MONASH University | ARMI AUSTRALIAN REGENERATIVE MEDICINE INSTITUTE 10 YEARS 2009–19

STUDENT RESEARCH PROJECTS 2021


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.

"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.

MARCELLE GROUP

The Marcelle Group is interested in understanding how functional skeletal muscle arises from a group of unspecialised mesodermal cells. They do this by studying chick and mouse embryos during the first few days of development.

This period is crucial to development because the fate of individual cells are decided, extensive cell migration occurs and tightly regulated cell division takes place. The focus of the group is to understand the cellular and molecular mechanisms at play during this complex process. The focus of the group insights into the cellular and molecular mechanisms at play during this complex process and have developed insights in how to build and restore muscles in damaged and diseased tissue.

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.

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 hypothese 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 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

HOBBS GROUP

The Hobbs group aims to uncover the self-renewal capabilities of adult stem cells, which will have importance to the fields of fertility, tissue regeneration and cancer. The group's understanding of the formation and regulation of male infertility is leading to improved treatment of human infertility.

The primary research aim of the Hobbs group is to identify and define the critical molecular mechanism underlying adult stem cells by using germline stem cells from the mouse testis as a model system.

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

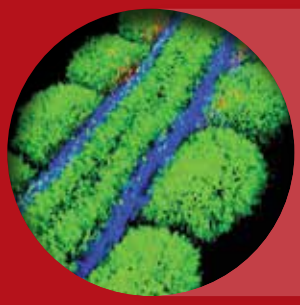
The Janovjak group combines synthetic biology and physiology to understand and manipulate the behavior of cells in health and disease. By applying physical actuators, such as light or sound, the Group aims to target cells in situ with spatial precision (for instance, selected cells in a tissue or organism)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

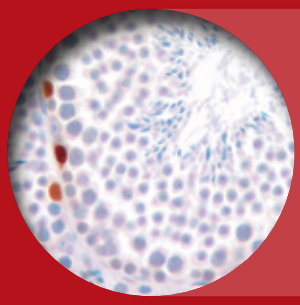


HEART AND MUSCLE DEVELOPMENT AND REGENERATION

Currie	www.armi.org.au/research-leadership/currie-group
Marcelle	www.armi.org.au/research-leadership/marcelle-group
McGlinn	www.armi.org.au/research-leadership/mcglinn-group
Ramialison	www.armi.org.au/research-leadership/ramialison-group
del Monte Nieto	www.armi.org.au/research-leadership/del-monte-nieto-group

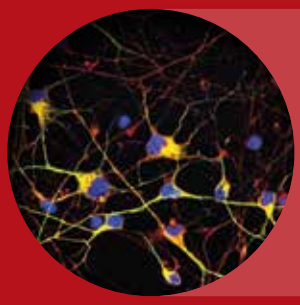
IMMUNITY AND REGENERATION

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



STEM CELLS AND REGENERATION

Hobbs	www.armi.org.au/research-leadership/hobbs-group
Laslett	www.armi.org.au/research-leadership/laslett-group
Nagy	www.armi.org.au/research-leadership/nagy-group
Nilsson	www.armi.org.au/research-leadership/nilsson-group
Polo	www.armi.org.au/research-leadership/polo-group
Zenker	www.armi.org.au/research-leadership/zenker-group



NEURAL REGENERATION

Bourne	www.armi.org.au/research-leadership/bourne-group
Kaslin	www.armi.org.au/research-leadership/kaslin-group
Merson	www.armi.org.au/research-leadership/merson-group
Nillegoda	www.armi.org.au/research-leadership/nillegoda-group

ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

Janovjak	www.armi.org.au/research-leadership/janovjak-group
Rossello-Diez	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:

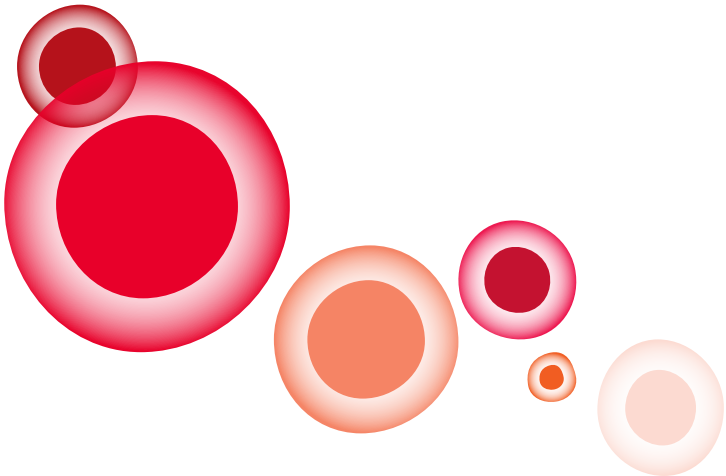
- Science
- Medical Science
- Health Science
- Engineering
- Pharmacy.

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: www.med.monash.edu.au/biomed/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:
http://www.med.monash.edu.au/biomed/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
Supervisors	Avnika Ruparelia

MARCELLE GROUP

Research Themes:

- How the process of morphogenesis of skeletal muscles is regulated at a cellular and molecular level
- Identifying putative candidate genes important in fusion
- Defining a core gene network governing “stem-cellness” in muscle.

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 Chamber Formation**
Project summary	The project aims to determine if the same cell decisions leading the normal formation of blood vessels control the formation of the specialized muscle tissue formed in the cardiac chambers during embryonic development. The process of endocardial sprouting is critical for the patterning and organization of the ventricular chambers (del Monte-Nieto et al., Nature 2018). This project will improve our understanding of the formation of these essential structural components performing the main force during heart contraction and the abnormal processes leading to congenital heart disease.
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	Evolutionary Conservation of ECM in cardiac trabeculation
Project summary	The project aims to determine if the ECM dynamics critical for the process of cardiac trabeculation (del Monte-Nieto et al., Nature 2018) are conserved through evolution. Preliminary analysis identified that these dynamics are not conserved in fish. Therefore, the project aims to identify the specific role of the ECM rich areas present in the ventricular chambers for the process of cardiac trabeculation. We will characterize trabecular development in different animal species including fish, sharks, chicken, emu and mouse.
Main techniques	Embryo dissection, immunofluorescence in wholemount samples, 3D light-sheet/ confocal microscopy imaging, 3D reconstructions and 2D and 3D image quantification.
Group leader	Dr Gonzalo del Monte Nieto
Supervisor	Dr Gonzalo del Monte Nieto

DEL MONTE-NIETO GROUP CONT.

Project title	Study the process of trabecular myocardium induction.
Project summary	The project aims to investigate the process by which the trabecular myocardium delaminates from the myocardial wall in the mouse. Recent studies have identified that the trabecular myocardium may originate earlier than previously described following a process very similar to the way it occurs in zebrafish (del Monte-Nieto et al., Nature 2018). This project will characterise the process of trabecular induction and will study the molecular and cellular processes controlling it.
Main techniques	Embryo dissection, immunofluorescence and in situ hybridization in wholemount samples, 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

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	Spatial modelling of gene regulatory networks during early embryogenesis
Project summary	Embryonic development is regulated by a network of genes that are expressed in precise spatio-temporal patterns. Any disruption in the deployment of this network will lead to embryonic defects. This project aims to create novel spatial dynamic models of embryonic gene regulatory networks, building on spatial transcriptomics and genomics information. This model will assist in predicting the effect of gene perturbations in defined domains of the embryo.
Main techniques	Mathematical modelling, bioinformatics (transcriptomics and genomics).
Group leader	A/Prof Mirana Ramialison
Supervisor	A/Prof Mirana Ramialison, Dr. Hieu Nim

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.

Project title	**Characterisation of neutrophils in a zebrafish laminB receptor mutant**
Project summary	LaminB receptor mutations are the basis of the hereditary form of the Pelger Huët anomaly of neutrophils, a variant of human neutrophils characterised by hypo-lobulated neutrophil nuclei. Exactly how this anomaly affects neutrophil function is still controversial. We have built a zebrafish model of this disorder to enable us to experimentally test how it impacts on neutrophil function in vivo.
Main techniques	Zebrafish genetics; widefield and confocal fluorescence microscopy; In vivo assays of neutrophil functions: migration, oxidative burst; Cytochemistry and in situ hybridisation
Group leader	Prof Graham Lieschke
Supervisor	Prof Graham Lieschke, assisted by Harriet Manley

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.

HOBBS GROUP

Research Themes:

- Identify and characterise novel molecular mechanisms underlying adult stem cell function using germline stem/progenitor cells from the mouse testis as a model system
- Define downstream targets of Plzf in SPCs and their role in SPC function, which is achieved using a combination of mouse genetics, flow cytometry analysis and in vitro SPC culture techniques.

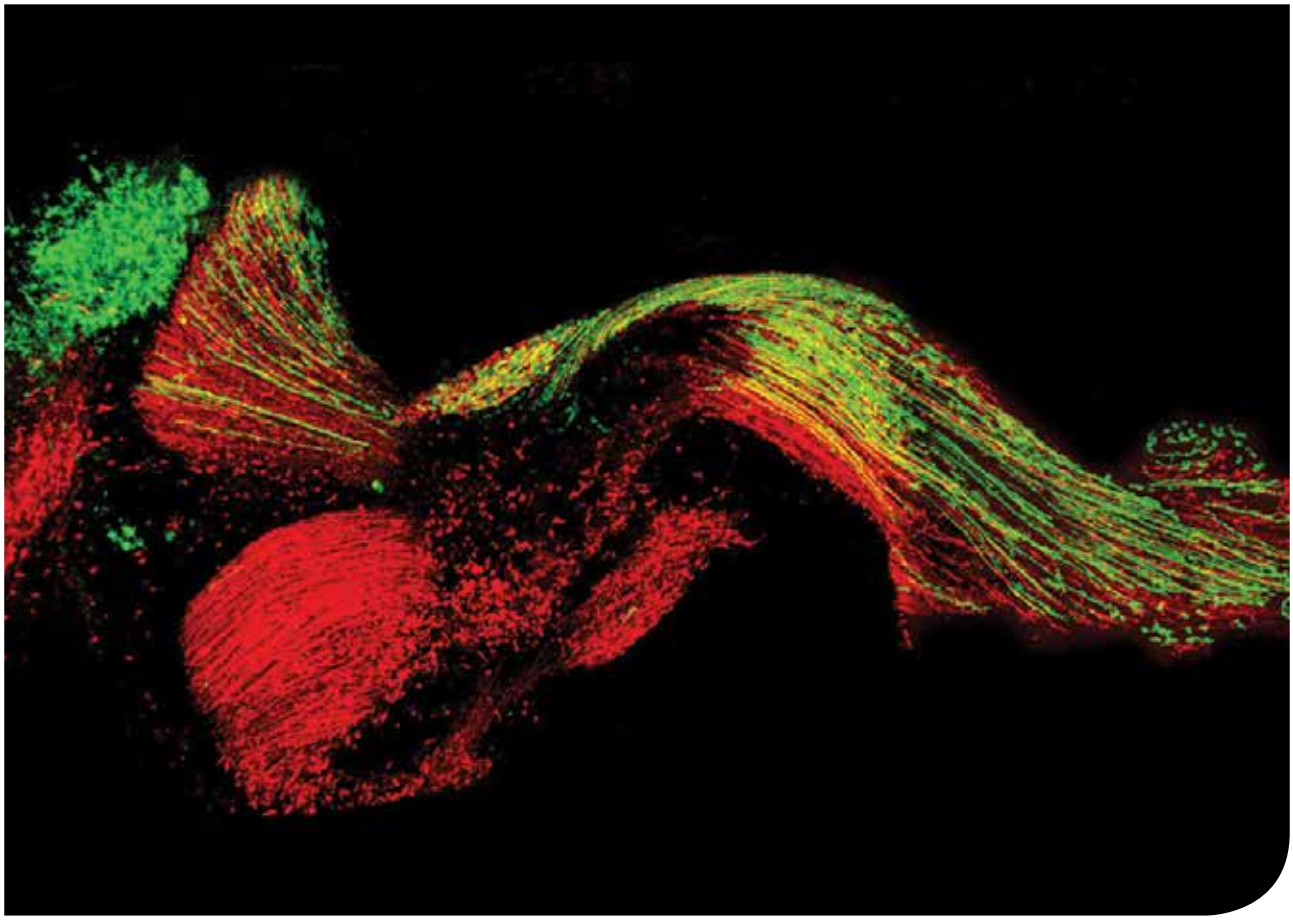
Project title	**Germline stem cells and male fertility**
Project summary	Maintenance of many adult tissues is dependent on a population of stem cells that self-renews and generates differentiating cells. In our lab, we use the male germline as a model system to study genes regulating stem cell function. Male germline stem cells enable continuous production of spermatozoa and maintain lifelong male fertility. We have identified a number of essential regulators of gene expression in germline stem cells and work to understand the mechanisms by which they function is ongoing. This project will focus on characterising the role of these factors using mouse models, in vitro culture of stem cells and cell/molecular biology techniques. These studies can have particular relevance to the stem cell and fertility fields.
Main techniques	Tissue culture, mouse models, molecular biology and cell biology (including RT-PCR, molecular cloning, western blot)
Group leader	Dr Robin Hobbs
Supervisor	Dr Robin Hobbs and Dr Julien Legrand

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.

Project title	**Functional uses for monoclonal antibodies that detect live human pluripotent stem cells**
Project summary	Characterisation of humanised monoclonal antibodies for use as antibody / drug conjugates or as carriers for transcription factors
Main techniques	Human pluripotent stem cell culture, molecular biology, immunocytochemistry, flow cytometry, video microscopy
Group leader	Dr Andrew Laslett
Supervisor	Dr Andrew Laslett Dr Hun Chy



RESEARCH GROUPS
STEM CELLS AND REGENERATION

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

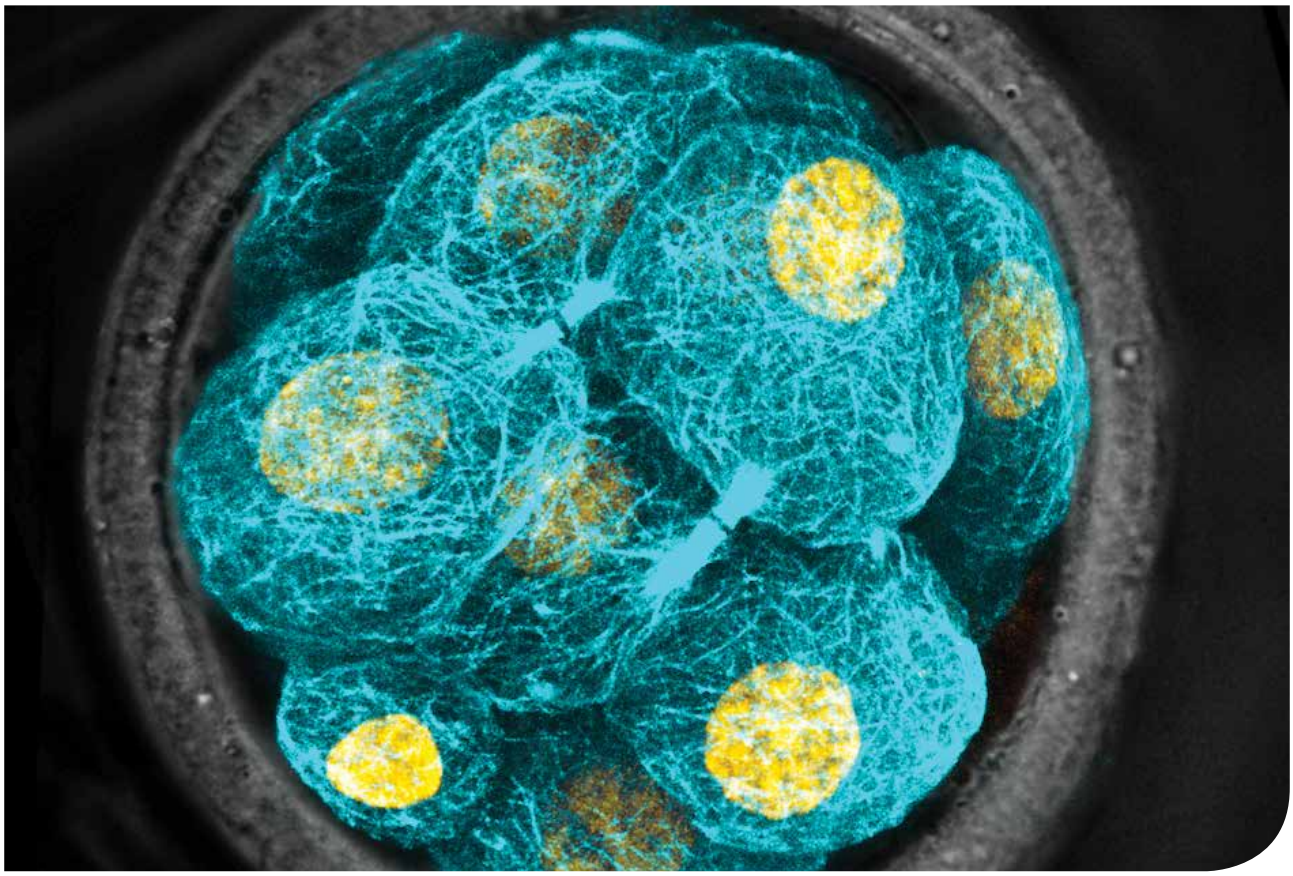
Project title	**Immune-cloaking to prevent rejection of allogeneic cell products**
Project summary	Immune rejection of cells from a different genetic background remains a critical barrier for cell therapies. This is because the immune system has evolved a complex set of mechanisms to recognise and eliminate "non-self" cells that express specific protein fragments that differ between donor and recipient. The current solution to preventing allograft rejection is treatment with broadly-directed immunosuppressant drugs, which act systemically and ultimately leave patients immunocompromised. To overcome this issue and allow the development of universal cells for therapeutic applications, we have identified a set of eight immune-modulating genes involved in allograft tolerance and rejection. Expression of these immune-cloaking transgenes in mouse embryonic stem cells (mESCs) allows the development and long-term survival of subcutaneous teratomas in major histocompatibility complex-mismatched recipients.
Main techniques	This project will focus on characterising the interaction between immune-cloaked mESCs and innate and adaptive immune cells using in vitro assays and a pre-clinical mouse model of multiple sclerosis.
Group leader	Prof Andras Nagy
Supervisor	Dr Natalie Payne, Prof Andras Nagy

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	**Visualizing microtubule remodelling in differentiating cells**
Project summary	Embryonic stem cells and induced stem cells are characterised by their ability to differentiate into all cell types of the adult body, called pluripotency. The overall aim of this project is to unravel how the architecture of the microtubule network regulates the differentiation process of such cells. To address this question, the inner skeleton of pluripotent cells in the living mouse embryo will be fluorescently labelled. The real-time changes of the microtubule network will be imaged as the cells start to differentiate in the developing embryo. 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

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.

Project title	**The evolution of the astrocyte: how brain glia have enabled more complex networks and cognition in the primates**
Project summary	Astrocytes are one of the most populous neural cell types in the brain, facilitating neural transmission, maintaining homeostasis and responding to injuries. Yet it remains unclear if astrocyte functions have expanded in higher order species to accommodate the increase in neuronal complexity and function throughout the evolutionary development of the mammalian brain. This project will explore the cellular and molecular characteristics of astrocytes in the nonhuman primate brain to gain new insights into the evolutionary expansion in the roles of astrocytes in primates including human.
Main techniques	Immunohistochemistry and immunofluorescence, histology, microscopy (brightfield, epifluorescent and confocal), morphological analysis, stereology, western blotting, qPCR, transcriptome analysis, calcium imaging, cell culture experiments.
Group leader	Prof James Bourne
Supervisor	Dr Leon Teo and Prof James Bourne

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

RESEARCH GROUPS
NEURAL REGENERATION

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

Project title	**Development of a novel tool for indelible labelling of cell-cell interactions**
Project summary	Myelin, the fatty insulating coating that surrounds the axons of neurons in the central nervous system, enables rapid conduction of electrical impulses. The student will develop and validate a novel molecular tool to permanently mark the myelinated segments of axons in the mouse brain. The approach will combine the use of bioluminescence resonance energy transfer and photoconvertible fluorescent reporter proteins.
Main techniques	Molecular biology, cell culture, immunocytochemistry
Group leader	Dr Tobias Merson
Supervisor	Dr Tobias Merson & Dr Yasuyuki Osanai

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 the human Hsp70-based disaggregase in neuronal cells**
Project summary	Neurodegeneration and dementia, coincide with the formation and accumulation of protein aggregates in neuronal tissue over time, leading to cellular proteostasis (protein homeostasis) breakdown. Often, symptoms linked to neurodegenerative disease conditions 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 disaggregation 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. This possibility has been brought into sharper focus with the observation that an enhanced artificial disaggregase from yeast can restore proteostasis and mitigate neurodegeneration in animal models. This project will focus on characterizing key regulatory elements of the human Hsp70-based disaggregase vital for boosting aggregate solubilization in neuronal cells.
Main techniques	Protein design and molecular cloning, mammalian cell culture, confocal microscopy, immunoprecipitation, western blot, proximity-based protein interaction assays.
Group leader	Dr Nadinath Nillegoda
Supervisor	Dr Nadinath Nillegoda

Project title	**Dissecting the role of an atypical molecular chaperone system in neuroinflammation**
Project summary	Neuroinflammation is considered as a double-edged sword that could produce both beneficial and detrimental effects on neurons under different (patho)physiological conditions. Many neurodegenerative diseases show prolonged neuroinflammation triggered by the exposure of protein aggregates, which promotes disease progression in patients. In this project, we are investigating various aspects pertaining to the interplay between protein disaggregation and neuroinflammation in neurodegenerative diseases such as Alzheimer's disease and Multiple sclerosis
Main techniques	Protein design and molecular cloning, mammalian cell culture, confocal microscopy, immunoprecipitation, western blot, proximity-based protein interaction assays.
Group leader	Dr Nadinath Nillegoda
Supervisor	Dr Nadinath Nillegoda

RESEARCH GROUPS
NEURAL REGENERATION

NILLEGODA GROUP CONT.

Project title	**Deciphering the J-domain protein network in human cells using Optogenetics**
Project summary	The J-domain proteins (JDPs) that regulate the Hsp70 chaperone system, constitute the largest and the most diverse chaperone family in human cells. These critical chaperones cooperate (in)directly to form a vital protein quality control layer that monitors proper folding and regulation of a large number of proteins including kinases, receptors and transcriptional factors from synthesis to degradation. Little is known about JDPs, and mutations and/or misregulation of these proteins are linked to a wide range of disease (e.g. neurodegeneration, diabetes to cancer) and cellular aging. Our lab has pioneered in dissecting the network components and regulatory elements of JDPs. Aim: The proposed project aims to develop and characterize the first set of human JDPs that can be artificially regulated using Optogenetics, a biological technique that involves the use of light to control protein function in living cells or tissues. Using blue/green light, these engineered JDPs will be activated in a spatio-temporal manner to modulate the levels of cytotoxic disease-linked protein aggregates in human cells.
Main techniques	Engineering light regulatable JDPs, protein purification and characterization in vitro using biochemical assays. CRISPR Cas9 based gene-editing, confocal microscopy. Modelling proteotoxic stress induced dynamics of the JDP network during cell repair.
Group leader	Dr Nadinath Nillegoda
Supervisor	Dr Nadinath Nillegoda

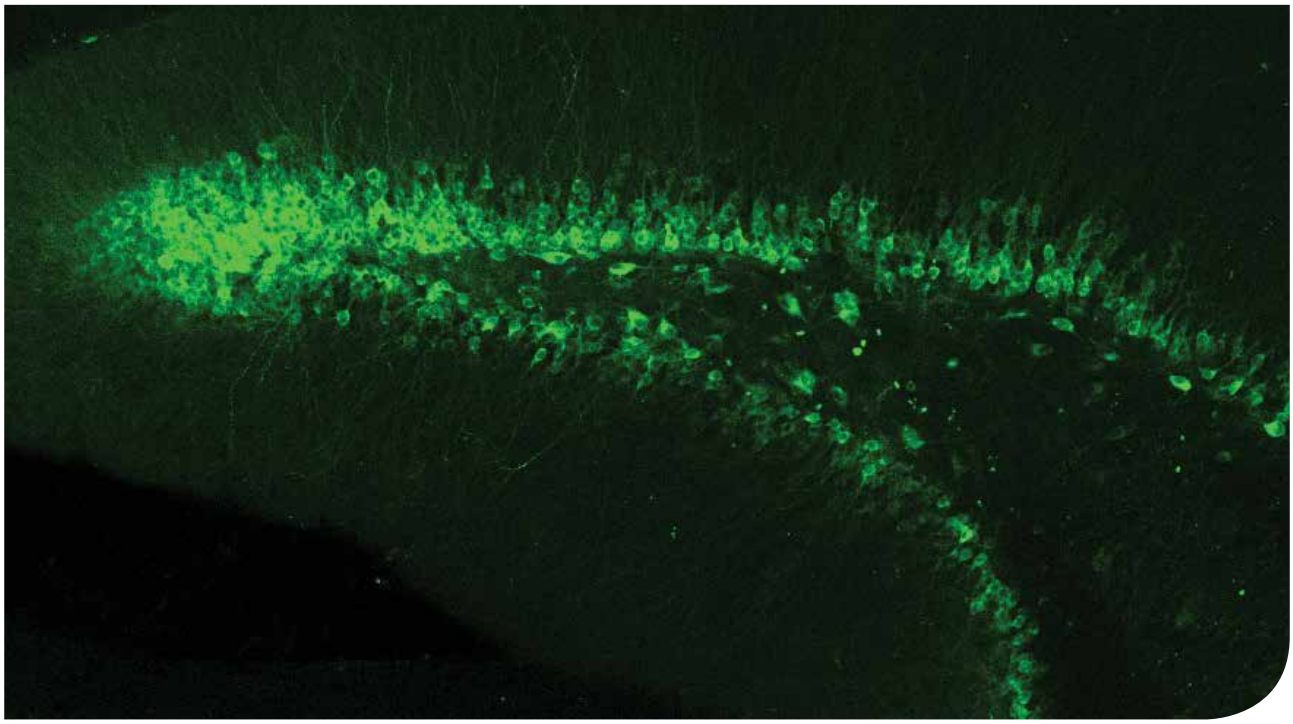
RESEARCH GROUPS
ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

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	**Pioneering synthetic neurobiology at the pre-synapse**
Project summary	The synapse is one of the most intricate biological structures and essential for nervous system function. Recent work in synthetic neurobiology has focused on manipulating synaptic signal transmission, e.g., using ‚designer receptors that were always targeted to the post-synaptic side. The goal of this project is to manipulate synaptic communication by modulating pre-synaptic terminals and synaptic vesicles. The group has recently identified a set of genes that are candidates to alter the neurotransmitter contents of synaptic vesicles by introducing ‚false neurotransmitters. The specific aims of this project are to characterize these genes in neuronal cell models and evaluate their potential as novel tools for manipulating synaptic communication and behaviour. This work builds on our past work published in *Nature Neuroscience* and the *Journal of Neuroscience Methods.*
Main techniques	cell culture, virus production, protein engineering, neurotransmitter assays
Group leader	Dr Harald Janovjak
Supervisor	Dr Harald Janovjak



RESEARCH GROUPS
ORGAN ENGINEERING AND SYNTHETIC BIOLOGY

JANOVJAK GROUP CONT.

Project title	**Embedded bacterial systems activated by light and sound**
Project summary	Synthetic biology research has in recent years focused on creating, designer cells that respond to artificial light and sound signals. These systems are promising for a range of technological and medical applications that would require ,packing them into deliverable formats (e.g., into hydrogels or matrices). The overall goal of this project is to functionally embed prototypical light- and sound-activated cells in two-dimensional and three-dimensional artificial environments. The specific aims of this project are to engineer light- and sound-responsive model cells and to test their functionality in gel matrices. This work builds on our past work in optogenetics published in, e.g., *Nature Chemical Biology* and the *EMBO Journal.*
Main techniques	cell culture, imaging, protein engineering, electrical engineering
Group leader	Dr Harald Janovjak
Supervisor	Dr 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, blastocyst complementation
Group leader	Dr Alberto Roselló-Díez
Supervisors	Dr Alberto Roselló-Díez

Project title	Characterising a highly reparative but transient 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, Dr Jonathan Bensley

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