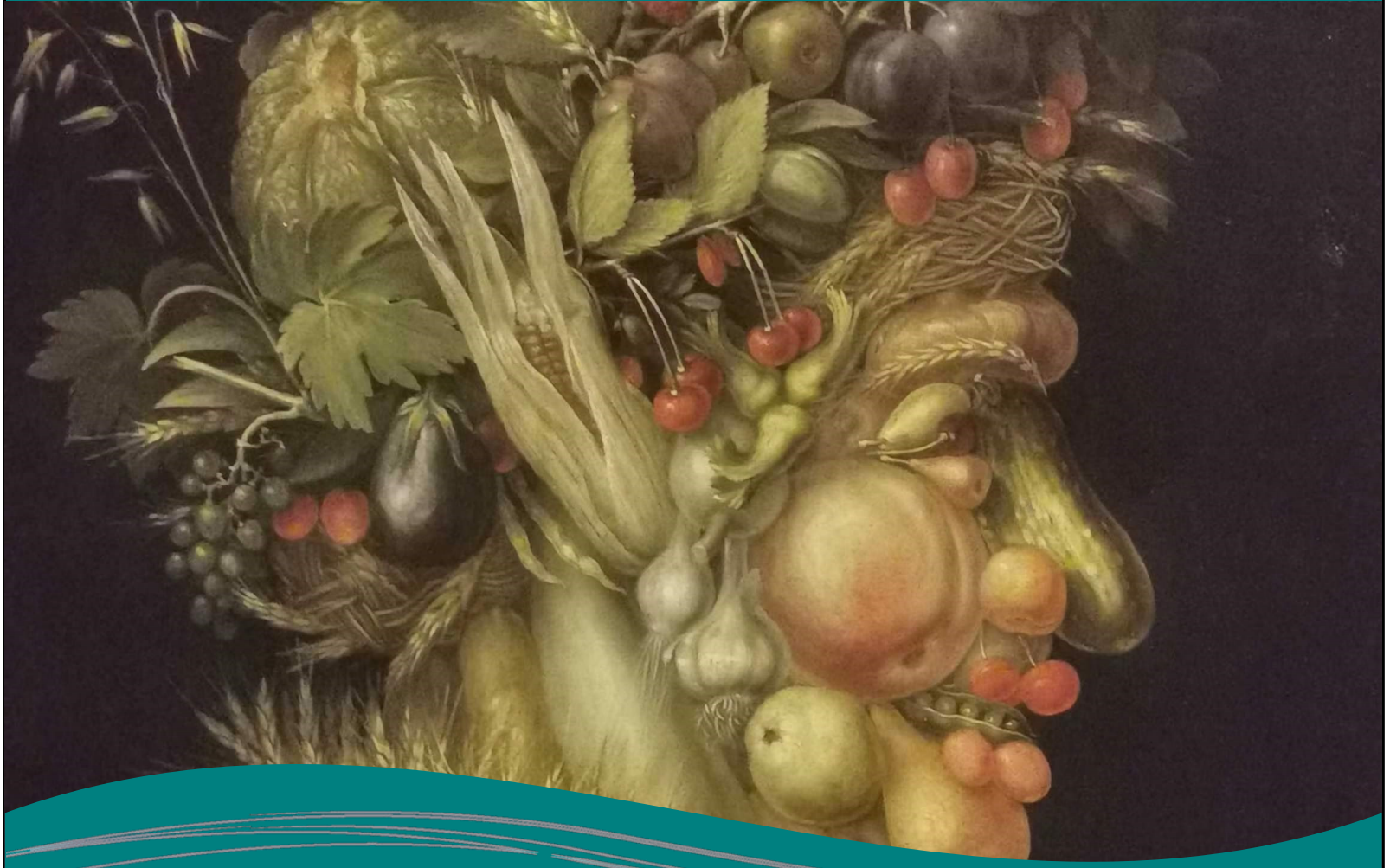


10th CUHK International Symposium on Stem Cell Biology & Regenerative Medicine

3rd Guangdong-Hong Kong-Macau Greater Bay Area International Conference on Regenerative Medicine

Musculo-Skeletal Regeneration: From Technology to Therapy

8-9 April 2024

1/F Auditorium, Main Clinical Block and Trauma Centre, Prince of Wales Hospital, Shatin, Hong Kong

Day 1 (8 April 2024)

1/F Auditorium, Main Clinical Block and Trauma Centre
Prince of Wales Hospital, Shatin, Hong Kong

09:20-09:50	**Welcome addresses by Co-organizers:** **Prof. Rocky Tuan, Vice-Chancellor and President of CUHK (5 min);** **Prof. Wei Ge, Vice Rector, UM (5 min);** **Prof. Ren-He Xu, University of Macau, GBRM (5 min);** **Prof Gang Li, History of CUHK SCRM (10 min);** **Photo Taken**	**Prof. Gang Li** **Prof. Ren-He Xu**
	Session 1: Emerging Technologies	**Moderators:** **Prof. Gang Li** **Prof. Ren-He Xu**
09:50-10:10	Prof. Rocky Tuan, PhD The Chinese University of Hong Kong, Hong Kong **Title: Societal Relevance of Stem Cell Research**	
10:10-10:30	Prof. Yufang Shi, PhD Soochow University, China **Title: Immune Regulation during Tissue Regeneration**	
10:30-10:50	Prof. Chunming Wang, PhD University of Macau, Macau **Title: Engineering a glycan matrix to reshape spleen tissue for ectopic liver regeneration**	
10:50-11:10	Prof. Jongpil Kim, PhD Dongguk University, Korea **Title: Recent advances in stem cells, cell reprogramming, and gene editing for Neurological diseases therapeutics**	
11:10-11:30	**Tea Break**	
	Session 2: Stem Cell Biology	**Moderators:** **Prof. Chuxia Deng** **Prof. Wei Li**
11:30-11:50	Prof. Wei Li, PhD Institute of Zoology, Chinese Academy of Sciences, China **Title: Development of novel stem cell tools for research and translation**	
11:50−12:10	Prof. Guokai Chen, PhD University of Macau, Macau **Title: Ion channel modulation induces cardiomyocytes from human pluripotent stem cells**	
12:10-12:30	Prof. Ying Wang, PhD Shanghai Institute of Nutrition and Health, CAS, China **Title: How non-essential fatty acids maintain tissue homeostasis**	
12:30-12:50	Prof. Xuexun Fang, PhD College of Life Sciences, Jilin, University **Title: Anti-inflammatory and anti-cancer properties of Amuc_1434, a mucin degrading protease from *Akkermansia Muciniphila***	
12:50-14:20	**Lunch break**	

Program Rundown

	Session 3: New Thoughts from and for Musculoskeletal System	**Moderators:** **Prof. Louis Cheung** **Prof. Bo Shen**
14:20-14:55	Prof. Gang Li, MBBS, DPhil The Chinese University of Hong Kong, Hong Kong **Title: Distraction Histogenesis: Biological Insights and Novel Applications**	
14:55-15:20	Prof. Bo Shen, PhD National Institute of Biological Sciences, Beijing (NIBS) and Tsinghua University, China **Title: Mechanosensitive Osteolectin+ Cells in Skeletal Development and Homeostasis**	
15:20-15:45	Prof. Haobo Pan, PhD Shenzhen institutes of advanced technology, Chinese Academy of Sciences, China **Title: Biological interaction between Materials and human body**	
15:45-16:10	Prof. Louis Cheung, PhD The Chinese University of Hong Kong, Hong Kong **Title: Advancing Sarcopenia Treatment: A Focus on Myosteatosis, Mitochondria, and Neuromuscular Health**	
16:10-16:35	**Tea Break**	
	Session 4: Clinical and Translational Research	**Moderators:** **Prof. Jian Yang** **Prof. Alan Li**
16:35-17:00	Prof. Alan Li, PhD The Chinese University of Hong Kong, Hong Kong **Title: Human Stem Cell-derived Joint-on-a-Chip Systems for Modeling Joint Degeneration and Developing Regenerative Therapies**	
17:00-17:25	Prof. Jian Yang, PhD Westlake University, China **Title: Citrate: The Nexus of Cellular Mechanism and Orthopedic Biomaterials Innovation**	
17:25-17:50	Prof. Fei Chang, MD, PhD Jilin University, China **Title: The Treatment of Osteochondral lesions: From Current Practices to Biomechanical Insights**	
18:30-21:30	**Invited Speakers, Guests and Faculty Members Dinner**	

Day 2 (9 April, 2024)

1/F Auditorium, Main Clinical Block and Trauma Centre
Prince of Wales Hospital, Shatin, Hong Kong

09:00-09:30	Take a walk from hotel to conference venue	**Lead by students from conference hotel Regal Riverside Shatin**
	Session 5: Emerging Technologies	**Moderators:** **Prof. Ren-He Xu** **Prof. Liming Bian**
09:30-09:50	Prof. Ren-He Xu, PhD University of Macau, Macau **Title: hESC-derived MSCs for clinical trials, developmental study, and cancer research**	
09:50-10:10	Prof. Liming Bian, PhD South China University of Technology, China **Title: Cell-adaptable hydrogels for cell delivery and 3D culture**	
10:10-10:30	Prof. Fan Zhou, PhD Tsinghua University, China **Title: Peri-implantation embryo development and regulation**	
10:30-10:50	Prof. Jiahong Lu, PhD University of Macau, Macau **Title: Fighting Alzheimer disease by targeting autophagy: from basic study to pharmacological application**	
10:50-11:10	Prof. Qi Zhao, PhD University of Macau, Macau **Title: Antibody-based Immune-cell Therapy Against Cancer**	
11:10-11:30	**Tea Break**	
	Session 6: Stem Cell Biology	**Moderators:** **Prof. Cynthia Jiang** **Prof. Jinyu Liu**
11:30-11:50	Prof. Huating Wang, PhD The Chinese University of Hong Kong, Hong Kong **Title: Regulation of skeletal muscle stem cells in aging**	
11:50-12:10	Prof. Nam-Hyung KIM, PhD Wuyi University, China **Title: Application of Stem Cell-Derived Organoids in Biomedical Research**	
12:10-12:30	Prof. Jinyu Liu, MD, PhD Jilin University, China **Title: PBX1 in regeneration medicine**	
12:30-12:50	Prof. Cynthia Jiang, MD, PhD The Chinese University of Hong Kong, China **Title: Unveiling the Potential of hESC-derived Neural Crest Models: Insights into Neuroblastoma and Therapeutic Strategies for Hypoxic-Ischemic Encephalopathy**	
12:50-14:00	**Lunch break**	

Program Rundown

	Session 7: Student Presentations	**Moderators: Prof. Sien Lin, Prof. Ning Zhang, Prof. Lu Feng, Prof. Xiaona Chen**
14:00-14:10	Ms. Mengqi Chen, PhD student, University of Macau **Title: An aging-promoting feedback loop interferes with cell migration and muscle repair**	
14:10-14:20	Ms. Naping Xiong, PhD student, The Chinese University of Hong Kong **Title: Engineered exosomes loaded with cGMM conduct dual functions for postsurgical osteosarcoma treatment**	
14:20-14:30	Mr. Shuai Liu, PhD student, University of Macau **Title: TET3 promotes pancreatic cancer malignancy and metabolic remodeling through GATA6-mediated TGF-β signaling pathway**	
14:30-14:40	Ms. Jiawei Huang, PhD student, The Chinese University of Hong Kong **Title: Multifaceted Activities of Human Pluripotent Stem Cell-Derived Ectomesenchymal Stromal Cells for the Treatment of Hypoxic-Ischaemic Encephalopathy**	
14:40-14:50	Mr. Yi Ye, PhD student, University of Macau **Title: How do MSCs help circulating tumor cells escape NK killing?**	
14:50-15:00	Mr. Xu Yan, PhD student, The Chinese University of Hong Kong **Title: The study of cranial bone transport and pulsed electromagnetic field in traumatic brain injury rehabilitation**	
15:00-15:10	Dr. Yeneng Dai, Postdoc fellow, University of Macau **Title: NIR-II self-assembly nanomedicines for targeted multimodal imaging-guided synergistic anti-tumor immunotherapy**	
15:10-15:20	Mr. Tongzhou Liang, PhD student, The Chinese University of Hong Kong **Title: Systemic supplementation of magnesium attenuates bone loss via acting on the central nervous system**	
15:20-15:30	Ms. Zhaoying Zhang, PhD student, University of Macau **Title: Endogenous protease activity regulates metabolic and cell fate patterns**	
15:30-15:40	Mr. Zhaowei Jiang, PhD student, The Chinese University of Hong Kong **Title: Tibial Cortex Transverse Transport Accelerates Diabetic Foot Ulcer Healing: The Role and Mechanism of Mesenchymal Stem Cell Mobilization**	
15:40-15:50	Mr. Qianjin Wang, PhD student, The Chinese University of Hong Kong **Title: Intervention Study of LMHFV and β-hydroxy-β-methylbutyrate Treatment on Sarcopenia: neuromuscular junction and mitochondria dysfunction**	
15:50-16:00	Mr. Jiaming Yang, PhD student, The Chinese University of Hong Kong **Title: The regulatory role of the focal adhesion protein Kindlin-2 in the osteogenesis process of distraction osteogenesis**	
16:00-16:20	**Tea Break**	
	Area of Excellence Session: Clinical and Translational Research in Musculoskeletal System	**Moderators: Prof. Ling Qin, Prof. Jiankun Xu**
16:20-16:40	Prof. Ling Qin, PhD The Chinese University of Hong Kong, Hong Kong **Title: AoE as a platform for Collaborative Research in Aging with Focus on Skeletal Degeneration and Regeneration**	
16:40-17:00	Prof. Fan Yang, PhD Shenzhen institutes of advanced technology, Chinese Academy of Sciences, China. **Title: Central neural regulation of parathyroid hormone and bone remodeling**	
17:00-17:20	Prof. Jiang Chang, PhD Shanghai Institute of Ceramics, Chinese Academy of Sciences, Chang **Title: Bioactive ceramics for tissue regeneration and disease therapy**	
17:20-17:50	**Student Awards Ceremony and Closing Remarks**	**Moderators: Prof. Gang Li, Prof. Ren-he Xu**
17:50	Meeting adjourns and free evening	

Message from organizing committee

Dear Colleagues and Friends:

The 10th CUHK international symposium on stem cell and regenerative medicine (SCRM) in Hong Kong continues with the momentum following 9 previous successful ones since 2011. The 9th CUHK SCRM meeting was held in Hong Kong in November 2019 and the meeting was halted for 3 years by the global pandemics of Covid19.

This year, the 10th CUHK SCRM symposium resumes and jointly run with University of Macau, Faculty of Health Sciences to co-organize the 3rd International Conference of the Guangdong-Hong Kong-Macau Greater Bay Area on Regenerative Medicine (GBRM). The main topics of the symposium this year consist of updated issues of stem cell biology and regenerative medicine, emerging technologies, musculoskeletal regeneration and clinical translational research. The year we have 30 plus speakers from China, South Korea as well as special administrative regions of China, Hong Kong and Macau.

The 10th SCRM and 3rd GBRM meeting is co-sponsored by University of Macau, Faculty of Health Sciences; CUHK Department of Orthopedics and Traumatology; CUHK School of Biomedical Sciences and CUHK Are of Excellence Research Center (RGC Reference No. AoE/402/20).

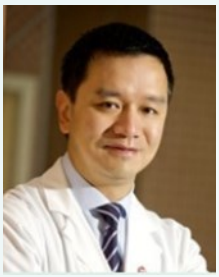
We welcome all academics and students who are interested in stem cells biology, regenerative medicine, and tissue engineering to join the meeting. On behalf of symposium organizers, we warmly welcome you and wish all an enjoyable stay in Hong Kong!

Organizing Committee, 10th CUHK SCRM and 3rd GBRM

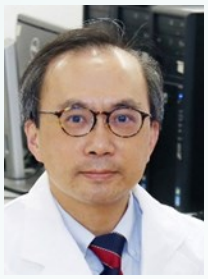
Prof. Gang Li
Co-Chairman
Professor
CUHK-ORT

Prof. Re-He Xu
Co-Chairman
Vice Director
UM-FHS

Prof. Wai-Yee Chan
Pro-Vice-Chancellor
CUHK



Prof. Patrick SH Yung
Chairman
CUHK-ORT



Prof. Andrew Chan
Director
CUHK-SBS

Organizing Committee Board Members

Co-chairmen:
Prof. Gang Li, CUHK
Prof. Ren-He Xu, UM

Advisors:
Prof. Rocky Tuan, CUHK
Prof. Wei Ge, UM
Prof. Wai-Yee Chan, CUHK
Prof. Chuxia Deng, UM
Prof. Patrick Yung, CUHK
Prof. Andrew Chan, CUHK

Members:
Prof. Ling Qin, CUHK
Prof. Chunming Wang, UM
Prof. Louis Cheung, CUHK
Prof. Guokai Chen, UM
Prof. Huating Wang, CUHK
Prof. Jiahong Lu, UM
Prof. Cynthia Jiang, CUHK
Prof. Qi Zhao, UM
Prof. Qiang Wu, MUST
Prof. Jiankun Xu, CUHK
Prof. Jack Chon Lok Lei, UM
Prof. Alan Li, CUHK
Prof. Ruiyu Xie, UM
Prof. Sien Lin, CUHK
Prof. Wakam Chang, UM
Prof. Lu Feng, CRMH
Dr. Weiwei Liu, UM

Secretary:
Ms. Debbie Ho, CUHK

Message from Vice-Chancellor and President

Welcome message

Professor Rocky S. Tuan
Vice-Chancellor and President
The Chinese University of Hong Kong

It is with great pleasure that I welcome all of you to the **10th CUHK International Symposium on Stem Cell Biology and Regenerative Medicine and 3rd International Conference of the Guangdong-Hong Kong-Macao Greater Bay Area on Regenerative Medicine.**

Regenerative medicine is a major advancement of biomedicine in the 21st century. The remarkable advances in the science of embryonic, adult and induced pluripotent stem cells and the engineering of smart biomaterials represent the essential building blocks of future promises for injured and diseased tissues to regenerate and for the understanding and treatment of various disease processes. Some of the significant developments in this fast-growing field include stem cell-based therapies, organoid and tissue-on-a-chip technologies for disease modeling and drug screening, and the application of bioactive scaffold materials to house exogenous stems and to recruit and stimulate the patient's own stem cells into reparative actions. An increasing number of challenging medical conditions, such as heart failure, nerve injuries and neurological disorders, fractures, severe wounds, and many degenerative diseases are now being treated effectively with regenerative medicine approaches.

CUHK has been expanding its research capacity in the field of regenerative medicine over the past decade. Dedicated research teams and research projects have been established, and state-of-the-art research facilities are in place to address the needs of research and clinical applications. A multidisciplinary, university-wide Institute for Tissue Engineering and Regenerative Medicine (iTERM) was established in 2016 as a hub of research excellence to enhance and support research collaborations on regenerative medicine. In 2021, CUHK established The Centre for Neuromusculoskeletal Restorative Medicine with the support of the Hong Kong SAR government to advance biomedical research and development related to neuromusculoskeletal medicine.

I am delighted to see the resumption of the CUHK International Symposium on Stem Cell Biology and Regenerative Medicine following a three-year hiatus due to the COVID-19 pandemic, in partnership with the 3rd International Conference of the Guangdong-Hong Kong-Macao Greater Bay Area on Regenerative Medicine. I am confident that it will be an exciting platform for the exchange of innovative research ideas and an inspiring learning and collaborative opportunity for our students and young scientists.

I wish all of you a stimulating and successful symposium, and an enjoyable stay in Hong Kong!

Rocky S. Tuan Ph.D.
Vice-Chancellor and President
Lee Quo Wei and Lee Yik Hoi Lun Professor of
Tissue Engineering and Regenerative Medicine
The Chinese University of Hong Kong

Message from Dean of Faculty of Medicine, CUHK

Welcome Message

Dear Colleagues and Friends,

Welcome to the 10th CUHK International Symposium on Stem Cell Biology and Regenerative Medicine (SCRM) and 3rd International Conference of the Guangdong-Hong Kong-Macau Greater Bay Area on Regenerative Medicine. Regenerative medicine is an emerging discipline using cells, genes, other biological factors, and tissue engineering approaches to repair or regenerate cells, tissues, and organs. It has enormous potential to develop new paradigms for medicine on tissue repair and regeneration obviating the need for organ replacement. This specialty will transform clinical practice, reducing dependence on invasive procedures and providing the potentials to treat currently intractable diseases. As such it is of great societal and economic importance. Stem cell biology and regenerative medicine research bring together the clinicians and research scientists from clinical and preclinical departments which are interdisciplinary research efforts.

The 1st CUHK International Symposium on Stem Cell Biology and Regenerative Medicine started in 2011 and the 9th CUHK SCRM meeting was held in November 2019 and the meeting was then halted for 3 years because of the global pandemics of Covid19. Thanks for the efforts of our colleagues in Department of Orthopedics and Traumatology and School of Biomedical Sciences, as well as the colleagues from University of Macau, Faculty of Health Sciences, I am glad to see the meeting resumes again this year, which is a remarkable event for our faculty. I hope that you take this opportunity to share research findings, make friends, build collaborations and also enjoy the hospitality of our colleagues at CUHK!

I wish you all have pleasant stay in Hong Kong and the symposium to be very fruitful and successful!

Yours sincerely

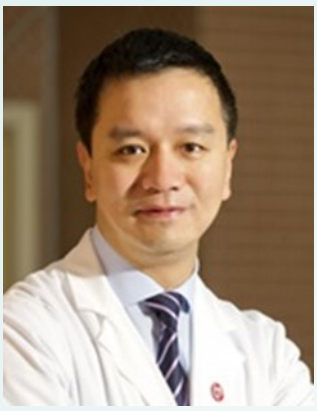
Philip Chiu

Dean, Faculty of Medicine,
The Chinese University of Hong Kong

Department of Orthopaedics and Traumatology
The Chinese University of Hong Kong

The department was established in 1982 under the foundation Chairmanship of Professor PC Leung. The first batch of medical students started to have their clinical orthopaedic teaching in 1983. Through the years, the department has grown and developed under the clear Mission and Vision "to provide the highest quality service in patient care, research, education and teaching for medical students and postgraduate training".

The department has grown from a single professor team to more than 40 clinical colleagues and 60 supporting clerical, technical and research staff now. It would be appropriate to divide the development of the department into three different phases, namely the establishment, the expansion and the consolidation phases. The initial establishment phase stretched from 1982 to 1990 and could be regarded as the infancy and childhood phase. This was followed by a rapid expansion phase from 1991 to 1996 by "hundred flowers blooming" phase which was quite similar to the pre - adolescent and adolescent phase. The past few years, from 1997-2001 featured the early consolidation and sustained growth of the department with the analogy of early and young adulthood phase.



Prof. YUNG Shu-hang, Patrick
Chairman, Department of Orthopaedics & Traumatology

Prof. PC LEUNG
Founding Chairman

On the clinical services, the department has developed along the major fields of subspecialties in orthopaedics, from Hand and Microsurgery, Sports Medicine, Traumatology, Paediatric Orthopaedics to Orthopaedic Oncology, Spinal injury, Orthopaedic Rehabilitation, Joint Reconstruction Surgery to the latest addition of Foot and Ankle surgery 3 years ago. Many of these subspecialties enjoy significant local, regional and international professional and academic recognition and achievements.

Commitment to quality teaching of medical students is one of the main keystones of the department. The department has been involving in the teaching of musculoskeletal system and orthopaedics in Med 3 and Med 5 students and with the introduction of the new curriculum in 2001, teaching has been extended further into year 1 and 2. With the setting up of a formal teaching committee and departmental teaching coordinator, the curriculum in musculoskeletal system is regularly reviewed and updated. Regular teaching quality assessment, meeting with students and annual curriculum review with honorary teachers has helped not only to update but continuous improvement of the quality of teaching as reflected by the evaluation results and recognition by the faculty and university.

Department of Orthopaedics and Traumatology
The Chinese University of Hong Kong

Significant growth has been achieved in the research area. From purely clinical reviews and research, the department has steadily expanded in the years to cover different areas of basic and applied basic research that spread from soft tissue, bone and cartilage to biomaterials, osteoporosis and traditional Chinese medicine. The research committee and the musculoskeletal research laboratory structure now have clear responsibility and function to plan, advice and implement defined policies related to research. Three main focused research programs and functionalisation have been established to incorporate all teaching and research staff of the department. The research output and research grants have increased significantly over the years both in quantity and quality. Up to now, 50 Mphil, 23 PhD and 2 MD have graduated from the department. Active collaborations with other departments, universities and research institutions locally, regionally and with other countries have opened up many new and important areas of research.

The department has put great emphasis on the development of information technology and audiovisual supporting services to all staff from administration to training, teaching, research to clinical services. The whole department is now connected by a sophisticated system of high-speed Intranet. Active research and application of IT in enhancement of web-based interactive teaching is well supported.One of the most important highlights of the department is the establishment of the Orthopaedic Learning Centre from generous donations around 2 million US$ in total. Since it's opening in April 1999, over 5,000 local, regional and international participants have attended different courses and workshops conducted in the centre. The centre has also been recognised as advanced training centre by various societies and also a favorite center for visit by any outside guest to the Faculty of Medicine.

Throughout the years, colleagues of the department have and will continue to be actively committed to the university, the professional and specialty development, and play important roles in public services, voluntary services and services to the community. With the support, spirit and dedication of colleagues at all levels, we can proudly look forward into the future, continue to strive, seek and develop "to provide the highest quality service in patient care, research, education and teaching for medical students and postgraduate training".

The Center for Neuromusculoskeletal Restorative Medicine (CNRM)

The Center for Neuromusculoskeletal Restorative Medicine has been established to advance biomedical research and development related to neuromusculoskeletal medicine. Combining the expertise in stem cells, biomaterials, 3D bioprinting, tissue engineering, and personalised and translational medicine of The Chinese University of Hong Kong and Sweden' s Karolinska Institutet, the Center is devoted to restoring structure and function to injured, diseased and degenerated (due to ageing or trauma) neuromusculoskeletal tissues and organs. This multi-disciplinary, international consortium aims to apply convergent principles and technologies of biomedical science and engineering to ultimately address mobility impairments and improve patients' overall well-being.

Prof. Woody CHAN &
Prof. Patrick YUNG
Co-Director,
The Center for Neuromusculoskeletal Restorative Medicine (CNRM)

Building on the talent and infrastructural research capabilities of CUHK and the research setup of the KI Hong Kong Ming Wai Lau Centre (MWLC) for Reparative Medicine in HKSTP, CNRM gathers multi-disciplinary investigators to lead projects across its five research programmes:

-Stem Cells and Cell-Based Therapies

-Tissue Engineering and 3D Microtissue Modeling

-Cellular and Molecular Mechanisms

-Preclinical and Clinical Translation

-Enabling Technologies

Faculty of Health Sciences, University of Macau

With the vigorous support and joint efforts from numerous supporters, the Faculty of Health Sciences (FHS) of the University of Macau (UM) has thrived since its establishment in 2013. As a fundamental academic unit, FHS, comprised of three departments (Department of Biomedical Sciences, Department of Pharmaceutical Sciences and Department of Public Health and Medicinal Administration), now offers three undergraduate programmes, two master programmes and two doctoral programmes. The programmes are delivered by an excellent team of academics who have guided and inspired over 750 young researchers and students in the lifelong quest of knowledge.

The research of FHS focuses on ten major themes, they are: (i) Precision Oncology, (ii) Stem Cell and Development (iii) Aging, Neural and Metabolism Disorders and Infectious Diseases, (iv) Biomedical Imaging, (v) Data Science, (vi) Drug Development, (vii) Neuropsychiatry, (viii) Structural Biology, (ix) Translational Medicine and x) Public Health. To support these research activities, FHS has established a state-of-the-art infrastructure that includes more than 40 research laboratories, 4 research centres and 4 core facilities. In addition, upon the approval of the Ministry of Education, UM established the first Frontiers Science Center in Hong Kong and Macao in 2021, namely "Frontiers Science Center for Precision Oncology", which is formed a team led by FHS, dedicating to carry out cutting-edge scientific research of common cancers in Macao. In addition, FHS initiated abundant projects as the principle unit, one of which is a National Key R&D Programme of China to support a multi-institutional project on stem cell therapy.

With this solid research support, FHS has recorded a steady increase in the quantity and quality of publications and scientific discoveries in the past decade. The accumulative number of papers published by FHS scholars increased from 43 in 2014 to over 2,100 in Dec 2023, with over 47,000 citations and over 400 accumulative publications with impact factor ≥10. The success and impact of FHS in research are also shown by the fact that health sciences-related subjects of UM, including clinical medicine, pharmacology & toxicology, biology & biochemistry, chemistry, and psychiatry/psychology have entered top 1% rank of the Essential Science Indicators (ESI). Based on World University Ranking in 2024, UM was ranked 193 in general and 201-250 in Life Sciences.

These research output signify the continual improvement in the overall influence worldwide of FHS in the health sciences. Equally important, FHS has organised numerous symposia and seminars including Macau Symposium on Biomedical Sciences (MSBS) and International Conference of the Greater Bay Area on Regenerative Medicine (GBRM) to deliver talks with topics both in cutting-edge science and popular science, and assisted local schools in devising and operating STEM education programmes, all of which benefit the general understanding of biomedical science and health sciences by the community.

https://fhs.um.edu.mo/

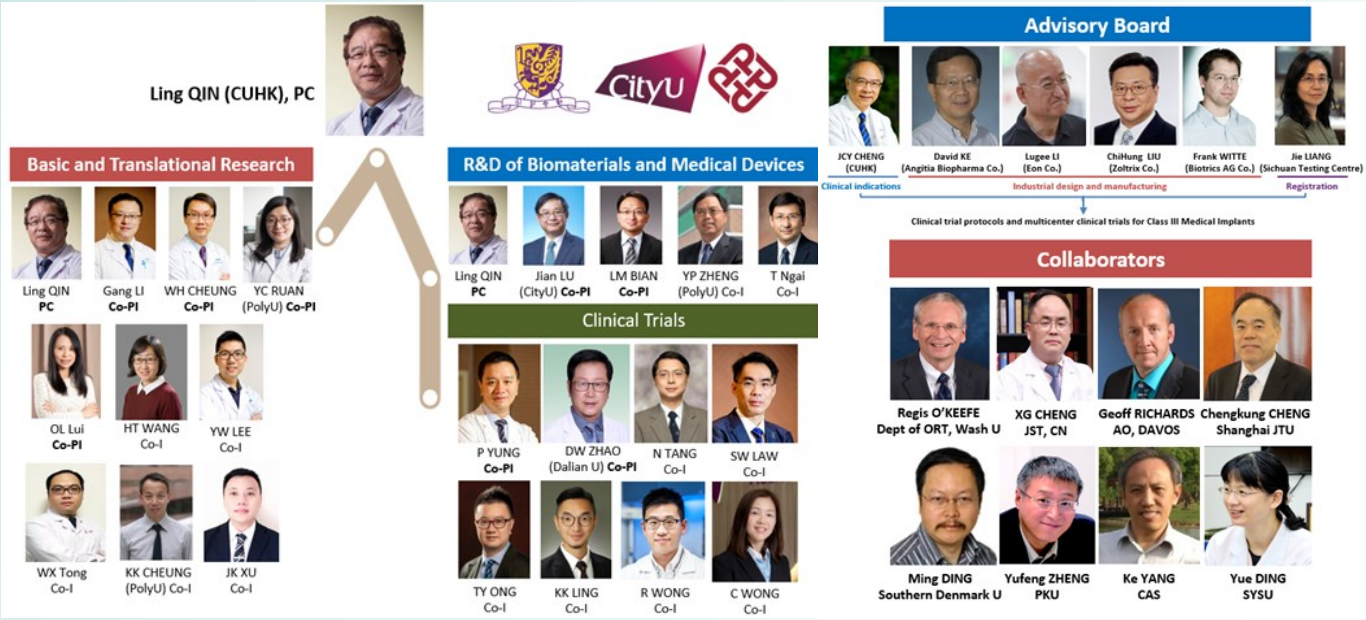
ORT-led Research Project as UGC Areas of Excellence

AoE/P-402/20

Aging, Skeletal Degeneration and Regeneration

Project Coordinator: Prof. Ling QIN

The world population is aging, particularly in Hong Kong. The Hong Kong Government has projected that the local population will see a rapid increase in its aging population from 15% in 2014 to 36% in 2064. The incidence of age-associated osteoporosis and bone fractures is high, with one osteoporotic fracture occurring every three seconds worldwide. Extensive research has been conducted on aging. Coordinated and multidisciplinary research facilitating skeletal regeneration in bone metabolic disorders and fragility injuries, especially in searching for bioactive and biodegradable implantable materials for temporal fixation and stimulating skeletal regeneration, is still highly desirable.



Our internationalized team recently identified the unique function of neuronal protein regulating the regeneration of skeletons via sensory nerves. Degradation of Magnesium (Mg) releases Mg ions and hydrogen gas and creates a local alkaline environment. They have delineated that Mg ions stimulate sensory nerve endings in the periosteum and upregulate and release calcitonin gene-related peptide (CGRP) from dorsal root ganglions. CGRP, an osteogenic neurotransmitter, facilitates differentiation of periosteum-derived stem cell into osteoblast linage, and thus benefits osteoporotic fracture repair, highlighting Mg as an excellent candidate for facilitating skeletal regeneration in elderlies.

With the support of AoE scheme, the team is engaging to apply advanced biotechnologies to address these scientific questions while continuing the translational work on innovative biodegradable implants towards multi-centre clinical trials and Class III medical product registration for broadening clinical applications. The collective efforts will enhance the regeneration of challenging musculoskeletal disorders and hence reduce the healthcare and socio-economic burden of the aging society.

Areas of Excellence Scheme 2020/21
(Ref. AoE/M-402/20)

Translational Medicine Research Model of
Magnesium-based Innovative Medical Biomaterials and Devices

MECHANISM
Identification of Cell Type
Exploration of Molecular Pathways
Publication of Scientific Articles

III

DESIGN II
Guided by Clinical Needs
Demonstration of Design Feasibility
Determination of Design Parameters

IV **VERIFICATION**
Selection of Experimental Animals
Construction of Animal Disease Model
Analysis of Experimental Results

CLINICAL NEEDS I
Analysis of Clinical Pain Point
Analysis of Existing Products
Design of Clinical Guidance

V **TRANSLATION**
Market Research
Manufacture of the Implant
Multicenter Clinical Trials
Device Registration
Launching and Commercialization of the Product

Consolidate the Scientific Foundation

Nature Highlight : Neuronal Origin of Osteogenic Effects of Magnesium
Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats.
***Nature Medicine**, 22(10):1160-1169, **2016**.*

Science Highlight Improved Healing of Rare Fractures
Magnesium facilitates the healing of atypical femoral fractures: A single-cell transcriptomic study.
***Materials Today** 52, 43-62,**2022**.*

Research on Nerve- Bone Axis
Implantable electrical stimulation at dorsal root ganglions accelerates osteoporotic fracture healing via calcitonin gene-related peptide.
***Advanced Science**,9(1), 2103005, **2022**.*

The First Clinical Study of Biodegradable Magnesium In China
Vascularized bone grafting fixed by biodegradable magnesium screw for treating osteonecrosis of the femoral head. ***Biomaterials** 81,84-92, **2016**.*

Magnesium-Based Hydrogel for Nerve and Tissue Regeneration
Magnesium-Encapsulated Injectable Hydrogel and 3D-Engineered Polycaprolactone Conduit Facilitate Peripheral Nerve Regeneration.
***Advanced Science**, 9(21), 2202102,**2022**.*

Research on Fat - Bone Axis
Macrophages in epididymal adipose tissue secrete osteopontin to regulate bone homeostasis.
***Nature Communications**, 13(1), 427, **2022**.*

The First One to Propose the Concept of Mg/Ti Hybrid Fixation Devices
An innovative Mg/Ti hybrid fixation system developed for fracture fixation and healing enhancement at load-bearing skeletal site.
***Biomaterials** 180, 173-183, **2018**.*

Magnesium-Based Sprays for Wound Healing
Green-Prepared Magnesium Silicate Sprays Enhance the Repair of Burn-Skin Wound and Appendages Regeneration in Rats and Minipigs.
***Advanced Functional Materials**, 2307439,**2023**.*

Research on Cartilage Degeneration
Wnt16 attenuates osteoarthritis progression through a PCP/JNK-mTORC1-PTHrP cascade.
***Annals of the rheumatic diseases**, 78(4), 551-561, **2019**.*

Recommend Industry Standard for the Development of Magnesium-Containing Devices
Recommendation for modifying current cytotoxicity testing standards for biodegradable magnesium-based materials.
***Acta Biomaterialia**,21, 237-249, **2015**.*

Magnesium-Based Membranes for Bone and Tissue Regeneration
Biosynthesized Bandages Carrying Magnesium Oxide Nanoparticles Induce Cortical Bone Formation by Modulating Endogenous Periosteal Cells.
***ACS nano**, 16(11), 18071-18089,**2022**.*

Research on Fat-Cartilage Axis
Blockage of Osteopontin-Integrin β3 Signaling in Infrapatellar Fat Pad Attenuates Osteoarthritis in Mice.
***Advanced Science**, 2300897, **2023**.*

Innovative Class III Medical Products (Patented)

Magnesium-Based Hybrid Devices
To promote bone, muscle and nerve regeneration in clinical bone fractures.

Magnesium-Based Biomaterials
To promote irregular bone defect and wound repair.

Multi-centre clinical trials

HuaMg Medical Technology (Shenzhen) Co. Ltd
Medical Magnesium Limited (Hong Kong)

School of Biomedical Sciences
Faculty of Medicine
The Chinese University of Hong Kong

Prof. Andrew Chan
School of Biomedical Sciences, CUHK

The School of Biomedical Sciences (SBS) was officially inaugurated on 8th January 2010, amalgamating the former four pre-clinical Departments of Anatomy, Biochemistry (Medicine), Pharmacology, and Physiology under the Faculty of Medicine. Since its establishment, SBS has been dedicated to advancing cutting-edge and translational research through interdisciplinary collaboration, while providing high-quality graduate and undergraduate education.

As the first of its kind in Hong Kong, SBS has made significant strides in research excellence. We have established three Thematic Research Programs (TRPs) that focus on key areas of biomedical sciences:

- Cancer Biology and Experimental Therapeutics
- Developmental and Regenerative Biology
- Neural, Vascular, and Metabolic Biology

Members of these three Programs, including those clinical Associate Members, have been supported by our Core Laboratories and Animal Holding Core which provide state-of-the-art equipment and specialized technologies. To demonstrate our commitment to research excellence, we regularly organize theme-based seminars and host the annual School of Biomedical Sciences Research Day to foster knowledge exchange and collaboration.

In addition to research, SBS places great importance on providing an exceptional learning environment for our graduate and undergraduate students. Through the consolidation of teaching manpower, we have achieved synergies in graduate and undergraduate teaching, ensuring a cohesive educational experience. Our MPhil-PhD Programme in Biomedical Sciences, which admitted its first cohort of students in 2010-11, has been instrumental in nurturing the next generation of researchers.

To further enhance our commitment to education, we established the Division of Education and organize the annual School of Biomedical Sciences Postgraduate Research Day. These initiatives demonstrate our dedication to fostering excellence in education and promoting intellectual growth among our students. In 2016-17, we introduced the new BSc Programme in Biomedical Sciences, aiming to equip graduates with comprehensive biomedical sciences knowledge and skills for diverse career paths such as scientific research, health system policy and management, or clinical, pharmaceutical, diagnostics, and healthcare-related professions. Additionally, the Advisory Board on Students' Career and Development, established in late 2016, works tirelessly to enhance the career competitiveness of our undergraduate and postgraduate students, maximizing their exposure to professional fields before graduation.

SBS actively seeks to establish strong academic and scientific collaborations with universities and research institutes worldwide, expanding our international outlook. We have signed Memoranda of Understanding (MOUs) with prestigious higher education and research institutions in the Mainland and overseas to facilitate collaborative research and exchange opportunities. Furthermore, we keep participating in outgoing and incoming visits, exploring potential partnerships that contribute to research and educational advancements.

For more detailed information about the School of Biomedical Sciences, including the academic profiles of our faculty members, please visit our website at https://www2.sbs.cuhk.edu.hk. If you have any comments or inquiries, please do not hesitate to contact us at sbs.med@cuhk.edu.hk.

Societal Relevance of Stem Cell Research

Prof. Rocky S. TUAN
Vice-Chancellor and President
Lee Quo Wei and Lee Yik Hoi Lun Professor of
Tissue Engineering and Regenerative Medicine
The Chinese University of Hong Kong, Hong Kong SAR

Research on stem cells represents one of the most active areas of biomedicine. The ability of stem cells to self-renew and develop into different specific cell types with specialized functions represents the main attraction. Stem cells may be derived as embryonic stem cells, adult progenitor and stromal cells, and induced pluripotent stem cells from reprogrammed somatic cells. Research successes in stem cells thus have significant relevance to the society, including therapeutics, regenerative medicine, biotechnology, and health. A fundamental benefit is scientific advancement of the basic biology of embryonic development, cell fate and differentiation, and the cellular basis of tissue/organ formation, and wound healing and repair, knowledge that should facilitate drug discovery and development. By harnessing the regenerative properties of stem cells, researchers aim to develop therapies for a wide range of clinical conditions, including neurodegenerative disorders, heart diseases, diabetes, spinal cord injuries, genetic disorders, musculoskeletal degeneration, and various types of cancer. Approaches being considered include direct introduction of stem cells (with or without genetic manipulations) as well as the use of pre-formed stem cell-derived mini-tissues (with or without the use of natural or synthetic scaffolds). A recent line of investigation utilizes stem cells as the starting cell source for the construction of organoids and organ-on-chip constructs, which may be used as a platform to investigate disease pathogenesis and test candidate therapeutics. The rapid growth in stem cell and cell-based research has led to a concomitant growth in GMP-grade biotechnology and bioinstrumentation industries, to support both basic research activities and pre-clinical and clinical trials. Finally, stem cell-based technologies must be assessed in terms of ethical considerations, e.g., the use of autologous *versus* heterologous cells, and particularly when embryonic stem cells are involved. There is an urgent need to establish clear regulatory frameworks that balance innovation and patient protection on the basis of robust scientific evidence and well-defined manufacturing processes.

Professor Rocky S. Tuan assumed office as the eighth Vice-Chancellor and President of The Chinese University of Hong Kong (CUHK) on 1 January 2018. Born and raised in Hong Kong, he pursued further studies in the United States and received his PhD in Life Sciences in 1977 from the Rockefeller University in New York. He is concurrently Lee Quo Wei and Lee Yick Hoi Lun Professor of Tissue Engineering and Regenerative Medicine at CUHK.

Immune Regulation during Tissue Regeneration

Prof. Yufang SHI
Institutes for Translational Medicine
Soochow University

Immune responses not only defend our body from infections and malignancies but also play a central role in tissue regeneration. Promptly activated immune responses are tightly regulated and their dysregulation can result in various types of diseases. Our early investigations focused on how rapidly proliferating T cells are controlled from overreaction. We discovered that reactivation of activated T cells leads them to undergo apoptosis. We termed this novel mechanism activation-induced cell death (AICD), which acts as a feedback mechanism for terminating an ongoing immune response and serves to maintain immune tolerance. This finding linked apoptosis to the maintenance of immune homeostasis during immune responses. Subsequently, we studied AICD in different T cell subsets and found that Fas, FasL, granzyme B, and TRAIL are differentially regulated in distinct T cell populations, providing critical information for the precise control of different immune responses under different pathophysiological processes. Immune cells reside in different tissue microenvironments, in which they closely interact with niche cells. To understand how in situ cellular components regulate immune cells, we turned our attention to a special population of tissue stromal cells, mesenchymal stem cells (MSCs). We cloned MSCs from bone marrow and found that MSCs are potent regulators of immune response both in vitro and in vivo. Ironically, we showed that the execution of such stem cell-mediated suppression of inflammation depends on inflammatory cytokines to stimulate the production of immunosuppressive factors. This novel finding initiated an active stem cell immunology research area. Additionally, we found that active tissue regeneration and damaged tissue repair also require ongoing inflammation, thus forming the theory of bidirectional regulation of stem cells and immunity. Through studying the roles of inflammatory cytokine dynamics in licensing stem cells to regenerate tissues and regulate immune responses, we established the concepts of “plasticity” and “empowerment” of MSCs during disease pathogenesis and applications to disease settings. This empowerment capacity of MSCs was found to be closely related to the inflammatory cytokine-induced secretion of a large number of growth factors at high amounts to activate and expand tissue-specific progenitors to regenerate and repair, a novel concept substituting the traditional cell replacement dogma. Since tumors can be considered as wounds that never heal, we investigated the role of MSCs in tumor progression and metastasis and found that the same mechanism also operates in the tumor stroma. Thus, our findings in immune regulation are important for understanding various pathogenesis processes as well as guiding the designing of regenerative medicine strategies.

In 1980’s-91990s, a series of Dr. Shi’s publications creatively defined activation-induced cell death (AICD) in proliferative T cells, linking the "life" and "death" of immune cells with the regulation of immune homeostasis and establishing the "brake" concept of immune cell self-limitation to prevent excessive proliferation of antigen-activated immune cells. Dr. Shi pioneered stem cell immunology, with 23 granted and filed patents and over 100 related publications in high-impact journals. By focusing on the interaction between stem cells and immune responses, he found that tissue stem cells are potent regulators of the immune response. Based on the roles of inflammatory cytokine dynamics in licensing stem cells to regenerate tissues and to regulate immune responses, he established doctrines of "plasticity" and "empowerment" of MSCs in the pathogenesis and therapy of inflammatory diseases and tissue damage. Dr. Shi established a novel therapeutic theory of stem cell-mediated tissue repair. He found that stem cells in damaged tissues, in addition to regulating inflammation, secrete large amounts of growth factors to promote tissue regeneration and repair through cell empowerment, a revolutionary concept substituting the traditional one of cell replacement through stem cell direct differentiation. Dr. Shi devoted enormous amounts of time to the MSC committee of ISCT. He also served as an Editor-in-Chief of *Cell Death and Disease* (2010 to present), receiving editor of *Cell Death and Differentiation* (2015 to present), and a member of the Executive Board of *Advanced Science* (2020 to present). Dr. Shi’s more than 300 publications have appeared in *Nature*, *Science*, *Nature Medicine*, *Nature Immunology*, *Cell Stem Cell*, *Immunity*, *Cell Metabolism*, *Nature Review Drug Discovery,* and other journals with more than 52,000 citations. His h-index is currently 94. Dr. Shi has been listed as one of the most cited scientists in the world and was elected to Academia Europaea in 2020.

Engineering a glycan matrix to reshape spleen tissue for ectopic liver regeneration

Prof. Chunming WANG
Director
N6-5011b, RSKTO
University of Macau, Taipa, Macau SAR

Ectopic regeneration of the liver in the spleen is a promising alternative to organ transplantation for treating liver failure. To accommodate transplanted liver cells, the splenic tissue must undergo structural changes to increase extracellular matrix (ECM) content, demanding a safe, efficient approach for tissue remodelling. Based on our previous research on glycan biomaterials (*Nat Comm* 2019 & 2020, *Adv Mater* 2021 & 2023) and spleen tissue transformation (*Sci Adv* 2020, *Gut* 2022), in this study, we design a glycan biomaterial system to remodel the splenic tissue by activating endogenously stored transforming growth factor-beta (TGF-β) into a supraphysiological level locally.

This system is based on a synthesised sulfated hyaluronic acid (sHA) with an affinity for the latent complex of TGF-β. It can crosslink into a stiff gel network (sHA-X) *via* click chemistry. Upon injection into the spleen, sHA-X efficiently binds the abundant latent TGF-β and provides the molecular force to liberate the active TGF-β dimers, mimicking the physiological 'bind-and-pull' mechanism and reshaping the splenic tissue to support liver cell adhesion and growth. Hepatocytes transplanted to the remodelled spleen develop into liver tissue with sufficient volume to exert potent functions for rescuing the animals with 90% hepatectomy and metabolic liver disorder (in $Fah^{-/-}$ transgenic model), with no adverse effects observed and no additional drugs required. These data highlight the efficacy and translational potential of sHA-X, as the first biomaterial to remodel a specific organ by mechanically activating one single cytokine, representing a novel strategy for designing biomaterials-based therapies for organ regeneration.

Chunming (CM) Wang is a Professor at the University of Macau (UM). He is currently the Director of the Research Services & Knowledge Transfer Office (RSKTO), the counterpart of a research support office and an IP management department in many other institutions. His research focuses on developing new methods to promote tissue repair, including immunomodulatory biomaterials and therapeutic cells, as supported by over 20 funding grants, such as the Outstanding Young Scholars Fund from the National Natural Science Foundation of China (NSFC), Macau Key R&D Projects, Joint Funding Support by the Macao Science and Technology Development Fund (FDCT) and NSFC, as well as industrial funding. He has been awarded the 'Qi-Huang' Youth Scholarship by the State Administration of TCM (China) and elected a Fellow of the Royal Society of Chemistry (FRSC, UK). CM joined UM in October 2012, starting his independent research as an Assistant Professor and being promoted to Associate Professor in August 2018 and full Professor in August 2022, respectively. Before that, he received his BSc and MSc degrees in Biochemistry from Nanjing University (China) and PhD in Biomedical Engineering from Nanyang Technological University (Singapore) and undertook his postdoctoral training at the University of Cambridge (UK).

Recent advances in stem cells, cell reprogramming, and gene editing for Neurological diseases therapeutics

Prof. Jonpil KIM
Professor
Dongguk University
Seoul, South Korea

Recent advancements in cellular and genetic engineering have garnered considerable interest in human disease modeling and cell replacement strategies. Our focus lies in harnessing these breakthroughs in stem cells, cell reprogramming, and gene editing technologies to deepen our understanding of neurological diseases and develop innovative therapies. Our recent research has identified quiescent neural stem cells as a promising target for autism spectrum disorders (ASDs), demonstrating the effectiveness of inhibiting their dormancy to alleviate ASD symptoms (Molecular Psychiatry, 2023). Additionally, we have reported electromagnetic field-based direct lineage reprogramming as a promising strategy for neurodegenerative disorders like Parkinson's disease (Nature Nanotechnology, 2017). This study offers a proof of concept for in vivo reprogramming as a potentially safe and viable therapeutic approach for Parkinson's disease. Finally, I will discuss recent advancements in in vivo therapeutic editing using CRISPR/Cas9 as a novel therapeutic agent for Alzheimer's disease (Nature Neuroscience, 2019).

Jongpil Kim, Ph.D obtained his doctoral degree from Columbia University(New York) and completed a postdoctoral fellowship at MIT's Whitehead Institute (Boston). Currently, Kim serves as a professor at Dongguk University, where he focuses on stem cell biology, cell reprogramming, and gene editing to develop novel therapeutics for neurological diseases such as Autism, Alzheimer's, and Parkinson's. Recently, his work has been published in respected journals like Nature Neuroscience (2019), Nature Nanotechnology (2017), and Nature communication (2023) reflecting his dedication to advancing understanding in his field.

SELECTED PUBLICATIONS

1. Park H et al., Nature Communications, (2023) Feb 13;14(1):802.
2. Kim H et al., Molecular Psychiatry. 2022 Jun;27(6):2751-2765.
3. Park H et al., Nature Neuroscience, 2019 Oct 22,524-528
4. Kim H et al., Stem Cell Reports. 2019 Mar 5;12(3):518-531
5. Yoo J et al., Nature Nanotechnology, 2017 Oct;12(10):1006-1014.
6. Kim H et al., Brain, 2017 Aug 1;140(8):2193-2209.
7. Kim J et al., Cell Stem Cell. 2011 Nov 4;9(5):413-9.
8. Kim J et al., Science. 2008 Aug 31;317(5842):1220-4.

Development of novel stem cell tools for research and translation

Prof. Wei LI
Deputy Director
State Key Laboratory of Stem Cell and Reproductive Biology
Institute of Zoology, Chinese Academy of Sciences

Stem cells have versatile applications owing to their unique features, such as rapid and unlimited proliferation capacity and broad differentiation potential. They can serve as a model for developmental study, as well as the perfect seed cells for regenerative medicine. Moreover, stem cells have amazing potential to be engineered for novel phenotypes and functions. Here we introduce several novel stem cell tools or platforms we have developed during the past several years and discuss their potential applications. The haploid embryonic stem cells (ESCs) are derived from the haploid blastocyst, which provide a convenient approach for large-scale genetic screen and rapid generation of genome-modified animals. Another novel stem cell type is the mammalian allodiploid ESCs, which contain stable allodiploid genome of two evolutionarily distant related species, and can self-renew indefinitely and differentiate into all three germ layers. These features make them a useful tool for the identification of genetic basis of phenotypic differences between species. Our studies hence show that stem cell engineering is promising to generate novel tools for biological research.

Wei Li, PhD, is a professor and Deputy Director of State Key Laboratory of Stem Cell and Reproductive Biology, Institute of Zoology, Chinese Academy of Sciences (CAS). Dr. Li's research interests concentrate on the research and development of innovative genome engineering and stem cell technologies, and utilizing these technologies to study the mammalian reproduction and regeneration, as well as to develop gene and cell therapies. He has published over 70 research papers as a corresponding author on scientific journals including Cell, Science, Nature, and Nature Biotechnology etc., and has developed 7 gene and cell drugs entering the clinical stage. Dr. Li has been awarded a number of awards and honors, including Outstanding Science and Technology Achievement Prize of the CAS, NSFC Distinguished Young Scientists Fund, International Award of the Japanese Association for Laboratory Animal Science etc.

Ion channel modulation induces cardiomyocytes from human pluripotent stem cells

Prof. Guokai CHEN
Faculty of Health Sciences
University of Macau, Macau SAR

Ion channels play a crucial role in cardiac functions, and their activities exhibit dynamic changes during heart development. However, the precise function of ion channels in human heart development remains elusive. In this study, we employed human embryonic stem cells (hESCs) to model the process of human embryonic heart development. During the differentiation of hESCs into cardiomyocytes, differential expression of ion channel genes was observed, with upregulation of ryanodine receptor 2 (RYR2), a gene encoding a calcium release channel. In addition, we discovered that suramin, an activator of RyR2, efficiently promoted cardiac differentiation even in the absence of classic WNT inhibitors. Furthermore, a set of modulators targeted sodium channels, potassium channels or chloride channels were subjected in chemically defined conditions during cardiac differentiation. We found that blocking the chloride channel with DIDS also enhanced hESC differentiation into cardiomyocytes. Both suramin and DIDS partially inhibited the WNT signaling pathway, and RYR2 knockdown attenuated cardiac differentiation induced by WNT inhibitors, suramin or DIDS. The resulting cardiomyocytes induced by these ion modulators exhibited specific expression patterns of cardiac genes and displayed typical electrophysiological signals. Notably, compared with WNT inhibitors, both suramin and DIDS led to increased generation of atrial-like cardiomyocytes, suggesting their potential as alternative inducers to drive specific cardiomyocyte lineage commitment during human cardiomyocyte induction processes. This study demonstrates that the regulation of ion channels plays a crucial role in determining the fate of cardiac cells, providing an effective approach for inducing cardiomyocytes from hPSCs and highlighting their critical involvement in human heart development.

Dr. Guokai Chen is a Professor in the Faculty of Health Sciences at University of Macau. Dr. Chen's group focus on technology development for human pluripotent stem cells (hPSC) and their clinical applications. He has developed the next generation of hPSC culture condition and differentiation methods to produce functional cells for potential cell therapy. Dr. Chen's inventions have been widely used in stem cell field, including E8 cell culture system. Dr. Chen's group currently studies the molecular mechanisms associated with cardiomyocyte fate determination. They hope to enhance cardiac induction method for large scale production, which would facilitate cell therapies with cardiomyocytes.

How non-essential fatty acids maintain tissue homeostasis

Prof. Ying WANG
Professor
Shanghai Institute of Nutrition and Health
Chinese Academy of Sciences
319 Yueyang Road, Shanghai 200031, China

The balance between stem cells and microenvironment is crucial for ontogeny, tissue homeostasis and regeneration. Fatty acids are the major components of lipid metabolism that actively modulate cell membrane composition, cellular signaling, lipid deposition, metabolic and epigenetic regulation and cell fate determination. In our study, we found that stearoyl-CoA-desaturase 1 (SCD1), an enzyme in catalyzing the generation of monounsaturated fatty acid, is critical in controlling adipose derived stem cell differentiation to maintain the function of adipose tissue and in regulating the formation of bulge to house quiescent hair follicle stem cells to support their periodic activity in hair growth and skin homeostasis. Notably, the expression of SCD1 in thymic epithelial cells impacts thymocytes and their subsequent differentiation to regulatory T cells in periphery, suggesting a new window and mechanism of in regulating T cell subset generation. Taken together, fatty acids can modulate tissue homeostasis and regeneration through various types of mechanisms.

Ying Wang received her M.D./Ph.D. from Shanghai Jiao Tong University, China, in 2009. She is a professor and principal investigator of Shanghai Institute of Nutrition and Health, Chinese Academy of Sciences. She has been working on stem cells and tissue microenvironment. Recently, she focused on investigating the crosstalk between stem cells and tissue microenvironments, including inflammation, metabolites and ECM, with the efforts to develop novel strategies to remodel tissue homeostasis and combat multiple immune diseases. Her recent studies have shown that fatty acids are crucial in controlling the quiescent status and differentiation potentials of many types of stem cells or progenitors in maintaining tissue homeostasis. Various signals received by immune cells during their development can metabolically and epigenetically determine their differentiation and function in the context of pathophysiological condition. Also, she revealed that plastic regulation of the immunoregulatory role of MSCs can be used to resolve the inflammation in the microenvironment of multiple inflammatory diseases. She has published 50 corresponding/first-author papers in *Nature Immunology, Cell Stem Cell, Cell Metabolism, Nature Metabolism, PNAS,* etc.

Anti-inflammatory and anti-cancer properties of Amuc_1434, a mucin degrading protease from *Akkermansia Muciniphila*

Prof. Xuexun FANG
Key lab for molecular enzymology and engineering
College of Life Sciences, Jilin University
Changchun, P. R. China

Intestinal flora participates in a variety of physiological processes of the host. Akkermansia muciniphila, a mucin degrading intestinal symbiont bacterium has shown many beneficial effects towards the host in disease treatments such as diabetes, inflammation and cancer. Here we present that a protein expressed by A. muciniphila named Amuc_1434 exhibits a good therapeutic effect on the mouse colitis model and anti-cancer effects towards several colorectal cancer cells lines.

Amuc1434 protein treatment significantly improved the survival status and physiological conditions of the DSS induced colitis mice. In addition, the treatment significantly reduced the levels of inflammatory cytokines in colon tissue and serum, and increased the abundance and diversity of gut microbiota in mice. These studies suggest that the therapeutic mechanism of Amuc1434 on colitis mice may be achieved by reducing inflammatory cytokine levels and restoring gut microbiota. Current data indicate that Amuc1434 protein is involved in regulating the TLR4-NF-κB/MAPK pathway. However, the specific targets of the Amuc1434 protein still requires further investigation.

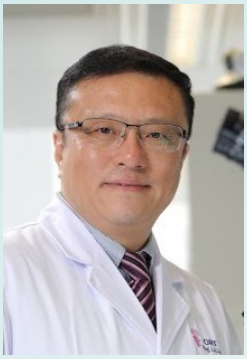
Colorectal cancer cells with high and low expression of mucin were subjected to Amuc_1434 treatment. Amuc_1434 reduced the cell viability and promote apoptosis in all colorectal cancer cells tested. Amuc_1434 increase the intracellular ROS level, and regulate the proteins expressions in the endogenous mitochondrial apoptosis pathway. In addition, Amuc_1434 could synergize with oxaliplatin to enhance its efficacy. Amuc_1434 raised cellular levels of ROS that may cause oxidative stress, which in turn activates the mitochondrial-dependent apoptosis pathway. This study suggests the importance of gut microbes and their components in the clinical treatment of CRC.

Dr. Xuexun Fang graduated from the Department of Molecular Biology, Jilin University in1990 with a bachelor degree in biochemistry; in 1997, Dr. Fang earned his Ph.D degree in Molecular Biology and Biochemistry from the Department of Biochemistry at the University of West Virginia School of Medicine; From 1997 to 2000, he received postdoctoral training at The Burnham Institute in California, US. In 2001, Dr. Fang was recruited and appointed as a professor by Jilin University. Dr. Fang's research projects were funded by the National Natural Science Foundation of China, provincial Department of Science and Technology, and private companies. Dr. Fang has published over 90 SCI papers and awarded more than ten patents. In 2003, he received the Jilin Province Outstanding Youth Researchers Fund, and in 2008, he received New Century Excellent Talents Fund from the Chinese Ministry of Education. He is a current committee member of the Protein Society of the Chinese Society of Biochemistry and Molecular Biology. Dr. Fang's main research focuses are the biological activities of traditional Chinese medicines and therapeutic benefits of the commensal bacterial components.

Distraction Histogenesis: Biological Insights and Novel Applications

Prof. Gang LI
MBBS, D. Phil. (Oxon), FIORS, FORS
Department of Orthopedics & Traumatology
Director of Stem Cells and Regeneration Laboratory of Li Ka Shing Institute of Health Sciences
Faculty of Medicine, The Chinese University of Hong Kong
Postal Address: Room 74038, 5/F, Lui Che Woo Clinical Sciences Building
Prince of Wales Hospital, Shatin, NT, Hong Kong, SAR, PR China

Distraction histogenesis (DH) techniques have been widely accepted and practiced in orthopedics, traumatology, and craniofacial surgery over the last two decades. Using DH methods, many previously untreatable conditions have been successfully managed with outstanding clinical outcomes. It is generally accepted that mechanical stimulation is the key in promoting and maintaining tissues' regenerating capacities. Under normal circumstances with adequate support of postoperative physiotherapy, DH treatment has good clinical outcome and needs no additional intervention(s). Being a great surgical technique for skeletal tissue repair and regeneration, DH also has a wider implication in understanding body's self-repair and self-regeneration potentials, and its new clinical applications are extended to functional tissue engineering, hip reconstruction surgery, management of vascular diseases and cosmetic limb lengthening surgery, as well as neurological disorders. DH theory opens a new page of human biology and physiology, its wider applications will continue bring us more surprises.



Trained as an orthopaedic surgeon and PhD scientist in China and UK, Prof. Li's research interests are on biology and clinical applications of distraction histogenesis and stem cells applicaitons. He has published more than 300 papers in journals such as Biomaterials, Nature Communications, Advanced Science, Bioactive Materials, etc., 16 monographs, and edited 2 books. His papers have been cited more than 19,000 times, with H index 76. He is the Executive deputy editor-in-chief of Journal of Orthopedic Translation, editorial board member of Bone and Joint Research, Bone, Journal of Orthopedic Research, etc. He is a visiting professor at Monash Australia; University of Science Malaysia, Nanjing Medical University, etc. His work received serval awards including 1st Class Award in Science Advances, Ministry of Science and Technology, PR China (2021); 2nd Class Award in Medical Science and Technology, China Medical Association (2017); 1st Class Research Award in Science and Technology, Ministry of Education, China (2014). He is elected as Fellow of International Combined Orthopaedic Research Societies (FIORS) in 2016 and Fellow of American Orthopaedic Research Society (FORS) in 2021. From 2020 to present, he has been on the list of the world's top 2% scientists (ranked among the 1% of the world's top scientists in 2022 and 2023). In 2023, he is ranked 9th of the top 100 scholars in the field of orthopedic surgery in PR China.

Mechanosensitive Osteolectin$^+$ Cells in Skeletal Development and Homeostasis

Prof. Bo SHEN
National Institute of Biological Sciences
Beijing (NIBS)
Tsinghua University

Osteolectin, an osteogenic growth factor recently identified, exhibits expression in chondrocytes, osteoblasts, and bone marrow stromal cells (eLife 5:e18782). To discern the cellular origin of Osteolectin and trace changes in the distribution pattern of *Osteolectin*-expressing cells during development, we engineered a membrane-bound tdTomato reporter into the endogenous *Osteolectin* locus. Our findings reveal that *Osteolectin* is exclusively expressed by peri-arteriolar LepR$^+$ stromal cells in adult bone marrow. Employing fate-mapping mouse genetics, we have identified *Osteolectin*-expressing stromal cells (Osteolectin$^+$ cells) as short-lived osteogenic progenitors responsible for adult bone formation (Nature 591:438). However, during neonatal development, *Osteolectin*-expressing cells display a broader distribution pattern. Through the use of *Osteolectin*-mTomato and *Gli1*-GFP reporter mice, we have observed significant overlap between *Osteolectin*-expressing cells and *Gli1*-expressing cells in the neonatal growth plate. Utilizing a dual-recombinase lineage tracing system for fate mapping Osteolectin$^+$Gli1$^+$ cells *in vivo*, we have established that growth plate Osteolectin$^+$Gli1$^+$ cells play a pivotal role in neonatal bone elongation. Importantly, these Osteolectin$^+$ cells also exhibit elevated levels of Piezo1. Notably, deletion of *Piezo1* from Osteolectin$^+$ cells in neonatal bone marrow results in a significant reduction in bone length, underscoring the critical role of mechanical loading in bone elongation. Furthermore, the deletion of *Piezo1* from Osteolectin$^+$ cells in adult bone marrow leads to a depletion of Osteolectin$^+$ cells and a reduction in osteogenesis. In summary, our findings demonstrate that mechanical loading is essential for Osteolectin$^+$ cells, not only in neonatal bone elongation but also in the maintenance of bone during adulthood.

Dr. Bo Shen is an Assistant Professor in the National Institute of Biological Sciences, Beijing (NIBS) and the Tsinghua Institute of Multidisciplinary Biomedical Research (TIMBR), Tsinghua University. He received his B.S. in Life Science from the National University of Singapore in 2008 and Ph.D. from the Department of Pharmacology, University of Illinois College of Medicine in 2015. He conducted his doctoral research on platelets and developed a novel anti-thrombotic drug based on selective inhibition of platelet integrin outside-in signaling and aggregation without interfering with platelet adhesions (Nature 2013). He performed his postdoctoral research in the laboratory of Dr. Sean Morrison at UT Southwestern Medical Center and Howard Hughes Medical Institute, where he identified integrin alpha11 as a receptor for a novel bone growth factor, Osteolectin. He also discovered that Osteolectin-expressing bone marrow stromal cells form a mechanosensitive peri-arteriolar niche for osteogenesis and lymphopoiesis (Nature 2021). His lab now works on how secreted factors, including growth factors and ECM proteins, regulate tissue homeostasis and regeneration. One such factor his lab recently worked on is Nerve Growth Factor (NGF), which is required for bone marrow innervation, and hematopoietic regeneration after bone marrow transplantation.

Biological interaction between Materials and human body

Prof. Haobo PAN
Director
Institute of Biomedicine and Biotechnology
Shenzhen Institute of Advanced Technology
Chinese Academy of Sciences
1068 Xueyuan Rd., Nanshan District, Shenzhen

Borosilicate is a kind of dual glass network together with [BO_3] and [SiO_4], the degradation behavior can be controlled with the adjusting of [BO_3] / [SiO_4]. As such, the modification of the structure can match the repair of hard or soft tissue by controlled release of essential components. From large animal evaluation, the large bone defect can be effectively achieved with the addition of essential trace elements such as Sr and Mg. The mechanism lies in the rapid enhance of vegf activity and thus facilitate the formation of channel to transport cells. In the meantime to adjust the direction of macrophages and determine the differentiation of stem cells. As a result, we can see the rapid formation of skin due to the common mechanism by rapid formation of newly formed blood vessel, and thus facilitate the restoration of nutrition supply. In summary, borosilicate is a family of new class of bioactive glass. The biological mechanism still needs to be further clarified to understand the repair mechanism.

Pan Haobo, Ph.D., professor, deputy director of the Institute of Biomedicine and Biotechnology, Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences, fellow of the International Society for Advanced Materials, chief scientist of the "14th Five-Year Plan" key research and development program of the Ministry of Science and Technology, director of the Research Center for Degeneration of Human Tissues and Organs, director of the Guangdong International Joint Research Center for Biomedical Materials, director of the Guangdong Provincial Marine Biomaterials Engineering Technology Center, director of the Shenzhen Key Laboratory of Marine Biomedical Materials, honorary professor of the University of Hong Kong, and selected as the top 2% in the world for three consecutive years Top Scientist List. He is also the director of the Chinese Association for the Promotion of Health Care, the chairman of the Department of Orthopedic Biomaterials, the director of the Chinese Society of Biomaterials, the chairman-elect of the Marine Biomaterials Branch, the vice chairman of the Bioceramics Branch, the deputy head of the Translational Medicine Group of the Orthopaedic Youth Committee of the Chinese Medical Association, and the vice chairman of the Translational Medicine Group of the Orthopaedic Branch of the Chinese Geriatrics Association. He has been engaged in the research of orthopedic biomedical materials for a long time, and put forward the scientific view of alkaline regulation of bone metabolism, which provides an important theoretical basis for the design of new orthopedic biomaterials. He has published more than 180 papers, more than 9,000 SCI citations, and an H-index of 51, including Prog Mater Sci, Adv Mater, Adv Funct Mater, Nat Commun, Adv Sci, Research, Bioact Mater, Biomaterials, ACS Appl Mater Interface, Acta Biomter, etc.

Advancing Sarcopenia Treatment: A Focus on Myosteatosis, Mitochondria, and Neuromuscular Health

Prof. Wing Hoi CHEUNG
Department of Orthopaedics&Traumatology
The Chinese University of Hong Kong

Introduction: Sarcopenia, characterized by the loss of muscle mass and function, is a consequence of aging. The etiology of sarcopenia is complex, involving factors such as myosteatosis, mitochondrial dysfunction, and neuromuscular junction (NMJ) degeneration, which remain insufficiently explored. Our team is investigating a range of interventions, both non-pharmaceutical and pharmaceutical, to mitigate the effects of sarcopenia.

Methods: We utilized senescence-accelerated male mice (SAMP8), a model known for onset of sarcopenia at 8 months of age. Our interventions encompassed non-pharmaceutical approaches, such as vibration therapy, oral supplement HMB, gut microbiota, and BAIBA, as well as a pharmaceutical strategy involving anti-RANKL antibodies. These treatments commenced when the mice were 6-month-old, with evaluations conducted 4 months later. We assessed outcomes by measuring grip strength, muscle cross-sectional area (MCSA), muscle weight, and *ex-vivo* muscle function.

Results: Our findings indicate that sarcopenia mice had myosteatosis, mitochondrial dysfunction and NMJ degeneration. Notably, mitochondrial and NMJ issues begin as early as 6 months of age, preceding the sarcopenia phenotype at 8 months. The combination of vibration therapy and HMB oral supplementation effectively reduces fat infiltration via the Wnt-β catenin pathway. Vibration therapy alone shows promise in mitigating NMJ degeneration by upregulating Dok7. Additionally, modulating gut microbiota contributes to improved mitochondrial biogenesis and overall gut health. BAIBA also plays a role in reducing inflammation.

Conclusions: The sarcopenic mouse model has highlighted issues related to myosteatosis, mitochondrial dysfunction, and NMJ degeneration. Our interventions have shown varying degrees of positive impact on sarcopenia, presenting potential for clinical translation. Furthermore, anti-RANKL antibodies emerge as a promising candidate for the first pharmacological treatment for sarcopenia.

Wing Hoi Cheung is a Professor and Deputy Director of the Musculoskeletal Laboratory in the Department of Orthopaedics & Traumatology at CUHK. He is also the Head of the Graduate Division and the Deputy Director of the MSc program in Musculoskeletal Medicine, Rehabilitation, and Geriatric Orthopaedics. He has courtesy researcher positions at CUHK Shenzhen Research Institute and the Hong Kong-Shenzhen Innovation and Technology Research Institute (FITRI).

His research focuses on the causes and treatments of sarcopenia and osteoporotic fracture healing, and the use of mechanical stimulation to address musculoskeletal ageing problems. He has received prestigious awards such as AO Berton Rahn Research Fund Prize, Beijing Municipal Science and Technology Award First Prize and 10th HOMA Academic Achievement Award in Osteoporosis Medical Research. He is a grant reviewer for prominent organizations, an Associate Editor and an Editorial board member for many international scientific journals. He has published 159 peer-reviewed international articles, 9 book chapters, more than 370 conference abstracts, and one book (as editor). He also has 4 patents (including 1 PCT and 3 US/China patents), showing his dedication to translating research into practical applications. His Google H-index is 44.

Human Stem Cell-derived Joint-on-a-Chip Systems for Modeling Joint Degeneration and Developing Regenerative Therapies

Prof. Z. Alan LI
Room 112C, Ho Sin Hang Engineering Building
Department of Biomedical Engineering (BME)
Chinese University of Hong Kong

Joint diseases such as osteoarthritis (OA) are highly prevalent and debilitating. Currently, there are no drugs capable of halting or reversing OA progression. While conventional joint disease models have significantly contributed to our understanding of disease mechanisms, traditional models have various limitations. For example, the endotype-specific pathogenic mechanisms were rarely addressed in conventional disease models. In addition, physiologically relevant disease models mostly do not possess high-throughput drug testing capability, and vice versa. Organ-on-a-chip (OoC) systems have emerged as highly promising *in vitro* platforms to study human-specific (patho)physiology. We have developed a series of joint-on-a-chip (JoC) systems using human stem cells and microfluidic systems to mimic the key functional features of synovial joints. Furthermore, inflammatory OA, one of the most common OA subtypes, has been modeled in our JoC systems. We demonstrated that the different tissue components underwent active bidirectional crosstalk in the JoC under "healthy" and "OA" conditions; we also used our JoC-based disease models to test clinically used OA drugs and those under development. Human stem cell-derived JoC systems hold promising potential in facilitating mechanistic studies on various joint conditions and accelerating the development of efficacious (personalized) regenerative medicine.

Dr. Alan Li joined the Department of Biomedical Engineering (BME), the Chinese University of Hong Kong as a Vice-chancellor Assistant Professor in 2022. He worked as a Postdoctoral Associate (with Prof. Rocky Tuan) and then a Research Assistant Professor (with Prof. Michael Gold) at the University of Pittsburgh School of Medicine (UPSOM) during 2018–2021. Alan obtained his Ph.D. (with Prof. Michael Khor) in bioceramics from Nanyang Technological University (NTU) Singapore, where he also worked as a Postdoctoral Research Fellow. Dr. Li directs the Biomaterials and Tissue Engineering Laboratory at the BME Department and leads a multidisciplinary team consisting of researchers with expertise in materials science, mechanical engineering, microfluidics, stem cell biology, and orthopaedic surgery. Research endeavors at the Li Lab are highly interdisciplinary and are focused on stem cells and biomaterials for bone and joint regeneration and musculoskeletal organ-on-chip systems. Among other honors, Alan received the Wake Forest Institute for Regenerative Medicine (WFIRM) Young Investigator Award and the Orthopaedic Research Society (ORS) 3Rs Award in 2019 and won the 2016 Young Persons' World Lecture Competition (YPWLC).

Citrate: The Nexus of Cellular Mechanism and Orthopedic Biomaterials Innovation

Prof. Jian YANG
Chair Professor, School of Engineering
Westlake University
Hangzhou, Zhejiang, China
Email: yangjian07@westlake.edu.cn

Tissue regeneration represents a substantial component of clinical practice. Although significant progress has been made in the development of degradable biomaterials, existing materials are limited by poor mimicking of the tissue compositions, often lacking the biochemical, biomechanical, and biological coordination necessary to mediate complex tissue healing. Developing regenerative materials that can promote wound healing and tissue regeneration remains a challenge. Leveraging the multifunctional nature of citrates in chemistry and inspired by its important biological roles in human, we have created a citrate-based biomaterials and small molecules platform that hold great promising for various regenerative engineering applications. The unprecedented knowledge on the previously under-explored citrate biology have enabled us to design the next generation of biomaterials that present citrate signals in demand during cellular and tissue development, which we now term it as "metabotissugenic biomaterials". Metabotissugenic citrate biomaterials have been successfully developed into FDA-approved implantable devices. The technology development and translation of citrate-based biomaterials are just at the beginning. The clinical successes of citrate materials-based medical devices will spur the rapid biomaterials and technology development to address the unmet challenges in complex tissue repair and regeneration.

Dr. Jian Yang is currently a Chair Professor in Biomaterials and Regenerative Engineering, the chair of Biomedical Engineering Program, and an Associate Vice President at the Westlake University. Prior to Westlake, he was a Professor of Biomedical Engineering and Dorothy Foehr Huck and J. Lloyd Huck Chair in Regenerative Engineering at the Pennsylvania State University. Dr. Yang is known for his pioneering contribution on citrate chemistry and biology for the development and applications of citrate-based biomaterials. He was a recipient of NSF CAREER Award (2010), Outstanding Young Engineering Faculty Award at UTA (2011), PSEAS Outstanding Research Award at Penn State (2018), and BMES Wallace H. Coulter Award for Healthcare Innovation Award (2023). Dr. Yang is an elected Fellow of American Institute of Medical and Biological Engineering (AIMBE, 2016), the National Academy of Inventors (NAI, 2018), the Biomedical Engineering Society (BMES, 2020), the American Association for the Advancement of Science (AAAS, 2021), and the International Academy of Medical and Biological Engineering (IAMBE, 2023). Dr. Yang is the Co-Editor-in-Chief of "Bioactive Materials", and an Associate Editor of "Science Advances". Dr. Yang is a co-founder and the Past-President of Chinese Association for Biomaterials (CAB) and the recipient of 2023 CAB Distinguished Leadership and Service Award.

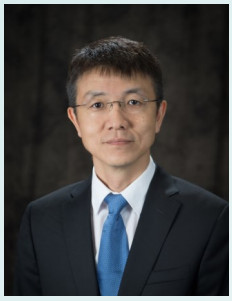
The Treatment of Osteochondral lesions: From Current Practices to Biomechanical Insights

Prof. Fei CHANG
Director
Department of Foot &Ankle Surgery
2nd Hospital of Jilin University

Osteochondral injuries, representing a significant challenge in orthopedic surgery, demand effective treatment strategies to restore joint function and alleviate pain. Recent developments in this field have emphasized the need for comprehensive approaches that not only address the immediate damage but also foster long-term regeneration of the affected tissues. Among prevalent treatment methods, autologous chondrocyte implantation (ACI) and matrix-associated autologous chondrocyte implantation (MACI) have gained recognition for their potential in promoting hyaline cartilage restoration. Additionally, techniques leveraging mesenchymal stem cells (MSCs) have shown promising outcomes due to their differentiation capacity and anti-inflammatory properties.

Our research extends beyond these current methodologies by investigating the role of the joint biomechanical environment in cartilage injury and repair processes. Through studies, we have uncovered that alterations in biomechanical forces not only contribute to the initiation and progression of cartilage damage but also significantly influence the efficacy of regenerative treatments. Our findings underscore the importance of modulating the biomechanical environment as part of a holistic treatment strategy. By integrating biomechanical considerations with advanced cellular and tissue engineering techniques, we aim to enhance the reparative capacity of injured cartilage, offering new insights into the optimization of osteochondral injury management.

Our work highlights the dynamic interplay between biomechanical factors and tissue engineering, proposing a nuanced approach to osteochondral injury treatment that capitalizes on the symbiosis of mechanical stimuli and cellular responses. This perspective opens up new avenues for research and therapy, potentially setting the stage for more effective and personalized treatment modalities in the future.



Fei Chang currently is the Director of the Department of Foot &Ankle Surgery at the Second Hospital of Jilin University, ChangChun, China. He received his PhD from both Jilin University in China and the Tsukuba University in Japan.

As a surgeon, his main direction of work is in foot-ankle surgery. He first established the foot and ankle surgery department as the founder in Jilin University, which was also the first professional foot and ankle surgery department in Jilin Province.

He is a Lifetime Member of International Chinese Musculoskeletal Research Society, a fellow of Chinese Orthopaedic Research Society (CORS), Chinese Association of Orthopaedic Surgeons (CAOS), Chinese Association of Rehabilitation Medicine (CARM), and International Society of Orthopaedic Surgery and Traumatology (SICOT). His research has been funded by a number of national research projects, including the National Key Research and Development Program and the National Natural Science Foundation of China.

He is the recipient of Chinese Medical Science and Technology Award, Scientific and Technological Progress Award in Jilin Province, and Natural Science Achievement Award in Jilin Province. In the field of basic research, he is mainly interested in cartilage damage and cartilage repair, and has done some research work in cartilage tissue engineering and biomechanics.

hESC-derived MSCs for clinical trials, developmental study, and cancer research

Ren-He XU
Faculty of Health Sciences
University of Macau
Avenida da Universidade
E12-4015, Taipa, Macau

Mesenchymal stem cells (MSCs) differentiated from human embryonic stem cells (hESC) (namely EMSCs) are advantageous to somatic tissue-derived MSCs for their unlimited source, stable quality, and remarkable efficacy in a variety of disease models. We have advanced EMSCs to a clinical trial on multiple sclerosis in U.S. and clinical studies on diabetic foot ulcer, graft-versus-host disease, and knee osteoarthritis in China. Recently, EMSCs were found to chimerize with the mouse blastocyst and contribute to cartilages and even the placenta. They also partially ameliorate skeletal defects caused by *Sox9* mutation. EMSCs can be used to study the NK resistance of circulatory tumor cells to form metastasis.

Dr. Ren-He Xu is a distinguished professor and associate dean (research) of the Faculty of Health Science, University of Macau, the president of Macau Society for Stem Cell Research, and a council member of Chinese Society for Stem Cell Research. He has studied stem cell development and applications for decades, published near 100 papers with around 10,000 citations, and obtained over 10 patents from U.S. and China. The mesenchymal stem cells differentiated from human embryonic stem cells via trophoblasts (T-MSCs) his team invented were approved by the U.S. Food and Drug Administration as an investigational new drug for a clinical trial on multiple sclerosis. Currently, Dr. Xu leads a Macau Key R&D project and a China National Key R&D project to study the clinical application of T-MSCs. Recently his lab demonstrated the developmental potency of T-MSCs via chimerism with the mouse blastocyst and the usefulness of T-MSCs to model the cancer-stromal cell interactions.

Website: https://fhs.um.edu.mo/en/staff/ren-he-xu/

Cell-adaptable hydrogels for cell delivery and 3D culture

Prof. Liming BIAN
International Campus
South China University of Technology
Panyu, Guangzhou

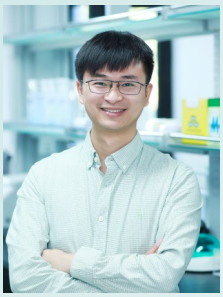
Although biopolymer-based chemical hydrogels, with biopolymers covalently crosslinked, have been widely used as scaffolds for tissue engineering due to good stability, their permanent network structures and brittleness limit their applications in repairing load-bearing tissues, such as cartilage. In contrast, biopolymer-based supramolecular hydrogels, which are usually formed via self-assembly of physically interacting biopolymers, are usually weak as shown in "inverted vials" instead of freestanding 3D constructs and less stable than chemical hydrogels. Herein, we describe a novel host-guest macromer approach for preparation of biopolymer-based freestanding supramolecular hydrogels. Such hydrogels are solely crosslinked by in situ formed multivalent host-guest nano-clusters, and show significantly reinforced mechanical properties yet still retain desirable supramolecular features. They can self-heal and be re-molded into freestanding 3D constructs which afford effective protection on the encapsulated stem cells during the compression re-molding, making them promising carriers for therapeutic cells that can quickly adapt to and integrate with surrounding tissues of the targeted defects. We demonstrate that such hydrogels supported in situ tissue regeneration via the delivery of therapeutic cells and drugs. Such dynamic hydrogels are not only desirable for potential clinical applications but also useful for 3D culture of cells and organoids to assist basic studies.

Prof. Bian Liming is currently a Changjiang Scholar Professor and the Associate Dean in the School of Biomedical Sciences and Engineering at the South China University of Technology after serving as a tenured professor in the Department of Biomedical Engineering at the Chinese University of Hong Kong. Prof. Bian completed his Ph.D. study in Biomedical Engineering at Columbia University in 2009. Prof. Liming Bian then conducted his postdoctoral research in the Department of Bioengineering, the University of Pennsylvania from 2009 to 2012. Prof. Bian's research focuses on the development of novel multiscale biomaterials not only for investigating the role of cell microenvironment factors on stem cell behaviors but also for facilitating the regeneration of diseased or injured tissues and organs. Prof. Bian's research work has been published in the leading journals including Science Translational Medicine, PNAS, Nature Communications, Science Advances, Advanced Materials, JACS, Angew Chemie, etc.

Peri-implantation embryo development and regulation

Prof. Fan ZHOU
Tsinghua University
Beijing, China

Connecting preceding blastocyst formation and following gastrulation respectively, peri-implantation embryogenesis is a key biological event during mammalian development. The embryo undergoes a series of cellular and molecular regulatory processes from pre- to post-implantation transition. In this presentation, we will discuss in vitro and in vivo models, omics measurement and molecular marker identification to explore the ingenious linkages among molecular program, lineage specialization, and polarity formation from a perspective of multidimensional molecular regulation. Relevant studies potentially provide clues to understand cell fate and regulation of embryo development, as well as the possible causes of habitual abortion and infertility.



Dr. Fan Zhou is now an associate professor and principal investigator at School of Life Sciences, Tsinghua University. Fan received his PhD from the Academy of Military Medical Sciences in 2016, and postdoctoral training at Peking University from 2016 to 2020. He joined Tsinghua as a faculty and set up his independent laboratory in August 2020. The current group now aims to integrate in vivo and in vitro functional identification, omics mining and genetic manipulation systems to study cell fate and peri-implantation embryo development. With newly-developed single-cell-initiated in vivo transplantation system, he revealed key signalling pathway during HSC emergence (*Nature,* 2016). Fan and his colleagues uncovered the gene networks and DNA methylome patterns of human implantation (*Nature,* 2019), the cellular and molecular dynamics of embryonic polarity formation across species (*Developmental Cell,* 2023), and the molecular characteristics of monkey blastoids (*Cell Stem Cell,* 2023). Fan has received the Ray Wu Prize (2016) and Young Elite Scientists Sponsorship Program from China Association for Science and Technology (2017). The research of human implantation was selected as the 2019 Top Ten Advances in Life Sciences in China.

Fighting Alzheimer disease by targeting autophagy: from basic study to pharmacological application

Prof. Jiahong LU
Room 9005, N22 building,
Institute of Chinese Medical Sciences
University of Macau
Avenida da Universidade, Taipa, Macao, China

Autophagy is a highly conserved cellular bulk degradation mechanism for materials recycle and clean-up of damage organelles and aggregated proteins. Aberrant autophagy has been linked to neurodegenerative diseases including Alzheimer disease (AD). Our Lab works on a novel autophagy related gene NRBF2 and reveals its implication in the pathogenesis of AD. Meanwhile, we identified a series of autophagy modulators from traditional Chinese medicine and evaluated their neuroprotective effects through cross-species models of AD.

Dr. Jiahong Lu is the associate professor at institute of Chinese medical sciences, University of Macau. Dr. Lu's major research interests are autophagy biology and pharmacological study of Chinese medicine. Dr. Lu has published more than 60 papers as corresponding author in high profile journal including: Nature Biomedical Engineering, EMBO Molecular Medicine, Cell Discovery, Autophagy (7), Molecular neurodegeneration, Acta Pharmaceutica Sinica B (3), …, with a total citation over 9,000 times. Dr. Lu's research work received wide recognition. He has been listed in the Stanford World's Top 2% Scientists list. He won the "Best Poster Prize" in EMBO autophagy conference (2013), the "Future of Science Fund Scholarship" from Keystone Symposia (2014) and the "Annual Young Scientist award" from TCM Brain Science Conference (2022). Dr. Lu is the editorial board member of Acta Pharmaceutica Sinica B and neurochemistry international.

Antibody-based Immune-cell Therapy Against Cancer

Prof. Qi ZHAO
Faculty of Health Sciences
University of Macau

In recent years, immune checkpoint therapy has emerged as a breakthrough strategy to reinvigorate anti-tumor immune responses. Targeting multiple non-small cell lung cancer antigens, we employed phage display antibody library screening techniques to identify several specific monoclonal antibodies. Utilizing yeast display combined with computer-assisted design, these antibodies were recombinantly engineered into high-affinity antibodies, mediating tumor cell killing through the mechanism of antibody-dependent cell-mediated cytotoxicity (ADCC). Additionally, these antibodies were engineered into bispecific antibodies targeting tumor cells and human NK cell markers, capable of engaging NK cells to kill tumors. Furthermore, we constructed chimeric antigen receptor (CAR)-modified T cells targeting non-small cell lung cancer cells. Simultaneously, based on immune cell formulations, we developed nanoparticle drug delivery systems for targeted delivery and controlled release of therapeutics in various in vitro and in vivo models. These data will support further development of therapeutic agents of this class in preclinical and clinical research.

Professor Zhao Qi is an Associate Professor at the Faculty of Health Sciences, University of Macau. He earned his bachelor's degree from the School of Life Sciences, Jilin University, and completed his Ph.D. in the Department of Biochemistry at the Chinese University of Hong Kong. He has held a postdoctoral fellow at the National Cancer Institute and as a Research Associate at the Memorial Sloan-Kettering Cancer Center in the USA. With a prolific research career spanning over numerous years, Professor Zhao Qi has authored and co-authored over 100 papers in peer-reviewed journals such as Nature Communications, Journal of Hematology & Oncology, Leukemia, and Clinical Cancer Research. His accomplishments also include 20 granted patents and prestigious awards. He has been honored with the US NIH Federal Technology Transfer Award. He has been actively engaged in various research projects, including the National Key Research and Development Program, Macao Science and Technology Development Fund, NSFC-FDCT Joint Fund, Zhong Nanshan Medical Foundation, Dr. Stanley Ho Medical Development Foundation, and Novo Nordisk Research Fund.

Regulation of skeletal muscle stem cells in aging

Prof. Huating WANG
507A Li Ka Shing Institute of Health Sciences
PWH, CUHK

Population aging is on the point of instigating one of the most important social-economic changes and also one of the resource-consuming health crises of the 21st century. Skeletal muscle, as a key organ of body homeostasis and mobility, suffers from age-associated sarcopenia, i.e. the decline of mass, function, and regenerating capacity. As a common geriatric condition with a prevalence of 10%–27% in adults, sarcopenia represents a major public health issue due to various resultant clinical and societal consequences, including reduced quality of life, falls, fractures, frailty, physical limitation, loss of independence, high health care cost and mortality, thus there is an urgent need to increase our collective efforts in understanding the underlying mechanisms and harnessing the knowledge to develop effective intervention strategies. It is commonly believed that sarcopenia can be partially attributed to the decrease in the number and function of adult muscle stem cells (MuSCs). MuSCs are indispensable for injury induced muscle regeneration and maintenance of muscle homeostasis. Here in this talk we will discuss how intrinsic alterations in MuSCs and extrinsic deregulations in the niche environment contribute to the age-related MuSC decline.

Professor Huating Wang is currently a Professor in the Department of Orthopedics and Traumatology at the Li Ka Shing Institute of Health Sciences, the Chinese University of Hong Kong. She received her bachelor's degree in Environmental Chemistry from Nanjing University, China, in 1996. In 1998, She went to the Ohio State University (OSU), USA to study for a doctoral degree, and received her PhD in Molecular Virology in 2004. She then did Postdoctoral training at The Ohio State University Comprehensive Cancer Center under the support of an F32 Postdoctoral Fellowship grant from the National Institutes of Health, USA. In 2009, she moved to Hong Kong as an Assistant Professor at the Faculty of Medicine at the Chinese University of Hong Kong. She was promoted to Associate Professor in 2015 and to Full Professor in 2020. Her team studies the intrinsic and extrinsic regulatory mechanisms of skeletal muscle stem cells in regeneration and aging. Since 2005, she has published more than 80 papers and been awarded more than 20 Hong Kong and China grants.

Application of Stem Cell-Derived Organoids in Biomedical Research

Prof. Hyung-kim NAM
Wuyi Univeristy
Jiangmen, Guangdong Province, China
namhyungkim@163.com

Stem cell research has marked a pivotal shift in biomedical sciences, particularly with the advent and maturation of organoid technology. Stem cell-derived organoids, three-dimensional cell cultures that mimic the complexity of organ architecture and function, have emerged as a revolutionary tool in modeling diseases, personalized medicine, and regenerative therapy. This presentation, titled " Application of Stem Cell-Derived Organoids in Biomedical Research" aims to encapsulate the current status of stem cell-derived organoid research, elucidating its potential, challenges, and future directions. Stem cell-derived organoids have provided serve as a bridge between traditional two-dimensional cell cultures and in vivo animal models, offering a more physiologically relevant and ethical approach to study human biology and disease. The application of organoids spans across various domains, modeling complex diseases such as cancer, neurodegenerative disorders, and infectious diseases, drug discovery and toxicology testing, and the exploration of regenerative medicine. The talk will highlight significant breakthroughs in the field, showcasing how stem cell-derived organoids have been instrumental in understanding the pathophysiology of diseases, in the development of targeted therapies, and in pioneering efforts towards organ transplantation and repair. Stem cell-derived organoids represent a significant leap forward in our ability to study human health and disease. By continuing to refine this technology and address existing challenges, the field is poised to make even more remarkable contributions to biomedical research, offering hope for the development of more effective treatments and therapeutic strategies. This talk aims to inspire continued innovation and collaboration in the quest to fully realize the promise of stem cell-derived organoids in advancing human health.

Nam-Hyung Kim, Ph.D. in Reproductive Physiology, Oregon State University, USA. Special appointed professor at Wuyi University, Guangdong province, China, with extensive experience in reproductive physiology, specifically in embryo physiology and the production of cloned transgenic animals. Director of the Guangdong province Key Laboratory of Large Animal Disease Model for Biomedicine. Academician of the Korea Academy of Science and Technology with a significant track record of leading major national projects, publishing over 350 SCI-included papers, authoring two books, and holding more than 20 patents. 1999 -2022 Professor of Chungbuk National University, Best Scientist Achievement Award, Korea, 2017, New Knowledge Management Conference Award, Korea, 2018, Highest Education Award, Ministry of Education of Korea, 2022, Best Foreign Expert Award, Jilin, 2019, Friendship Award, Guangdong Province, 2023. Recent his ocus are on stem cell research and organoid application for industrialization.

PBX1 in regeneration medicine

Prof. Jinyu LIU
Xinmin Street 1163
School of Public Health, Jilin University
Changchun, PR China

Stem cell therapy holds promises in regenerative medicine. Even though, the maintenance of stem cell self-renewal and multipotency, and alleviation of stem cell senescence is prerequisite in stem cell therapy in view point of safety and efficacy. Increasing evidence shows that transcription factors orchestrate interaction networks to maintain stem cell self-reviewal and pluripotency. Pre-B-cell leukemia transcription factor 1 (PBX1) is a member of the triple amino acid loop extension family of homologous transcription factors and acts as a key transcriptional regulator in the development of multiple tissues and organs. SIRT1 is a highly conserved NAD-dependent lysine deacetylase and ADP-ribosyl transferase. It is widely involved in the regulation of cellular senescence and contributes to organism longevity via acetylation and deacetylation of substrates. Our recent studies showed that PBX1 and SIRT1 forms a positive interaction feedback loop, separately or synergistically downregulates PARP1 expression, and attenuates ROS-mediated HF-MSC senescence and apoptosis. The newly found positive interaction feedback loop between PBX1 and SIRT1 open a new insight in stem cell senescence research.

Dr. Jinyu Liu earned his MD and PhD from Norman Bethune University of Medical Sciences, China. 1999-2004 he undertook skin tissue engineering and wound healing at the Department of Dermatology, Zurich University Hospital, Switzerland. Where he set up a novel bioreactor microcarrier cell culture system for high yields of autologous skin stem cells, and subsequently put these cells into clinical trial for treatment of hard to heal leg ulcers and stable vitiligo, with promising results obtained. 2004-2008, he undertook cardiovascular tissue engineering at the Department of Chemical and Biological Engineering, State University of New York at Buffalo. Where he tissue-engineered functional small diameter vascular constructs using bone marrow- or hair follicle-derived stem cells as cell sources. 2009-present, he undertook stem cell biology and regenerative medicine at Jilin University. Where he explored the role of pioneering transcription factor PBX1 in alleviation of stem cell senescence and enhancement of tissue regeneration. His main research focus on stem cell biology and regenerative medicine, tissue engineering and gene therapy, biopharmacy and toxicology, tumor pathobiology.

Unveiling the Potential of hESC-derived Neural Crest Models: Insights into Neuroblastoma and Therapeutic Strategies for Hypoxic-Ischemic Encephalopathy

Prof. Cynthia Xiaohua JIANG
Room 126A, School of Biomedical Sciences
Area 39, the Chinese University of Hong Kong

One of the major challenges faced by cancer biologists is the development of model systems that accurately recapitulate human diseases. To date, studies on neural crest (NC) development and biology have predominantly relied on model organisms. Human embryonic stem cells (hESC) hold great promise as sources of regenerative tissue and therapeutics. Additionally, their value as tools for studying the genesis and biology of human diseases cannot be underestimated. Given that childhood cancers often arise from disruptions in embryonic development, hESC represents an invaluable resource for investigating pediatric tumorigenesis. In this talk, I will present our recent study utilizing a hESC-derived NC model to investigate the cellular and molecular origin of neuroblastoma. Through this platform, we have discovered that MYCN plays a critical role in shaping CD55 as a novel cancer stem cell regulator, which serves as both a prognostic marker and a potential therapeutic target for neuroblastoma.

Hypoxic-ischemic encephalopathy (HIE) is a severe birth complication that affects neonates and infants. Mesenchymal stromal cell (MSC)-based therapy has emerged as a promising treatment approach for HIE. In the second part of the talk, I will discuss our recent findings on the application of human NC-derived ectomesenchymal stromal cells in a rat model of HIE.

Professor JIANG is an Associate Professor in the School of Biomedical Sciences at CUHK, actively contributing to the Developmental and Regenerative Biology Thematic Research Program. She received her medical degree from Shanghai Second Medical University (currently School of Medicine, Shanghai JiaoTong University) and completed her internship and residency at RuiJin Hospital, Shanghai. She obtained her PhD degree in cell biology from the University of Hong Kong. Following her doctoral studies, Prof. JIANG continued her research journey as a postdoctoral fellow at the Department of Medicine, UCLA, and the University of Southern California, supported by the CIRM (California Institute for Regenerative Medicine). In 2013, she established an independent laboratory within the School of Biomedical Sciences at the Chinese University of Hong Kong. Prof. JIANG's research primarily focuses on stem cell biology and regenerative medicine, with a particular interest in understanding the molecular regulation of stem cells, investigating the stem cell microenvironment, and exploring stem cell therapy for neurological diseases. Prof. JIANG has published more than 100 peer-reviewed papers with over 5000 citations and a H-index of 40, including *Nature Medicine*, *Cell Research*, *iScience*, *Cell Death and Differentiation*, *Stem Cells*, *Stem Cell Reports* and *Neuro-oncology*. She serves as editorial board member for various international journals and reviewers for numerous journals and grants.

An aging-promoting feedback loop interferes with cell migration and muscle repair

Mengqi CHEN
Faculty of Health Science, University of Macau
E12-3049, Avenida da Universidade, Taipa, Macau, China

Impaired cell migration commonly occurs in aged cells and contributes significantly to the time-related deterioration of many physiological functions, like tissue repair and regeneration. Productive cell migration requires a proper and persistent direction which is determined by a front-to-back, centrosome-to-nucleus polarity. We found that such a polarity is lost in dermal fibroblasts from aged but not young people. Mechanistically, aging elevates the expression of SUN1, an inner nuclear protein, which stabilizes and recruits microtubules to the nucleus and prevents rearward nuclear movement. We further found that SUN1 expression caused the cells to secret a protein to inhibit nuclear movement in other cells. The polarity inhibitor also existed in conditioned medium from aged cells and plasma from aged people. We have identified the protein and named it as factor released by aged cells (FRAC). Treating cells with recombinant FRAC blocked nuclear movement in wildtype fibroblasts as expected. Interestingly, FRAC treatment induced SUN1 expression and acted through SUN1 and microtubules to interfere with cell polarity. This SUN1-FRAC feedback loop promoted the occurrence of multiple aging cellular phenotypes besides cell polarity and migration defects. To examine the physiological impacts of this feedback loop, we studied myotube differentiation in vitro and muscle repair in vivo and found that FRAC significantly inhibited myotube formation and impaired muscle repair after injury. Altogether, we have discovered a positive feedback loop that promotes aging impairments at both the cellular and organismal levels.

Full Name: Chen Mengqi
Tel: +85363978719
Email:YC07655@ umac.mo

Academic Qualification

University of Macau 2020.8-2024.8
PhD student of Biomedical Science

Sichuan University, Western China Hospital 2016.9-2019.7
Master's Degree in Biomedical Engineering

Taiyuan Normal university 2012.9-2016.7
Bachelor's Degree in Biology

Published Research

Li Y, Chen M, Chang W. Roles of the nucleus in leukocyte migration. Journal of Leukocyte Biology, 2022 Oct; 112(4):771-783.

Chen M, Ma Y, Chang W. SARS-CoV-2 and the Nucleus. International Journal of Biological Sciences, 2022 Jul; 18(12):4731-4743.

Chen, Mengqi. Li, Rui. Yin, Wen. Wang, Tao. Kang, Y. (2020). Copper promotes migration of adipose-derived stem cells by enhancing vimentin-Ser39 phosphorylation. Exp Cell Res. doi:10.1016/j.yexcr.2020.111859

Lu, Zu. Jiang, Xia. Chen, Mengqi. Feng, Li & Kang, Y. (2019). An oxygen-releasing device to improve the survival of mesenchymal stem cells in tissue engineering. Biofabrication. 11.10.1088/1758-5090/ab332a.

Research Experience

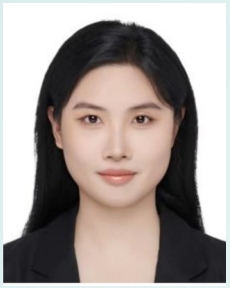
University of Macau, Macau (Supervisor: Wakam Chang) 2020-now
An ApoD-SUN1 positive feedback loop promotes aging

Sichuan University West China Hospital, Sichuan (Supervisor: Y. James Kang) 2016-2019
Copper promotes the migration of adipose-derived stem cells by enhancing vimentin Ser39 phosphorylation

Engineered exosomes loaded with cGMM conduct dual functions for postsurgical osteosarcoma treatment

Naping XIONG
Department of Orthopaedics and Traumatology
Faculty of Medicine, The Chinese University of Hong Kong
Shatin, N.T., Hong Kong

Osteosarcoma (OS) is a highly aggressive primary malignant bone tumor that predominantly affects children and adolescents. While current immunotherapy has not met the curative expectations in the treatment of osteosarcoma. Therefore, there is an urgent to develop a high-efficiency targeting delivery system to transport the immunotherapeutic drugs. In this study, we designed a cGAMP@MnO2 composite material, in which MnO2 serves as a carrier of cGAMP and these two components synergistically activate the cGAS-STING pathway. OS-targeting exosomes as vehicles to deliver cGAMP@MnO2 into the tumor cells indicates the potential precise therapeutic strategy for OS. Meanwhile, the Mg hydrogel (MeHA-Mg) was employed to carry these cGAMP@MnO2 loaded OS-targeting exosomes to form an all-in-one system (cGMM) for anti-tumor and promoting osteogenesis. By observing the in vivo tumor growth curve, we found that cGMM significantly inhibits the recurrence and growth of OS. By examining the systemic immune responses in mice, we discovered that cGMM significantly increases the maturated DCs (CD86+ , CD80+) in tumor-draining lymph nodes. CD103+ /CD8a+ DCs, the most competent antigen presenting cells (APCs) for cross-priming CD8+ T cells, were also increased by cGMM treatment. Consistently, we observed a significant increase of CD4+ and CD8+ T lymphocytes in the peripheral blood of mice. On the other hand, the magnesium-containing hydrogel facilitates bone regeneration based on the scans of bone defect repair using microCT. In summary, we have developed an all-in-one system for postoperative of osteosarcoma by activating the immune system, inhibiting tumor recurrence, and promoting bone regeneration.



Naping XIONG focuses on the role of metalloimmunotherapy in osteosarcoma. She graduated from Yichun University in 2018 with a bachelor's degree, where she was recognized as an outstanding graduate. In the same year, she joined Prof. Zhaocai ZHOU's group at the Shanghai Institute of Life Science, Chinese Academy of Science, to pursue a master's degree. In 2020. She joined Prof. Yifeng ZHANG's group at Shanghai Tech University, where she continued her research on the role and mechanisms of manganese ions metal immunotherapy in osteosarcoma. In February 2023, she co-authored a related paper published in Nanotoday (IF: 17.4) as a co-first author. In August 2022, Naping XIONG joined Prof. Ling QIN's research group in the Department of Orthopedics and Traumatology, Faculty of Medicine, the Chinese University of Hong Kong, to pursue a doctoral degree. She is currently in her second year of the doctoral program. During her doctoral studies, her main research area focuses on the immunostimulatory effects of Mn ions combined with Mg ions and their application in promoting bone repair in postoperative rehabilitation of osteosarcoma. Her goal is to design and synthesis integrated materials for suppressing postoperative recurrence and metastasis of osteosarcoma while promoting bone defect repair.

TET3 promotes pancreatic cancer malignancy and metabolic remodeling through GATA6-mediated TGF-β signaling pathway

Shuai LIU
Faculty of Health and Sciences
University of Macau, Macau SAR, China

Aberrant expression of ten-eleven translocation (TET) enzymes has been reported in patients with pancreatic ductal adenocarcinoma (PDAC). However, the molecular mechanisms in which TETs affect PDAC progression remain elusive. Analysis of pancreatic cancer data from TCGA and GTEx suggested that increased expression of TET3 was negatively correlated with patient survival. Using CRISPR-Cas9 to genetically delete endogenous TET3 in various human pancreatic cancer cell lines, we found that cell migration, invasion, and tumor growth were significantly inhibited. Transcriptome analysis revealed that differential expression genes were significantly enriched for TGF-β and cell metabolic pathways in TET3-depleted cells. Our subsequent analysis demonstrated that loss of TET3 results in an energy switch from glycolysis to oxidative phosphorylation. In addition, fatty acid synthesis was suppressed by downregulating various rate-limiting enzymes including SCD, FASN, and FADS2 in TET3-knockout cells, suggesting that TET3 contributes to metabolic reprogramming in pancreatic cancer. Moreover, we found that TET3 suppressed GATA6 which negatively regulated TGF -β2 and therefore inhibited the TGF-β signaling pathway in a SMAD4-dependent manner. In summary, our findings illuminate the distinct mechanism of TET3 in SMAD4-positive PDAC and provide implications for the development of novel therapeutic strategies for pancreatic cancer patients.

Liu Shuai is a 4th year PhD student in Faculty of Health Science, University of Macau. He received BSc and MSc in pharmacy and pharmacology from Shenyang Pharmaceutical University, followed by 2 years research assistant at The University of Hong Kong. Currently, he works on the molecular mechanism in pancreatic cancer, elucidating the role of DNA- and histone-modifying enzymes, and exploring novel anti-cancer strategies by targeting key epigenetic pathways.

Multifaceted Activities of Human Pluripotent Stem Cell-Derived Ectomesenchymal Stromal Cells for the Treatment of Hypoxic-Ischaemic Encephalopathy

Jiawei HUANG

Room 126, Lo Kwee-Seong Integrated Biomedical Sciences Building

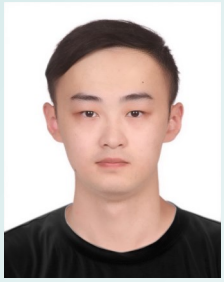
Area 39, The Chinese University of Hong Kong

Hypoxic-ischaemic encephalopathy (HIE) is one of the most serious complications in neonates and infants. Mesenchymal stromal cell (MSC)-based therapy is emerging as a promising treatment avenue for HIE. However, limitations such as cell heterogeneity, low isolation efficiency, and unpredictable effectiveness hinder the clinical application of MSCs. In our previous study, we discovered that human pluripotent stem cell-derived ectomesenchymal stromal cells (hPSC-EMSCs) exhibited superior therapeutic effects compared to hUC-MSCs in promoting brain functional recovery in a rat model of HIE. Intranasal delivery of conditioned medium (CM) derived from hPSC-EMSCs reduced brain lesion size, stimulated endogenous neurogenesis, and attenuated inflammatory responses. *In vitro* studies demonstrated that hPSC-EMSC-derived CM exerted neuroprotective and neurorestorative effects by enhancing anti-apoptosis, neurite growth, and neurogenesis. Notably, our recent findings revealed that hPSC-EMSC-derived CM also promoted oligodendrocyte progenitor cell (OPC) differentiation *in vitro* and facilitated remyelination *in vivo*. Through comprehensive RNA-seq, MASS-SPEC, and enzyme-linked immunosorbent assays, we identified differential secreted factors between hPSC-EMSCs and hUC-MSCs. Of particular interest was the enrichment of periostin (POSTN), which binds to integrins αvβ3, αvβ5, and α6β4, thereby activating multiple signaling pathways. Preliminary results suggest that POSTN promotes OPC differentiation *in vitro*. In conclusion, our findings demonstrate that hPSC-EMSCs exhibit multifaceted neuromodulatory activities through paracrine/trophic mechanisms, leading to functional recovery in HIE. These insights shed light on the potential of hPSC-EMSCs as a novel therapeutic approach for HIE treatment.

How do MSCs help circulating tumor cells escape NK killing?

Yi YE
Faculty of Health Sciences
University of Macau
Taipa, Macau, China

Circulating tumor cells (CTCs) shed from primary tumors must overcome the cytotoxicity of immune cells, particularly natural killer (NK) cells, to form metastasis. The tumor microenvironment (TME) protects tumor cells from the cytotoxicity of immune cells partially executed by cancer-associated mesenchymal stromal cells (MSCs). However, the mechanisms by which MSCs influence the NK resistance of CTCs remain poorly understood. This study demonstrates that MSCs enhance NK resistance of cancer cells in a gap junction-dependent manner, thereby promoting survival and metastatic seeding of CTCs in immune-compromised mice. Tumor cells crosstalk with MSCs through an intercellular cGAS-cGAMP-STING signaling loop, leading to increased production of interferon-b (IFNb) by MSCs. IFNb reversely enhances the type I IFN (IFN-I) signaling in tumor cells and hence their expression of human leukocyte antigens class I (HLA-I) on the cell surface, protecting the tumor cells from NK cytotoxicity. Disrupting the loop results in the reversal of NK sensitivity in tumor cells and a decrease in tumor metastasis. Moreover, positive correlations between IFN-I signaling, HLA-I expression, and NK tolerance were found in human tumor samples. Thus, the NK-resistant signaling loop between tumor cells and MSCs may serve as a novel therapeutic target.



Mr. Ye Yi obtained his bachelor's and master's degrees in clinical medicine from Central South University before pursuing his Ph.D. study in the Faculty of Health Sciences, University of Macau. During his Ph.D. study, he focuses on effects of mesenchymal stromal cells on tumor progression under the supervision of Prof. Ren-He Xu. His work has been published in Advanced Sciences, International Journal of Biological Sciences, and Journal of Cancer. The highest cited paper has more than 1000 citations.

The study of cranial bone transport and pulsed electromagnetic field in traumatic brain injury rehabilitation

Xu YAN
Department of Orthopedics and Traumatology
Faculty of Medicine, The Chinese University of Hong Kong
Shatin, HKSAR, China

Traumatic Brain Injury (TBI) is a leading cause of death and disability in young people, affecting 69 million people annually, worldwide, leading to primary and secondary brain damage. cranial bone transport (CBT) has therapeutic effects on the central nervous system. In our previous study, CBT remarkably improved brain function after an ischemic stroke and revealed the therapeutic effects of CBT on Alzheimer's disease (AD). Those results shed light on the relationship between bone transport and the regeneration of meningeal lymphatic vessels (MLVs). Pulsed electromagnetic field (PEMF) treatment is a safe physical therapy that is usually used to promote bone, cartilage, and blood vessel regeneration.

TBI rats model, Cranial bone transport rats model, and Combined therapy rats model are successfully established. Rotarod test, NOR test, Y-maze and open field test, Nissl stain, H&E stain. Immunofluorescence and flow cytometer are involved.

In the result, the PEMF-CBT combined therapy shows therapeutic effects on TBI. New theories and technologies help us understand the mechanisms underlying of CBT in the treatment of brain disease. We have made initial progress in biological processes. In the future, bones may be redefined as endocrine organs responding to mechanical stimuli.

Mr. YAN Xu obtained his bachelor's in clinical medicine from Second Military Medical University and his master's degree in surgery (Orthopedics) from Shanghai Jiao Tong University before pursuing his Ph.D. study in the ORT department, in CUHK. He focuses on brain-bone crosstalk, cranial bone transport, distraction osteogenesis, fracture non-union, and mechanobiology under the supervise of Prof. Gang LI in CUHK.

NIR-II self-assembly nanomedicines for targeted multimodal imaging-guided synergistic anti-tumor immunotherapy

Dr. Yeneng DAI
Cancer Centre, Institute of Translational Medicine
Faculty of Health Sciences, University of Macau
Macau SAR, 999078, China

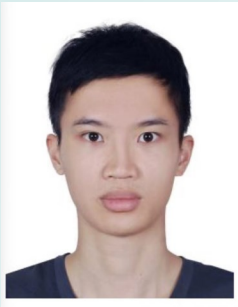
The effectiveness of phototheranostics induced immunotherapy is still hampered by limited light penetration depth, the complex immunosuppressive tumor microenvironment (TME) and the low drug delivery efficiency. To overcome these obstacles, a series of NIR-II self-assembly nanomedicines with high drug loading and TME reprogramming capabilities are constructed through metal ion (Fe^{3+}, Cu^{2+}, Mn^{2+}) mediated coordination self-assembly, followed by camouflaging of tumor cell membranes or modified with aPD-L1 nanobody (Nb), for targeted and amplified immunotherapy. Under the triggering of TME, these nanomedicines responsively disintegrated and released therapeutic components, which enable tumor-specific NIR-II fluorescence/photoacoustic imaging-guided NIR-II photothermal-chemodynamic therapy. Specially, the released Cu(I) induces the aggregation of lipoylated mitochondrial proteins accompanied by the loss of iron-sulfur proteins, leading to severe proteotoxic stress and eventually cuproptosis, simultaneously provoking significant immune surveillance and triggering the immunogenic cell death (ICD) to promote cytotoxic T lymphocyte infiltration together with aPD-L1-mediated immune checkpoint blockade. In addition, the released glycolysis inhibitor markedly inhibits lactate generation through glycolysis obstruction. The decreased lactate efflux remodels immunosuppressive TME through suppressing the M2 macrophage proliferation and downregulating regulatory T cell levels, thus further amplifying the efficiency of NIR -II photothermal immunotherapy.

Dr. Dai graduated from Institute of Advanced Materials (IAM), Nanjing University of Posts & Telecommunications with a doctor's degree of Organic and Bio Optoelectronics in 2022. He is now a post-doctoral fellow of Faculty of Health Sciences, University of Macau. His research interests focus on smart responsive NIR-II (1000-1700 nm) phototheranostic probes and biomimetic drug delivery system for targeted and activatable oncology theranostics, and developing self-assembly NIR-II nanoadjuvants for regulating and remodeling immunosuppressive tumor microenvironment to amplify anti-tumor immune response. His works have been published in *Advanced Functional Materials*, *Biomaterials, Small, Chemical Engineering Journal and Acta Biomaterialia.*

Systemic supplementation of magnesium attenuates bone loss via acting on the central nervous system

Tongzhou LIANG
Department of Orthopaedics and Traumatology, Faculty of Medicine
The Chinese University of Hong Kong
Shatin, N.T., Hong Kong

Osteoporosis (OP) is a prevalent disorder that disrupts bone quality and may result in devastating osteoporotic fractures. Magnesium supply can reverse the progression of osteoporosis, but the magnesium content in bone and serum is relatively unaffected, suggesting a different mechanism instead of local interaction. In the central nervous system (CNS), oral magnesium-L-threonate (MgT) supply improved memory. Therefore, we speculated that magnesium could regulate bone metabolism by acting on the CNS. In this study, we used CNS penetrable MgT to achieve high bioavailability in the cerebrospinal fluid. After being treated with MgT for 1 month, MgT-treated mice showed increased micro-CT parameters compared with osteoporotic mice treated with saline or MgCl2. The osteogenic differentiation in the trabecular region increased, marked by increased Sp7 and Runx2 positive cells. Using retrograde tracing virus, we identified an anatomical connection between the femur and parabrachial nucleus (PBN) in the brainstem. Chemogenetic activation of the CGRP+ subpopulation in PBN increased the BV/TV of trabecular bone. Transcriptome analysis of the bone suggested that a specific neuroactive ligand, neurotensin, may serve as the downstream effector of PBN. Deletion of magnesium transporter-1 (Magt1), an important magnesium transporter, in PBN's Calca+ neurons, resulted in deteriorated trabecular bone parameters and abolished the protective effect of MgT's treatment. In summary, we identified that systemic magnesium supply by MgT activated neurons in PBN, thus affecting osteogenic differentiation and improving bone quality.



Mr. Tongzhou LIANG has a great interest in the regulatory mechanism, biological nature, and treatment of certain orthopedic diseases. He obtained a bachelor's degree in clinical medicine from Sun Yat-sen University in 2018. During his bachelor's period, he was awarded the first award in the competition for undergraduate experimental design in basic medical sciences. In 2018, he was admitted to the Sun Yat-sen Memorial Hospital, Sun Yat-sen University to pursue his master's degree in surgery. Under the supervision of Prof. Dongsheng HUANG and Prof. Peiqiang SU, he focused on the regulatory mechanism of retinoic acid receptor-related orphan receptor alpha on bone and cartilage metabolism. His serial work has been published in Cell Death & Disease and the International Journal of Biological Sciences as first author or co-first author. He obtained his master's degree in 2021 and was awarded the national scholarship and recognized as an outstanding postgraduate student. In August 2021, He joined Prof. Ling QIN's team and worked as a PhD candidate at the Department of Orthopedics and Traumatology, Faculty of Medicine, the Chinese University of Hong Kong. In the PhD period, he showed his interest in the research area of the neuroregulatory role of Mg ion, and the role of such regulatory function mediating brain-bone interaction. The goal of his study is to identify novel mechanisms and therapeutic targets of osteoporosis via the nervous system.

Endogenous protease activity regulates metabolic and cell fate patterns

Zhaoying ZHANG
Faculty of Health Sciences, University of Macau
Room 2008, Building N22, Avenida de Universidade
Taipa, Macau SAR

Pattern formation is one of the most important processes during embryogenesis. It is commonly accepted that pattern formation is mainly driven by morphogen gradient. However, heterogeneous pattern still exists in 2D monolayer culture system that does not have obvious growth factor gradient. In this project, we use 2D monolayer human pluripotent stem cell (hESC) culture to study pattern formation in hPSC colonies. We observe that cell fate pattern is determined by the location of individual cells in a colony. The spatial distribution is associated with the pattern of metabolic activities in a colony. We show that endogenous protease influence metabolic pattern through the activation of protease-activated receptor (PAR). PAR pathway further regulates metabolism related signaling pathway such as mTOR that is important for fate pattern. This study highlights a novel autocrine feedback important for pattern formation and cell fate determination.

Zhaoying Zhang is a PhD Student in University of Macau. She received her bachelor degree in Biomedical Sciences from University of Macau in 2020. Her major project is to study the factors that could influence cell fate determination in human pluripotent stem cells.

Tibial Cortex Transverse Transport Accelerates Diabetic Foot Ulcer Healing: The Role and Mechanism of Mesenchymal Stem Cell Mobilization

Zhaowei JIANG

507, Li Ka Shing Institute of Health Sciences

Prince of Wales Hospital, Shatin, NT, Hong Kong

Tibial cortex transverse transport (TTT), a novel surgical technique based on DO principle, has shown promising result in treating peripheral ischemic conditions, including diabetic foot ulcer (DFU). However, the underlying biological mechanisms for TTT surgery remain unclear. This study aimed to unveil the mechanism by which the TTT technique confers therapeutic benefits for treatment of DFU, with a specific focus on mesenchymal stem cells (MSCs) mobilization. Result indicated that TTT technique showed significant benefits in accelerating DFU closure and improving the quality of newly formed skin tissues. Additionally, TTT induced the migration of MSCs to the peripheral blood after cortex transport, and these mobilized MSCs was recruited to the site of the chronic wound, thereby accelerating wound healing. Serum isolated from rats treated with TTT significantly promoted mobilization of BMSCs in vitro, which potentially facilitated wound healing. Furthermore, the concentration of stromal cell-derived factor 1 (SDF-1) protein in the peripheral blood was upregulated by TTT treatment. Importantly, knockdown of CXCR4 receptor or use of the ADM3100 (SDF-1 inhibitor) attenuated the MSCs mobilization effects induced by TTT serum in vitro and delayed the wound healing in vivo. In conclusion, The TTT technique accelerated DFU healing via enhancing the mobilization of MSCs. These mobilized MSCs, in turn, may promote angiogenesis and regulate the immune response at the ulcer site potentially through their paracrine factors such as VEGF and IL-10. However, further investigations are required to fully elucidate the specific mechanisms by which mobilized MSCs promote wound healing.

JIANG Zhaowei is a Ph.D. student in Prof. Li Gang's team at The Chinese University of Hong Kong. He holds a bachelor's degree (2017) and an M.Phil. degree (2020) from Nankai University. In 2021, JIANG Zhaowei embarked on his Ph.D. journey in the department of Orthopaedics and Traumatology, at The Chinese University of Hong Kong. His research focuses on investigating the mechanism of Tibial Cortex Transverse Transport (TTT) surgery for the treatment of diabetic foot ulcer. Under the esteemed guidance of Professor Li Gang, he is conducting in-depth studies to unravel the TTT treatment's efficacy in addressing diabetic foot complications and its mechanism with specific focus on the mobilization of mesenchymal stem cells (MSCs). During His Ph.D. studies, he was honoured with The Best Poster Award at the 43rd Annual Congress of Hong Kong Orthopaedic Association (HKOA) and the Golden Award at the 2023 TERMIS-AP webinar student presentation contest.

Intervention Study of Low-Magnitude, High-Frequency Vibration and β-hydroxy-β-methylbutyrate Treatment on Sarcopenia: neuromuscular junction and mitochondria dysfunction

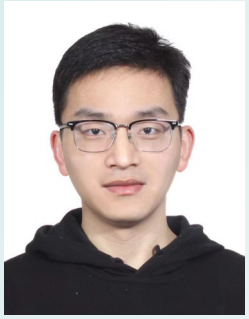
Qianjin WANG
10F, Li Ka Shing Health and Science Institution
Prince of Wales Hospital, Shatin

Background: Sarcopenia is a multi-etiology disorder characterized by progressive decline in skeletal muscle mass and strength and has become one of the most common problems of elderly individuals. As one of the key factors in affecting sarcopenia, neuromuscular junction (NMJ) is a high degree of subcellular specialization characteristic of chemical synapses composed of pre- and post-synaptic compartments between motor neuron terminals and muscle fibers, which can convert the neural electrical impulses into muscular contractile response. β-hydroxy-β-methylbutyrate (HMB) is a leucine metabolite produced in tissues of humans and animals, which has been shown to increase muscle mass and strength. Also, low-magnitude high-frequency vibration (LMHFV) was demonstrated to alleviate the NMJ degeneration in sarcopenic mice during ageing. However, the detailed mechanism of HMB combined with LMHFV in attenuating NMJ degeneration in the elderly is still not clear. We hypothesized that LMHFV combined with HMB treatment could attenuate NMJ degeneration.

Methods: This study was divided into in vivo and in vitro studies. Senescence-accelerated (SAMP8) male mice were randomized into control (CTL), LMHFV (VIB), HMB and combined HMB with LMHFV (COM) groups. Interventions were started at age of month 6 and assessed at 4-month post-intervention. In HMB group, HMB supplement (500 mg/kg/day, 5 days/week) was given to mice. In VIB group, mice were given LMHFV treatment (35 Hz, 0.3 g, 20 min/day, 5 days/week) according to our previous protocol. In COM group, both LMHFV and HMB supplement were provided accordingly. In vitro study, the C2C12 cells were used to show the NMJ and mitochondrial changes during combined treatments.

Results: After 4 months of intervention, the grip strength of control SAMP8 mice was significantly lower than those of HMB and COM groups. Twitch force, tetanic force and specific tetanic force of HMB and COM groups showed significantly higher values than those of CTL group. Besides, HMB and COM groups showed higher MCSA and wet weight of triceps surae as compared with CTL group at 10 months old. The IF staining of NMJ showed that AChRs clusters in CTL group presented severe fragmentation, discreteness, and dispersion, whereas AChRs were significantly less fragmented in HMB and COM groups. Furthermore, ex-vivo NMJ function was significantly improved in COM group at 4-month post-treatment. Type I muscle fibres in CTL group were higher than those of HMB, VIB, and COM groups. In AAV9 treated mice, the number of fragmented postsynaptic membrane was significantly increased compared with negative treated mice. In vitro study, we found that HMB combined with vibration treatment increased AChR clustering and decreased the ROS production in myotubes.

Conclusions: Sarcopenic mice presented obvious NMJ function and morphology deterioration at 10 months old. HMB combined with LMHFV interventions could better attenuate NMJ degeneration and mitochondrial dysfunction in SAMP8 mice as compared with either treatment alone. Hence, HMB combined with LMHFV treatment can achieve the muscle enhancement through alleviating NMJ degeneration during ageing.



Mobile: 852-91049295
E-mail: 1155186148@link.cuhk.edu.hk

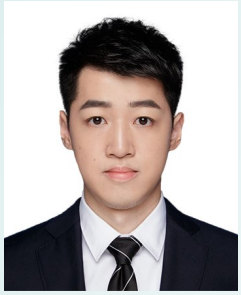
Academic Achievement

The Influence of Different THA Surgical Approaches on Patient's Early Postoperative Anxiety and Depression. (co-first author) (***Muscleskeletal Disorders* 2021)**.
Is the femoral component flexion affected by the sagittal femoral shaft bowing in conventional intramedually guided TKA (co-first author) ***(JOSR* 2021).**
Exercised Skeletal Muscle Accelerated the production of Muscle-derived Kynurenic Acid and Alleviated the Postmenopausal Osteoporosis through Gpr35/NFκB p65 pathway. (fifth author) ***frontiers in endocrynology* (JOT 2022)**
Osteocyte-derived sclerostin impairs cognitive function during ageing and Alzheimer's disease progression **(Nature Metabolism 2024)**
Atrophic skeletal muscle fibre-derived small extracellular vesicle miR-690 inhibits satellite cell differentiation during ageing **(JCSM 2022)**
Iron Oxide Nanoparticles-Loaded polyvinylpyrrolidone/ethylcellulose Coaxial Electrospun Nanofibers with Enhanced Osteogenic Capability for Bone Tissue Regeneration. (first author) **(under review).**
Inhibition of PI3K-AKT signaling pathway promotes repair of articular chondrocytes and alleviates inflammatory response of osteoarthritis in mice. (first author) **(Ready to submit).**
The Accuracy of an Extramedullary Femoral Cutting System in Total Knee Arthroplasty in Patients with Severe Coronal Femoral Bowing: A Radiographic Study. (first author) ***Journal of Orthopaedic Surgery and Research* (Under review)**.

The regulatory role of the focal adhesion protein Kindlin-2 in the osteogenesis process of distraction osteogenesis

Jiaming YANG
[1]*The Chinese University of Hong Kong, Hong Kong SAR, China*
[2]*Southern University of Science and Technology, Shenzhen, China*

Distraction Osteogenesis (DO) effectively stimulates the formation of fresh bone tissue through slow distraction, which has been widely used in orthopedic clinics. However, the molecular mechanisms whereby extracellular mechanical stress signals translate into intracellular biochemical signals during the DO process and promote bone formation remain poorly defined. It is known that osteocytes buried in the bone matrix play an important role in mediating mechanical loading induction of osteogenesis. Kindlin-2, as a key molecule in focal adhesion, plays an important role in regulating bone mass and bone formation. However, the underlying biological mechanisms of Kindlin-2 in the osteogenesis process of distraction osteogenesis still need to be clarified. In this study, a custom-made unilateral external fixator was applied on the mouse DO model. Wide-type C57BL/6 mice were used to establish DO model and to determine the dynamic expression of Kindlin-2 during DO procedure. The DO protocol consisted of 5 days of latency, 10 days of distraction at a rate of 0.3 mm daily and several durations of consolidation. Femoral samples were harvested 10, 15, 28, 42 days after the surgery (POD) for micro-computed tomography (μCT), histology, immunohistochemistry, and in situ hybridization to determine the expression of Kindlin-2 and osteogenic markers. Then, specific knockout of Kindlin-2 in osteocyte transgenic mice, $Dmp1^{Cre/+}$; $Kindlin\text{-}2^{fl/fl}$, were subjected to the same DO procedure as above. Cre-negative $Kindlin\text{-}2^{fl/fl}$ mice are regarded as controls. In addition to the aforementioned assessments, ELISA examination was conducted to identify specific osteogenic-related cytokines in serum that were affected by Kindlin-2 deficiency. The knowledge gained through these findings offers valuable insights into the molecular links of Kindlin-2 in mechanical tension-mediated bone regeneration in DO. Furthermore, it may lead to the further development of new strategies for targeting Kindlin-2 to improve outcomes of DO clinical applications with reduced costs to healthcare providers, pain and suffers to patients and their families.



Mr. Jiaming YANG obtained his bachelor's degree in clinical medicine from Shenzhen University and his master's in surgery from Sun Yat-sen University before pursuing his Ph.D. at the Chinese University of Hong Kong. He is also a senior Southern University of Science and Technology scholar fellow. He focuses on the biomechanical microenvironment in intervertebral disc degeneration and distraction osteogenesis under Prof. Gang Li's supervision at CUHK. He has conducted academic exchanges at national and global orthopedic annual meetings such as CAOS, COA, ORS, etc., and has published 4 SCI papers.

AoE as a platform for Collaborative Research in Aging with Focus on Skeletal Degeneration and Regeneration

Prof. Ling QIN
Dept. of Orthoapedics & Traumatology
The Chinese University of Hong Kong,
Hong Kong SAR, PRC China

The world population is aging, with high incidence of age-associated osteoporosis and bone fractures. Our mission focuses on clinical translation by providing innovative and effective treatment for age-associated musculoskeletal disorders. Extensive research has been conducted on aging, coordinated and multidisciplinary research facilitating skeletal regeneration in bone metabolic disorders and fragility injuries, especially in searching for bioactive and biodegradable implantable materials for temporal fixation and stimulating skeletal regeneration, are still highly desirable. We recently identified the unique function of neuronal protein regulating the regeneration of skeletons via sensory nerves; highlighted as an important milestone in biodegradable metals. Our collaborative achievements include identifying the unique biomechanical and biological function of biodegradable metals, especially Magnesium (Mg) as revolutionary biometal. Degradation of Mg releases Mg ions and hydrogen gas and creates a local alkaline environment. We have delineated that Mg ions stimulate sensory nerve endings in the periosteum and upregulate and release of calcitonin gene-related peptide (CGRP) from dorsal root ganglions. CGRP, an osteogenic neurotransmitter, facilitates differentiation of periosteum-derived stem cell into osteoblast linage, and thus benefit osteoporotic fracture repair, highlighting Mg as an excellent candidate for facilitating skeletal regeneration in elderlies. The alkaline environment and hydrogen gas may also contribute to new bone formation via regulating local inflammation, reducing oxidative stress, and attenuating cell senescence. However, the underlying mechanisms are not well defined. For this AoE proposal, we have built up a multidisciplinary team to apply advanced biotechnologies to address these scientific questions and further moving towards multi-centre clinical trials for translating our innovative biodegradable implants as Class III medical product for facilitation of bone regeneration, especially in osteoporotic conditions. Further local and international collaborations are essential for enhancing regeneration of challenging musculoskeletal disorders for reducing our healthcare and socio-economic burden of our aging society, including endeavors in establishing TEA-NET (Translational European-Aisa Network for Excellence of Translational Medicine).

Professor Ling QIN is Choh-Ming Li Professor of Orthopaediatrics and Traumatology and Director of CUHK SZ-HK Innovation Technology Institute (Futian). Professor Qin has been working on basic and translation research in orthopaedics with focus on diagnosis and pathophysiology of bone metabolic disorders and their treatment using innovative biometals as Class III medical implants over the past 30 years. Professor Qin is editor-in-chief of Journal of Orthopaedic Translation and past president of ICMRS. As principle investigator, Dr. Qin has received over 36 competitive research grants, including one on Area of Excellent (AoE) in Musculoskeletal Aging, Degeneration and Regeneration. He has published 9 books and over 460 SCI journal papers. He also holds over 30 inventions or new utility patents from PRC and USA. His pioneer scientific and translational research work in developing innovative biodegradable Mg-based metals for orthopaedic applications has been highlighted in ***Nature*** and ***Science***. Professor QIN received many prestigious honors and awards, including Member of Academy of Europe (MAE) and Fellow of AIMBE, ICORS, ASBMR, and IUSBSE attributed to his contribution to musculoskeletal research and innovation of biomaterials for orthopaedic applications.

Central neural regulation of parathyroid hormone and bone remodeling

Prof. Fan YANG
Xueyuan Avenue 1068,
Nanshan District, Shenzhen, China

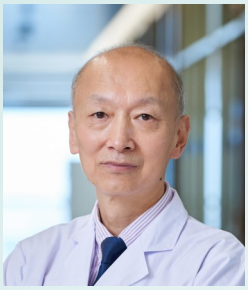
Parathyroid hormone (PTH) is one of the most important hormones for bone turnover and calcium homeostasis. It is unclear how the central nervous system regulates PTH. The subfornical organ (SFO) lies above the third ventricle and modulates body fluid homeostasis. Through retrograde tracing, electrophysiology, and in vivo calcium imaging, we identified the SFO as an important brain nucleus that responds to serum PTH changes in mice. Chemogenetic stimulation of GABAergic neurons in SFO induces decreased serum PTH followed by a decrease in trabecular bone mass. Conversely, stimulation of glutamatergic neurons in the SFO promoted serum PTH and bone mass. Moreover, we found that the blockage of different PTH receptors in the SFO affects peripheral PTH levels and the PTH's response to calcium stimulation. Furthermore, we identified a GABAergic projection from the SFO to the paraventricular nucleus, which modulates PTH and bone mass. These findings advance our understanding of the central neural regulation of PTH at cellular and circuit level.

Yang Fan is a professor in Shenzhen institutes of advanced technology, Chinese Academy of Sciences. He received his Bachelor and Master degree from Peking University. Then he obtained his PhD degree from faculty of Medicine, University of Hong Kong. Now he is a professor in Shenzhen institutes of advanced technology, Chinese Academy of Sciences. Prof Yang’s research interests mainly focused on how neural circuits, neurons and neural molecules regulate peripheral bone metabolism, now he is using cutting-edge technology including optogenetics, chemogenetics and neural tracing to dissect the mechanism of crosstalk between the brain and the bone. Prof Yang’s recent research work has been published in high impact journals including Neuron, JCI; Nature Communications et al.

Bioactive ceramics for tissue regeneration and disease therapy

Jiang CHANG
Shanghai Institute of Ceramics
Chinese Academy of Sciences
1295 Dingxi Road, Shanghai 200050

Bioactive ceremics are ceramics materials which reveal biological activity to stimulate cellular behavior and enhance tissue regeneration. They have been developed first for bone and dental applications, and with the progress of the biological studies more and more functions of bioactive ceramics have been identified in regulating different type of cells and tissues, which demonstrate huge potential of this type of biomaterials for applications in the whole field of regenerative medicine and the treatment of tissue/organ related diseases. In this presentation, a brief summary of our recent progress in the study of bioactive ceramics and composites in the application of different tissue regeneration and disease treatment.



Professor, Shanghai Institute of Ceramics, Chinese Academy of Sciences, Fellow of International Union of Societies for Biomaterials Science and Engineering (FBSE), Fellow of Royal Society of Chemistry (FRSC), and Fellow of American Institute of Medical and Biological Engineering (AIMBE). Ph.D in 1991 in Chemistry from the Technical University of Darmstadt in Germany. Research Assistant Professor in the Medical School at New York University in USA (1997-1999); Professor and founder of the Biomaterials and Tissue Engineering Research Center of the Shanghai Institute of Ceramics; and vice president of the Interdisciplinary Research Society for Bone and Joint Injectable Biomaterials (GRIBOI). His research focuses on bioactive materials including bioceramics and composites for tissue regeneration and tissue engineering. Professor Chang has over 500 scientific papers published in international peer-reviewed scientific journals (with more than 30000 citations and H-index 99) and 70 patents.

Rohto Advanced Research Hong Kong Limited

Rohto Advanced Research Hong Kong Limited (ARHK) was established in January 2019 by a Japanese company called Rohto Pharmaceutical Co., Ltd (ROHTO). The core businesses of ROHTO are skincare, OTC drugs (eye drops, gastrointestinal medicine, etc.), and functional foods and food products. In research field, ROHTO specializes in developing cell culture techniques and as well as utilizing an aseptic automated system for manufacturing their products such as eye drops and cosmetics.

One of the main research areas ROHTO focuses on is regenerative medicine. In 2017, ROHTO started its first clinical trial using allogenic adipose-derived mesenchymal stromal cells against liver cirrhosis. In 2020, a clinical trial against severe COVID-19 pneumonia was also initiated, entering Phase II trials in 2021. Several more clinical trials are ongoing against various target indications in Japan.

In accordance with the strategic planning and development of regenerative medicine and its related businesses, ARHK utilizes ROHTO's expertise and cutting-edge technologies to contribute to the advancement of scientific research and people's wellness.

ARHK is currently conducting scientific research on mesenchymal stromal cells in collaboration with multiple parties in Hong Kong, and worldwide.

As ARHK is celebrating our 5th year anniversary in 2024, we aim to further expand our R&D activities worldwide, as well as looking forward to the discovery and encountering novel technologies.

Company name
Rohto Advanced Research Hong Kong Ltd.

Location
Room 310-313, 3/F, Building 15W, Phase 3, Hong Kong Science Park, Pak Shek Kok, New Territories, Hong Kong

Foundation
28th January 2019

Managing director
Dr. Eiji Kobayashi

Business overview
Overseas R&D center and hub for new business, looking at opportunities in Mainland China

R&D in regenerative medicine (cell culture, cell therapy)

- **Gene editing**
We use gene modification techniques to unlock the potential of mesenchymal stem cells (MSCs).

- **Cell derived-components**
We conduct basic research using components derived from MSCs for therapeutic applications.

- **Culture medium research**
We continue to research on Animal Origin Free medium suitable for MSCs culture.

- **Other collaboration**
We create new values through collaboration with various universities and companies, not limited in Hong Kong.

- **Animal research**
We make use of different animal models to verify the therapeutic effects of MSCs.

- **iPSCs research**
We conduct stem cells research using induced Pluripotent Stem Cells (iPSCs).

Contents

Contents

10th CUHK International Symposium on Stem Cell Biology & Regenerative Medicine

3rd Guangdong-Hong Kong-Macau Greater Bay Area International Conference on Regenerative Medicine

Location (Site):

1/F Auditorium, Main Clinical Block and Trauma Centre

Prince of Wales Hospital, Shatin, Hong Kong

香港新界沙田銀城街30-32號威爾斯親王醫院

住院主樓暨創傷中心一樓演講廳

（第一城地鐵站B出口）