



Ming Wai Lau Centre for Reparative Medicine

Ming Wai Lau Centre
for Reparative Medicine
劉鳴煒復修醫學中心



**Karolinska
Institutet**

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Karolinska Institutet Ming Wai Lau Centre for Reparative Medicine – An Introduction



Ming Wai Lau Centre for Reparative Medicine (MWLC) at Karolinska Institutet (KI) was inaugurated in October 2016 and became operational during spring 2017. The Centre is the first overseas establishment of a Swedish public university.

KI has a strong tradition for collaboration and international interactions. MWLC is a continuation of this tradition, representing an inter- and multi-disciplinary approach in biomedical science that brings together scientists with different backgrounds and expertise to solve complex problems in reparative medicine. KI has welcomed the exciting opportunity to create a branch in Hong Kong, a city with commitments to biomedical research, technology and innovation as described in the Chief Executive's policy addresses. With its two nodes, one in Hong Kong and one in Stockholm, MWLC offers a unique, collaborative environment for research in one of the most rapidly evolving fields with relevant translational implications.

The research activities at MWLC focus on tissue repair, with special emphasis on the *nervous system*, *heart* and *skin*. A key component of MWLC's research is related to the development of frontline technologies applicable for imaging and tracing, drug delivery and tissue engineering to be used in various domains of reparative medicine. By reading this booklet you will get a more detailed overview of the fascinating research performed in our Centre.

To achieve MWLC's aims we have four major strategies based on our vision.

1. to provide a stimulating environment and appropriate infrastructures for outstanding research in reparative medicine;
2. to reinforce and create collaborative synergies with the research communities in Hong Kong and Mainland China;

3. to catalyze interactions between the academia and biotech industry with open innovation initiatives.
4. to foster young researchers by creating job opportunities and assisting them in their career development.

To promote a policy of transparency with regard to research quality assessment, career development and recruitments, we have recently established a Scientific Advisory Board consisting of internationally recognized researchers, and a Local Reference Group consisting of prominent representatives of the local universities in Hong Kong. The MWLC initiative aims at improving human health and quality of life through excellent research based on fruitful and successful international teamwork and collaborations. The unique environment and synergies created by the Stockholm-Hong Kong partnership likely ensure a successful outcome of these considerable investments and efforts.



Prof Sandra Ceccatelli
Director

Vision and Mission



Vision

As part of Karolinska Institutet, the vision of the Ming Wai Lau Centre for Reparative Medicine is to significantly contribute to the improvement of human health by conducting cutting edge research in reparative medicine and related subjects, by creating a new platform for synergies between academia and innovation in Sweden and Hong Kong as well as China, and fostering future leaders in both academia and industry.

Mission

Reparative Medicine is a rapidly expanding area of biomedical research and clinical practice. Early applications include cell-based therapies that are evaluated in numerous ongoing clinical trials. The realization of reparative medicine requires interdisciplinary expertise and collaborations of institutions and countries.

By building a frontline technology-focused hub in Hong Kong, KI aims to strengthen the scientific interactions with the Hong Kong and Chinese scientific communities to further contribute to the progress of this research field and its implementation into medical innovation.

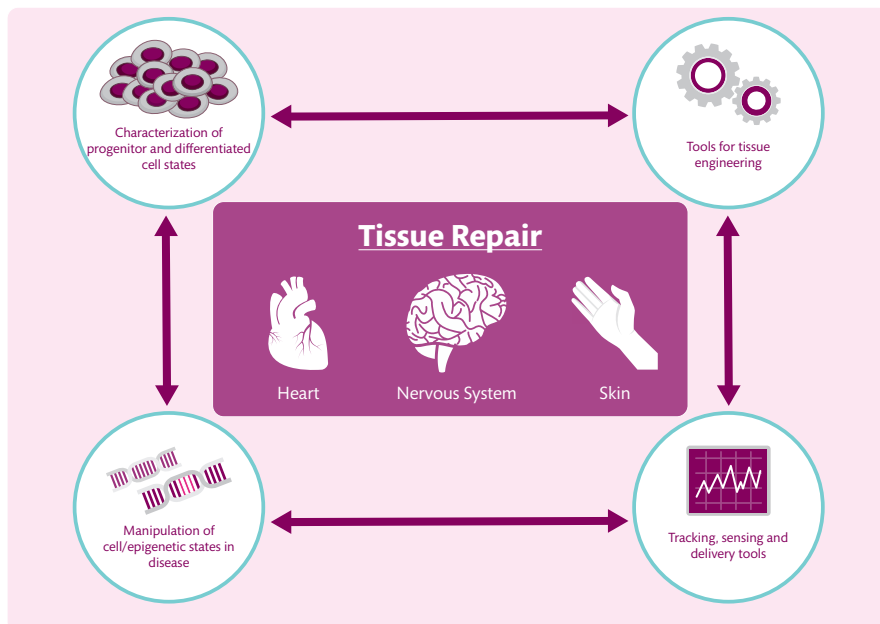
KI has a strong track record in medical innovation and Hong Kong has established world-class financial, legal and medical systems. There are growing needs and opportunities in life science involving the academia and private sector throughout the Greater Bay Area. Indeed, Stem Cell Biotechnologies and Regenerative Medicine have been identified as top priorities in the 12th and 13th 5-year Plans of PRC.

The MWLC will contribute to the development of this research field by:

- Creating a leading technology hub in stem cell research and a KI platform for interactions with partners in Hong Kong and elsewhere fostering the next-generation science leaders
- Using the Hong Kong site as a starting and bridging point to facilitate collaborations with leading institutions in Asia, Europe, and North America
- Contributing to the establishment of a regulatory framework for reparative medicine and development and commercialization in this and related technologies
- Serving as a “catalyst” for the interactions among academia, biotech industry, and society (e.g., regulatory policy, clinical trials) in the development of the reparative medicine field
- Creating job opportunities within the field of reparative medicine by being an active member of the Hong Kong, Shenzhen, and Greater Bay Area research and innovation communities

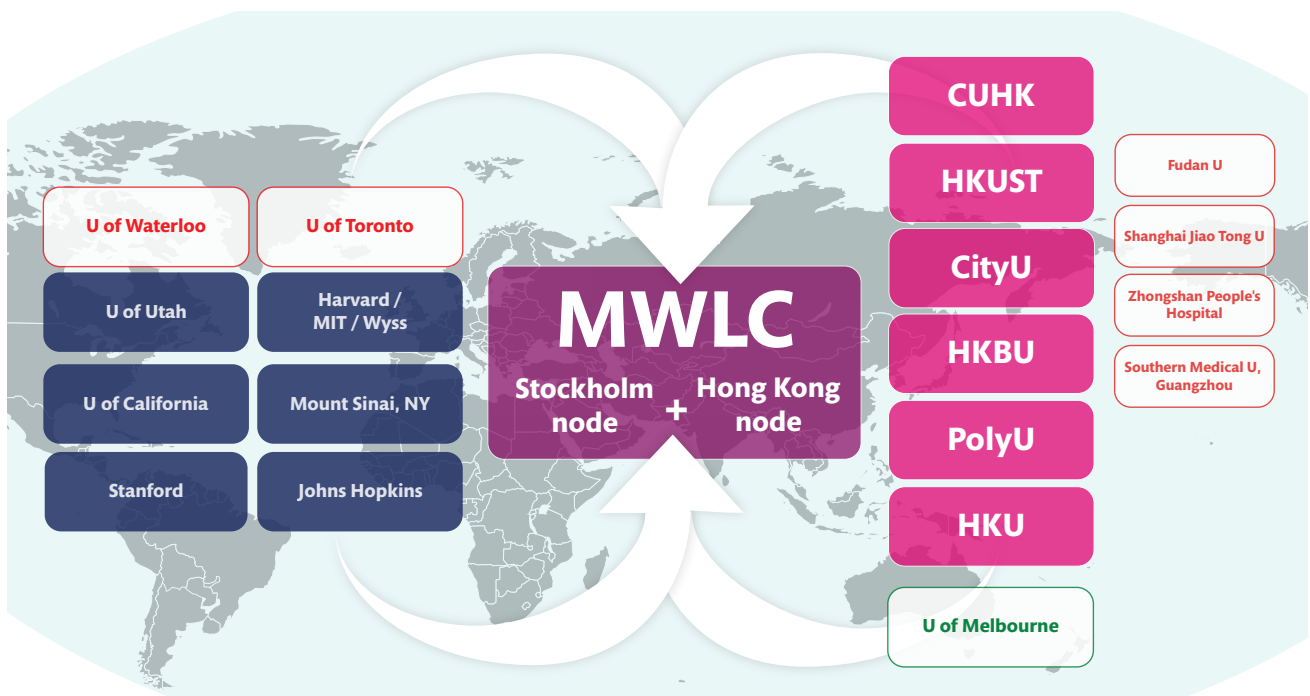
An International Research Centre

MWLC has two nodes, one in Hong Kong located in Hong Kong Science Park and one in Stockholm, currently with four and six research teams respectively with different expertise in reparative medicine.



Areas of expertise of MWLC.

To promote the collaborations between the two nodes, several initiatives have been implemented, such as organising world leading courses and conferences in Stockholm and Hong Kong in the scientific areas of interest of MWLC. Seminars are streamed between the two nodes to share unpublished results and foster collaboration. Interactions are further promoted by infrastructure within the centre, such as common core facilities co-directed by principal investigators.



Local and international collaborators.

The researchers are submitting common research applications to funding bodies both in Sweden and Hong Kong to seek funds for their collaborative projects.

The research at the two nodes are presented by the ten research groups in more details in this booklet.

Miniature Human Hearts and the Cardiac Initiative by Prof Ronald Li



Mini-heart made of human pluripotent stem cell-derived cardiomyocytes.

Human pluripotent stem cells can divide infinitely and differentiate into any cell types, including heart muscle cells termed ventricular cardiomyocytes, which can be used as fundamental building blocks for constructing more complex tissues such as heart patches, contracting muscle strips and 3D fluid-pumping chambers (a.k.a. mini-hearts). Normal mini-hearts from different ethnic groups as well as sick ones that carry particular mutations can be cloned. At MWLC, Prof Li and his team are applying these technologies for studying various heart conditions including contractile defects and arrhythmias for identifying new biomarkers. Specifically, Asian-prevalent conditions are of interest. On the translational front, these human heart prototypes are being used by industrial partners for discovering and developing novel drugs, devices and therapeutics.

In collaboration with the Dr Li Dak-Sum Research Centre at The University of Hong Kong (HKU) and Queen Mary Hospital, Prof Li's team recently completed an Innovation and Technology Fund project to establish a "Molecular Encyclopaedia" for the human heart. Patient samples in Hong Kong with congenital heart diseases such as single ventricle associated with heterotaxy syndrome, pulmonary atresia with intact ventricular septum and Tetralogy of Fallot, were converted into engineered heart tissues at MWLC. Dr Zongli Zheng at MWLC then characterized their single-cell gene profile for insights into potential future cures. Prof Li's group collaborates with Dr Gary Tse, Dr Faye Tsang and Prof Xiaoqiang Yao at The Chinese University of Hong Kong (CUHK) to study congenital cardiac ion channelopathies common in the region, including Brugada syndromes and polycystic kidney diseases with cardiac complications. Internationally, other long-term collaborators include Johns Hopkins University (JHU) (Gordon Tomaselli, Leslie Tung, Linzhao Cheng), Stanford University (Joseph Wu), Wyss Institute (Christopher Chen), University of California (Michelle Khine, Deborah Lieu) and Icahn School of Medicine at Mount Sinai in Manhattan (Roger Hajjar and Kevin Costa).

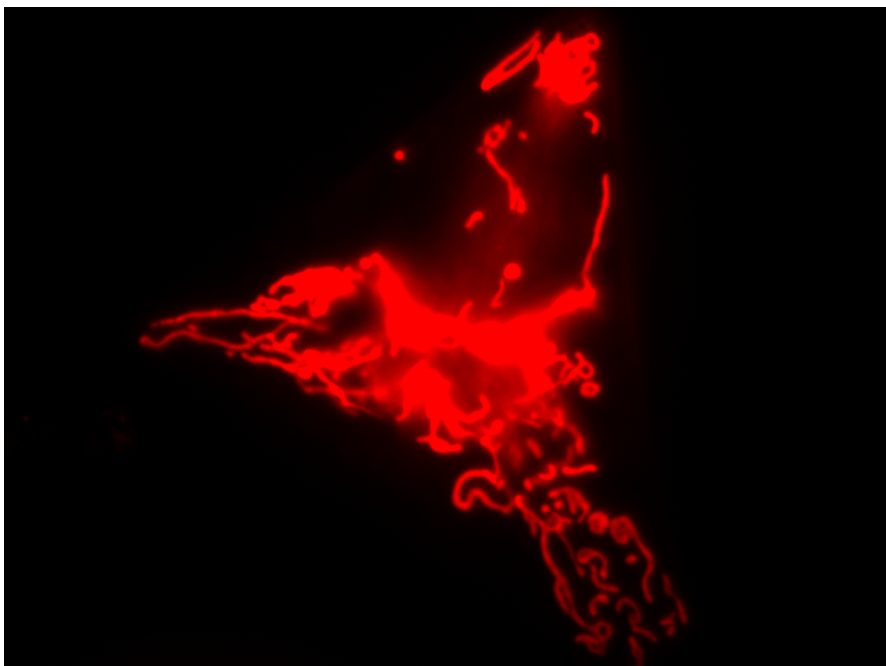
These investigators collectively form the Cardiac Initiative of MWLC, which objective is to develop next-generation heart therapies.

Prof Li is concurrently Hong Kong Director of MWLC and professor at HKU. After graduating from University of Waterloo and University of Toronto (UT), he joined JHU as a fellow in Cardiac Electrophysiology, and subsequently promoted to Assistant Professor. At JHU, he was a 2-time recipient of the Top Young Faculty Award (2002, 2003), Top Young Investigator, 1st Prize by the Heart Rhythm Society, and Career Award of C.A.R.E. Foundation. In light of California's \$3-billion stem cell bill, Prof Li was recruited to found the Human Embryonic Stem Cell Consortium at UC Davis. He later joined the Mount Sinai Hospital in Manhattan as Professor and Co-Director for Cardiovascular Cell and Tissue Engineering. During 2010-15, Prof Li was Endowed Professor and the Founding Director of Stem Cell & Regenerative Medicine Consortium at HKU. With over 150 publications, his group was the first in the world to generate genetically engineered human heart cells and, more recently, the first human "mini-heart" with accolades such as Best Study of 2005 and Ground-breaking Study of 2006 by the American Heart Association, Distinguished Visiting Professorship at UT Lewar Heart Center, Distinguished Alumnus of U of Waterloo, Spirit of Hong Kong by SCMP. His lab has received over US\$40 million from RGC, ITC, NIH, California Institute of Regenerative Medicine, etc. His inventions have led to several spin-outs in the US, Canada and Hong Kong.



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Seeing is Believing – Fluorescent Probes by Dr Sijie Chen



A cancer cell stained by a fluorescent probe developed by Dr Chen and her colleagues in their previous studies. The probe selectively stains a specific organelle inside the cell called mitochondria.

The best way to unveil the mystery of life is to make the biological targets and events visible. Biomolecules and cells are usually too small, and with signals too weak to be observed. Abnormal cellular microenvironments often lead to diseases, but remain invisible until reaching advanced stages when the damages done are already irreversible. Therefore, the development of tools and techniques for visualising various biological targets and for evaluating the intracellular as well as extracellular environments is of great academic and translational significance.

Fluorescence, a dominant methodology used extensively in biology, offers high sensitivity and spatiotemporal resolution to visualise biological events on site and in real time. Fluorescent probes light up the molecules of interest, or show light signal changes (e.g. colour change, intensity change) for tracking biological events. As such, fluorescence-based methodology is widely used in both biological studies and clinical diagnosis, helping scientists and surgeons to track stem cells, image tumours and detect disease-related biomarkers, etc.

Dr Chen's lab is particularly interested in developing novel fluorescence-based tools and techniques for visualising cell structures to understand how these biological fundamental building blocks work and how they intriguingly interact with each other in response to the environments. These tools and techniques are important for regenerative biology and cancer biology, and collectively serve as the basis for developing novel diagnostic methods and therapeutic approaches for various diseases.

Dr Chen has collaborations with Dr Linxian Li and other investigators in Hong Kong, Mainland China, Sweden, and

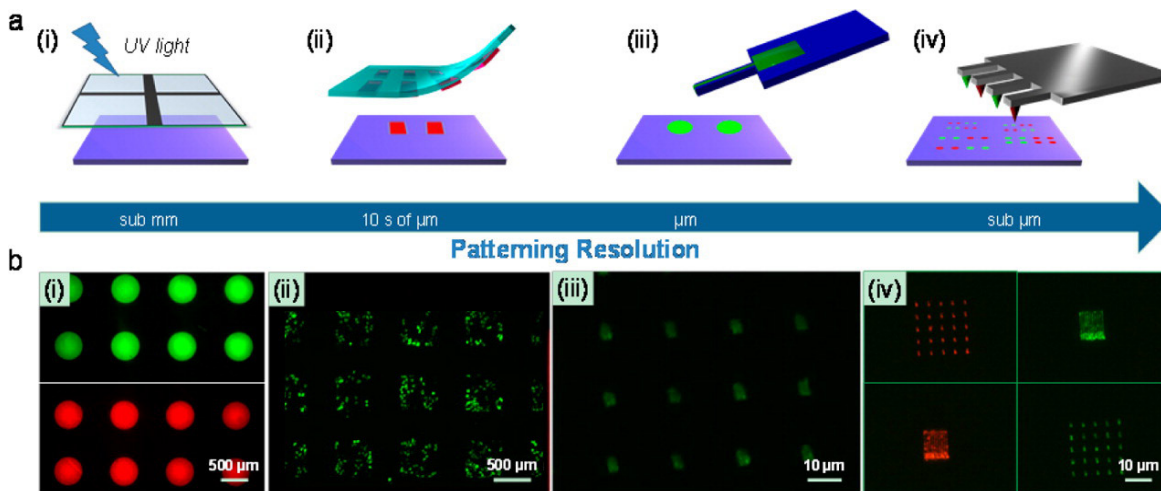
Australia, including Prof Alfonso Ngan (HKU), Prof Ben Zhong Tang of Hong Kong University of Science and Technology (HKUST), Dr Puxiang Lai Hong Kong Polytechnic University (PolyU), Dr Weiping Wang (HKU), Dr Xin Zhao (PolyU), Prof Li-li Li (National Center for nanoscience and technology, China), Dr Ning Xu Landén (KI), Dr Yuning Hong (La Trobe University) and Prof Treavor Smith (University of Melbourne). These inter-institutional research teams with complementary expertise in chemistry, biology, bioengineering, material science, bioimaging and physics work closely on developing novel imaging and sensing techniques.

Dr Chen received her BSc in Biology from Wuhan University, China in 2009 and PhD in Bioengineering from HKUST in 2013. She worked as a Postdoctoral Fellow in HKUST and then as an Endeavour Fellow in University of Melbourne, Australia and a visiting scientist in Walter and Eliza Hall Institute of Medical Research, Australia. She later joined Prof Ana Teixeira's group as a Postdoctoral Fellow at KI in 2015 before her recruitment to MWLC. Dr Chen has published more than 40 scientific papers, three of which were published after she joined MWLC and with the Centre's support.



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Engineering Advanced Biomaterials by Dr Linxian Li



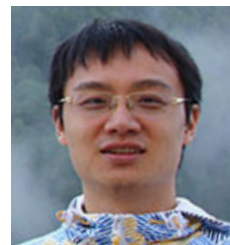
Patterning molecules on polymer surfaces at the range of features from submillimeters to submicrometers.

In gene and cell therapy, it is important to engineer the cells by delivering macromolecules, such as RNA, into the proper cells or engineer surfaces by utilising cell-biomaterials interactions to improve their functions. However, the rational design of biomaterials are often laborious and inefficient, since the design criteria are difficult to define. The lack of efficient and accurate tools has limited the development of novel biomaterials for innovative clinical treatment.

Dr Li's lab is dedicated to integrating the combinatorial biomaterials libraries, high-throughput screening and artificial intelligence to break the rate-limiting steps in preclinical research and accelerate the development of biomaterials for clinical therapy. The goal is to develop innovative technology platforms to find the ideal biomaterials for the cell of interest and accelerate the development of novel biomaterials for global healthcare challenges. With a focus on technological advancement, Dr Li and his team are developing new biomaterials for RNA and cell therapeutics.

Dr Li is a biomedical engineer with interdisciplinary expertise in organic chemistry, molecular biology, materials science, and bioengineering. After obtaining his PhD at Heidelberg University, Germany in 2014, he pursued postdoctoral research at Massachusetts Institute of Technology (MIT), Boston, USA, from 2014-2017. Committed to translating new materials for medical use, Dr Li focuses on developing biomaterials to deliver RNA therapeutics and engineering biomaterials to control cell behaviour. His work has resulted in over 20 publications including papers, patents and patent applications. These patents have been licensed to chemical

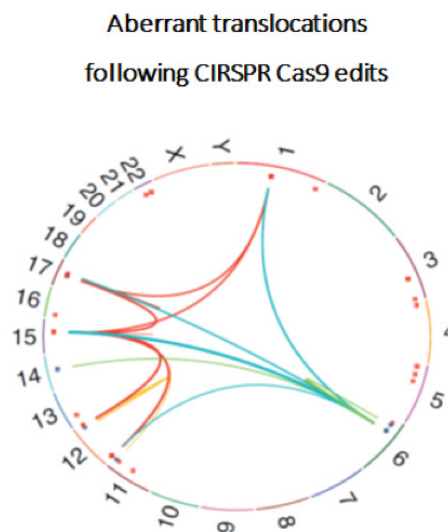
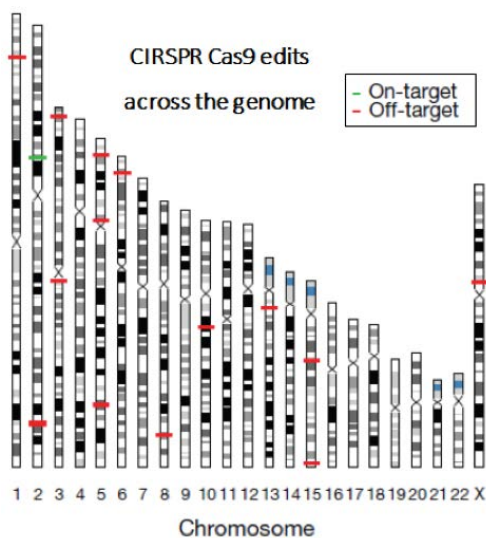
and biotechnology companies, and several products that have been commercialised. Dr Li is named to the list of MIT Technology Review Innovators Under 35 China in 2017.



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Small and Precise – Single-cell and Gene Editing

by Dr Zongli Zheng



Unbiased genome-wide identification and characterisation of unwanted cuts and chromosomal translocations following CRISPR gene editing.

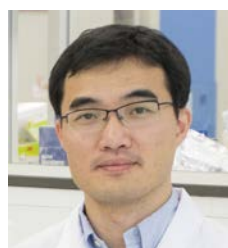
Adaptive immunity is one of the two main immune defence strategies found in vertebrates. The adaptive immune system is highly adaptable because of somatic hypermutation and V(D)J recombination. This gene rearrangement mechanism allows a small number of genes to generate a vast number of different antigen receptors expressed on lymphocytes. The advances in the next-generation sequencing technology has facilitated high-resolution studies of lymphocyte dynamics along with adaptive immunity. Dr Zheng has developed novel next-generation sequencing technologies and computational algorithms that have been adopted globally for molecular diagnosis of gene rearrangement in cancer patients. Based on single-cell and the powerful gene rearrangement technologies, Dr Zheng's lab is interested in characterizing dynamics of adaptive immunity in aging related disorders. Further, the team is interested in developing new technologies for genomic characterisation and genome-wide functional screening to identify biomarkers and therapeutic targets for aging diseases.

Fundamentally, numerous diseases are rooted in the genetic abnormality at the DNA level. The genetic defects may be inherited from parents or acquired due to environmental stimuli. New technologies like cell manipulation using CRISPR gene editing tools allow one to perform "microsurgery" to repair DNA anywhere in the genome with a great ease, and the modification can be passed down to new cell generations. Hence, this technology holds great promises for the treatments of a variety of diseases. However, the tool is not yet precise enough, limiting its use both in research, where confounded results may arise from off-target edits, and in clinical applications where safety is of paramount importance. Dr Zheng's lab is interested in developing new technologies for assessing and refining CRISPR gene editing off-target changes

in the genome. Highly sensitive technologies and personalized approaches are needed for fully assessing risks and benefits before potential clinical applications.

Dr Zheng's lab has established collaborations with Drs Gonçalo Castelo-Branco, Fredrik Lanner, Ning Xu Landén, Fang Fang and Weimin Ye from KI, Drs Anderson Shum (HKU), Alan Wong (HKU), Mingliang He (City University of Hong Kong, CityU) and Jin Young Kim (CityU) from Hong Kong, and Dr Mingfang Ji (Zhongshan People's Hospital, Guangdong) from Mainland China.

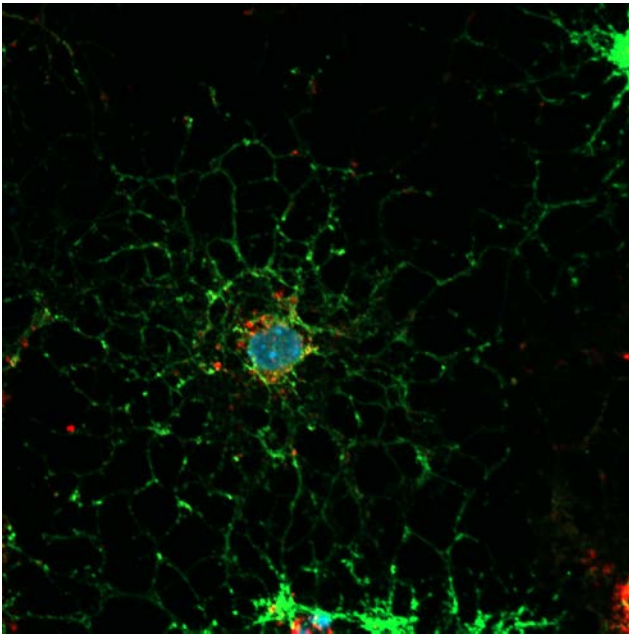
Dr Zheng received his PhD degree from KI in 2011 and completed postdoctoral training in Harvard Medical School, Boston, USA. Dr Zheng has developed novel technologies and computational algorithms for molecular diagnostics. The simple and robust diagnostics method named AMP has been adopted globally in both research and clinical settings. The AMP method has become *the* clinic assay for gene fusion diagnosis and has helped accelerate recent FDA approvals of new targeted therapies. Dr Zheng has published 35 original articles that have been cited over 5,000 times since 2013.



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Tackling Multiple Sclerosis One Cell at the Time

by Dr Gonçalo Castelo-Branco



Oligodendrocyte lineage cell expressing MHC class II, after interferon gamma treatment. Photo: Mandy Meijer.

Oligodendrocytes insulate neuronal axons through their myelin containing membranes. Myelin allows the fast and efficient impulse transmission between neurons through saltatory conduction and is important for axonal integrity, thereby being essential for the proper functioning of the central nervous system. Several diseases, such as multiple sclerosis (MS), are characterized by abnormal or defective myelination. Spontaneous remyelination occurs at initial stages of MS, promoted by endogenous oligodendrocyte precursor cells (OPCs). However, this process progressively starts occurring with less efficiency, until it eventually fails.

All cells in a given organism are derived from a single cell (zygote) and thereby share an identical genome. Additional layers of epigenetic information overlaid on the genome achieve the plethora of cellular phenotypes present in development and in the adult body. This epigenetic information is stored at the level of chromatin, the complex where nuclear DNA is packaged together with histones. DNA methylation and post-translational modifications at histones define the epigenetic state of a cell and ultimately cell fate, by controlling key processes, including transcription. Non-coding RNAs have also emerged recently as key regulators of chromatin and cell fate.

The epigenetic and transcriptional states of oligodendrocyte lineage cells define their ability to remain as a precursor cell, differentiate and produce myelin or even de-differentiate into a stem cell state or a glioma initiating cell state. The main focus of Dr Castelo-Branco's research group is to investigate how distinct epigenetic/transcriptional states within the oligodendrocyte lineage are established, by identifying key transcription factors, chromatin modifying complexes and

non-coding RNAs that are involved in epigenetic transitions, using technologies such as RNA-Seq (single-cell and bulk), quantitative proteomics and epigenomics, among others. The long term aim of this research group is to design epigenetic based-therapies to induce regeneration (remyelination) in demyelinating diseases, such as MS. Dr Castelo-Branco's lab has performed single cell RNA-Seq and identified several cell states within the oligodendrocyte lineage in development and disease (Science 2015, Science 2016, Dev Cell 2018, Nature Medicine 2018). His lab has generated several web resources from their single-cell and bulk transcriptomic datasets, compiled in the OligoInternode interface (<https://ki.se/en/mbb/oligointernode>), where one can enter a gene of interest and investigate its expression pattern in the identified oligodendrocyte lineage populations/states or determine how specific genes of interest are differentially expressed.

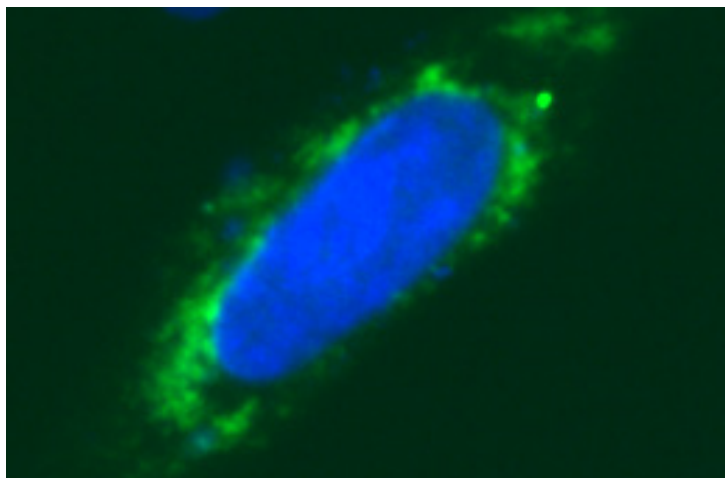
Dr Castelo-Branco received his PhD in Medical Biochemistry, KI in 2005. He completed post-doctoral fellowships first at KI and then at University of Cambridge, UK. Dr Castelo-Branco started his research group in 2012 and is an Associate Professor of Neurobiology at the Department of Medical Biochemistry and Biophysics at KI. He has received many prestigious awards and grants, including the European Research Council Consolidator Grant.



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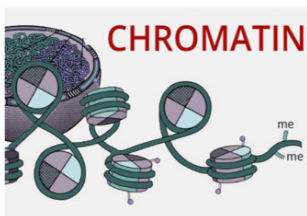
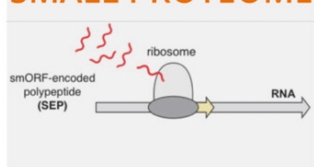
Function of Peptides Encoded by Short Open Reading Frames

by Dr Simon Elsässer

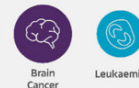


A short open reading frame encoded peptide labeled with a synthetic amino acid that allows subsequent attachment of a fluorescent label (green) in live human cells. The peptide localizes to the vesicular structures surrounding the nucleus (blue).

SMALL PROTEOME



STEM CELLS DEVELOPMENT CANCER



Proteins perform a myriad of functions in every living cell. Biomedical research on proteins has historically been focused on those that can be easily detected, isolated and characterized. Much less attention has been paid to shorter amino acid chains referred to as “peptides” of fifty or less amino acids. Intriguingly, new research suggests that our human genome contains many thousands of translated short open reading frames (sORFs) that encode such peptides, with entirely unknown functional repertoire.

Being small, fast evolvable, and more versatile in their biochemical and biophysical properties than larger proteins, peptides may modulate processes that happen in cells, or mediate communication between cells or organs. Yet to date, only a handful of short polypeptides have been studied in detail, as technical limitations of detection and isolation hamper profiling their function at a global scale.

Dr Elsässer’s laboratory has started to address this void. The group is using CRISPR technology to probe the function of thousands of candidate peptides in a variety of phenotypic screens. Collaboration with Fellows and Faculty at MWLC, as well as other groups at Karolinska Institutet, Sweden opens up a wide range of medical relevant screening assays, e.g. related to myelination pathology (Castelo-Branco), wound healing (Xu Landén), Alzheimer’s disease (Tjernberg, Sakmar).

To advance the study of proteins and peptides in cells and tissues, Dr Elsässer’s lab is pioneering new technologies based

on synthetic amino acids. Their technology provides novel ways to probe or control proteins in living cells, e.g. fluorescent labeling and microscopy. The same technology provides opportunities for bioengineering and the development of advanced protein-based therapeutics, so-called “biologicals”.

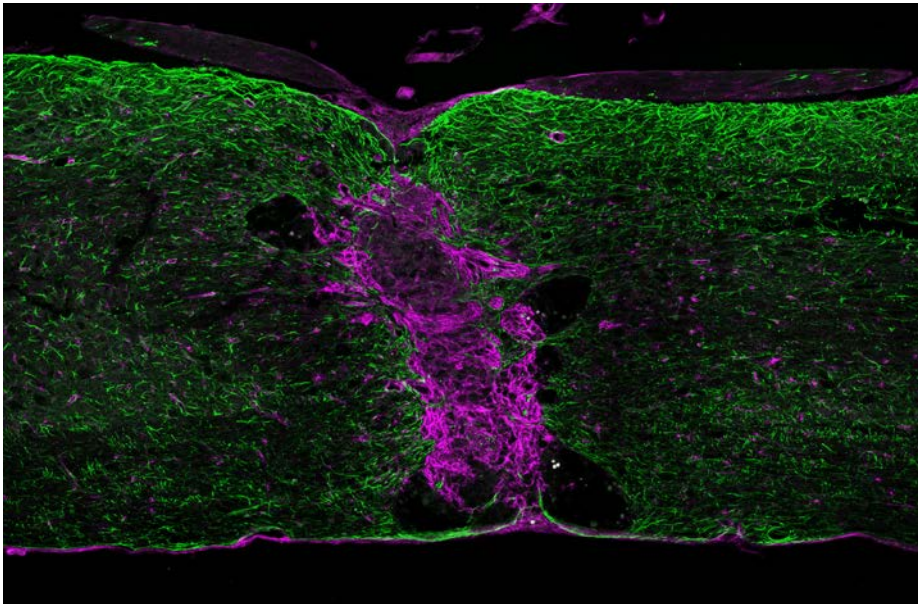
Other research interests in Dr Elsässer’s lab concern the regulation of pluripotency and differentiation, and the packaging of genome into chromatin.

Dr Elsässer studied Biochemistry at University of Tübingen, Germany before joining the Graduate Program in Bioscience at The Rockefeller University, New York, United States in 2007 from where he received his PhD in 2012. He was a Junior Research Fellow at MRC Laboratory of Molecular Biology, Cambridge, UK from 2012 and joined KI as a SciLifeLab Fellow in 2015. Dr Elsässer is an Assistant Professor at the Division of Chemical Biology and Translational Medicine, Department of Medical Biochemistry and Biophysics, KI.



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Repair of Central Nervous System Lesions by Dr Christian Göritz



Sagittal view of the spinal cord fourteen days after a full crush injury showing reactive astrocytes (green) flanking the injury core filled with fibroblast-like cells (magenta).

The healing ability of the central nervous system is very limited and injuries to the brain or spinal cord often result in permanent functional deficits. In many organs, damaged tissue can be repaired by generating new cells of the type that were lost. However, after an injury to the central nervous system, a special type of scar tissue is formed which inhibits this regeneration. Injuries to the brain and spinal cord therefore often lead to permanent loss of functional ability.

It was recognised more than a century ago that nerve fibres of the central nervous system fail to grow through the scar tissue that forms at a lesion. However, this scar tissue is a complex mesh of different cell types and molecules, and it has been unclear exactly how the scar tissue blocks nerve fibre regrowth. The research group of Dr Göritz investigates the origin of scar forming cells, the mechanisms of scar formation and explores possible therapeutic interventions to improve functional recovery.

Recently, Dr Göritz and his co-workers have identified an important mechanism explaining how scar tissue inhibits nerve fiber regeneration after an injury. They found that a very small population of cells lining blood vessels, which gives rise to a large part of the scar tissue, inhibits nerve fiber growth after a spinal cord injury. When they inhibited scar formation by the blood vessel-associated cells, some nerve fibers could regenerate and reconnect with their targets. This resulted in improved functional recovery after spinal cord injury in mice.

“Our findings give an important explanation as to why functional recovery is so limited following injury to the central nervous system,” says Christian Göritz, Associate Professor at the Department of Cell and Molecular Biology and Lau Fellow at MWLC, KI.

Further studies are now needed to explore whether this knowledge can be used to promote recovery following injury to the central nervous system in humans. For this Christian Göritz is establishing close collaborations with Dr Linxian Li (MWLC) and other investigators in Hong Kong, including Dr Kai Liu (HKUST).

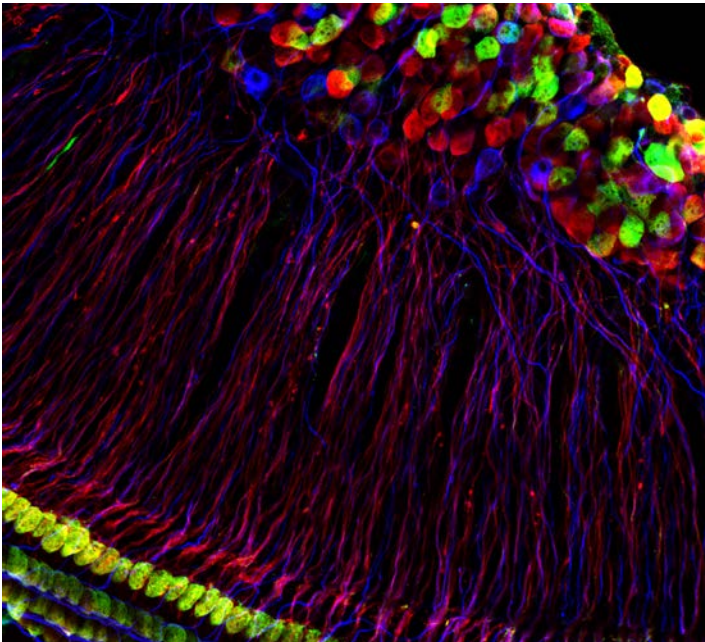
Dr Göritz studied Biochemistry in Berlin, Germany. He performed his PhD studies in Strasbourg, France, in a joint Max Planck / CNRS research environment in the field of Neuroscience. For his postdoctoral training, he joined the lab of Prof Jonas Frisé at KI. In 2012 Dr Göritz established his own research group. He is currently an Associate Professor at the Department of Cell and Molecular Biology, KI.



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Sensory Circuits – Developmental Principles and Network Mapping

by Dr Francois Lallemand



Cochlear neurons innervating hair cells. Photo: Charles Petitpre

Dr Francois Lallemand and his research group is interested in understanding the molecular principles underlying the neuronal specification and neural circuit formation in the peripheral nervous system. In addition, they propose to shed light on how developmental processes make use of either stochastic or predetermined molecular mechanisms or both simultaneously during the formation of the nervous system. The research projects in the laboratory employ an integrated approach involving molecular and cell biology, advanced genomics, genetic strategies in the mouse, complemented by anatomical and physiological methods.

An important process in the construction of a functional nervous system is the death of “unwanted” neurons during early development. This cell death helps scaling the population size and thus the connectivity between neurons and their target, which is necessary for building up a functional organ. However how and which cells are selected to survive and participate in the construction of a mature neural circuit is still largely unknown. Dr Lallemand’s lab recently uncovered a new cell selection model for neuronal survival during development, where a molecular fitness heterogeneity in sensory neurons predicts their survival probability and the selection of the fittest cells for the establishment of functional neural networks.

Another central theme in developmental neurobiology is to understand how the large diversity of neurons types in mammals is generated during development. One model proposes that neurons acquire the potential to differentiate into a distinct subtype at the level of progenitors; the competing model postulates that their identity is established later, after becoming postmitotic, through interactions with the environment at their homing site. Using the diversity of sensory neurons of the somatosensory system, Dr Lallemand’s research

group recently unveiled the existence of distinct subsets of neuronal progenitors that are molecularly specified to particular neuron fates.

Studying the neuronal diversity in the peripheral auditory system, Dr Lallemand’s lab discovered that the main axon tracts that composed the cochlear nerve are in fact made of three main neuron types. This study, published in *Nature Communications*, will have long lasting impact in the auditory field as it for the first time provides a cellular basis of the functional diversity in the peripheral auditory system. It will also permit the identification of specific ascending auditory pathways needed to centrally process the various peripheral information encoded by each individual auditory afferent type, and for linking their alteration with specific hearing disorders.

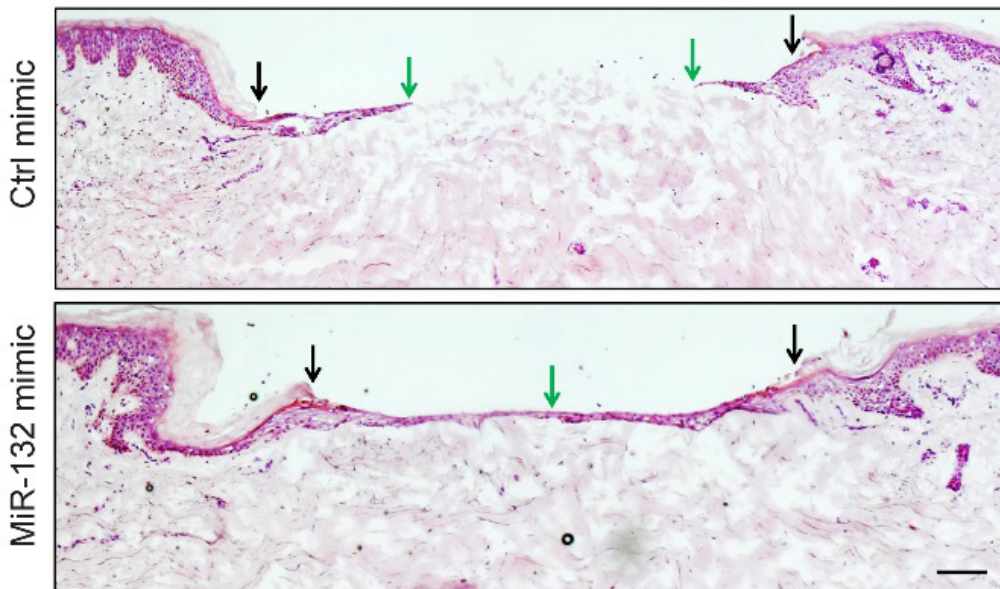
Dr Lallemand received his PhD at the GIGA Neuroscience, in Liege, Belgium in 2005, followed by a postdoctoral research at the Department of Medical and Biochemistry and Biophysics, KI from 2006 to 2010 working on neural crest cell lineage. Dr Lallemand established his research group in 2011, and was recruited to the Department of Neuroscience, KI in 2013, where he heads the lab of neuronal specification and connectivity since then. Dr Lallemand is an Associate Professor at the Department of Neuroscience, KI.



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Targeting Regulatory RNAs in Skin Wounds: a New Opportunity of Healing?

by Dr Ning Xu Landén



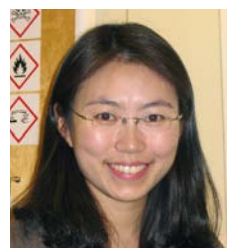
Hematoxylin and eosin staining of human *ex vivo* skin wounds topically treated with microRNA-132 mimics or control oligonucleotides for 5 days. Black arrows point to initial wound-edges; green arrows denote the newly formed epidermis.

The immense economic and social impact of deficient wound healing e.g. chronic ulcers, post-surgical wounds care and skin scarring calls for attention and allocation of resources to understand biological mechanisms underlying wound complications. Due to the complex nature of wounds, efficient targeted approaches to enhance healing is essentially lacking today. The recent discovery of non-coding RNAs (ncRNAs) as powerful gene regulators provides hope to develop novel RNA-based treatments for a wide variety of diseases.

The objective of Dr Xu Landén's research is to reveal the role(s) of ncRNAs, i.e. microRNAs (miRNAs), long-non-coding RNAs (lncRNAs) and circular RNAs in skin wound healing and to explore the potential of RNA-based therapy for chronic wounds. Her research network is composed of both clinicians and scientists, which allows performing "Bench-to-Bedside" research. At present, her team is investigating the novel roles of ncRNAs in skin wounds using a unique collection of human wound tissues. In the next step, they aim to translate their basic scientific findings into therapeutic interventions for wound patients.

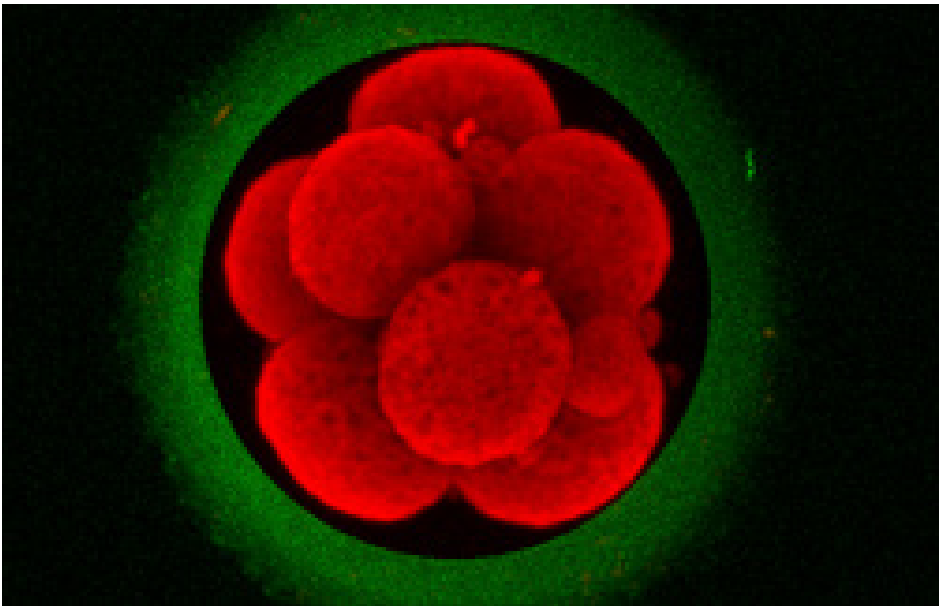
To achieve the goals of this multidisciplinary project, Dr Xu Landén's team collaborate with many investigators with different expertise, including Drs Sijie Chen, Zongli Zheng, Gonçalo Castelo-Branco and Simon Elsässer at MWLC.

Dr Xu Landén received her Bachelor in Medicine from Peking University, China in 2003 and PhD in Medical virology from Uppsala University, Sweden in 2008. She worked 2009 to 2013 as a Postdoctoral Fellow in Prof Mona Ståhle's group at KI. Dr Xu Landén started her own research group in 2014 focusing on skin wound healing and is an Associate Professor at Department of Medicine, KI since 2017.



For further information, please contact
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Uncovering the Secrets of Early Human Embryo Development and Treating Blindness Using Embryonic Stem Cells by Dr Fredrik Lanner



Human embryo consisting of 8 cells, three days after fertilization. Photo: Alvaro Plaza Reyes.

Embryonic stem cells, which are isolated from the human blastocyst, can be propagated indefinitely and directed to mature into virtually any cell type of the adult human, offering great potential for reparative medicine to replace lost or damaged tissues. However, we have a very superficial knowledge of how these early immature cells are established and controlled in the embryo. Better understanding of these cells will not only improve our possibilities in efficiently and safely mature them to clinically cell types, but could also shed light on understanding the causes of infertility.

Dr Fredrik Lanner's lab has mapped the first week of human development using single cell mRNA sequencing and uncovered new insights into how the first cell types are established and when the equivalent of embryonic stem cells emerge (Petropoulos et al Cell 2016). They have further established novel markers of these immature pluripotent stem cells, which can be used to classify the stem cells into different developmental stages (Collier et al., Cell Stem Cell 2017). The Lanner lab is now extending these studies to functional studies of the genes that they have identified during this first week, using pioneering genome editing technologies. Together with Prof William Yeung at HKU, they are now extending their studies into the second week, which is the period when the human embryo implant in the uterine wall and the pluripotent stem cells start maturing.

Within their clinically oriented research the Lanner lab has established new embryonic stem cells of clinical quality within the GMP facility at Karolinska University hospital. Next they have developed a xeno-free and defined maturation process to generate retinal pigmented epithelial cells, the cells that degenerate in age-related macular degeneration (Plaza-Reyes

et al., Stem Cell Reports 2016 and manuscript in preparation, Patent filing: #62/687,416). The cells have been tested in preclinical animal models to show functional integration in the retina and they have performed safety testing including whole genome sequencing, bio-distribution and tumorigenicity assays in preparation for future clinical trial. Finally they are exploring various approaches to reduce immunological rejection of the transplanted stem cell derived retinal cells.

Dr Lanner undertook his PhD studies at KI with focus on generating vascular cells from embryonic stem cells. He then joined Janet Rossant's team at The Hospital for Sick Children in Toronto from 2009-2012 to study early mammalian biology where he identified the fundamental role of FGF signaling during the formation of pluripotent cells in the mouse blastocyst and embryonic stem cells (Yamanaka et al., Development 2010, Lanner et al., Stem Cells 2010, Lanner and Rossant Development 2010). Returning to KI in 2012 he initiated his own lab with a focus towards human embryo development. In addition to the MWLC Lau Fellow grant in 2016, he is a Ragnar Söderberg Fellow, Wallenberg Academy Fellow, CIMED Junior Investigator and recipient of the Swedish Research Council Junior Investigator grant.



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Establishment of the State-of-the-Art Core Facility

by Prof Ronald Li

An objective of MWLC is to facilitate local and international collaborative research in Reparative Medicine. This goal is being accomplished with the establishment of a State-of-the-Art Core Facility consisting of platforms for Bioinformatics, Molecular and Cell Biology, Single-Cell Profiling and Biomedical, Interfacial and Optical Engineering.

Single-Cell Profiling

Co-directors – Drs Gonçalo Castelo-Branco, Zongli Zheng

Single-Cell Profiling platform is set up to enable single-cell genomics and transcriptomics research. Further integration of gene editing in single cells allows for pooled CRISPR screening, and flexible and scalable single-cell multi-analyte analyses are at the global forefront of biotechnology development. Current expertise and capability include next-generation sequencing, single-cell genomics, and CRISPR gene editing.

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Bioinformatics

Co-directors – Drs Gonçalo Castelo-Branco, Zongli Zheng
Experts – Drs Virpi Ahola and Shangli Cheng

MWLC has established a bioinformatics platform in Hong Kong. The platform collaborates with various research projects conducted in Stockholm and Hong Kong nodes. The platform has and will further develop expertise in single-cell genomics, epigenomics, system biology and other next generation sequencing-based methodology. It also has a network between bioinformaticians in the Stockholm and Hong Kong nodes to build up knowledge in important areas.

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Molecular and Cell Biology

Experts – Mr Patrick Chan, Dr Ryan Gao

Molecular and Cell Biology platform is set up to facilitate the development of basic and translational stem cell research. The platform has expertise in the latest gene transfer technologies, human pluripotent stem cell culture and differentiation, and various functional phenotyping assessments such as patch-clamping, electrophysiological assays, imaging, etc. These integrated services and equipment are provided to investigators at MWLC and other collaborators.

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Biomedical, Interfacial, and Optical Engineering

Co-directors – Drs Sijie Chen, Linxian Li

Biomedical, Interfacial, and Optical Engineering platform is established to meet the needs of researchers who focus on developing new biomaterials and biotechnologies, especially but not limited to fluorescent probes, fluorescence-based techniques, biomaterials for 2D and 3D cell culture, microfluidic devices, and nanomaterials for drug and gene delivery. The platform provides a platform for the fabrication, characterization, and performance evaluation of novel bio-probes and biomaterials in physiologically relevant contexts, facilitating the development of materials, tools and techniques for biological studies. The platform houses essential resources including ultrasonic system, ultra-high-spinning evaporation system, collimated UV lamp and photomask, 3D-bioprinter, drop shape analyser, light microscope instrumentation, wide-field fluorescence microscope, FLIR thermal imaging camera, multi-detection microplate reader with cuvette ports and accessories for microfluidics systems.

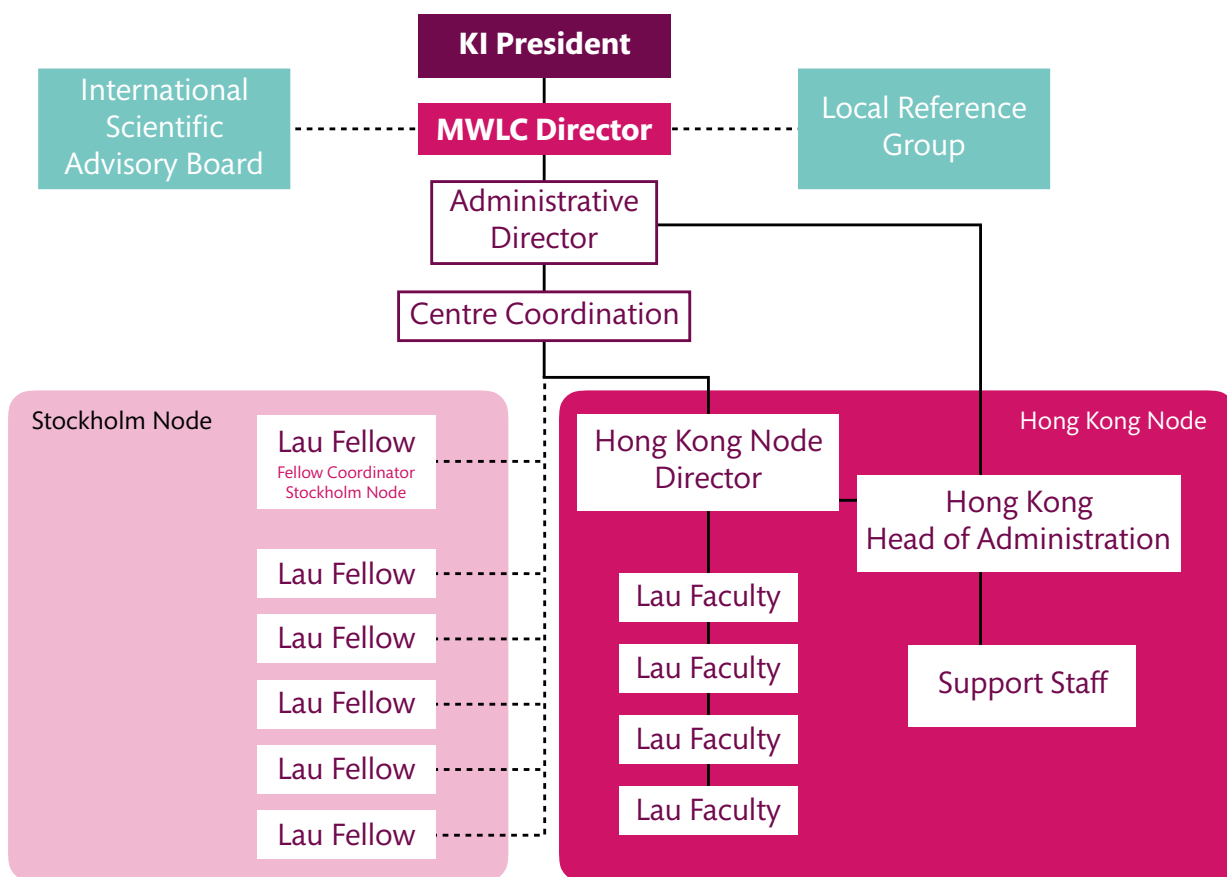
sijie.chen@ki.se / linxian.li@ki.se

Institutional and Administrative Development

by Administrative Director Marie Tell

The building of a solid institutional and administrative infrastructure for MWLC started long before the Centre was inaugurated in 2016. The early focuses had been on setting up the office and lab, recruiting researchers and assimilating the Swedish and Hong Kong rules, standards and routines.

During MWLC's second year of operations KI welcomed its new President, Prof Ole Petter Ottersen. Promoting and enabling international, academic work is one of his long-time priorities, and his interest in and commitment to KI's first overseas establishment has been a positive factor as we develop the organisation further. One immediate result of this commitment was a decision to organise MWLC directly under the President's office, and to appoint a new Director, Prof Sandra Ceccatelli, who took up her assignment on 1 September 2018.



Organisation chart of MWLC.

The past year has been a year of consolidation for MWLC in many aspects. In terms of administrative development, we further streamlined local rules and processes to comply with KI's regulations as well as relevant laws in Sweden and Hong Kong. The two administrative offices in Stockholm and Hong Kong communicate daily to work together as one. It has been a process of facts findings and learning, both together and from each other. The hard work has paid off with positive remarks given by KI's internal auditors who scrutinised MWLC in spring 2018.

In terms of institutional development, KI and MWLC are reaching out to set up partnership with local universities. A Memorandum of Understanding (MOU) was signed between KI and HKU in December 2017. During 2018, the existing MOU with CUHK was extended for another five years, and a new MOU was signed between KI and CityU, to signify the signing parties' commitment for closer academic exchange. HKU has granted honorary appointments to three of our researchers, and reciprocally, a member of the Li Dak-Sum Research Centre, HKU, is seconded to conduct research at MWLC.

International Scientific Advisory Board

From November 2018 MWLC has a Scientific Advisory Board (SAB) formed by highly qualified and internationally respected scientists with expertise in areas relevant for the Centre.

Membership of SAB is as follows:

Prof Eero Castrén (Chair)

Academy Professor
Neuroscience Center
University of Helsinki

Prof Karl Deisseroth

D.H. Chen Professor of Bioengineering and of Psychiatry and of Behavioral Sciences, Department of Bioengineering, Stanford University
Investigator, Howard Hughes Medical Institute

Prof Tak Wah Mak

Professor, Departments of Medical Biophysics and Immunology
University of Toronto
Director, The Campbell Family Institute for Breast Cancer Research at The Princess Margaret Cancer Centre

Prof Lee Rubin

Professor of Stem Cell and Regenerative Biology, Department of Stem Cell and Regenerative Biology
Director of Translational Medicine, Harvard Stem Cell Institute
Harvard University

Prof Fiona M. Watt

Director, Centre for Stem Cells and Regenerative Medicine
King's College London

Local Reference Group

In addition, we have established a Local Reference Group (LRG) with advisory function consisting of prominent leaders and academics from universities in Hong Kong.

Membership of LRG is as follows:

Prof Wai Yee Chan

Pro-Vice-Chancellor / Vice President
Professor of School of Biomedical Sciences
The Chinese University of Hong Kong

Prof Roland Chin

President and Vice-Chancellor
Chair Professor of Department of Computer Science
Hong Kong Baptist University

Prof Nancy Ip

Vice-President for Research and Graduate Studies
Morningside Professor of Life Science
Director of the State Key Laboratory of Molecular Neuroscience
Hong Kong University of Science and Technology

Prof Paul Tam

Provost and Deputy Vice-Chancellor
Li Shu-Pui Professor in Surgery
Chair Professor of Paediatric Surgery
Director of Dr. Li Dak-Sum Research Centre
The University of Hong Kong

Prof Wing-Tak Wong

Chair Professor of Chemical Technology
Dean of Faculty of Applied Science and Textiles
The Hong Kong Polytechnic University

Prof Yuan-Ting Zhang

Chair Professor of Biomedical Engineering
City University of Hong Kong

Both the SAB and the LRG will help by providing expert, non-binding advice to make better strategic decisions fundamental to accomplish the mission of MWLC.

Activity Timeline

Oct 2016

Inauguration Ceremony

On 7 October 2016 MWLC was inaugurated in Hong Kong as the first hub for KI outside Sweden. The ceremony was officiated by Acting Vice-Chancellor of Karolinska Institutet Prof Karin Dahlman-Wright, Mr CY Leung, the Chief Executive of the HKSAR, donor Mr Ming Wai Lau and Mrs Helena Storm, Consul General of Sweden to Hong Kong and Macau.



Oct 2016

Inauguration Scientific Symposium

An inaugural scientific symposium was held in conjunction with the inauguration ceremony. Two of the Centre's researchers, Drs Sijie Chen and Zongli Zheng outlined their research initiatives. Scientists from BaptistU, CityU, CUHK and HKU also put forward plans for inter-institutional collaborations.

Dec 2016

Visit of delegation led by Prof BAI Chun Li, President of Chinese Academy of Sciences

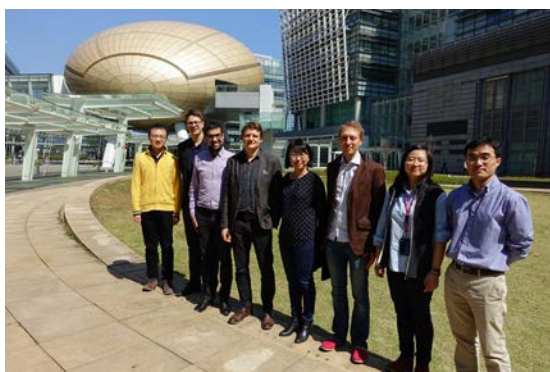
Feb 2017

Visit of delegation led by Ms Madeleine Harby-Samuelsson, Ministry of Health and Social Affairs, Sweden

Feb 2017

MWLC Internal Retreat and Training for Researchers

Principal investigators from the Stockholm node and the Hong Kong node, and management and administration met in Hong Kong for an intensive internal workshop to discuss fundamental issues like laboratory setup, research ethics, IP rights and logging research data, as well as scientific directions and plans, laying the blueprint for developments in the upcoming few years.



Feb 2017

Symposium on “Reparative Medicine and Beyond”

A kick-off symposium where a total of 22 investigators from KI, CityU, CUHK, HKU, HKUST, and PolyU met up and introduced their research interest with a total of over 60 participants. Joint projects took shape after this “match-making” occasion!



Feb 2017

Joint Roadshow with InvestHK in Stockholm and Umeå, Sweden

Feb 2017

Visit of Delegation led by Mr Brian Krieger, Ministry of International Trade, British Columbia Provincial Government, Canada

Mar 2017

Visit of Mr Per Bengtsson, University Director of KI

University Director Mr Per Bengtsson, KI visited MWLC in March 2017 to witness the overall infrastructural and administrative progresses made. He also met the then Chief Executive Mr CY Leung and Secretary for Innovation and Technology Mr Nicholas Yang to discuss how to jointly develop Innovation and Technology in Hong Kong, the Greater Bay Area and Sweden.

Mar 2017

Visit of Panel on Information, Technology and Broadcasting, Legislative Council, Hong Kong



Apr 2017

Visit of Delegation led by Ms Holly Vineyard, Department of Commerce, U.S.A.

May 2017

MWLC Faculty Training and Exchange with Researchers in Stockholm

Jun 2017

Meeting with Mr Antonio Vicente, Head of Cabinet of the EU for Research, Science and Innovation, hosted by Ms Carmen Canto, Head of EU Office in Hong Kong

Jun 2017

Interview by Shenzhen Media Group for documentary “20 years of Shenzhen-Hong Kong Connections”

Jun 2017

National Day of Sweden and Sweden Innovation Forum

On 6 June 2017, the National Day of Sweden, MWLC participated as an official partner in the Sweden Innovation Forum organised by the Consulate General. At the National Day reception held in the same evening, MWLC representatives met with guests from other institutions and companies of Swedish background.

Jun 2017

Visit of Delegation led by Ms Anne Linde, Minister for EU Affairs and Trade of Sweden

Ms Anne Linde, Minister for European Union Affairs and Trade of Sweden, and Mr Stefan Noreén, Acting Consul General of Sweden to Hong Kong and Macau, led a delegation to visit MWLC in June 2017. A laboratory tour followed where our principal investigators introduced their key research to the guests.



Jul 2017

Visit of Dr David Chung, Under Secretary for Innovation and Technology of the HKSAR Government, and Dr Pascal Touchon, Novartis Oncology

Aug 2017

Doctoral course on “Medical Developmental Biology” in Stockholm

Aug 2017

Doctoral course on “The Developing Brain” in Stockholm

Aug 2017

MWLC Hong Kong and Stockholm researchers exchanged ideas in GOSSIPER retreat held in Stockholm



Sep 2017

Internal retreat in Stockholm with participation from both MWLC nodes

Nov 2017

Seminar by Prof Eric Honoré – “The Mechanobiology of Ion Channels: May the Force Be with You!”

Prof Eric Honoré from Institute of Molecular and Cellular Pharmacology-CNRS reviewed the new findings on selectivity and gating mechanisms of stretch-activated ion channels, which hopefully will pave the road for the identification of novel therapeutic strategies.

Nov 2017

Doctoral Course “In Situ Hybridization: Theory and Practice” in Stockholm

The course covered the basics about theory and practice of in situ hybridization techniques, and focused on demonstrating and explaining current in situ hybridization techniques to detect RNAs (microRNA, long-non-coding RNA and mRNA) and DNA molecules in tissues/cells.

Dec 2017

Visit of HRH Prince Carl Philip

During his first official visit to Hong Kong, HRH Prince Carl Philip visited MWLC as part of his official program. After a short introduction to MWLC by Administrative Director Marie Tell and Local Director Ronald Li, the Prince together with his delegation and Consul-General Helena Storm met with our staff.

During the tour of the laboratory, our principal investigators presented examples of their ongoing projects and some of the equipment. The delegation was both very interested and impressed by the prospects of future applications of their work.



Dec 2017

Visit of KI President and Chairman of the KI Board

President of KI, Prof Ole Petter Ottersen together with the Chair of the Board, Mr Mikael Odenberg visited MWLC for the first time on 19 December. It was a great opportunity for the President and Chairman to meet with staff members and learn about our research.



Jan 2018

Internal Retreat Between Stockholm Node and Hong Kong Node

Jan 2018

Scientific Symposium 2018

The scientific symposium was co-organised by MWLC, Aarhus University, BGI, HKBU, HKUST, CUHK, PolyU and HKU.

This was the second opportunity for our scientists, both from the Hong Kong and Stockholm nodes, to connect with other researchers from universities in Hong Kong, and further explore possibilities of collaboration. It was a densely packed day with 20 presentations limited to 20 minutes each on various topics.

The four sessions covered topics on epigenetics of stem cells, biomedical engineering, tissue repair and gene-editing. Speakers, junior lab members, as well as students mingled for exchange of ideas during breaks. New project ideas were brought up.



Feb 2018

Nobel Media AB Visit

Mar 2018

AstraZeneca Visit

Mar 2018

Seminar by Prof Staffan Holmin - "Imaging and Micro-endovascular Navigation - Time to Redraw the Map"

Prof Staffan Holmin from KI illustrated the last years dramatic improvement in invasive stroke treatment and described different strategies for achieving super-selective delivery of cells and substances, and sampling via the endovascular route.

Mar 2018

Swedish University Directors' Visit

KI's university Director Mr Per Bengtsson, together with a group of colleagues representing several of Sweden's largest universities as part of a study visit to Hong Kong, visited MWLC to learn more about establishing a Swedish university branch in Hong Kong.



Apr 2018
Singapore CG Visit

May 2018
Nature Masterclass

A Nature Masterclass in Scientific Writing and Publishing was held at MWLC, on how to write high-quality scientific manuscripts and optimise their chances of being published in high-impact journals.

Jun 2018
Summer Internship Programme

The first MWLC Internship Programme was launched in June. Overwhelming response was received from 13 local and overseas universities with over 50 applicants. 14 interns were selected and allowed to attach to the assigned research group for a period of 4-6 weeks, and received laboratory safety training, observed and assisted in experiments, attended laboratory meetings, scientific seminars and other academic activities of MWLC.



Jun 2018
Dr Li Dak-Sum Research Centre of HKU Visit

Aug 2018
Seminar by Dr Puxiang Lai - "Noninvasive High-resolution Optical Imaging, Focusing, and Stimulation at Depths in Tissue"

Dr Puxiang Lai from PolyU presented his endeavours in the past years of using the synergy of light and sound to achieve non-invasive high-resolution optical imaging, focusing, and stimulation in thick biological tissue. Applications and future direction were also discussed.

Aug 2018
Doctoral Course "Medical Developmental Biology" in Toronto

The international exchange course between KI and University of Toronto, also known as Developmental and Perinatal Biology, was held in Toronto this year. The course covered everything from basic research on stem cells and early embryonic development to clinical aspects of pregnancy, early childhood, epigenetic and ethics.

Sep 2018
Doctoral Course "The Developing Brains" in Stockholm

Oct 2018
The Swedish Foundation for International Cooperation In Research and Higher Education (STINT) Visit

Nov 2018
Reception "Moving Forward Together : Shaping the Future of Ming Wai Lau Centre for Reporative Medicine"

Nov 2018
Internal Retreat Between Stockholm Node and Hong Kong Node

Dec 2018
Symposium on "Human Pluripotent Stem Cell-based Precision Medicine and Therapies for Heart Diseases: From Concepts to Realities"

Grants and Awards to Researchers at the Hong Kong Node 2017-2018

MIT Technology Review Innovators Under 35 China (2017)

The MIT Technology Review Innovators Under 35 Awards is organized annually by the Massachusetts Institute of Technology (MIT) publication to recognize outstanding innovators under the age of 35 around the globe whose superb technical work promises to shape the coming decades. The awards span a wide range of fields, including biotechnology, materials, computer hardware, energy, transportation, communications, and the web. Past winners include Sergey Brin (2002), one of the founders of Google, and Mark Zuckerberg (2007), the founder of Facebook. In 2017, a China chapter was created, and Dr Linxian Li, Assistant Professor at MWLC Hong Kong was among the first group of Chinese young researchers to receive this prestigious award.

Dr Li is listed as a pioneer for exploring the therapeutic potentials of human messenger RNA (mRNA). These molecules are a new class of drugs that can direct cells in the human body to make proteins to prevent or fight diseases, which can potentially replace the current recombinant proteins and monoclonal antibodies. The major challenge limiting the clinical use of mRNA as therapeutics is the inefficient delivery. The platforms Dr Li developed can rapidly and accurately identify the clinical biomaterials candidate for efficient and safe *in vivo* mRNA delivery. His was awarded for being able to integrate the combinatorial biomaterials libraries and high-throughput screening to break the rate-limiting steps in preclinical research and accelerate the development of biomaterials for clinical therapy.



Dr Linxian Li.

VR International Postdoc Grant by Swedish Research Council



Drs Sijie Chen (left) and Sheng Xie (right).

The VR International Postdoc Grant by Swedish Research Council is a career support programme for recently qualified researchers with a doctoral degree from a Swedish university to expand their research network and competence. Dr Sheng Xie, from Dr Sijie Chen's lab at MWLC Hong Kong, was awarded a grant of SEK 2.1 million for a period of two years for his project "Exploration and Development of Soft Supramolecular Assemblies of Mechanoresponsive Fluorescent Materials for Mapping Mechanic Properties & Visualizing Physical Forces in Developing Tissues". The aim of the project is to develop fluorescent tools to visualize the changes of forces and mechanic properties of a tissue in a physiological process. It is a collaboration between Prof Alfonso Ngan's lab at HKU and MWLC Hong Kong.

MWLC Members

Senior Management



Sandra Ceccatelli
Director



Marie Tell
Administrative Director



Ronald Li
Director, Hong Kong node

Centre Coordination



Agneta Wallin Levinovitz
Centre Coordinator



Anna Däckfors
Administrative Coordinator

Bioinformaticians



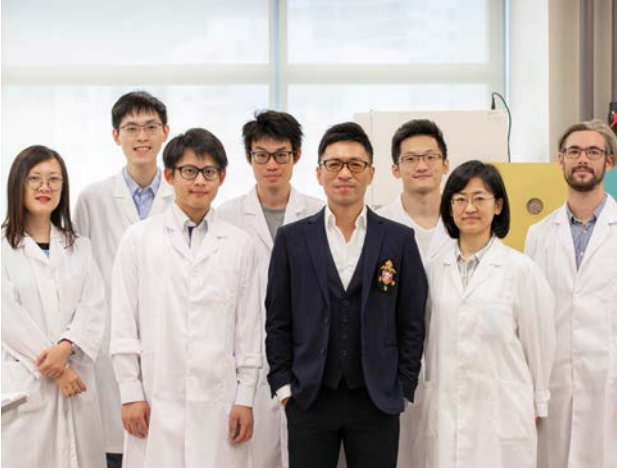
Virpi Ahola
Computational Biologist



Shangli Cheng
Postdoctoral Researcher

Hong Kong Node

Ronald Li MWLC/LDSRC Joint Lab



Back, from left to right: Yin Yu Lam, Joe Lai, Ben Chan; Front, from left to right: Wendy Keung, Nicodemus Wong, Ronald Li, Lin Geng, David Brenière-Letuffe

Sijie Chen Lab



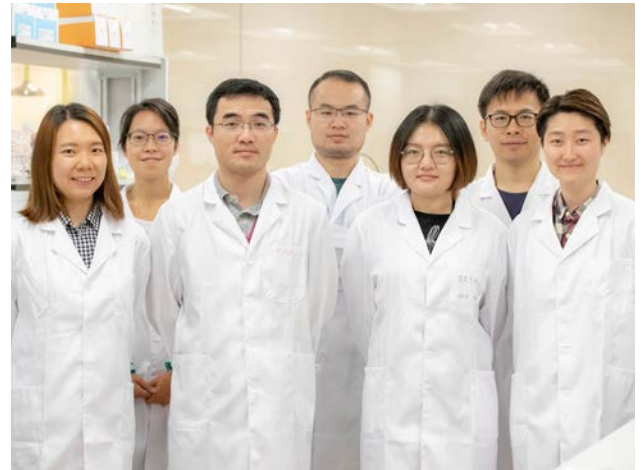
Back, from left to right: Mingyu Wu, Sheng Xie, Fei Li, Alex Wong; Front, from left to right: Miller Leung, Sijie Chen, Hui Gao

Linxian Li Lab



Back, from left to right: Gaofeng Zha, Joe Lai, Jiabing Ran; Front, from left to right: Fei Li, Linxian Li, Jinsong Han

Zongli Zheng Lab



Back, from left to right: Athena Chu, Baifeng Zhang, Qinle Zhang; Front, from left to right: Maggie Chow, Zongli Zheng, Siyu Bao, Jan Keung

Administrative Team



From left to right: Molly Yang, Emily Ip, Lorain Leung

Technical Team



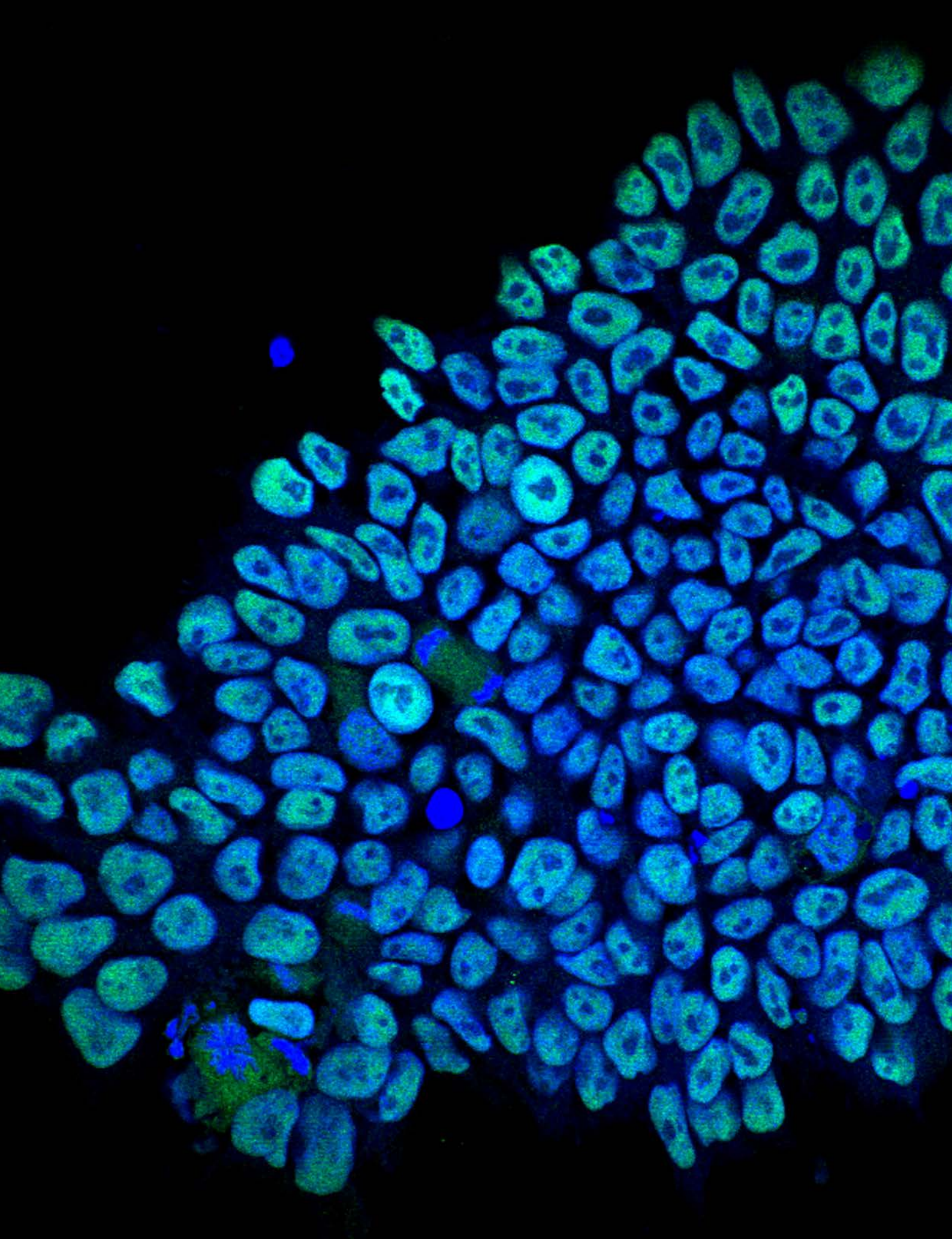
From left to right: Patrick Chan, Joe Lai, Ryan Gao, Eva Fung

Stockholm Node

Lau Fellows



From left to right: Gonalo Castelo-Branco, Simon Elsasser, Christian Goritz, Francois Lallemand, Ning Xu Landen and Fredrik Lanner



Human induced pluripotent stem cells (iPSCs) reprogrammed from peripheral blood mononuclear cells. Photo: Ronald Li.

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