease in a dish” models using human induced pluripotent stem cells
- Investigation of culture substrates for the maintenance and differentiation of human pluripotent 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



RESEARCH GROUPS

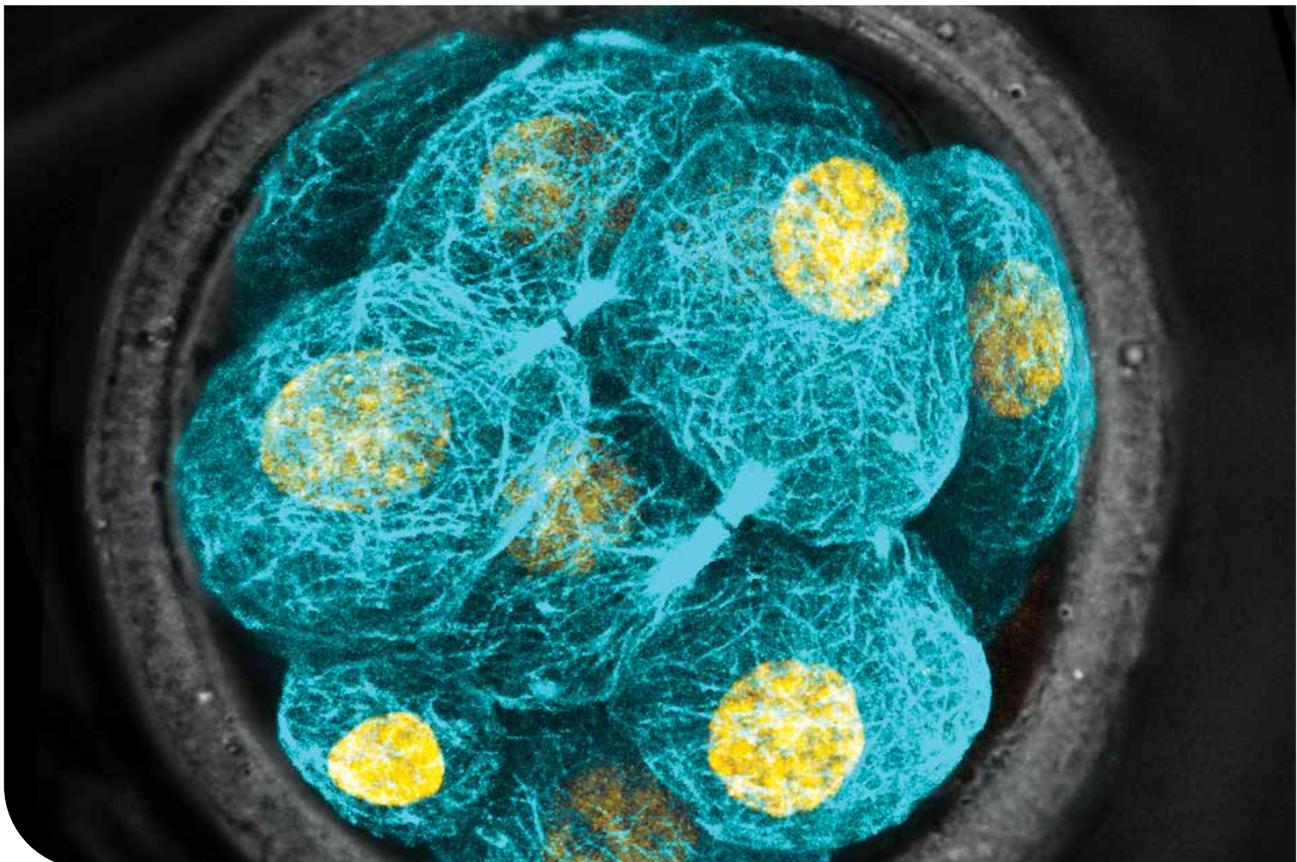
STEM CELLS AND REGENERATION

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	Real-time effects of embryo-microbe interactions on mammalian embryo implantation
Project summary	The effect of the reproductive tract microbiome on embryonic development and the initiation of a healthy pregnancy is not well understood. A unique data base collected from a case-control cohort of women with recurrent implantation failure undergoing IVF treatment will provide hypotheses as to how different uterine “microbiome contexts” may directly affect the successful implantation of a mammalian embryo. The successful completion of the proposed project will establish a physiological mammalian model system for mechanistic studies of embryo-microbiome interactions in reproductive health.
Main techniques	Mouse embryo handling and imaging, computational data analysis, cloning, cell culture
Group leader	Jennifer Zenker
Supervisor	Jennifer Zenker



RESEARCH GROUPS

NEURAL REGENERATION

BOURNE GROUP

Research Themes:

- The development and maturation of the cerebral cortex of primates and other mammals, with a focus towards the visual cortex, which is responsible for visual perception and visual guidance of behaviour
- Clarifying the functional bases of disturbances of visual perception that emerge as a consequence of perinatal lesions
- How the mechanism of neuroplasticity could aid in brain injury rehabilitation
- Using cultures of cells and organ tissues in situ hybridisation and RNA expression profiling.



RESEARCH GROUPS

NEURAL REGENERATION

KASLIN GROUP

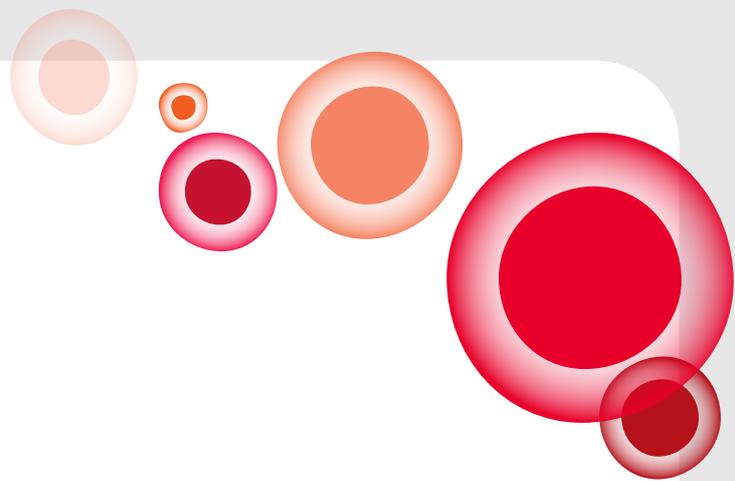
Research Themes:

- 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
Supervisor	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 leader	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 leader	Jan Kaslin, Minni Anko (Hudson)
Supervisor	Dr Jan Kaslin



MERSON GROUP

Research Themes:

- To dissect the mechanisms that regulate myelin formation in health and disease
- To establish the cellular and molecular players that induce axonal pathology following oligodendrocyte death
- To develop methodologies for optimising myelin regeneration and restoring neuronal function in the damaged CNS



RESEARCH GROUPS

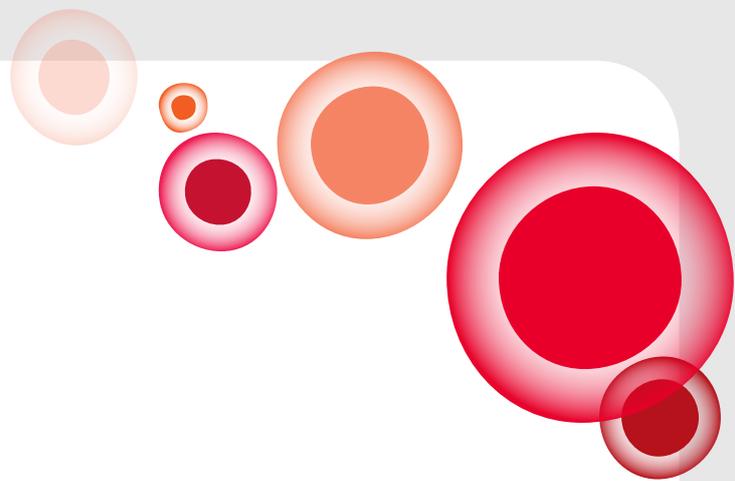
NEURAL REGENERATION

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

Project title	Regulation of a novel protein disaggregation activation pathway during neuronal cell differentiation
Project summary	<p>Neurodegeneration and dementia, coincide with the formation and accumulation of protein aggregates in neurons over time, leading to cellular proteostasis (protein homeostasis) breakdown. Often, symptoms linked to neurodegenerative diseases such as Alzheimer's disease become apparent only in the long-lived, aging communities and thus, largely limits our ability to develop preventive therapeutics. The therapeutic gain of boosting protein disaggregation (aggregate solubilization) activity as a potential treatment (i.e. after onset of the disease symptoms) to clear disease-linked aggregates and promote cellular repair, therefore, becomes highly attractive.</p> <p>Project Aim: To characterize a novel protein disaggregation activation pathway during neuronal cell differentiation.</p> <p>Rationale & hypothesis: We have identified three stress inducible configurations of the Hsp70-based disaggregase system in stem cells. Intriguingly, 2/3 of the disaggregases get inactivated during cell differentiation. We hypothesize that stem cells have a superior aggregate clearance capacity to counteract proteotoxicities associated with protein aggregation. Re-harnessing that power in neuronal cells will help develop novel therapeutic avenues to treat neurodegenerative diseases.</p> <p>Plan: The project involves monitoring the activation and dynamics of distinct disaggregases under various stress conditions related to neurodegeneration (e.g. oxidative stress) in stem cells, neural progenitor cells and in differentiated dopaminergic neurons using a cutting edge in situ protein-protein interaction technique. Perform a genetic screen to identify key regulatory elements that control the cellular protein disaggregase system during cell differentiation.</p> <p>Significance: This is a pioneering study involved in understanding protein quality control functions such as aggregate solubilization in stem cells and how such activities change during cell differentiation.</p> <p>Relevant publications: Nillegoda et al., 2015, Nature; Nillegoda et al., 2016 eLife; Gao et al., 2015 Mol. Cell; Kirstien et al., 2017 Aging Cell, Rosenzweig*, Nillegoda* (*equal cont.) et al., 2019, Nat. Rev. Mol. Cell Biol. Wentink, Nillegoda et al., 2020, Nature.</p>
Main techniques	Protein design and molecular cloning, stem cell and mammalian cell culture, cell differentiation, cell toxicity assays, confocal microscopy, immunoprecipitation, western blotting, proximity-based protein interaction assays.
Group leader	Dr Nadinath Nillegoda
Supervisor	Dr Nadinath Nillegoda



NILLEGODA GROUP CONT.

Project title	Post translational modifications that modulate the assembly of protein disaggregases in human cells
Project summary	<p>Neurodegeneration and dementia, coincide with the formation and accumulation of protein aggregates in neurons over time, leading to cellular proteostasis (protein homeostasis) breakdown. Often, symptoms linked to neurodegenerative diseases such as Alzheimer's disease become apparent only in the long-lived, aging communities and thus, largely limits our ability to develop preventive therapeutics. The therapeutic gain of boosting protein disaggregation (aggregate solubilization) activity as a potential treatment (i.e. after onset of the disease symptoms) to clear disease-linked aggregates and promote cellular repair, therefore, becomes highly attractive.</p> <p>Project Aim: To characterize a post translational modification that regulates the assembly of Hsp70 protein disaggregases in neurodegenerative diseases.</p> <p>Rationale & hypothesis: Recent findings from the Nillegoda lab points towards a novel strategy that regulates the abundance of protein disaggregase targeting factors in human cells via a specific phosphorylation event. This particular post translational modification (PTM) destabilizes the J-domain of J-domain proteins (JDP), which results in their inactivation and rapid degradation. We postulate that this modification may be misregulated in neurodegenerative diseases such as tauopathies, Parkinson's disease to Huntington's disease and disrupt the efficient assembly of disaggregases that counteract potentially toxic amyloid formation, which drives premature apoptosis of neurons.</p> <p>Plan: The student will develop two approaches to dissect the PTMs that modulate DNAJA1 and DNAJB1 subunits of the disaggregase via semi high throughput screening (mutation-based; 2. proteomics-based).</p> <p>Significance: The first description of PTMs that universally regulates JDP family proteins and protein disaggregases in human cells and an analysis of their disease relevance.</p> <p>Relevant publications: Nillegoda et al., 2015, Nature; Nillegoda et al., 2016 eLife; Gao et al., 2015 Mol. Cell; Kirstien et al., 2017 Aging Cell, Rosenzweig*, Nillegoda* (*equal cont.) et al., 2019, Nat. Rev. Mol. Cell Biol. Wentink, Nillegoda et al., 2020, Nature.</p>
Main techniques	Confocal microscopy, proximity-based protein interaction assays, mammalian cell culture, western blotting, Analysis of PTMs on proteins, protein purification and characterization in vitro using biochemical assays, CRISPR Cas9 based gene-editing.
Group leader	Dr Nadinath Nillegoda
Supervisor	Dr Nadinath Nillegoda

RESEARCH GROUPS

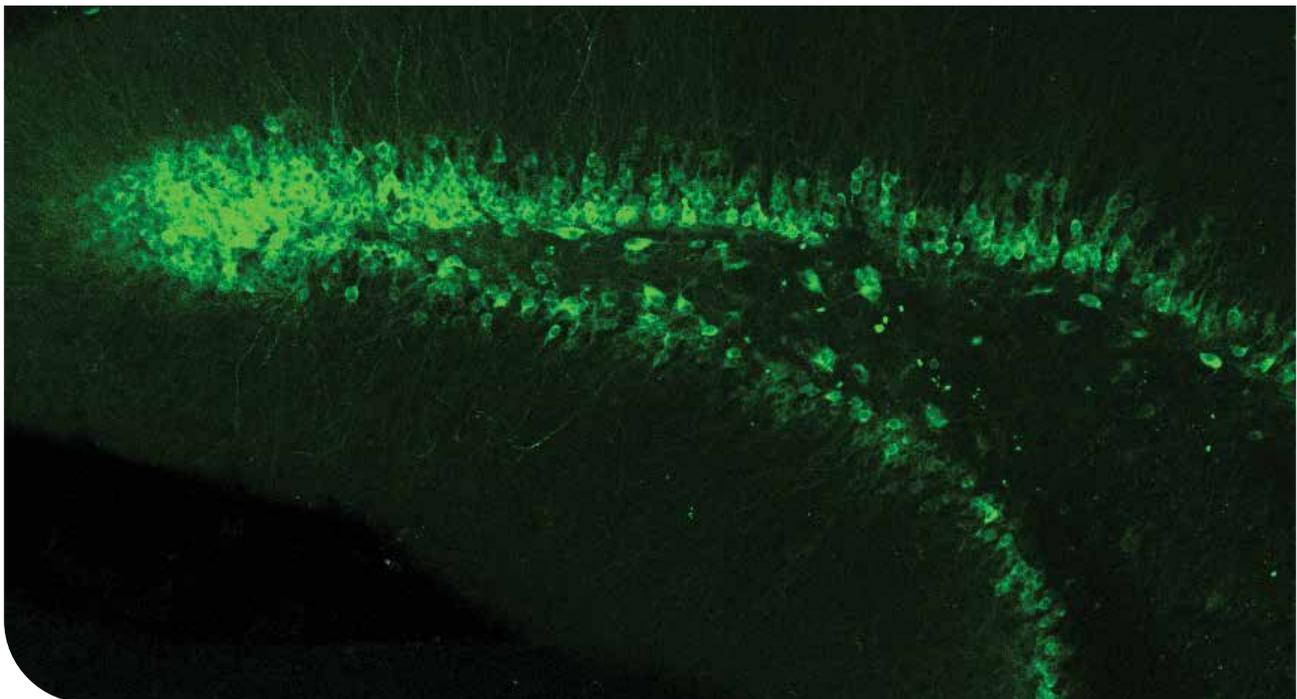
ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

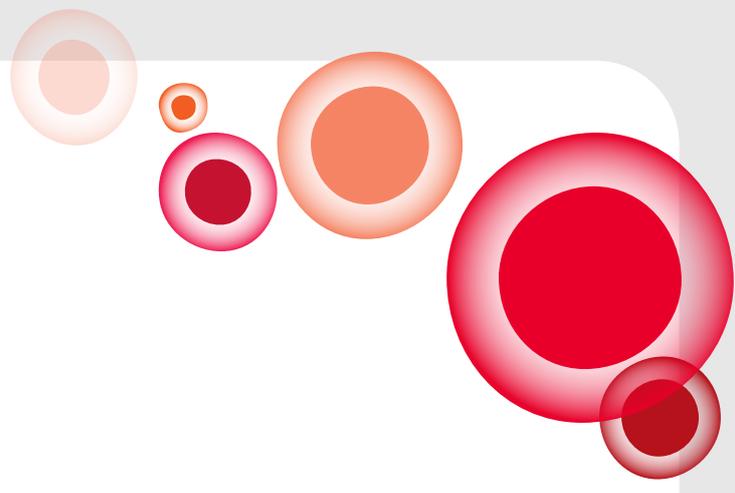
JANOVJAK GROUP

Research Themes:

- Developing new methods for controlling cell behaviour with high spatio-temporal precision (e.g. optogenetics)
- Engineering of new genes and proteins for synthetic biology
- Deciphering the function and physiology of orphan receptors
- Controlling cell proliferation and survival in models of degenerative disorders

Project title	Genome-wide protein engineering
Project summary	The goal of this project is to study the distribution and function of entire protein families in living cells on an unprecedented scale. Currently, no methods are available that allow genetic modification of hundreds of protein-coding genes with high throughput, fidelity and speed. A new research genetic technology with this capability will be developed here and applied to, e.g., fluorescent modification or optogenetic modification of all members of disease-related protein families (e.g., all kinases or all transcription factors). This technology will be achieved through combination of cutting-edge methods, including but not limited to high throughput cloning, long-read next generation sequencing and high content microscopy. The end goal is to obtain genome-wide information of protein function and protein localization to understand molecular mechanisms of disease occurrence and progression. Ultimately, this project will lead to the first demonstration of genome-wide protein engineering.
Main techniques	genetic engineering, next generation sequencing, cell culture, fluorescence microscopy
Group leader	A/Prof Harald Janovjak
Supervisor	A/Prof Harald Janovjak





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	Establishing new models of genetic chimeras to study limb growth regulation
Project summary	Classic transplantation studies have shown remarkable autonomy of limb growth, such that when limb primordia are grafted from a big salamander species into a related species of smaller size (or the other way around), the grafted limb grows to the size of the donor, not the host. However, internal organs such as the pancreas show the opposite behaviour, adapting to the size of the host when generated in situ via pluripotent stem cells. To determine whether this discrepancy depends on where the organ progenitors are generated (donor vs. host), we plan to generate a model of inter-species chimeras in mice, in which the limbs are generated from pluripotent stem cells injected into mouse embryos that cannot generate limbs. This project will be the proof-of-principle to establish such a technique.
Main techniques	Mouse timed mating and embryo collection, generation and culture of induced pluripotent stem cells, histology, immunofluorescence on tissue sections, image analysis.
Group leader	Dr Alberto Rosello-Diez
Supervisors	Dr Alberto Rosello-Diez Prof Jose Polo 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 extinguished around birth during normal mouse growth, but that expands and lingers for a longer time in response to cartilage injury. We plan to characterise these progenitors in several models of injury, using single-cell RNA-seq, as well as their requirement during catch-up growth (recovery of the normal growth trajectory after a transient developmental perturbation).
Main techniques	Mouse timed mating and embryo collection, PCR genotyping, flow cytometry, single-cell preparation.
Group leader	Dr Alberto Roselló-Díez
Supervisors	Dr Chee Ho H'ng Xinli Qu

RESEARCH GROUPS

ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

ROSELLO-DIEZ GROUP CONT.

Project title	Exploring lipid-mediated cell communication in the injured cartilage
Project summary	Long bones grow by forming a cartilage template that provides a scaffold to be replaced by mineralised bone. Developmental perturbations in this cartilage are compensated for by surrounding cells. Based on scRNA-seq data, we hypothesize that the injured cartilage has altered lipid metabolism, which alters key signalling pathways in the responding cells. We will quantify the expression of key biosynthetic enzymes and responding signalling pathways, determine the spatial distribution of free cholesterol and use ex vivo cultures to test the role of key candidates in bone growth.
Main techniques	Mouse timed mating and embryo collection, PCR genotyping, histological staining, qRT-PCR, microscopic imaging and analysis, ex vivo bone culture.
Group leader	Dr Alberto Roselló-Díez
Supervisors	Dr Alberto Roselló-Díez Dr Chee Ho H'ng





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