Our First Year

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

Karolinska Institutet

Hej Hong Kong!

The Ming Wai Lau Centre for Reparative Medicine (MWLC) will soon celebrate its first year of operations and, while still being busy with solving many practical issues associated with the establishment of a new research unit, we at Karolinska Institutet (KI) already count ourselves as proud members of Hong Kong's academic community.

MWLC is KI's first overseas branch and the first example of a Swedish public university establishing a unit outside of its national borders. This is a significant milestone in KI's strides to participate in the global effort to promote international collaboration, the generation and free exchange of knowledge, and the implementation of such knowledge into innovation for the improvement of human health.

MWLC will be a strong reinforcement of KI's research in the field of reparative medicine with one node in Stockholm and one node in Hong Kong. It will promote the sharing of knowledge and technical platforms between the two sites, while providing fantastic opportunities for the establishment of many new collaborations with the scientific communities of Hong Kong and the neighboring mainland China.

During the first year of operations, our activities have mainly focused on recruitment and on the organization of research facilities and technical platforms. A significant part of our efforts was devoted to setting up robust administrative routines that will allow operation in compliance with both Swedish and Hong Kong regulations. We are now moving towards the end of the start-up phase, to be completed by the end of 2017, with the establishment of academic leadership, educational programmes, and full integration between the Stockholm and Hong Kong nodes. In 2018, we will initiate a consolidation phase with focus on the realization of our research and education programmes, initiation of local and international collaboration, and work towards the long-term sustainability of the Centre. An International Scientific Advisory Board will be appointed during the spring.

It has been a year of hard work! We have often walked on uncharted territory and we can still see some difficulties ahead but we have learned a lot. Our enthusiasm has increased as we have met new colleagues and embraced the merging of our different cultures. On behalf of KI and the MWLC Steering Group I wish to thank all of you who have worked hard to make this possible!

Prof Maria Masucci
Deputy Vice-Chancellor for International Affairs
Chair of the Steering Group of the Ming Wai Lau Centre for Reparative Medicine

Left to Right: Prof Ronald Li, Director MWLC, KI, Hong Kong; Prof Anders Gustafsson, Dean of Research, KI; Prof Paul Tam, Provost and Deputy Vice-Chancellor, The University of Hong Kong; Mrs Fanny Law, Chairperson, Hong Kong Science and Technology Parks Corporation; Mr Nicholas Yang, Secretary for Innovation and Technology, HKSAR Government; Mr Ming Wai Lau, Donor; Chairman of Chinese Estates Holdings Limited; Ms Tong Xiaoling, Acting Commissioner of the Ministry of Foreign Affairs of the People's Republic of China in the HKSAR ; Mr CY Leung, Chief Executive of the HKSAR; Mr Lars Leijonborg, Chancellor of KI; Prof Karin Dahlman-Wright, Acting Vice-Chancellor, KI; Ms Helena Storm, Consul General of Sweden to Hong Kong and Macau; Prof Maria Masucci, Deputy Vice-Chancellor for International Affairs, KI; Ms Marie Tell, Deputy University Director, KI; Dr Ola Hermanson, Scientific Director, MWLC, KI.

MWLC 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 Ms Helena Storm, Consul General of Sweden to Hong Kong and Macau.

"Hong Kong is a global hub for research and innovation and provides unique opportunities for collaboration and knowledge exchange. By establishing MWLC in Hong Kong, KI will both strengthen its research within reparative medicine as well as take a significant step forward in an area that can have important future implications for human health." Prof Karin Dahlman-Wright pinpointed the strategic position of the Centre in her welcoming remarks.

Prof Karin Dahlman-Wright.

"I have a deep belief in the impact that stem cell research will bring to the medical field and the human race as a whole. Hong Kong is equipped with all the favourable conditions to become a regional hub in this highly specialised area and I take great pride in supporting this meaningful initiative." said Mr Ming Wai Lau. "The establishment of this Centre in Science Park will provide the intended practitioners in Hong Kong a springboard to take their research projects to the world stage in reparative medicine."

Mr Ming Wai Lau.

In her congratulatory speech, Ms Helena Storm highlighted the exciting opportunities for both Sweden and Hong Kong brought by the setting up of the Centre. Researchers from around the world will be able to conduct research in reparative medicine at the new facility with the future goal of being able to replace damaged or lost tissue.

Vision and Mission of MWLC

Vision

As part of KI, the vision of the MWLC 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.

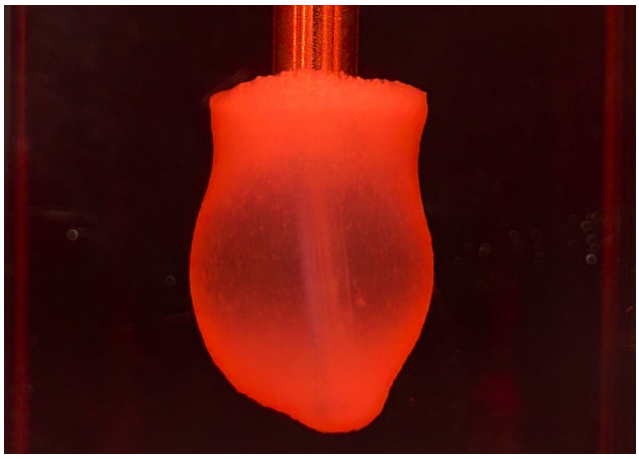
The MWLC will contribute to the development of this research field by:

1. 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
2. Using the Hong Kong site as a starting and bridging point to facilitate collaborations with leading institutions in Asia, Europe, and North America
3. Contributing to the establishment of a regulatory framework for reparative medicine and development and commercialisation in this and related technologies
4. Serving as a "catalyst" for the interactions between academia, biotech industry, and society (e.g., regulatory policy, clinical trials) in the development of the reparative medicine field
5. 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

A Centre with Two Nodes - Hong Kong and Stockholm

MWLC of KI has two nodes, one in Hong Kong and one in Stockholm, currently with 4 and 7 scientific teams, respectively, specialising in different aspects of reparative medicine. Each scientific team is led by a principal investigator; the eleven teams closely interact as one centre for collaborative efforts via a series of workshops and seminars interchangeably held in Hong Kong and Stockholm, as well as other routine investigator-initiated communications. Such interactions are further promoted by our internal infrastructure such as common core facilities co-directed by principal investigators.

Beating Miniature Human Hearts in Your Palm - 3D Human Heart Organoid and *the Cardiac Initiative of MWLC* by Prof Ronald Li



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

Human pluripotent stem cells are able to divide infinitely and differentiate into any cell types of the body, including heart muscle cells termed as ventricular cardiomyocytes. Single ventricular cardiomyocytes can serve as fundamental blocks for building more complex tissues such as patches, contracting muscle strips and 3D fluid-pumping chambers (a.k.a. mini-hearts or cardiac organoids). Normal mini-hearts from different ethnic groups as well as sick hearts that carry particular human disease mutations can be cloned or fabricated for studying genetic diversity and disease mechanisms.

Prof Li and his co-workers at MWLC are now applying these technologies to study the fundamental biological mechanisms underlying a range of heart conditions with contractile defects and/or arrhythmias (i.e. electrical disturbances of the heart) with the goal of identifying new biomarkers for these diseases that afflict tens of millions of patients every year. On the translational front, such human heart prototypes are being used by industrial partners as the basis for developing high-throughput instrumentation and analytical programmes to facilitate the discovery and development of novel drugs and therapeutics.

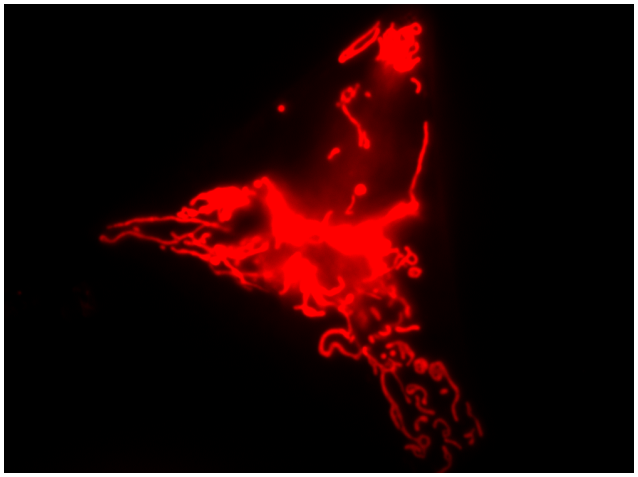
In collaboration with the Dr Li Dak-Sum Research Centre at The University of Hong Kong (HKU), MWLC has been awarded an Innovative and Technology Fund for establishing a "Molecular Encyclopaedia" for the early human heart development. The team, which includes Prof Yiu-Fai Cheung, Prof Godfrey Chan, Dr Wendy Keung of HKU and Profs Kenneth Chien, Ronald Li and Emil Hansson representing KI, converts a range of patient samples locally available in Hong Kong with congenital heart conditions (e.g., single ventricle associated with heterotaxy syndrome, pulmonary atresia with intact ventricular septum, Tetralogy of Fallot) to human pluripotent stem cell-derived ventricular cardiomyocytes, followed by systematically characterising their single-cell transcriptomes (with Dr Zongli Zheng, MWLC; see P.7) for discovering new biomarkers so as to gain insights into patho-physiological developments for potential cures in future.

Prof Li's group also collaborates with Dr Gary Tse, Dr Faye Tsang and Prof Xiaoqiang Yao at CUHK to elucidate the molecular mechanisms underlying atrial and ventricular tachycardia at the systems level, attempting to explain arrhythmogenesis by electrical abnormalities, and the roles of TRP channels in cardiac functions, using a combination of induced pluripotent stem cells and their various engineered cardiac tissue constructs for producing human disease models such as congenital cardiac ion channelopathies that include Long QT and Brugada syndromes.

In addition to the above-mentioned KI and Hong Kong investigators, other long-term collaborators with over one or even two decades of relationships from Johns Hopkins University (Prof Gordon Tomaselli, Prof Leslie Tung, Prof Linzhao Cheng), Stanford University (Prof Joesph Wu), Wyss Institute (Prof Christopher Chen), University of California (Prof Michelle Khine, Dr Deborah Lieu) and Icahn School of Medicine at Mount Sinai in Manhattan (Prof Roger Hajjar and Dr Kevin Costa) in the U.S. collectively form the Cardiac Initiative of MWLC, whose objective is to develop next-generation therapeutics, devices and therapies for debilitating heart conditions.

For further information, please contact **Prof Ronald Li**, *ronald.li@ki.se*

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 or even cells are usually too small, and with signals too weak to be observed. Abnormal cellular microenvironments often lead to diseases, but remain invisible until later 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 will 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 or detect disease-related biomarkers, etc.

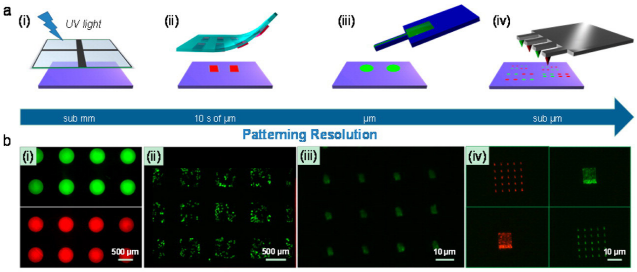
Dr Chen's lab is particularly interested in developing novel fluorescence-based tools and techniques for visualising cell structures so as to understand how these biological fundamental building blocks work and how they intriguingly interact with each other in response to the environments. These tools 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 is establishing close collaborations with Dr Linxian Li and other investigators in Hong Kong, including Prof Alfonso Ngan (HKU), Prof Benzhong Tang (HKUST), Dr Weiping Wang (HKU) and Dr Xin Zhao (PolyU). 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 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 and a visiting scientist in Walter and Eliza Hall Institute of Medical Research. She later joined Prof Ana Teixeira's group as a Postdoctoral Fellow at KI in 2015 before her recruitment to MWLC.

For further information, please contact **Dr Sijie Chen**, *sijie.chen@ki.se*

One Cell, One Surface, One Vector – Surface Engineering and RNA Delivery 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-surface interactions to improve their functions. However, the rational design of delivery systems and surfaces 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.

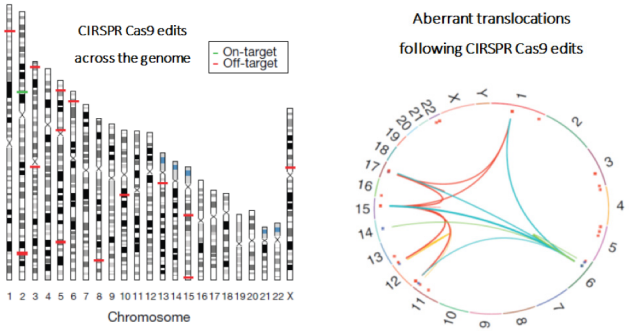
Dr Li's lab is dedicated to integrate the combinatorial biomaterials libraries, cell microarrays, and high-throughput screening to break the rate-limiting steps in preclinical research and accelerate the development of biomaterials for clinical therapy. The goal is to develop innovative tools and technology platforms to find the ideal surface and gene vector for the cell of interest. The tools and platforms will be used to accelerate the development of novel biomaterials for global healthcare challenges and lead the next generation of technological breakthroughs.

With a focus on technological advancement, along with collaborations with investigators at the Stockholm node, including Drs Gonçalo Castelo-Branco, Christian Göritz and Ning Xu Landén, Dr Li and his team are developing new technologies 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, he pursued postdoctoral research at Massachusetts Institute of Technology. Committed to translating new materials for medical use, he focuses on developing biomaterials to deliver RNA therapeutics and engineering biointerfaces 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.

For further information, please contact **Dr Linxian Li**, *linxian.li@ki.se*

Less is More - Next-generation Sequencing and Single-cell Profiling
by Dr Zongli Zheng



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

Fundamentally, numerous diseases are rooted at the DNA level. The DNA 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 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.

In Dr Zheng's lab, the scientists are interested in developing new technologies for assessing and refining CRISPR off-target changes in the genome. Highly sensitive technologies and effective approaches are needed for fully assessing risks and benefits before potential applications. Also, the team is interested in developing new technologies for genomic characterisation and genome-wide functional screening to identify pathways and biomarkers for predicting a variety of disease states and progression, and therapeutic targets.

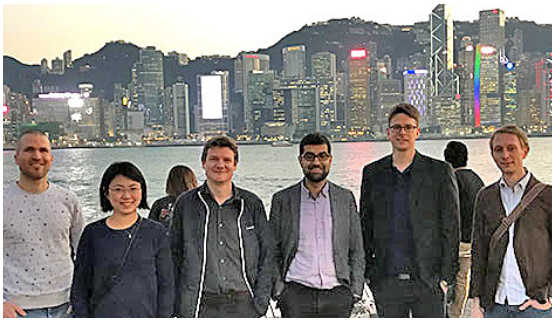
Dr Zheng has developed novel technologies and computational algorithms for discovering new therapeutic targets in cancer patients, and the simple and robust diagnostics method named AMP has been adopted globally in both research and clinical settings. The AMP method has become a new gold standard as the clinical assay for gene fusion diagnosis and has also helped accelerate recent FDA approvals of new targeted therapies.

With a focus on technological advancement, along with initial collaborations with Drs Gonçalo Castelo-Branco, Ning Xu Landén and Fredrik Lanner at the Stockholm node as well as Drs Mingliang He (CityU), Jin Young Kim (CityU) and Anderson Shum (HKU) in Hong Kong, Dr Zheng and his team are developing new technologies for integrating next-generation sequencing, single cell and genome editing platforms to improve the scalability, flexibility, resolution and precision of gene editing and omics technologies. The goal is to answer important biological questions, and to contribute to the practice of precision medicine for aging-related and other diseases

Dr Zheng received his PhD degree from KI in 2011. Based on large-scale longitudinal cohort, his doctoral study focused on the identification of molecular determinants in *Helicobacter pylori* and its host for the development of stomach cancer. He also developed a novel titration-free library preparation method for next generation sequencing. He then joined the Harvard Medical School, Boston as an International Postdoctoral Fellow supported by the Swedish Research Council, where he focused on clinical sequencing for cancer patients for targeted therapy and the CRISPR genome editing tools to characterize and refine its off-targets..

For further information, please contact **Dr Zongli Zheng**, *zongli.zheng@ki.se*

The Six Lau Fellows at a Glance



Left to Right: Drs Francois Lallemend, Ning Xu Landén, Christian Göritz, Gonçalo Castelo-Branco, Fredrik Lanner, Simon Elsässer

The Lau grants were established to support world-leading research in reparative medicine performed at KI and to deepen existing and establishing new research partnerships with top universities in Hong Kong and China. The grants are designed to support group leaders employed by KI at the stage where they are consolidating their own independent research. After rounds of selection, the following six researchers have been identified with cutting-edge expertise consistent with the mission and vision of MWLC. The Lau Fellows are MWLC investigators who form an integrated part of the Centre.

Dr Gonçalo Castelo-Branco

Associate Professor
Department of Medical Biochemistry and Biophysics

The main focus of Dr Castelo-Branco's research group is to investigate how distinct epigenetic 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.

Dr Simon Elsässer

Assistant Professor
Department of Medical Biochemistry and Biophysics

Short peptides encoded by short open reading frames (sPEPs) are translated abundantly in prokaryotic and eukarytic cells, yet their functions remain mysterious. Dr Elsässer's group aims to elucidate the role of Short peptides encoded by sPEPs in stem cell biology and lineage specification.

Dr Christian Göritz

Associate Professor
Department of Cell and Molecular Biology

The research of the Dr Göritz's lab focuses on the mechanisms that mediate scarring and repair of the central nervous system. The group aims to develop and test strategies that could be utilized to enhance tissue repair, with the long-term goal to facilitate repair in humans.

Dr Francois Lallemend

Associate Professor
Department of Neuroscience

The main focus of Dr Lallemend's research is to investigate how neurons are integrated into functional circuits during development. His team aims to identify key molecular players of neuronal cell death and modulate them in neural tumours to provide new efficient treatment.

Dr Ning Xu Landén

Associate Professor
Department of Medicine Solna

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 goal of Dr Landén's research is to develop novel RNA-based treatments to improve healing of human skin wounds.

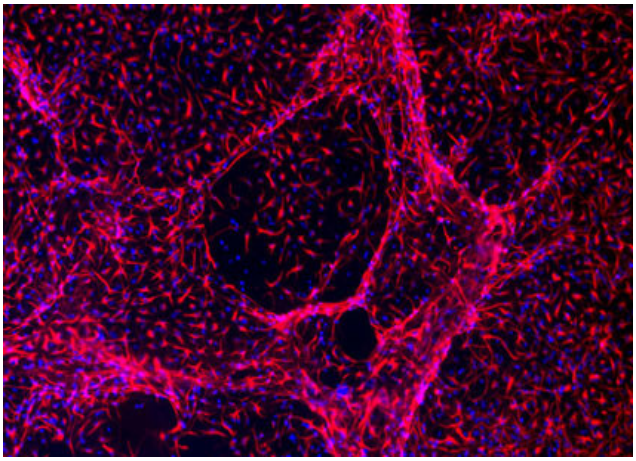
Dr Fredrik Lanner

Assistant Professor
Department of Clinical Science, Intervention and Technology

The main focus of Dr Lanner's group is to explore how pluripotent stem cells are regulated in the human embryo and how embryonic stem cells could be used for treatment of age-related macular degeneration.

The Lau Fellows and their research will be presented in more details in our future newsletter series.

Brain Reign: ***The Neural Initiative of MWLC*** by Dr Ola Hermanson



Cortical stem cells grown on 3D-substrate generated by recombinant spider silk protein and differentiated into functional astrocytes.

KI has a strong tradition of pursuing groundbreaking science in various aspects of neurobiology. The research spans from clinical neurology, surgery, and psychiatry, to basic neuroscience including electrophysiology and histology. More recently, neural stem cell research, developmental, and molecular neuroscience have emerged as intense focus areas.

MWLC is now the home for many successful developmental neuroscientists at KI. Dr Gonçalo Castelo-Branco and his colleagues have successfully implemented single cell technologies to decipher the cell types of the developing brain (Science 2015, 2016), and is now collaborating with Dr Zongli Zheng who has successfully established the single cell technology at the node in Hong Kong. Dr Francois Lallemend focuses on the neural crest and peripheral nervous system (Cell 209, Science 2017) and Dr Christian Göritz studies the role of pericytes in nervous system repair (Science 2011, 2014).

In addition to the single cell analysis and biomedical engineering, MWLC is setting up a functional bioprinting unit for 3D bioprinting of biomaterials and stem cells to enable reproducible generation of neural organoids, such as minibrains generated from human iPS cells. This is done in collaboration with Dr Hermanson and his colleagues who have vast experience in bioprinting and 3D cell cultures (Biomaterials 2007, 2012, Nature 2007).

There are already numerous collaborations between KI in general, MWLC, and local universities in Hong Kong in developmental and molecular neuroscience. These include e.g. Prof Paul Tam and Prof Mai Har Sham (HKU), Prof Ken Yung (BaptistU), Dr Danny Leung (HKUST), Dr Anna Falk (Cell Reports 2016, Mol Psychiatry, 2017) who is the director of the central KI unit for generation of hiPSC-derived neural progenitors, and Dr Igor Adameyko (eLife 2017, Science 2017), a leading imaging specialist focusing on neural crest development.

During 2017-18, several workshops, courses, and conferences with an emphasis on developmental neuroscience will be held in Hong Kong and Stockholm to foster new interactions and collaborations. Two courses/conferences took place in Stockholm in August 2017 ("Medical Developmental Biology" and "Developing Brain"). MWLC will further take advantage of the close collaborations KI has developed with other leading institutions in the field, including University of Toronto. The course/conference in "Medical Developmental Biology" in August hosted speakers and participants from KI, University of Toronto, and several Hong Kong universities including HKU, CityU, and HKUST, and further triangular collaborations among the three cities are on-going. A rapid and synergistic development in the field is expected in the very near future where MWLC will play a key role.

For further information, please contact **Dr Ola Hermanson**, *ola.hermanson@ki.se*

Our First Year

Since the official inauguration on October 7, 2016, our primary focus has been to fully establish our infrastructure such as laboratory, human resources, recruitments, and other administrative aspects that are crucial to long-term development, all in addition to the groundwork for scientific development. In our first year, MWLC has organized two scientific symposia and two doctoral courses, received more than 15 official delegations, student interns as well as numerous individual academic, governmental, and industrial partners from around the world to our Hong Kong site, while making serious efforts to reach out to the international community in the spirit of globalisation.

Oct 2016
Inauguration Ceremony

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 (Drs Ola Hermanson, Gonçalo Castelo-Branco, Simon Elsässer, Christian Göritz, Francois Lallemend, Ning Xu Landén, Fredrik Lanner) and the Hong Kong node (Prof Ronald Li as Director of Hong Kong node, and Drs Sijie Chen, Linixian Li, Zongli Zheng), 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, Pearl River Delta 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.

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"

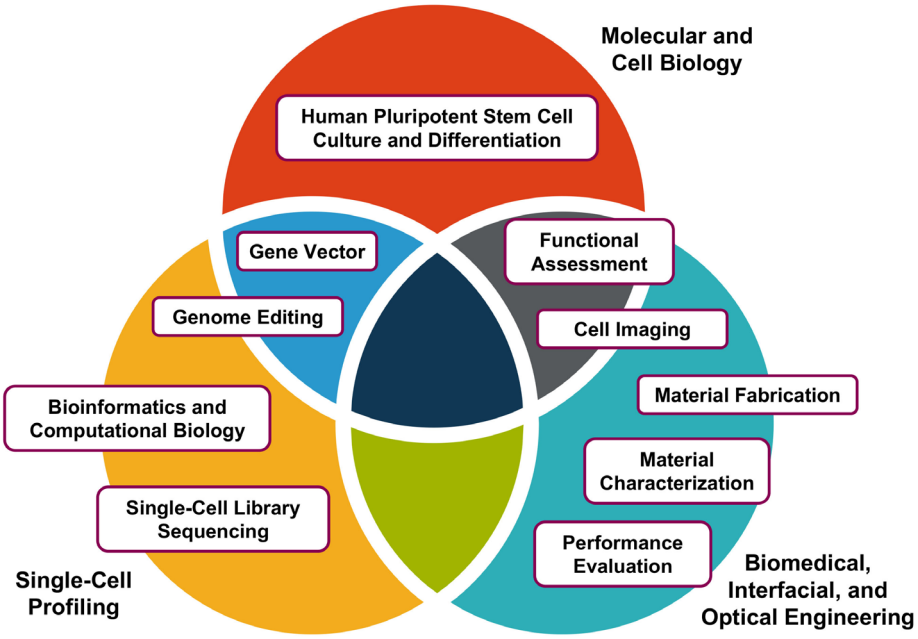
Aug 2017
Doctoral course on "The Developing Brain"

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

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

The MWLC Core Facility is established to facilitate local and international collaborative research. Currently, the MWLC Core Facility consists of 3 Divisions - Molecular and Cell Biology Division, Single-Cell Profiling Division, and Biomedical, Interfacial, and Optical Engineering Division. Our specialists offer a range of cutting-edge service at the Core equipped with state-of-the-art expertise, devices and instruments.



Molecular and Cell Biology Division
Laboratory Manager: Mr Patrick Chan; Laboratory Officer: Dr Ryan Gao
Committee members – Dr Sijie Chen, Dr Wendy Keung (HKU), Dr Linxian Li, Prof Ronald Li, Prof Ken Yung (BaptistU), Dr Zongli Zheng

Molecular and Cell Biology Division is set up to facilitate the development of basic and translational stem cell research. The Division 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 collaborating institutions. *patrick.chan@ki.se / ryan.gao@ki.se*

Single-Cell Profiling Division
Co-directors – Drs Gonçalo Castelo-Branco, Zongli Zheng
Committee members – Drs Wendy Keung (HKU), Fredrik Lanner

There are growing demands in the broad molecular biology research field for single cell-based analyses, including transcriptomics and genomics, and on larger scales. The goal of the Single-Cell Profiling Division is to provide scalable single-cell profiling and related bioinformatics analysis, facilitated by a central infrastructure and resource support from MWLC, leveraging on the world-leading single-cell expertise from KI. *goncalo.castelo-branco@ki.se / zongli.zheng@ki.se*

Biomedical, Interfacial, and Optical Engineering Division
Co-directors – Drs Sijie Chen, Linxian Li
Committee members – Drs Simon Elsässer, Anderson Shum (HKU), Weiping Wang (HKU), Xin Zhao (PolyU)

Biomedical, Interfacial, and Optical Engineering Division is established to meet the needs for 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 Division 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 Division 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*

Representative Publications

While MWLC is new and just turning 1-year old, our established investigators have joined the Centre by bringing with them significant scientific momentum along with years of technical experience as well as collaborative relationships from within and outside of KI. MWLC teams have published during the first 10 months a total of 31 peer-reviewed scientific publications, of which 13 were completed at MWLC and with the Centre's support. Selected representative publications are given below to illustrate our investigators' expertise and recognition by the international scientific community.

A. Furlan, V. Dyachuk, M. E. Kastriti, L. Calvo-Enrique, H. Abdo, S. Hadjab, T. Chontorotzea, N. Akkuratova, D. Usoskin, D. Kamenev, J. Petersen, K. Sunadome, F. Memic, U. Marklund, K. Fried, P. Topilko, F. Lallemend, P. V. Kharchenko, P. Ernfors, I. Adameyko, **Multipotent peripheral glial cells generate neuroendocrine cells of the adrenal medulla**. Science 357 (2017).
Adrenalin, a key stress hormone in our body, is produced by the chormaffin cells of our adrenal glands that were thought to originate from neural crest cells. Instead, results of this study show that these cells originate from Schwann cell precursors using the motor nerves as a scaffold to reach their homing site and differentiate into adrenal medulla cells.

C. Peng, L. Li, M. D. Zhang, C. Bengtsson Gonzales, M. Parisien, I. Belfer, D. Usoskin, H. Abdo, A. Furlan, M. Haring, F. Lallemend, T. Harkany, L. Diatchenko, T. Hokfelt, J. Hjerling-Leffler, P. Ernfors, **miR-183 cluster scales mechanical pain sensitivity by regulating basal and neuropathic pain genes**. Science 356, 1168-1171 (2017).
Pain serves the useful purpose of alerting us to danger. Chronic pain, however, can arise from dysfunctional responses. This study shows that pain threshold in nociceptors can be modulated by mechanisms involving a specific cluster of microRNAs, and that the same cluster also regulates the threshold of neuropathic pain in skin touch mechanoreceptors, which normally do not elicit pain. This report provides important new insights into molecular mechanisms that control pain threshold, both in normal and pathological conditions.

X. Li, D. Li, J. D. Wikstrom, A. Pivarcsi, E. Sonkoly, M. Stahle, N. X. Landen, **MicroRNA-132 promotes fibroblast migration via regulating RAS p21 protein activator 1 in skin wound healing**. Scientific Report 7, 7797 (2017).
We have previously shown that microRNA-132 facilitates inflammation-proliferation transition in epidermal keratinocytes, and here we further demonstrate that microRNA-132 promotes dermal fibroblasts migration, both of which processes are impaired in chronic non-healing wounds. Thus, we propose that microRNA-132 holds great promise for treating chronic wounds.

A. J. Collier, S. P. Panula, J. P. Schell, P. Chovanec, A. Plaza Reyes, S. Petropoulos, A. E. Corcoran, R. Walker, I. Douagi, F. Lanner, P. J. Rugg-Gunn, **Comprehensive Cell Surface Protein Profiling Identifies Specific Markers of Human Naive and Primed Pluripotent States**. Cell Stem Cell 20, 874-890 e877 (2017).
In this study, we identify novel cell surface markers of the very first cell of the human body which will be very useful in understanding the nature of pluripotent stem cells. With these markers, we can now physically sort out cells as the transition between the two pluripotent states, termed naive and primed.

A. Plaza Reyes, F. Lanner, **Towards a CRISPR view of early human development: applications, limitations and ethical concerns of genome editing in human embryos**. Development 144, 3-7 (2017).
In this review, we summarize our view of how we think genome editing using CRISPR can be utilized to study how the early human embryo is regulated and how pluripotent emerge. We also relate to the ethical perspective associated with this field of research. We anticipate that such studies will shortly show the power of this methodology and open for functional gene studies in the human embryo. This is one of the main goals of my research programmes within MWLC.

N. Winblad, F. Lanner, **Biotechnology: At the heart of gene edits in human embryos**. Nature 548, 398-400 (2017).
In this News & Views we discuss the Nature paper from the Mitalipov group which suggests that CRISPR based genome editing of the early human embryo may become a feasible approach to treat monogenic inherited disease.

S. Hildebrand, S. Hultin, A. Subramani, S. Petropoulos, Y. Zhang, X. Cao, J. Mpindi, O. Kalloniemi, S. Johansson, A. Majumdar, F. Lanner, L. Holmgren, **The E-cadherin/AmotL2 complex organizes actin filaments required for epithelial hexagonal packing and blastocyst hatching**. Scientific Report 7, 9540 (2017)
In this study, we identify that AMOTL2 is a regulator of cell shape in the pre-implantation embryo. Without it the cells fail to properly form their hexagonal shape and fail as a consequence to hatch from the zona pellucida. We also show that AMOTL2 control cell shape in most epithelial cell types in addition to the trophectoderm of the preimplantation blastocyst.

E. K. Lee, D. D. Tran, W. Keung, P. Chan, G. Wong, C. W. Y. Chan, K. Costa, R. A. Li, M. Khine, **Machine learning of human pluripotent stem cell-derived engineered cardiac tissue contractility for automated drug classification**. Stem Cell Reports (in press).
This study reports a novel software-based approach of using artificial intelligence or machine learning in combination with the various engineered human heart tissues for automatically classifying drugs based on their toxicity and functions, representing a potential scalable industrial method for the discovery and development of new drugs.

A. M. Shum, H. Che, A. O. Wong, C. Zhang, H. Wu, C. W. Chan, K. Costa, M. Khine, C. W. Kong, R. A. Li, **A Micropatterned Human Pluripotent Stem Cell-Based Ventricular Cardiac Anisotropic Sheet for Visualizing Drug-Induced Arrhythmogenicity**. Advanced Materials 29, (2017).
This study reports the engineering of a novel human heart patch by design that enables for the first time the visualisation of the toxic lethal arrhythmogenic side effect of a few "anti-arrhythmic" drugs under development that previously escaped conventional animal studies but ended up being withdrawn from clinical trials that involved over 1500 patients after ironically causing deaths by lethal arrhythmias. This kind of in vitro diagnostic tool could have prevented patient deaths.

MWLC Members and Associates

Steering Group

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Postgraduate Students

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Job Opportunities

MWLC is home to scientists who share a passion for cutting-edge research in reparative medicine and related subjects. We are always looking for candidates who share the same passion, and are determined to improve human health.

We will soon be announcing several computational biologists positions to lead the development of computational algorithms and pipelines for analysing large-scale next-generation sequencing data derived from in-house newly developed technologies for single-cell and CRISPR experiments to solve important biomedical problems.

We welcome applications from candidates with PhD degree in Computational Biology, Biostatistics, Bioinformatics, or relevant fields, with strong programming skills in C, C++, Java, JavaScript, Python, PERL or R.

If you are interested in joining us, please feel free to contact us at mwlc@ki.se or visit our website for specific job opportunities (http://ki.se/en/research/job-opportunities).