

9<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine (SCRM)

1<sup>st</sup> International Chinese Musculoskeletal Research Society (ICMRS) Stem Cells and Regenerative Biology Symposium

Joint Hong Kong Society for Cell Biology Symposium

11-12 November 2019

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

Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong



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Dear Colleagues and friends:

The 9<sup>th</sup> SCRM (9<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine) continues with the momentum of the previous successful ones with special highlights in musculoskeletal regeneration as the theme. This year, the 9<sup>th</sup> SCRM meeting will join hand with International Chinese Musculoskeletal Research Society (Stem Cells and Regenerative Biology Sector) and Hong Kong Society for Cell Biology, a newly formed Hong Kong based organization for Hong Kong researchers, scientists and postgraduate students interested in cell biology and molecular biology.

The main topics of the symposium this year consist of new thoughts from and for musculoskeletal system, stem cells biology study, emerging technologies development as well as clinical and translational research. There are about 30 speakers from, Australia, Europe, China, Malysia, Thailand, Taiwan and Hong Kong.

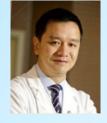
The 9th SCRM is co-sponsored and/or organized by CUHK Institute for Tissue Engineering and Regenerative Medicine (iTERM); CUHK Department of Orthopaedics and Traumatology; CUHK SMART Programme, Lui Che Woo Institute of Innovative Medicine; MOE Jinan-CUHK Key Lab for Regenerative Medicine, China; Functional Bone Regeneration in Challenging Bone Disorders and Defects (RGC Reference No. T13-402/17N). We also acknowledge the support from International Chinese Musculoskeletal Research Society (ICMRS) and Hong Kong Society of Cell Biology (HKSCB).

We welcome professionals and academics in the field of regenerative medicine, orthopaedics, bio-medical science and engineering and other related disciplines. On behalf of symposium organizers, we warmly welcome you and wish you all an enjoyable stay in Hong Kong!

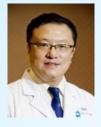
## Organizing Committee The 9<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine



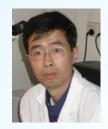
Prof. Wai-Yee Chan Pro-Vice-Chancellor/ Vice-President and Director CUHK-SBS



Prof. Patrick SH Yung Chairman and Professor CUHK-ORT iTERMs



Prof. Gang Li Professor CUHK-ORT iTERMs



Prof. Dong-Qing Cai Co-Director MOE Jinan-CUHK Key Lab for Regenerative Medicine, PR China

Message from Vice-Chancellor and President

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 9<sup>th</sup> CUHK International Stem Cell and Regenerative Medicine Symposium.

Regenerative medicine represents a major advancement of medicine in the 21th century. The remarkable advances in the science of embryonic and adult stem cells and the engineering of smart biomaterials are the exciting building blocks of future promises for injured and diseased tissues to regrow and regenerate. Some of the significant developments in this fast growing field include stem cell-based therapies, and the application of bioactive scaffold materials that are able to stimulate the patient's own stem cells into reparative action. Many challenging medical conditions, such as bone fractures, severe burns, blindness, heart failure, nerve injuries, neurological disorders, and a number of degenerative diseases are now actively being investigated with regenerative medicine approaches.

CUHK has been expanding its research potential and capacities in the field of regenerative medicine over in the last decade. Dedicated research teams and research projects have been established, and state-of-theart research facilities are in place to address the needs of research and clinical applications. Importantly, a multidisciplinary, university-wide Institute for Tissue Engineering and Regenerative Medicine (iTERM) was established in 2016 as a centre of research excellence to enhance and support research collaboration and cooperation in regenerative medicine.

I am delighted to see that the 9<sup>th</sup> CUHK International SCRM Symposium has attracted a great number of accomplished scientists, engineers, and clinicians, along with many young and energetic researchers. I am confident that you will find the Symposium to be an exciting platform for the exchange of innovative research ideas and the education of our young students and scientists.

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

Mochtuan

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

# 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. Throughout 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 phases 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.

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 Orthopaedic Oncology, to 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 and departmental formal teaching committee 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.









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 functionalization 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".











Key Laboratory for Regenerative Medicine (Ji Nan University - The Chinese University of Hong Kong) Ministry of Education, China

The Key Laboratory for Regenerative Medicine, Ministry of Education (Ji Nan University-The Chinese University of Hong Kong), was established by Ji Nan University, Guang Zhou, and the Chinese University of Hong Kong, Hong Kong, on the basis of the previously established Joint CUHK-JNU Lab for Regenerative Medicine in April 17th 2007. To further strengthen the expertise and resources of both universities, the Lab then applied for as a Key Lab of Regenerative Medicine, in the Ministry of Education, which was approved in Dec. 2007 to start building the Lab. Moreover, the Key Lab was approved in 2008 as an International Collaborative Base for Science and Technology, by the Department of Science and Technology, Guang Dong Province. In 2009, the key lab was further approved as International Collaborative Base for Science and Technology, by the Department of Science and Technology, P.R.China. Currently, the Key Lab has 31 permanent staffs with an average age of 45 years old. There are 20 high ranking members (Professor), 1 member with title in the "New Century National Hundred, Thousand and Ten Thousand Talent Project", 1 member of Oversea Outstanding- Youth. Almost all of the principal investigators have been trained oversea. The expertise of the staffs includes almost all areas of regenerative medicine, which are medical regeneration, developmental biology, regenerative biology, cell and molecular biology, tissue engineering, physiology, and immunology etc. The total lab space is about  $3600 \text{ m}^2$ , which includes laboratories for molecular biology, cell biology, stem cells, biological imaging, morphology, functional analysis, and up-to 1000-grade cell culture rooms. The labs are furnished with state-of-the-art equipment. The equipment and apparatus procured are worth about 50 million RMB. Post-graduate students from both laboratories move freely and conduct research at both sites. Our mission is to improve the lives of our community by conducting research to find cures for degenerative diseases, such as ischemic heart diseases, skeletomuscular degeneration, eye disease and tissue degeneration caused by cancer/aging. Stem cell-and small molecule- based therapies are currently being developed by principle investigators in the Key Lab to treat the various forms of degenerative diseases mentioned.



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

Through amalgamating the former four pre-clinical Departments of Anatomy, Biochemistry (Medicine), Pharmacology and Physiology, the School of Biomedical Sciences was formed under the Faculty of Medicine, The Chinese University of Hong Kong on 1 June 2009. Since its formation, our School has put tremendous efforts and resources in promoting cutting-edge and translational research through interdisciplinary collaboration as well as quality graduate and undergraduate education.

Being the first of its kind in Hong Kong, our School has established three Thematic Research Programs (TRPs), namely:



Prof. Wai-Yee Chan Pro-Vice-Chancellor/ Vice-President and Director CUHK-SBS

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 which provide state-of-the-art equipment and specialized technologies. The different theme-based seminars and the annual School of Biomedical Sciences Research Day are two of the examples showing our commitment to the pursuit of research excellence.

Similarly, we have placed great importance on the provision of quality teaching and learning environment to our graduate and undergraduate students. With the consolidation of teaching manpower, synergies in graduate and undergraduate teaching have been made possible. The MPhil-PhD in Biomedical Sciences Program admitted its first cohort of students in 2010-11. The establishment of the Teaching and Learning Unit and the annual School of Biomedical Sciences Postgraduate Research Day are yet another two prominent examples showcasing our dedication to the quest of excellence in education. In the academic year 2016-17, our School will introduce the new BSc in Biomedical Sciences Programme with a view to nurturing young talents conversant with biomedical sciences knowledge and skills who can engage themselves upon graduation in multiple career paths such as scientific research, health system policy and management, or clinical, pharmaceutical, diagnostics and healthcare related professions.

To promote stronger academic and scientific collaboration with overseas universities and research institutes and to further broaden the international outlook of our investigators and students, we have signed Memoranda of Understanding (MOU) with a number of prestigious higher education and research institutions in the Mainland and overseas. Our School has also actively taken part in many outgoing and incoming visits to explore possible research and educational collaborations.

The different pages of this new website will give you more details on our School, including the profiles of our academic and teaching staff. Meanwhile, our SBS 5th Anniversary Booklet - Reminiscences of the First Quinquennium and other publications can give you more ideas on the efforts and achievements we have made so far in different domains. If you have any comments or need any information, please feel free to write to us at sbs.med@cuhk.edu.hk.

# SMART Programme Lui Che Woo Institute of Innovative Medicine Faculty of MedicineThe Chinese University of Hong Kong

**LCW IIM SMART Programme** is a new initiative of Hong Kong Centre of Sports Medicine and Sports Science, CUHK

## Mission

To provide top-quality clinical service with educational objectives to both undergraduates and postgraduates, and to conduct comprehensive research programmes in clinical, basic and applied domains.

#### Vision

To assume regional leadership with international highlights of excellence and achievement. We are the pioneer in Sports Medicine and Health Science, with important Milestones:

1983	First Sports Clinic in Jubilee Sports Centre (now known as the Hong Kong Sports Institute)
1984	First Sports Injuries Clinic in Hong Kong established at the Prince of Wales Hospital and first to promote the development of arthroscopic surgery
1988	First Founding President of the Hong Kong Association of Sports Medicine (HKASMSS)
1990	First pioneer to establish Asian Federation of Sports Medicine (AFSM)
1995	First pioneer to establish the Asia-Pacific Orthopaedic Society for Sports Medicine (APOSSM)
1996	First Sports Medicine Centre designated as the WHO Collaborating Centre in Sports Medicine and Health Promotion (1996-2009)
2002	First Asian Presidency of International Federation of Sports Medicine (FIMS) (2002-2006)
2004	First Taught Programs (MSc & PgDip) in Sports Medicine & Health Sciences organized by a university in Hong Kong
2007	First SMART (Sports Medicine and Rehabilitation Therapy) Convention to promote knowledge transfer and community education
2008	First World Congress of Sports Trauma (WCST) held in Hong Kong, with over 1000 attendance First established centre in Sports Medicine and Health Sciences with the generous donation of HKD 88.72 million from Hong Kong Jockey Club Charities Trust
2010	First International Symposium of Ligaments and Tendons (ISL&T) held in Hong Kong
2011	First CUHK Stem Cell & Regenerative Medicine (SCRM) Conference held in Hong Kong
2013	First launch of Sport Medicine And Regenerative Technology (SMART) programme in the Insti- tute of Innovative Medicine (IIM) and Musculoskeletal Regenerative Research Network (MRN)
2014	Academic visits to Karolinska Institutet, UMC Utrecht and Stanford Unviersity - three key collab- orators of LCWIIM-SMART programme and MRN. Signed a MOU with UMC Utrecht in June and with Stanford University in November respectively
2015	Co-organized the 1st International Symposium of Musculoskeletal Regenerative Research Net- work (MRN), June 1-2, 2015, Karolinska Institutet, Sweden. Academic visit to Odense University Hospital, Denmark and signed a MOU in June.
2016	Co-organized the 2 <sup>nd</sup> International Symposium of Musculoskeletal Regenerative Research Network (MRN), June 16, 2016, UMC Utrecht University, the Netherlands.

#### **Clinical Service**

Sport Team has been the pioneer dedicated to the prevention, treatment and rehabilitation of sports-related injuries since its establishment in 1983. Through close collaborations with various clinical departments, a one -roof, one-stop comprehensive and multi-disciplinary diagnostic, treatment and rehabilitation service is provided not only to the general population, but also to professional and amateur athletes. A full spectrum of sports-related injuries, including ligament, meniscus & cartilage injuries around the knee; instability, rotator cuff and bicep tendon injuries around the shoulder; cartilage injuries, instability, impingement and tendon problems around the ankle, and labrum injuries, impingement, cartilage and tendon problems around the hip are managed by us. We are now taking care of over 5000 sports injury cases in our clinic every year. At the Hong Kong Sports Institute, we provide general medical and orthopaedic consultations, sports injury prevention programmes. Each year, about 300 elite Hong Kong Team athletes receive our care in Hong Kong Sports Institute.

We are also the pioneers in arthroscopic surgeries for treatment of sports injuries through our introduction of the first knee arthroscopy in Hong Kong, and we continue to take the lead in the field. With our expertise and state-of-art technology developed, arthroscopic surgeries are very safe and effective surgeries, and allowing patients return to sports much earlier than before. Our knee arthroscopic surgeries include Anterior Cruciate Ligament (ACL) reconstructions, Posterior Cruciate Ligament (PCL) reconstructions, multi-ligament reconstructions and reconstructions for patellofemoral joint (PFJ) instability, while shoulder arthroscopic operations consist of rotator cuff repairs, arthroscopic stabilization for recurrent shoulder dislocations and SLAP repairs etc. With the aid of computer navigation system and high-definition camera system, higher level of precision and better surgical outcome particularly for knee operations is guaranteed. With close collaborations with Foot & Ankle Team and Hand team, our arena of arthroscopic service extends to ankle arthroscopy, wrist arthroscopy and elbow arthroscopy. Each year, with our operative services provided at Prince of Wales Hospital and Alice Ho Miu-Ling Nethersole Hospital, we operate on more than 350 sports injuries cases, with about 250 ACL cases and 50 shoulder arthroscopic procedures. Our team holds various arthroscopy workshops such as the advanced cadaveric arthroscopy workshops of the knee and shoulders annually with a view to sharing our surgical experiences with orthopaedic surgeons from Hong Kong, China and over the world. Our close collaboration with experts from renowned orthopaedic centres around the world has granted us ample opportunities for the exchange of new surgical technologies.

#### Research

Research in sport team is bon marriage of clinical, applied and basic science research. Our major research focuses are prevention and treatments for sports injuries. We have published more than 264 articles in SCI journals. We have successfully secured 17 (General Research Fund) grants and 9 ITF (Innovation and Technology) grants in the past 30 years. In 2006, we were also awarded a 12 million UGC grant in developing a joint university centre in Sport medicine and rehabilitation. In 2008, the establishment of the CUHK-Jockey Club Sports Medicine and Health Sciences Centre (with a funding of 88 million) has significantly enhanced our research capabilities, with the state-of-the-art facilities such as animal gait analysis; in-vivo cell imaging system; multi-channel flow cytometer and high resolution ultrasound imaging system. To achieve innovative solutions for management of orthopaedic sport medicine conditions and musculoskeletal disorders and to provide platform for multi-disciplinary research on musculoskeletal regeneration, the Sport Medicine And Regenerative Technology (SMART) programme was established under the Institute of Innovative Medicine (IIM) in 2013.

Our Clinical team is actively participating in clinical researches. We have a very broad spectrum of interests, from sports injuries epidemiology, diagnostic skills, injury prevention programme, surgical technique development to rehabilitation and performance enhancement program. Our current main focus essentially is on Knee and shoulder sports injuries, with special interests in ACL injuries particularly randomize-controlled trials in single-bindle ACL versus double-bundle ACL reconstructions etc. We have published more than 30

clinical papers in different peer-reviewed international journals.

Our Basic Science team is one of the prominent tendinopathy research groups in the world and we pioneered the studies on clinical samples of tendinopathies. We also investigated various strategies to promote tendon healing, including growth factors, stem cells, traditional Chinese medicine and biophysical intervention. With respect to ACL injuries, the basic research team works closely with the clinical and applied research team in order to achieve clinical translation of research findings. A number of patents are filed and we looking forward to bringing more research findings into clinical application.

Our Applied team established the CUHK Sports Performance and Biomechanics Laboratory. We apply the technology of biomechanics to predict the occurrence of ankle sprain, and by micro-electrical muscle stimulation, excessive joint motion could be prevented. This innovative idea has led to the development of anti-sprain shoe and hopefully a series of anti-sprain "smart" devices will be launched into the market in the near future. We have also newly invented a new knee rotational laxity meter to assess the dynamic and static rotational stability of the ACL, which provides an innovative objective biomechanical assessment technique of the knee.

We are honored to be the regional hub of knowledge transfer with respect to tendon and ligament research. We have hosted the world renowned "International Symposium of Tendon and Ligament (ISL&T) in 2008 and 2010. In 2013, the 3rd CUHK Stem Cell & Regenerative Medicine Conference will continue to have the top scientists in the fields of regenerative medicine to join us. With the establishment of musculoskeletal research network, we shall be able to enhance the academic, professional and scientific output of members by facilitating more international collaboration.

## Education

We are a leading center for sports medicine education. For Undergraduate teaching, we are dedicated in educating CUHK MB,ChB Med I, III and V students. We were awarded the University Grants Council (UGC) Restructuring and Collaboration Fund (RCF) to set up the Joint Universities Sports Medicine and Rehabilitation centre with the Rehabilitation department of Hong Kong Polytechnic University in 2007. Though this collaboration, our medical students from CUHK and physiotherapist students from HKPU is now having the opportunities to enjoy a two-way learning, particularly acquiring more knowledge on the principle and applications of rehabilitation in sports injuries, as well as developing good long term working relationship. For post-graduate education, 21 research master students and 15 PhD students have completed their research projects on areas such as tendon and ligament regenerations and biomechanics studies. Our team successfully launched the first ever Master Course in sports Medicine & Health Science in Hong Kong in 2004. With a strong teaching international faculty equipped with collective expertise in research and education, rigorous trainings were provided to learners from a diversified background such as medical doctors, physiotherapists, nurses, sports scientists, allied health, fitness professionals and sports enthusiasts. We have now trained more than 400 people with our MSc course. Many of these alumni are contributing and playing a significant role in the sports medicine profession and industry in HK and around the world.

#### Future

Orthopedic sport medicine is an integral part of orthopedics. It is a vibrant and emerging sub-specialty that traverses boundaries in other disciplines in medicine in general and orthopedics in particular. A well-trained orthopedic surgeon will benefit from a comprehensive program of training as highlighted in this discipline with knowledge and skill applicable to other sub-specialties.

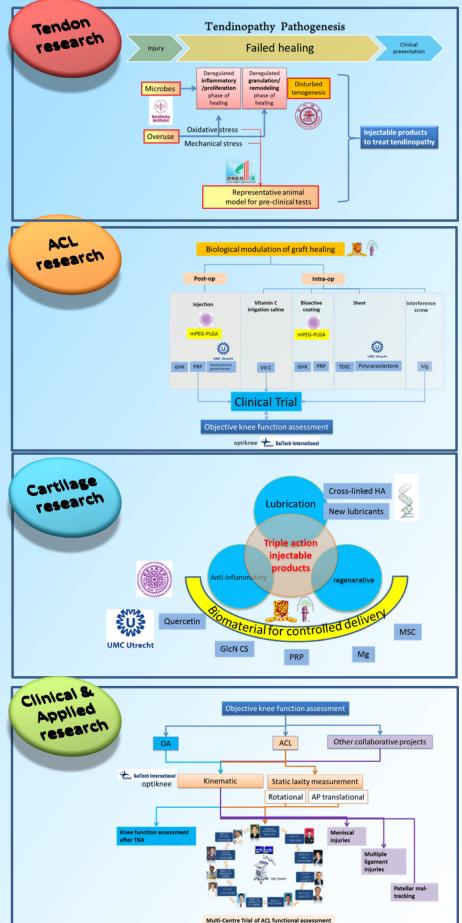
The CUHK Sport Medicine Centre will maintain this momentum of sporting spirit to achieve "Higher, Faster and Stronger" goals to reach new height in clinical service, education and research. We shall bring the next generation of clinician and scientist to a new platform of opinion leadership in this discipline.



#### IIM-SMART International Collaboration

Sport Medicine and Regenerative Technology (SMART) research programme focuses on prevention and treatments for sports injuries. Apart from clinical and applied research, we chiefly devote to translational research on tendon, ACL and cartilage healing.







組織工程與再生醫學研究所

## Institute for Tissue Engineering & Regenerative Medicine

## The Institute for Tissue Engineering and Regenerative Medicine (iTERM)

The Institute for Tissue Engineering and Regenerative Medicine (iTERM), under the Chinese University of Hong Kong (CUHK), is newly founded on January 13, 2016. Our Institute, with a solid background of top-ranked scientists and cutting-edge technologies, aims at integrating multiple disciplines in biomedical sciences, engineering, and clinical medicine, ultimately to facilitate and fortify the development of neuromusculoskeletal tissue engineering (TE) and regenerative medicine (RE). We envision that, the quality of life will be enhanced with the application of biomedicine in the upcoming future.

With the consortium of distinguished scientists and clinicians around the world, our Institute will pitch into the research of the 4 main program areas, with a view to fostering the translational research and beefing up the clinical development of Hong Kong at full-stream:

- Stem Cells and Cell-Based Therapies
- Tissue Engineering for Regenerative Medicine
- 3-Dimensional Microphysiological Tissue Models
- Clinical Trials and Precision Medicine

Under the support from the University and the Faculties of Medicine and Engineering, our Institute is wellequipped with comprehensive infrastructure and core facilities, which lay a solid foundation for our team to start a new chapter in the study of TE and RM. We will make every endeavor to advance and translate multidisciplinary scientific knowledge into clinical trials and product development, through various crossdisciplinary collaborations between our Principal Investigators and the faculty members from different academic departments upon the accrued valuable research experiences.

In addition, TE and RM have already become the prevailing trend of research in the globe, with an aim to serve as the panacea against the illnesses appeared among the aging population. To extend our nexus and strengthen the interaction with local and overseas prestigious universities and institutions, our team members have attended numerous international conferences exchanging ideas and experiences with scientific researchers from the fields of biomedicine and bio-engineering. And our Institute has also built up synergistic relationships with different renowned institutions, for example, Karolinska Institute Center of Regenerative Medicine and the Chinese Academy of Sciences Guangzhou Institutes of Biomedicine and Health (GIBH).

As the center of excellence of the CUHK, sustainable development of educational program is critical and crucial for the future growth of the Institute. Our faculty members, therefore, will take an active role in the educational activities and nurturing our fellow students with skillset and depth of scientific knowledge. We believe, with intensive and professional trainings, our students will evolve into accomplished and committed investigators, as the invaluable assets, contributing significantly to the future expansion of the industry.

You are welcomed to visit our website at <u>www.iterm.cuhk.edu.hk</u>, so as to get acquainted with our Institute and to be kept pace with the news and any updated information. If you wish to share any ideas or comments with us, please feel free to contact us via <u>iterm@cuhk.edu.hk</u>.

# **International Chinese Musculoskeletal Research Society** 動学学へ学術学会 <u>https://www.icmrs.net/</u>

**History:** Founded in August 1994 at Sun Valley, Idaho, the International Chinese Musculoskeletal Research Society (ICMRS, renamed from the International Chinese Hard Tissue Society, known as ICHTS) is a non-profit professional organization, striving to facilitate the exchange of ideas and to promote collaboration among scientists in the fields of musculoskeletal research.

**Mission:** ICMRS seeks to promote scientific and professional excellence and to enhance communication among scientists of Chinese heritage and other international scholars in the field of musculoskeletal research and related areas.

**Goals:** ICMRS does not, and will not have any political affiliation with any specific nation or region. As a world-wide organization, ICMRS is open to all professionals and trainees in all areas of musculoskeletal and related research or clinical practice.

- Provide members with opportunities for communication, networking, and collaboration;
- Develop and implement a strong mentoring program to promote career and technical advancements of our global members;
- Encourage and recognize the scientific contributions of our members by providing achievement and travel awards to attend scientific meetings;
- Provide an esteemed unit of scientific and technical consultants to assist China in supporting scientific research and drug development in the field of musculoskeletal research.

**Membership:** (1) Student member: Any students, residents or fellows who are currently in training. No doctoral degree or publication is required to apply for student membership. The annual membership fee is \$30 for a student member. (2) Regular member: Any individual with a doctoral degree or sufficient research/clinical experience who has at least one publication in the musculoskeletal field. The annual membership fee is \$50 for a regular member. (3) Lifetime member: individuals who are a regular member with good standing, have demonstrated contributions to the musculoskeletal field, and are willing to make a long-term commitment to the development, activities and the mission of ICMRS. Applicants must submit their curriculum vitae or resume to icmrs@icmrs.net for approval. The membership committee will review your curriculum vitae or resume. If the application is approved, the applicant will be invited to pay one time membership fee of \$500.

Please join us at: https://www.icmrs.net/join-us



Hong Kong Society for Cell Biology

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Hong Kong Society for Cell Biology (HKSCB) is a regional scientific organization which connects scientists that work on various aspects of Cell Biology in Hong Kong. HKSCB is established in January 2018. The aims of the organization are to advance scientific discovery, advocate sound research policies, promote professional development and facilitate research collaboration among its members. In addition, HKSCB will provide education to young scientists and non-professionals with latest knowledge of cell biology and its implication in human diseases, as well as to raise the awareness of social and economic impacts to the local society. HKSCB will also establish liaison with other cell biology societies, including those in Mainland China, U.S.A, Europe and other Asian pacific countries.

Individuals who are currently working in the field of cell biology or who are desirous of becoming members of the Society shall apply to the Council of the Society. Applications for membership shall be on the form to the Secretary via HKSCB Website: <u>https://hkscb.org/</u>

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## **Biomimetic Materials Controlling Cellular Activity**

#### Prof. Alan Rowan

Director Australian Institute for Bioengineering and Nanotechnology (AIBN) The University of Queensland

Fibrous networks of biopolymers are found in both the intracellular and extracellular matrix (ECM). From the microscopic scale of a single cell to the macroscopic scale of fibrous tissues, biopolymers with different stiffness control cellular processes such as cell differentiation, proliferation and communication. Recently, a large number of hydrogels has been developed to create an artificial ECM for biomedical applications. However, the mechanical environment inside and outside the cell is not determined by a single component. Multiple biopolymers with different structural and mechanical properties which physically interact with each other, make the mechanical environment of a cell in vivo much more complicated than the environment of a cell in a single-component artificial matrix.

The mechanics of natural biopolymer gels are very different from most synthetic hydrogels because they show strain stiffening behavior. Reconstituted networks of cytoskeletal polymers such as intermediate filaments or extracellular biopolymers such as collagen show a large increase in stiffness upon an applied stress. The stiffening response prevents these networks from breaking under external stresses and also enables communication between cells growing in these materials. Recently a new biomimetic polymer hydrogel was developed with unique cytomimetic properties, based upon oligo (ethylene glycol) grafted polyisocyanopeptides. These extremely stiff helical polymers form gels of materials properties almost identical to those of intermediate filaments and ECM. The unique ability of these materials and their application in cell growth and drug therapeutics revealed the importance of polymer stiffness and material non-linear mechanics. How to control the nonlinear mechanical properties and how the stiffening response is affected by the composite nature of natural biopolymer networks will be presented.



Professor Alan Rowan, is currently an ARC Laureate fellow, Chair of the Scientific Advisory Board for the ARC Centre of Excellence in Convergent Bio-Nano Science and Technology, and board member of: The UQ Confucius Institute; The Dow Centre for Sustainability; and of UQ Senior Management group. As the Director of AIBN, Prof. Rowan oversees a team of 500 researchers and professional staff. In recognition of his translational effort Prof. Alan Rowan was nominated in 2013 as one of the Netherlands Science Entrepreneurs of the year. In the last three years he has been granted five patents and have five pending in the area of nanomedicine. Prof. Alan Rowan has also been involved in the start up of four companies: Encapson, Noviotech, NovioSense and Secmatix.

## **CaP Micro-/nano-Biomimetic Scaffolds Induce Regeneration of Interface Tissues**

#### Prof. Sheng-min Zhang

Chair Professor & Head Advanced Biomaterials and Tissue Engineering Center Huazhong University of Science and Technology & Founding Chair of China-Korea Center for Biomaterials and Nano-biotechnology Life Science Building, 1037 Luoyu Rd. 430074 Wuhan, P.R.China

Based on CaP nano-biomaterials, a biomimetic osteochondral scaffold with continuous multilayer architecture and gradient composition from articular cartilage layer to subchondral bone layer was fabricated by a microsphere-based SLS technique. Our results demonstrated that the resultant gradient hierarchical scaffold featured highly interconnected porosity and desirable mechanical properties as well as excellent biocompatibility. In vivo animal evaluation further verified that multilayer scaffolds could simultaneously induce regeneration of cartilage and subchondral bone. Consequently, our current work realizes the regeneration of two kinds of tissues, cartilage and subchondral bone, only by using one scaffold without addition of any cell and biological growth factor, which greatly advances the potential application of bio-inspired multilayer scaffolds to regenerative medicine. We defined this finding as "one scaffold, two tissues".



Dr. Zhang received his Ph.D. in Materials Science from Wuhan University of Technology, China. Starting in 2003 he became a Professor, then the Chair Professor, the Director of the Advanced Biomaterials & Tissue Engineering Center, and the Director of Institute of Regulatory Science for Medical Devices at Huazhong University of Science and Technology in Wuhan, China. His previous academic positions were Professor (2000-2003), Associate Professor (1996-2000) and Assistant Professor (1992-1996) in Materials Science at Wuhan University of Technology. Prof. Zhang has over 20-year experience in biomaterials, tissue engineering and regenerative medicine fields and has authored more than 100 original papers, 5 books and given more than 100 Plenary, Keynote or Invited speeches in various conferences. He is the inventor of about 40 patents, some of which were further developed into 4 medical device products authorized by CFDA and FDA. He serves on the editorial boards of several leading international journals, such as Tissue Engineering, Biomedical Materials (IOP, UK), etc. He is a Member of the CFDA Advisory Committee for Medical Devices Evaluation and a Member of the CFDA Technical Committee for Medical Devices Classification.

Dr. Zhang was elected as Fellow of International Union of Societies for Biomaterials Science and Engineering (IUSBSE Fellow, FBSE) in 2016, and has been recognized for his distinguished contributions to development and translation of regenerative medical materials, and to public promotion of biomaterials science. In August, 2019, Dr. Shengmin Zhang was elected as the Vice President of Chinese Society for Biomaterials (2019-2023). He is also a Council Member of TERMIS-AP.

## **Injectable Bioactive Materials for Bone Regeneration**

#### Prof. Yu-lin Li

The State Key Laboratory of Bioreactor Engineering and Key Laboratory for Ultrafine Materials of Ministry of Education Key Laboratory for Ultrafine Materials of Ministry of Education Engineering Research Centre for Biomedical Materials of Ministry of Education East China University of Science and Technology, Shanghai 200237, China E-mail: yulinli@ecust.edu.cn

maintainence and self-renewal of tissues/organs Normal function depend on proper microenvironments in human body<sup>[1]</sup>. Facing the increasing bone diseases as the population aging, it is fascinating to develop bioactive materials with biomimicry features to activate endogenous stem cells for tissue engineering in situ<sup>[1]</sup>. This report aims to develop a series of injectable bioactive materials (IBMs) with bone-mimicking compositions and architectures, and their regulation of cell behaviors and tissue regeneration functions will be discussed <sup>[2]</sup>. In vitro evaluation indicates that the developed injectable materials are able not only to effectively recruit stem cells, but also to guide a directional osteogenic differentiation in the absence of growth factors. In vivo biological study shows that the IBMs present good ectopic bone formation ability both under the skin and inside muscle using a rabbit model. After that, the injectable materials are then composited with inert LARs artificial ligament used at clinical level, which are then implanted in a rabbit extra-articular model for bone regeneration evaluation. The introduction of the injectable materials can effectively enhance the osteo -integration of the LARS ligament with bone tissue via forming new bone at both the ligament's periphery and inner. This study may offer an insight for designing a new type of injectable bioactive materials for bone-related tissue regeneration.



Dr. Yulin Li is an Associate Professor in Engineering Research Centre for Biomedical Materials of Ministry of Education at East China University of Science and Technology (ECUST), Shanghai, China. In 2009, he is was appointed as a Research Assistant Professor at University of Madeira, Portugal. In 2014, he joined Prof. Changsheng Liu's group. Dr. Li's research interests are involved in the exploration of bioactive materials for bone regeneration and drug delivery application. He has published 1 edited books, and more than 60 journal papers. In the past five years, Dr. Li's citation index (h-index: 18) has risen significantly with more than 1600 citations.

## Lineage divergence of synovial joint progenitor cells: Implication to tissue repair

#### **Prof. Danny Chan**

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The developing synovial joint contains progenitor cells within the interzone, site of the future joint. These cells are know to express Gdf5 and Wnt9a as part of the earliest cellular processes in the establishment of the interzone. However, lineage specification and progression toward the different tissues of the joint are not well understood. By lineage tracing studies, we identify a population of Lgr5+ interzone cells that contribute to the formation of cruciate ligaments, synovial membrane and articular chondrocytes of the joint. We show that Col22a1, a marker of early articular chondrocytes, is co-expressed with Lgr5+ cells prior to cavitation as an important lineage marker specifying the progression towards articular chondrocytes. Interesting, Lgr5+ cells also contribute to the formation of the cruciate ligaments of the developing knee joint. Our *in vivo* cell fate mapping analysis indicates a divergent between ligament and articular cartilage lineages, establishing committed progenitors that are mutually exclusive with respect to genes marking ligament cells (Scx) and juvenile articular cartilage chondrocytes (Col22a1) within the Lgr5+ progenitor cell pool. This finding is supported by single cell transcriptome analyses and pseudo timeline projections. Furthermore, Lgr5+ cells contribute to the repair of a joint defect with the re-establishment of a Col22a1-expressing superficial layer.



Danny Chan is a professor and Acting Director of the School of Biomedical Science at the University of Hong Kong, and Assistant Dean for research and research postgraduate studies at the Faculty of Medicine. He graduated from the University of Melbourne, Australia

His research interest is in skeletal biology, focusing on development, growth and degenerative processes of the skeleton in health and disease. He has a particular interest in rare diseases of the skeleton. He has received more than 35M HKD of research funding as principal investigator and 200M HKD as Co-investigator, and with more than 170 publications and in high impact journals such as Nature, JCI, AMHG, PNAS, PLOS Biol, PLOS Genetics, eLife, EMBO and JCB.

In recognition of his achievements, he received an award for excellence in medical research from the Premier of Victoria in Australia, and recently, the Croucher Senior Research Fellow Award in Hong Kong, and the SY and HY Cheng Endowed Professor in Stem Cell Biology and Regenerative Medicine.

He helped to initiate "The Little People of Hong Kong" Foundation in Hong Kong, an NGO for the patient groups, and to increase the community's awareness of the needs of patients with rare skeletal disorders. He is a council member of Hong Kong Alliance for Rare Diseases, advocating for the needs of rare disease people in our society.

## **GSDM** protein and immunity

#### Prof. Xiang Gao

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Gasdermin is a protein family whose physiological functions are largely unknown. Several GWAS studies suggest that Gasdermin family associated with many autoimmune diseases. Recently, Gsdmd and Gsdme are demonstrated to be the executors of pyroptosis, which is a type of pro-inflammatory programmed cell death. Our lab is focus on analyzing the roles of Gasdermin family in physical status and autoimmune diseases. We also develop therapies based on the uncovered molecular mechanisms. We discovered that Gasdermin directly trigger cell death and inflammation firstly. Our recent works are mainly about the regulation of Gsdmd and Gsdme in pyroptosis. We found that inhibition of ROS reduces the cleavage of Gsdmd in canonical pyroptosis and inhibition of GSDMB reduces the cleavage of GSDMD in non-canonical pyroptosis. We developed several the methods to block pyroptosis in autoimmune diseases. One of the methods is using magnesium to block the membrane translocation of Gsdmd. Furthermore, supplement of magnesium could greatly enhance the survival rate of sepsis mice model.



Xiang was an alumina of Nanjing University. He received his Ph.D. degree from Thomas Jefferson University in 1994, then did his postdoctoral training at the Jackson Laboratory and University of North Carolina at Chapel Hill. In 2000, Xiang was recruited back to Nanjing University. He later founded both Model Animal Research Center of NJU and National Resource Center of Mutant Mice of China. He is also the current director for the State Key Laboratory of Pharmaceutical Biotechnology. Xiang is the recipient for Cheung Kong Scholar from Ministry of Education and Distinguished Young Scholar from National Science Foundation. His lab has been focused on understanding the physiological homeostasis of metabolic and immunological processes. He has been funded by multiple national grants and published more than 180 research papers. Xiang is recipient of many national and international awards, including the National Science and Technology Progress Award.

## LIM domain proteins Pinch1/2 regulate bone homeostasis

#### Prof. Guo-zhi Xiao

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Mammalian focal adhesion proteins Pinch1 and Pinch2 regulate integrin activation and cell-ECM adhesion and migration. Here we show that deleting Pinch1 in osteocytes and mature osteoblasts using the 10-kb mouse Dmp1-Cre and Pinch2 globally (double knockout or dKO) results in severe osteopenia throughout life, while ablating either gene does not cause bone loss, suggesting a functional redundancy of both factors in bone. Pinch deletion in osteocytes and mature osteoblasts generates signal(s) that inhibit osteoblast and bone formation. Pinch-deficient osteocytes and conditioned media from dKO bone slices cultures contain abundant sclerostin protein and potently suppresses osteoblast differentiation in primary BMSC and calvarial cultures. Pinch deletion increases adiposity in the bone marrow cavity. Primary dKO BMSC cultures display decreased osteoblastic, but enhanced adipogenic, differentiation capacity. Pinch loss decreases expression of integrin- $\beta$ 1, ILK, and  $\alpha$ -parvin and increases that of active caspases 3 and 8 in osteocytes. Pinch loss increases osteocyte apoptosis in vitro and in bone. Pinch loss upregulates expression of both Rankl and Opg in the cortical bone and does not increase osteoclast formation and bone resorption. Finally, Pinch ablation exacerbates hindlimb unloading-induced bone loss and impairs active ulna loading-stimulated bone formation. Thus, we establish a critical role of Pinch in control of bone homeostasis.



Professor Guozhi Xiao is an internationally renowned bone biologist. Dr. Xiao obtained his PhD degree in biochemistry and molecular biology from Peking University in 1994. He finished his post-doc training (1994-1998) and worked as a research scientist (1998-2005) at the University of Michigan Ann Arbor. In 2005, he assumed an independent faculty position as a tenure-track assistant professor at the University of Pittsburgh School of Medicine and was promoted to the level of associate professor with tenure in 2011. In 2012, he joined Rush University Medical Center in Chicago and assumed a prominent academic position as the Dr. Ralph and Marian C. Falk Endowed Chair Professor of Biochemistry and served as the director of research of the department of biochemistry. In 2013, he joined the SUSTech as a tenured full professor and later became the chair of the biological department. Dr. Xiao is the director of the Center for Experimental Animals at SUSTech. Dr. Xiao is the dean of Zhicheng College at SUSTech. Dr. Xiao has made several contributions to our understanding the molecular control of skeletal development and homeostasis. His work is reported in more than 120 peer-reviewed publications, many in high profile journals such as the Journal of Clinical Investigation and Nature Communications. He serves as a reviewer for the US National Science Foundation, the Italian Ministry of Health and the National Natural Science Foundation of China and sits on the editorial boards of the Journal of Bone and Mineral Research (JBMR) and the Journal of Biological Chemistry (JBC). Dr. Xiao's research interests focus in the following areas: (1) to determine how osteoblast, osteoclast, and chondrocyte formation is controlled during skeletal development and homeostasis under physiological and pathological conditions; (2) to define the mechanisms that modulate bone angiogenesis; and more recently, (4) to study the roles of cell adhesion signaling molecules, such as Kindlin-2, Migfilin and Pinch1/2, in skeletal development and homeostasis. By working on these projects, Xiao laboratory has also maintained a focus on important medical issues involving bone --osteoarthritis, osteoporosis, metastatic osteolytic lesions, and fracture healing. Information obtained from these studies will enhance our understanding of these pathological processes.

## Hippo signaling and skeletal diseases

#### **Prof. Kingston Mak**

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Musculoskeletal diseases such as osteoporosis, osteoporotic bone fracture and osteoarthritis are very common in the aged population. It is therefore important to understand the signaling mechanisms that govern bone and cartilage regeneration and protect them from degeneration. Our recent works uncovered the importance of the Hippo signaling in the skeletal system for tissue homeostasis and repair. In this talk, we will discuss the functional roles of the Hippo pathway in both chondrocyte and osteoblast lineages respectively and reveal the mechanistic networks that contribute to the pathogenesis of some of the common bone degenerative diseases. Specifically, we demonstrated that Yap1 inhibits chondrocyte differentiation and maturation that consequently inhibits bone repair. In the context of articular cartilage, Yap1 preserves articular cartilage integrity. Mst1/2 kinases that regulate Yap1 activity, modulate glucose uptake for osteoblast differentiation and bone formation that may be implicated in diabetic-induced bone loss.



Mak received his Ph. D from the University of Hong Kong and continued his postdoctoral training at the National Institute of Health (NIH). He started his own research group as Assistant Professor from 2010 at the School of Biomedical Sciences, The Chinese University of Hong Kong and recently joined the Guangzhou Regenerative Medicine and Health, Guangdong Laboratory as Principle Investigator. His research interest focuses on the regulation of the developing cartilage and bone and how these dysregulated processes contribute to common musculoskeletal diseases. He received several awards for his works including American Society of Bone and Mineral Research Young Investigator Award and Webster Jee Young Investigator Award.

## Photocrosslinkable materials for bone regeneration

#### Prof. Xin Zhao

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In this work, inspired by the gecko feet covered with millions of small hairy setae which could solely interact with the substrate and provide strong overall interaction to bear high load, we present a photocrosslinkable composite materials consisting of tri-block poly (lactide-*co*-propylene glycol-*co*-lactide) dimethacrylate ( $P_mL_nDMA$ ) and hydroxyethyl methacrylate-functionalized hydroxyapatite (nHAMA). Upon UV exposure, an inorganic-organic co-crosslinked network can be rapidly formed within 120 seconds. Such inorganic-organic co-crosslinked network has brought in a 10-fold increase in the mechanical properties compared to its organic counterpart. The significant improvement in the mechanical performance, comparable to natural cancellous bone, has made the composites highly favorable for various load-bearing applications. In addition, via changing the lactide-to-propylene glycol ratio in the  $P_mL_nDMA$  and the content of nHAMA, we could readily tune the rheological behaviors (for use as injectable materials or for 3D printing), wettability and degradation of the composites. Moreover, due to the low exothermal heat generation during crosslinking, the composites allow for loading and release of bioactive molecules. Together with the superior biological performances in supporting the *in vitro and in vivo* osteogenesis and angiogenesis, we envision that our composites have great potential in bone tissue engineering.



Dr. Xin Zhao is an Assistant Professor at the Department of Biomedical Engineering, the Hong Kong Polytechnic University, Hong Kong SAR, China. She received her PhD in Biomaterials and Tissue Engineering from University College London (UCL), UK (2010). Prior to her current position, Dr. Zhao worked as a postdoctoral research fellow at Harvard University, Harvard-MIT Health Science & Technology (HST) and School of Engineering of Applied Sciences (SEAS). Dr Zhao is dedicated to interdisciplinary research involving topics such as biomaterials, tissue engineering, drug delivery, cell micro-environment and microfluidics. She uses multi-disciplinary approach including material science, nanotechnology, cell biology and microfluidics to generate tissue-engineered organs and control cell behaviours for addressing clinical problems. So far she has published over 80 peer-reviewed journal articles and book chapters and applied for three national patents. Her work has been published in leading journals of the biomaterials field such as Chemical Reviews, Materials Today, Advanced Functional Materials, Angewandte Chemie International Edition, Biomaterials, Small, Theranostics, etc.

## **Stem cell spheres for therapeutic applications**

#### **Profesor Ren-he Xu**

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Mesenchymal stem cells (MSCs) have been extensively studied and used in clinical trials. However, traditionally MSCs rely on donated fetal or adult tissues. After transplantation, MSCs in a single cell state are rapidly cleared by innate immune cells. We demonstrate that MSCs differentiated from human embryonic stem cells through trophoblasts (T-MSC<sup>TM</sup>) have high efficacy in disease models such as mouse and monkey multiple sclerosis, inflammatory bowel disease and osteoarthritis. In addition, MSCs enter the "hibernation" state after forming a sphere and can withstand ambient temperature and anoxic conditions for up to 10 days. T-MSC spheres (rather than single-celled T-MSCs) remarkably promote skin wound healing due to increased cell survival and enhanced CXCL12 signaling.



Prof. Ren-he Xu focuses his study on the biology and therapeutic application of human embryonic stem cells (hESCs) and their derived mesenchymal stem cells via trophoblasts (T-MSC<sup>TM</sup>) and has published more than 70 papers with over 6,000 citations. He first discovered the key factors to sustain self-renewal and prolonged culture of hESCs (Nat. Biotechnol. 2002; Nat. Methods 2005; Cell Stem Cell 2008) and revealed recurrent copy number variations in human induced pluripotent stem cells (Nat. Biotechnol. 2011). He treated murine and monkey models of multiple sclerosis, colitis, and spontaneous osteoarthritis with T-MSCs with superior efficacy (Stem Cell Rep. 2014; Stem Cells 2016; Theranostics in press). His team invented a novel method for stem cell transportation in spheres under ambient conditions without need for the costly and inconvenient cryopreservation methods (Biomaterials 2017). He obtained a number of patents with successful commercialization and received many awards from Israel, U.S., Iran, Macau, and Portugal. Prof. Xu obtained Ph.D. at University of Tokyo and is currently a professor and associate dean of the Faculty of Health Sciences, University of Macau, and a member of the council of the Chinese Society for Stem Cell Research.

## Molecular regulation of muscle stem cell quiescence exit

#### Prof. Tom H. Cheung

S H Ho Associate Professor of Life Science Division of Life Science, The Hong Kong University of Science and Technology

Quiescent adult stem cells have the ability to respond rapidly to external stimuli, but mechanisms of such rapid activation remain elusive. Using quiescent skeletal muscle stem cells (QSCs), we showed that intron retention (IR) is prevalent. Genes possessing IR are essential for various fundamental cellular functions including RNA splicing, protein translation, cell cycle entry and lineage specification. Further analysis revealed that IR is a post-transcriptional mechanism that regulates QSC quiescence exit, which is dependent on the phosphorylated-Dek protein. While Dek is absent in QSCs, overexpression of Dek in QSC in vivo results in a global decrease of IR, quiescence exit, and consequently undermine muscle regeneration. Moreover, IR analysis on public RNA-seq data shows that other quiescent adult stem cells are enriched with retained introns, indicating IR as a feature of quiescent adult stem cells. Altogether, these findings suggest that intron retention plays an important role in stem cell quiescence exit.



Dr. Tom Cheung received his B.A. (2001) and Ph.D. (2006) in Biochemistry from the University of Colorado at Boulder. He then moved Stanford University School of Medicine to continue his postdoctoral training. He joined the Division of Life Science at the Hong Kong University of Science and Technology (HKUST) in 2013 where he current serves as an assistant professor. He is currently a member of the Center for Stem Cell Research, the State Key Laboratory of Molecular Neuroscience, and the Center for Systems Biology and Human Health. In 2017, he was named the S H Ho Assistant Professor of Life Science.

The main area of research interest of the Cheung laboratory at HKUST is somatic stem cell biology. The focus of the laboratory is to specify the molecular pathways that control stem cell quiescence and stem cell-mediated tissue regeneration to achieve a better understanding of somatic stem cell function in the context of tissue regeneration and diseases. The long-term goal of the Cheung laboratory is to understand molecular pathways that are essential for stem cell function during the process of biological ageing.

# Adipose-derived stem cell application in reconstructive surgery and musculoskeletal disorder

#### Prof. Nattawat Onlamoon

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Adipose-derived stem cell (ADSC) is adult stem cell isolated from human adipose tissue which can be taken by surgical resection or liposuction. However, liposuction yields a large volume of adipose tissue and has been considered as the typical method for clinical harvest of ADSC. ADSC are potential for selfrenewal and differentiation which are similar to mesenchymal stem cells. Utilization of ADSC from white adipose tissue also has advantages of accessibility and abundance compared to other types of stem cells. ADSC has also been reported to possess the same properties as the stem cells derived from bone marrow and is able to differentiate towards adipogenic, osteogenic, chondrogenic and myogenic lineages. ADSC has long been introduced to reconstructive surgery with broad applications in many organs. In particular, the soft tissue and skin are main targets for reconstructive surgery. With respect to oncoplastic breast surgery, ADSC is abundantly presented in the processed lipoaspirates used in lipotransfer during breast reconstruction procedure. ADSC is also considered to play important roles in a resorption rate of the transferred fat. The desirable outcomes may then rely on the quantity and quality of ADSC. Besides reconstructive surgery, ADSC also represents a new therapeutic strategy in musculoskeletal disorders with supportive evidences in both preclinical and clinical studies. Administration of ADSC has been demonstrated for their efficacy in muscle, tendon, bone and cartilage regeneration. Therefore, ADSC is considered as a promising tool in the treatment of musculoskeletal disorders.



Nattawat Onlamoon obtained his Ph.D. in Immunology from Mahidol University (Bangkok, Thailand) and pursued his postdoctoral training in the Department of Pathology and Laboratory Medicine, Emory University, School of Medicine in Atlanta (Georgia, USA). He is currently an Associate Professor in the Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, as well as a group leader of Siriraj Research Group in Immunological responses against infectious pathogens, such as HIV and dengue as well as the applications of flow cytometry technique in various research fields. By applying knowledge from basic research to translation, an ongoing research is conducted to develop an immune-based therapy for HIV-1 infected patients. Based on this therapeutic cell manufacturing experience, he decided to further utilize cell-based therapy by focusing on the application of stem cells in clinical practice. The current stem cell research focuses on using adiposederived stem cell (ADSC) for breast reconstruction in breast cancer patient after mastectomy.

## Neuronal intrinsic inhibitors regulating axon regeneration

#### Prof. Kai Liu

Cheng Associate Professor of Science Division of Life Science The Hong Kong University of Science and Technology

The failure of axon regeneration in the adult mammalian central nervous system (CNS) attributed to two properties of the adult CNS, the inhibitory extrinsic environment and a diminished intrinsic regenerative capacity of mature CNS neurons. Deleting Pten (phosphatase and tensin homolog) in retinal ganglion cells (RGCs) and corticospinal motor neurons (CSMNs) promotes robust axon regeneration. Importantly, the loss of the regrowth potential of axons is accompanied by a corresponding down-regulation of mTOR activity in neurons upon completion of development. An injury further diminishes neuronal mTOR activity. Our recent findings suggest that Pten deletion promotes regeneration in a chronic spinal cord injury model, and enhancing neuronal activity by melanopsin/GPCR signaling promotes axon regeneration in adult CNS. We also demonstrated that rapamycin-resistant mTOR function is required for sensory axon regeneration induced by a conditioning lesion. By doing single cell analysis on isolated regenerated neurons, we further revealed the downstream effectors of mTOR signaling in the axon regeneration.



Kai Liu is currently Cheng Associate Professor of Science in Division of Life Science at The Hong Kong University of Science and Technology (HKUST). Liu received his Bachelor degree from School of Life Sciences at Peking University in 1998, and received his Ph.D. from Rutgers University at New Brunswick in 2006. Then he did his postdoc research at Children's Hospital Boston/Harvard Medical School. In 2011, Liu joined Division of Life Science at HKUST as Assistant Professor. His research interest focuses on the intrinsic mechanisms regulating axonal regeneration.

#### **Selected publications**

- 1. Wang H, Wang X, Zhang K, Wang Q, Cao X, Wang Z, Zhang S, Li A<sup>#</sup>, Liu K<sup>#</sup>, Fang Y<sup>#</sup>. Rapid depletion of ESCRT protein Vps4 underlies injury-induced autophagic impediment and Wallerian degeneration. *Science Advances* 2019 Feb 13:Vol. 5, no. 2.
- Weng Y-L, Wang X, Ran A, Cassin J, Vissers C, Liu Y, Liu Y, Xu T, Wang X, Wong S, Joseph J, Dore L, Dong Q, Zheng W, Jin P, Wu H, Shen B, Zhuang X, He C, Liu K, Song H, Ming G-L. Epitranscriptomic m6A Regulation of Axon Regeneration in the Adult Mammalian Nervous System. *Neuron*, 2018 Jan:97 (2), 313-325. e6
- 3. Li S\*, Yang C\*, Zhang L, Gao X, Wang X, Liu W, Wang Y, Jiang S, Wong YH, Zhang Y, Liu K. Promoting axon regeneration in the adult CNS by modulation of the melanopsin/GPCR signaling. *Proc. Natl. Acad. Sci. USA*. 2016 Feb 16;113(7):1937-42.
- 4. Du K\*, Zheng S\*, Zhang Q\*, Li S, Gao X, Wang J, Jiang L, Liu K. Pten deletion promotes regrowth of corticospinal tract axons 1 year after spinal cord injury. *Journal of Neuroscience* 2015 July 1;35(26): 9754-9763.
- Li S\*, He Q\*, Wang H, Tang X, Ho KW, Gao X, Zhang Q, Shen Y, Cheung A, Wong F, Wong YH, Ip NY, Jiang L, Yung WH, Liu K. Injured adult retinal axons with Pten and Socs3 co-deletion reform active synapses with suprachiasmatic neurons. *Neurobiology of Disease* 2014 Oct 16;73C:366-376. [Epub ahead of print].

## FoxO3 protects against the paraquat-induced heart injury

## Prof. Xu-feng Qi

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Paraquat (PQ) promotes cell senescence in brain tissue, which contributes to Parkinson's Disease. Furthermore, PQ induces heart failure and oxidative damage, but it remains unknown whether and how PQ induces cardiac aging. Here, we demonstrate that PQ induces phenotypes associated with senescence of cardiomyocyte cell lines and results in cardiac aging-associated phenotypes including cardiac remodeling and dysfunction in vivo. Moreover, PO inhibits the activation of FoxO3, an important longevity factor, both in vitro and in vivo. We found that PQ-induced senescence phenotypes, including proliferation inhibition, apoptosis, SA-β-Gal activity, and p16<sup>INK4a</sup> expression were significantly enhanced by FoxO3 deficiency in cardiomyocytes. Notably, PQ-induced cardiac remolding, apoptosis, oxidative damage, and p16<sup>INK4a</sup> expression in hearts were exacerbated by FoxO3 deficiency. In addition, both in vitro and in vivo deficiency of FoxO3 greatly suppressed the activation of antioxidant enzymes including catalase (CAT) and superoxide dismutase 2 (SOD2) in the presence of PQ, which was accompanied by attenuation in cardiac function. The direct in vivo binding of FoxO3 to the promoters of the Cat and Sod2 genes in the heart was verified by chromatin immunoprecipitation (ChIP). Functionally, overexpression of *Cat* or *Sod2* alleviated the PQ-induced senescence phenotypes in FoxO3-deficient cardiomyocyte cell lines. Overexpression of FoxO3 and CAT in hearts greatly suppressed the PQ-induced heart injury and phenotypes associated with aging. Collectively, these results suggest that FoxO3 protects the heart against an aging-associated decline in cardiac function in mice exposed to PQ, at least in part by upregulating the expression of antioxidant enzymes and suppressing oxidative stress.



Professor Xufeng Qi is a PI in the Key Lab of Regenerative Medicine of Ministry of Education, Jinan University, China. He received PhD at Yonsei University Wonju College of Medicine in 2010, Korea and subsequently took the position in Jinan University. Professor Qi's research focuses on: 1) the molecular mechanisms that control heart aging and regeneration; 2) genome editing and disease model construction using CRISPR/Cas9. So far, he has published more than 30 papers in peer-reviewed journals, including Aging Cell, FASEB J, J Mol Cell Cardiol, Cell Death Dis, J Cell Physiol, Sci Rep, Br J Pharmacol, Mol Immunol, and J Cell Mol Med.

## **Fracture healing and bone regeneration: where are we?**

## Dr. David Hua-zhu Ke

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Nonunion fractures represent a devastating condition with significant impact on the lives of patients (pain, loss of function and working time, and social withdraws and other sufferings) and significant burden on the health care cost. Patients diagnosed with a long bone non-union have a very low quality of life as compare with that of the general population as well as estimates reported for other conditions such as diabetes, AIDS and stroke. Lack of new bone regeneration causing by multi-factors is thought to be the major mechanism for fracture nonunion. It has been hypothesized that bone anabolic pathways that can up-regulate bone regeneration and stimulate bone formation may reduce the rate of nonunion. Much effort has been put toward this area of preclinical research and clinical trials. Unfortunately, there is no currently approved pharmacologic therapy for nonunion care to promote fracture healing and improve patients' function outcome. This presentation will summarize the current understanding of the effects of bone anabolic pathways on bone regeneration, present the most up-to-day research we are currently carrying on, and discuss the potential area of continuing interest for research and development of novel therapeutics for improving fracture healing.



David Ke is currently the founder and CEO of Angitia Biopharmaceuticals with operation sites in China and in the States. He has the adjuct appointments as Adjucnt Professor at University of Utah, USA, Chinese University of Hong Kong, China, and Guangdong Medical University, China, and the Center for Musculoskeletal Research, Guangzhou Regenerative Medicine Guangdong Laboratory, China.

David Ke's research interests include bone biology, osteoporosis, fracture healing, muscle frailty and kidney diseases. David has been involving and leading the drug discovery research and development in estrogen receptor modulator (lasofoxifene), EP2 and EP4 receptor agonists, RANKL antibody (denosumab, approved for human use in 2010, with annual sales of 2018 greater than \$4 billion) and sclerostin antibody (romosozumab, approved for human use in May 2019) at **Pfizer**, Groton, Connecticut, USA (1992 – 2005, from Senior Research Scientist to Research Fellow), **Amgen**, Thousand Oaks, California, USA (2005 – 2014, from Scientific Director to Scientific Executive Director and Head of Bone and Mineral Research) and **UCB** Pharma, Slough, United Kingdom (2015 – 2018, Vice President and Head of Bone Therapeutic Area).

David has published 148 peer-review scientific publications and invited reviews, and is the inventor of 26 patents. He and his group has delivered more than 250 scientific presentations in the forms of international scientific conferences, research seminars and invited presentations.

# Clinical trial of cartilage defects and osteoarthritis treatment using bone marrow mesenchymal stem cells and infrapatellar fat pad mesenchymal stem cells

#### Prof. Chih-Hung Chang

Far Eastern Memorial Hospital Department of Orthopaedic Surgery President of Taiwan Association of Regenerative Medicine E-mail:orthocch@icloud.com

Osteoarthritis (OA), one of the most common joint disease, affects more than 80% of the population aged 70 or over. Nonoperative treatment for OA, despite NSAIDs, hyaluronic acid (HA) or platelet-rich plasma (PRP) injection, had also developed in Taiwan. Mesenchymal stem cells (MSCs) show multi-potent differentiation and self-renewal capability, and, after exposure to an inflammatory environment, also exhibit immunosuppressive properties. Currently, we cooperated with EMO Corp. to conduct a phase I clinical trial study of infrapatellar fat pad MSC (IPFP-MSC) for OA treatment. Twelve subjects enroll in the study. Results showed that the IPFP-MSC can express CD73, CD90 and CD105, and they do not express CD11b, CD19, CD34, CD45 and HLA-DR. They have highly proliferative and differentiate capability. Importantly, they possess anti-inflammatory ability to inhibit peripheral blood mononuclear cell proliferation and TNF- $\alpha$ production. Preliminary phase I clinical trial outcome indicated that there is an improvement with time in keen pain (VAS score) and knee function (IKDC, KOOS score) without severe adverse event.

For the treatment of cartilage defect, mosaicplasty and microfracture surgeries are the most common treatment method in Taiwan. However, some regenerative approaches had been developed for cartilage defect. Engineered cartilage bio-product Kartigen© is an MSC-derived pre-chondrocyte bioproduct. This technique is developed by Dr. Hwa-Chang Liu, Prof. Feng -Huei Lin and Dr. Chih-Hung Chang. It is derived from bone marrow MSC, and there is no need to harvest autologous cartilage. After 5 years, clinical results showed significant improvement of the knee function in IKDC scoring. A new phase I clinical trial is also ongoing.

Recently, Taiwan's government had launched regulations "Specific Medical Management Regulation" for the autogenous cell therapy, the draft of regulations for regenerative medicine also had been announced. Medical care institution could draft a proposal and submit to the central competent for specific autologous cell therapy technics. We believe these polices will be very encouraging to the Taiwan's regenerative medicine industries.



#### **Current position:**

President, Formosa Association of Regenerative Medicine Professor, Yuan Ze University, Taoyuan Chief, Department of Orthopedics, Far Eastern Memorial Hospital, New Taipei City

#### Individual specialty:

- Orthopedic surgery, Elbow surgery, Traumatology, Arthroplasty
- Biomedical engineering
- Tissue engineering & Regenerative medicine

#### **Representative and awards:**

- 2008 5th National Innovation Award
- 2010 8th Y. Z. Hsu Scientific Award: Outstanding Professor Award
- 2011 8th National Innovation Award
- 2014 3rd New Taipei Medical Charity Award: Educational Research Award
- 2017 JMBE Annual Excellent Paper Award

#### **Recent SCI publications:**

- Yu-Chun Chen, Yu-Wei Chang, Kinn Poay Tan, Yi-Shan Shen, Yao- Horng Wang, <u>Chih-Hung Chang\*</u>. (2018, Nov) Can mesenchymal stem cells and their conditioned medium assist inflammatory chondrocytes recovery? *PLoS ONE 13(11): 0205563*. (SCIE)
- Yu-Chun Chen, Yuan-Ming Hsu, Kinn Poay Tan, Hsu-Wei Fang, <u>Chih-Hung Chang\*</u>. (2018, Oct) Intraarticular injection for rabbit knee osteoarthritis: effectiveness among hyaluronic acid, platelet-rich plasma, and mesenchymal stem cells. *Journal of the Taiwan Institute of Chemical Engineers*. 91, 138-145. (SCI)
- Cheng-Tzu Wang, Jia-Wan Chen, Karl Wu, Chiang-Sang Chen, Wen-Chih Chen, Jwo-Luen Pao, <u>Chih-Hung Chang</u> and Tsung-Yu Lan. (2018 Jun) Suboptimal outcomes after closed reduction and internal fixation of displaced femoral neck fractures in middle-aged patients Is internal fixation adequate in this age group. *BMC Musculoskeletal Disorders*, 9;19(1):190. (SCIE)

## **Biological therapies for articular cartilage repair:** from basic research to clinical outcome

#### Dr. Pan Pan Chong

PhD, Senior Lecturer Department of Orthopaedic Surgery Faculty of Medicine, University of Malaya E-mail: pan2chong@gmail.com

The ability of cartilage to undergo self-repair as the result of an injury is limited due to the absence of neurovascular supply. To avoid the problem of limited tissue regeneration, the potential of mesenchymal stem cells (MSCs) to be employed in biological therapies for cartilage regeneration has recently generated much interest in the challenging arena of repairing damaged joint cartilage. This project focused initially on isolation and expansion of adult MSCs derived from bone marrow and peripheral blood, followed by inducing chondrogenic differentiation in vitro. Subsequently, such MSCs and MSC-driven chondrocytes were fully characterised prior to embedding in biocompatible alginate scaffolds and then transplanted into surgically created cartilage defects in knee joints of animal models. The project was further conducted to investigate the plausible mechanism of osteoarthritis by determining the interplay of hyaline cartilage loss and subchondral bone changes in the patients with established knee osteoarthritis, followed by the evaluation of the biosynthesis of isolated osteoarthritic chondrocytes to varying dynamic compressive strain and loading duration. Based on data arising from the animal and human studies, similar protocols were adapted for implementation in clinical trials involving suitable screened patients with grade I and II knee osteoarthritis to undergo repair through platelet-derived extracellular vesicles (PEV) treatment. The patients were classified into four groups, namely PEV, PEV and hyaluronic acid (HA), HA, and conservative treatments. A total number of 62 patients were recruited in these trials. When comparing the efficacy of these treatment options, the patients treated with PEV showed the best improvement.



Dr. Chong Pan Pan is a senior lecturer at the Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, Malaysia. Her work focuses on driving the adult mesenchymal stem cells (MSCs) from bone marrow, peripheral blood and adipose tissue along chondrogenic lineages for later transplantation to replace worn out joint cartilage in patients suffering from joint disorders, including trauma or osteoarthritis. Additionally, she has also been put in charge of the newly provided clinical service using platelet-derived extracellular vesicles (P-EVs) to treat musculoskeletal diseases. To attest her work, Dr. Chong has published in several high quality (Q1/high impact factor) peer-reviewed journals and presented her works extensively and globally at numerous international level conferences. At that time, she has also won several awards, including top prizes at the regional level, such as Young Investigator Awards, Young Investigator Best Paper Award, L'Oréal Malaysia for Women in Science, Best Poster/Oral Presentations and travel fellowships, etc. In addition, she has participated in several biotechnology exhibitions and business idea competitions. She won many innovation awards for her works on MSCs and P-EVs as biological therapies for tissue regenerations. She has also developed intellectual property related to the novel work which has been successfully patented.

UM expert: <u>https://umexpert.um.edu.my/panpanchong</u> Google scholar: <u>https://scholar.google.com.my/citations?user=Q945HfkAAAAJ&hl=en</u>

# The synergistic promoting effect on osteoarthritis chondrocytes regeneration displayed by combined application of both AAV-P65shRNA and AAV-BMP4

#### Prof. Guang-heng Li

Department of Osteopaedic Surgery, Shenzhen People's Hospital The Second Clinical Medical College of Jinan University Shenzhen 518035, Guangdong Province, China E-mail: liguangheng@hotmail.com

#### Aims:

To explore the combined effect on regeneration of OA chondrocytes by application of both AAV-p65shRNA and AAV-BMP4.

#### Methods and Materials:

1) Cells isolation and sorting. 2) Adeno-associated virus(AAV) package and infection. 3) Quantitative real-time PCR (qRT-PCR). 4) Chondrogenesis assay

#### **Results:**

Figure1.(A) There is no distinct different cell morphology observed under bright field microscope.(B) the mRNA level of RUNX2 ,Inflammatory chondrocytes was higher than the normal chondrocytes, whereas, the mRNA level of CollagenII,Sox9 and NKX3.2 have the opposite results.(C)(D)P65 is knocked down and BMP4 is overexpressed in Inflammatory chondrocytes.

Figure2. Chondrogenesis assay of the six cells (A) Distinct gross morphology of pellets from six populations. Combining AAV-P65shRNA and AAV-BMP4 and Inflammatory chondrocytes make the largest and the smallest pellet among these six cell groups, respectively.(B)(C)(D) Alcian blue, Safranin O and Immunohistochemistry at day28. Among them, Combining AAV-P65shRNA and AAV-BMP4 have the strongest potential for chondrogenic differentiation, whereas Inflammatory chondrocytes was weakest of the six cells.

#### **Conclusion:**

Combine inhibiting the NF-KB inflammation signal by AAV-p65shRNA and stimulating chondrogenic differentiation by AAV-BMP4 will yield the synergistic promoting effect of OA chondrocytes regeneration



Guangheng Li, M.D, PhD. Professor, Director of Orthopaedic Surgery, Shenzhen People's Hospital, Second Clinical Medical College of Jinan University and First Affiliated Hospital of Southern University of Science and Technology.

Education/training					
Institute Henan Medical University	<b>Degree</b> M.D.	<b>Year (s)</b> 1991 – 1996	<b>Field of study</b> Preventive Medicine		
Henan Medical University Shanghai 2 <sup>nd</sup> Medical Univ	M. Med Ph.D.	1996 – 1999 1999 – 2002	Orthopaedics Orthopaedics		
University of Pittsburgh	Postdoc	2002 - 2009	Muscle derived stem cell, Bone and cartilage tissue engineering		
Oregon H&S University	Postdoc	2010 - 2012	Rhabdomyosarcoma		

#### Personal statement.

As a physician-scientist, I pursue laboratory-based research to benefit the orthopaedic patients I serve through the study of bone and musculoskeletal progenitor (stem) cells and the cancers these cells give rise to. My knowledge of bone and soft tissue stem cells also allows me to address regeneration with respect to degenerative joint disease, which shares features with sarcomas as being a disease of the tissue microenvironment.

#### **Positions and Honors.**

09/96-07/99	Master candidate, Dept of Orthopaedics, Henan Medical University	
09/99-07/02	Ph.D. candidate, Dept of Orthopaedics, Shanghai Second Medical University	
08/02 to 07/07	Postdoctoral Fellow, University of Pittsburgh, Dept. of Orthopaedic Surgery	
07/07 to 09/09	Research Associate, University of Pittsburgh, Dept. of Orthopaedic Surgery	
10/10 to 06/12	Postdoctoral Research Fellow, Oregon Health & Science University	
06/12 to 04/13	Professor, Second affiliated hospital of Zhengzhou University	
04/13 to 05/19	Professor, First affiliated hospital of Zhengzhou University	
05/19 to present	Professor, First Affiliated Hospital of Southern University of Science and	
-	Technology, Shenzhen.	

## **Epigenetic and functional characterization of histone demethylases KDM3A and KDM4C in MSC senescence and bone aging**

#### **Prof.** Cynthia Jiang

Room 409A, 4/F, Lo Kwee-Seong Integrated Biomedical Sci. Bldg., Area 39, CUHK The Chinese University of Hong Kong E-mail: xjiang@cuhk.edu.hk

MSCs are extremely important adult stem cells for tissue homeostasis, regeneration and repair. However, the regenerative capacity of MSCs declines in aged people and their exhaustion is recognized as an important hallmark of aging. Thus, a better understanding of the molecular mechanisms underlying MSC senescence will not only provide important guidance for how to maintain the natural physiological function of stem cells and delay the aging process, but also offer new strategies for stem cell-based therapies.

In the present study, we show that MSC senescence is accompanied by heterochromatin organization. Using three different senescence models, we have identified two conserved histone H3 Lys 9 demethylases KDM3A (also known as JMJD1A) and KDM4C (also known as JMJD2C), which cooperatively mediate the heterochromatin organization in aging MSCs. Mechanistically, KDM3A and KDM4C transcriptionally activate chromosome condensation genes, in particular, components of condensins such as NCAPD2 and NCAPG2. Suppression of KDM3A or KDM4C by either genetic or biochemical approach leads to robust DNA damage response and aggravates cellular senescence. In contrast, overexpression of *KDM3A/KDM4C* or *NCAPD2* alleviates Doxorubicin-induced DNA damage response and MSC senescence. Moreover, MSCs and bone tissues derived from *Kdm3a -/-*mice exhibit defective chromosome organization and exacerbated DNA damage response. Importantly, a marked downregulation of KDM3A and KDM4C associated with a decrease in H3K9me3/2, HP1g and chromosome condensation genes is found in MSCs derived from old human individuals. Consistently, analysis of human bone marrow MSCs transcriptome database reveals inverse correlation of KDM3A/KDM4C and NCAPD2/NCAPG2 with aging.

Collectively, we have revealed a previously unrecognized role of histone demethylases in modulating condensin-mediated heterochromatin organization, which functions as a surveillance mechanism to restrain DNA damage during stem cell aging.



Professor JIANG is an Associate Professor in the School of Biomedical Sciences, CUHK. She is an active member in the Developmental and Regenerative Biology Thematic Research Program, Institute of Tissue Engineering and Regenerative Medicine (iTERM), MOE Key Laboratory for Regenerative Medicine. Prof. JIANG graduated 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. Prof. JIANG undertook her postdoctoral training at the Department of Medicine, UCLA and the University of Southern California as a CIRM (California Institute for Regenerative Medicine) fellow. In 2013, she established an independent laboratory within School of Biomedical Sciences at the Chinese University of Hong Kong. Her major research interest is in stem cell biology and regenerative medicine, in particular, molecular regulation of stem cells, stem cell microenvironment and stem cell therapy in neurological diseases. Prof. JIANG has published more than 80 peer-reviewed papers with over 3000 citations and a H-index of 30, including Nature Medicine, Cell Research, iScience, Cell Death and Differentiation, Stem Cells, Stem Cell Reports and Cancer Research. She serves as editorial board member for various international journals such as *cancer cell international*, *cell biology international* and reviewers for numerous journals and grants. Until 2019, she has presided as PI/co-PI in ~20 local and national competitive grants including GRF, ITF, HMRF and NSFC.

## KIAA1199, a secreted factor of stromal stem cells, promotes bone marrow adipocyte differentiation and inhibits bone density

## Prof. Li Chen

Assistant Professor Molecular Endocrinology Laboratory (KMEB) Odense University Hospital, University of South Denmark DK-5000 Odense C, Denmark

We identified KIAA1199 as a novel secreted factor in hBMSC during osteoblast differentiation using quantitative proteomic analysis, but the role of KIAA1199 in hBMSC bone biology is undisclosed. In the present study, we detected KIAA1199 expression in osteoprogenitor cells and scattered marrow cells. Knockdown of KIAA1199 in hBMSCs resulted in impaired adipocyte (AD) differentiation, but enhanced the osteoblast (OB) differentiation. Its role in osteogenic differentiation and adipogenic differentiation are both mediated by p-AKT and p-ERK MAP kinase signaling. Consistently, KIAA1199 knockout (KO) mice exhibited significant decreases of bone marrow fat and total body fat, while enhanced trabecular bone density. Stromal MSC from KIAA1199 KO exhibited impaired AD differentiation. KIAA1199 KO mice have better and faster bone healing, resistant at osteoporosis. Under high fat diet (HFD) condition, KIAA1199 KO mice also have less weight gain, total body fat gain, and also protected from the glucose tolerance under obesity condition. Relative clinical correlations were also found in human patients with KIAA1199, bone, fat and metablism. Our findings identify KIAA1199 as a novel regulator of fat and bone through its regulations at stem cell lineage differentiations.



Li Chen, Ph.D., (born in 1971) is an assistant professor at Molecular Endocrinology Laboratory (KMEB), Odense University Hospital, and University of South Denmark. She earned her BS at Fudan University, Shanghai, China (1993), and work as researcher and lecturer at the Fudan University Medical College and got her MS at National Laboratory of Medical Neurobiology, Fudan University (2000). She gained her Ph.D. at Aalborg University, Denmark (2005). She had the postdoctoral fellowship at the NCI, NIH, Bethesda, MD, USA where she worked at signaling regulation at cell apoptosis and necrosis. Li Chen's research focus on the molecular mechanisms of stromal stem cell differentiation that regulated by kinases, miRNA, secreted factors, small chemical molecule, and nano-materials; and the use of MSCs and relative factos for aging, osteoporosis, obesity and diabetes.

## Centrosome biology and regenerative potential in striated muscle cells

## Prof. David C. Zebrowski

Department of Medicine and Therapeutics Centre for Cardiovascular Genomics and Medicine Chinese University of Hong Kong E-mail: davidzebrowski@cuhk.edu.hk

One cause of heart failure is a heart attack - which results in the death of specialized contractile cells of the heart called cardiomyocytes. Unlike cardiomyocytes of fish and amphibians, cardiomyocytes of mammals/humans are terminally differentiated. As a result, the mammalian heart is unable to regenerate after injury. Being able to induce mammalian cardiomyocytes to reverse their terminally differentiated state and once again divide/renew represents a therapeutic strategy to regenerate the diseased heart and cure heart failure in humans. However, to date, how mammalian cardiomyocytes undergo terminal differentiation remains largely unknown.

The centrosome is an organelle which is required for cells to divide/renew. Cardiomyocytes of fish and amphibians, which are not terminally differentiated, have a centrosome. In contrast, cardiomyocytes of mammals, which are terminally differentiated, disassemble their centrosomes shortly after birth. Thus, the centrosome represents a novel 'bio-marker' that can predict the regenerative potential of cardiomyocytes.

Unlike cardiomyocytes, skeletal myoblasts undergo terminal differentiation prior to myogenic differentiation. This divergence in proliferative potential and acquisition of a myogenic phenotype in these two straited muscle cell types has suggested that cardiomyocytes and skeletal myoblasts utilize different mechanisms to achieve a terminally differentiated state. However, as with cardiomyocytes, skeletal myoblasts disassemble their centrosomes during terminal differentiation. Accumulating evidence with regards to centrosome biology indicates that similar mechanisms may be at play in establishing a terminally differentiated, and non-regenerative, state in both cardiomyocytes and skeletal myoblasts.



Dr. David Zebrowski, Ph.D. is currently an Assistant Professor in the Department of Medicine and Therapeutics and the Centre for Cardiovascular Genomics and Medicine at the Chinese University of Hong Kong. Dr. Zebrowski received his PhD from Rutgers Medical School (USA) before going on to pursue his postdoctoral studies at Harvard Medical School/Children's hospital Boston/ Depatment of Pediatric Cardiology (USA) and then at the Max Planck Institute of Heart and Lung Research/Erlangen Medical School (Germany). Upon completion of his academic fellowships, Dr. Zebrowski turned his career interest towards the pharmaceutical industry where he identified and developed heart failure targets and therapeutics first at AstraZeneca (Sweden) and then NovoNordisk (Denmark). While Dr. Zebrowski's research interests range across all aspects of heart failure, he is an expert in the field of cardiac regeneration - publishing his research in leading journals such as eLife, Cell, and Developmental Cell.

## Mitochondria-rich human pluripotent stem cell derived-cardiomyocytes uniquely recapitulate disease phenotype and drug responses

## **Prof. Ellen Poon**

Laboratory A, 8/F, Tower A, Hong Kong Children's Hospital, 1 Shing Cheong Road, Kowloon Bay, Kowloon, Hong Kong

Human (h) pluripotent stem cell (PSC)-derived cardiomyocytes (CMs) are of significant value to cardiac disease modelling, drug and cardiotoxicity testing, but their uses are limited by the immaturity of hPSC-CMs and their inability to recapitulate some (patho)physiological attributes of adult CMs.

Using a chemoproteomic approach, we identified LP1 as a surface marker of maturation that can be used to immunophenotype distinct subsets of hPSC-CMs in culture. LP1hi CMs are phenotypically and functionally more mature than LP1lo CMs and are characterized by improved cell morphologies, improved calcium signals and electrophysiological traits, and significantly improved mitochondrial and metabolic function. These cells have significantly increased sensitivities to oxidative stress induced by chemical (H2O2), physiological (hypoxia/reperfusion) and cardiotoxic (doxorubicin) stimuli. Focused studies on doxorubicin-induced cardiotoxicity show that LP1hi CMs, unlike mixed and LP1lo CMs, recapitulate known clinical responses to cardioprotective drugs. This response has not been previously observed with unsorted hPSC-CMs, showing that LP1hi CMs have drug responsive traits more consistent with an adult phenotype. Our results validate the use of chemoproteomics and immunophenotyping to resolve issues of CM immaturity, and this approach should be broadly applicable to any stem cell-derived lineage where matured cells are required. Specifically, we show that LP1hi hPSC-CMs can more accurately predict adult human responses for improved disease modeling and drug testing, and will drive efforts to understand mitochondrial maturation processes and advance investigations of adult cardiac syndromes that involve mitochondrial dysfunction.



Dr. Ellen Poon is currently an Assistant Professor in the Department of Medicine and Therapeutics and the Centre for Cardiovascular Genomics and Medicine at the Chinese University of Hong Kong. She received her BSc degree from the Department of Inorganic Chemistry in the University of Sydney and completed her DPhil studies in the University of Oxford. After graduation, she has worked in local and international institutions including the University of Hong Kong, the University of California, San Francisco and Imperial College London.

Her research focuses on the applications of human pluripotent stem cell-derived cardiomyocytes for disease modeling and drug screening. The immaturity of human pluripotent stem cell-derived cardiomyocytes has long been a barrier to the use of these cells for research and therapy, since their embryonic phenotype makes them poor predictors of adult cardiac responses. Combining transcriptomic, proteomic and microRNA profiling, she revealed novel mechanisms which facilitate the generation of mature cardiomyocytes with adult-like metabolic properties. Her present aim is to apply her hPSC-CM platform for studies of mitochondrial disorders and drug-induced cardiotoxicity to dissect disease mechanisms and to identify novel therapeutics.

# Two critical checkpoints during early activation of adult muscle satellite cells

#### Prof. Zhen-guo Wu

Division of Life Science Hong Kong University of Science & Technology

Adult skeletal muscle stem cells, also called muscle satellite cells (MuSCs), remain in the quiescent state in uninjured muscles but can be rapidly activated to promote regeneration upon muscle injury. However, the molecular mechanisms controlling early activation of satellite cells are not fully understood. Recently, our group demonstrated that the phosphatidylinositol 3-kinase (PI3K)-mediated signaling pathway controls a key checkpoint during early activation of MuSCs. It is both necessary and sufficient for quiescence exit: genetic inactivation of PI3K in adult MuSCs permanently arrests them in the quiescent state, while genetic activation of PI3K in MuSCs promotes their spontaneous exit from quiescence in the absence of muscle injury resulting in gradual depletion of MuSCs. Moreover, our recent work revealed that Paxbp1, a Pax7-binding protein identified in our group, is also indispensable for early activation of MuSCs: genetic deletion of *Paxbp1* in adult MuSCs prevented them from cell cycle re-entry, which resulted in a total failure of injury-induced muscle regeneration. Further analysis showed that loss of Paxbp1 in adult MuSCs were defective in both mitochondria biogenesis and several other metabolic pathways. Thus, Paxbp1 appears to regulate another previously-unrecognized checkpoint during early activation of MuSCs.

This study is supported by a GRF grant (16101517) from the Hong Kong Research grant Council.



Dr. Zhenguo Wu received his Bachelor degree in from Nanjing University in China and his Ph.D. degree in Biochemistry from Western University (formerly the University of Western Ontario) in Canada under the supervision of Dr. George Chaconas. He did his postdoctoral training with Prof. Michael Karin in the University of California at San Diego to study the MAP kinase-mediated cell signaling. He set up his own laboratory in the Hong Kong University of Science & Technology in 1999.

Dr. Wu's laboratory has a long-standing interest in elucidating the roles of different intracellular signaling pathways in regulating muscle stem cells and muscle differentiation using both primary and immortalized mouse myoblasts as well as different mouse models.

Dr. Wu is currently the acting Head of the Division of Life Science, a co-director in the Center for Stem Cell research, and a member in the Center for Systems Biology and Human Health at HKUST.

### **Genomics Technologies for Cell Engineering**

#### Prof. Alan S. L. Wong

School of Biomedical Sciences Department of Electrical and Electronic Engineering The University of Hong Kong E-mail: aslw@hku.hk

The orchestrated action of genes controls cell type specifications, yet the systematic discovery of gene combinations for cell engineering is labor-intensive and challenging to scale. Harnessing the power of synthetic biology and next-generation sequencing technologies, we developed CombiGEM (Combinatorial Genetics En Masse) as a powerful platform for high-throughput functional characterization of combinatorial genetic perturbations in human cells. CombiGEM enables rapid, scalable assembly of high-order barcoded combinatorial genetic libraries, and multiplexed quantification of all library members by using next-generation sequencing technologies. The genetic elements included in CombiGEM libraries can be arbitrary, including microRNAs, gene expression/ knockdown constructs, and programmable CRISPR-Cas genome editing tools. This technology platform is applicable to a broad range of biological settings, and will enable the systematic identification of genetic combinations that engineer specific cell types.



Dr. Alan Siu-lun Wong is an Assistant Professor of the School of Biomedical Sciences at the University of Hong Kong (HKU). He is also jointly appointed at the Department of Electrical and Electronic Engineering of HKU. Before he joined HKU, he obtained his B.Sc. and M.Phil. degrees in Biochemistry and Molecular Biotechnology from the Chinese University of Hong Kong in 2005 and 2007 respectively, and completed his Ph.D. in Biochemistry at the Hong Kong University of Science and Technology in 2011. He joined the Synthetic Biology Group at Massachusetts Institute of Technology from 2012-2016 for postdoctoral training. Dr. Wong was awarded with the Croucher Foundation Studentship (2008), the Butterfield-Croucher Award (2008), the Croucher Foundation Fellowship (2012), the Hong Kong Institution of Science Young Scientist Award in life science (2011), and the RGC Early Career Award (2016). Dr. Wong's current research focuses on developing and applying cutting-edge technologies for studying complex disease biology and devise new therapeutic strategies. His research takes an integrative approach leveraging on various techniques in synthetic biology, CRISPR-based genome engineering, high-throughput sequencing, molecular biology, and genetics to decode the complex genetic bases of human diseases, as well as rationally design and engineer genetic circuits for providing new biomedical and biotechnological solutions.

## TRPV1 channels regulate the electrophysiology of embryonic stem cells-derived cardiomyocytes

#### **Prof. Suk Ying Tsang**

Rm 607, Mong Man Wai Building, School of Life Sciences The Chinese University of Hong Kong, Shatin, Hong Kong SAR E-mail: fayetsang@cuhk.edu.hk

Embryonic stem cell-derived cardiomyocytes (ESC-CMs) is an important source of cardiomyocytes for regenerative medicine and drug screening. Calcium is key player in the excitation-contraction coupling in cardiomyocytes. Transient receptor potential vanilloid 1 (TRPV1) channels are non-selective cation channels which permeate calcium. How TRPV1 channels would regulate the intracellular calcium and electrophysiological characteristics of ESC-CMs has not been explored. In this study, we found that TRPV1 channels are expressed in differentiating ESC-CMs. By calcium imaging, we found that TRPV1 controls calcium release from the sarcoplasmic reticulum of ESC-CMs. By electrophysiology and calcium imaging, TRPV1 blockade and functional knockdown of TRPV1 were found to decrease the rate and diastolic depolarization slope of spontaneous action potentials, and the amplitude and frequency of global calcium transients (CaTs) through the suppressing the Na<sup>+</sup>/Ca<sup>2+</sup> exchanger (NCX) activity. This study not only gives a better understanding of calcium homeostasis of ESC-CMs, but also provides insights into the future cell replacement therapies.



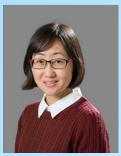
Professor Faye Suk-Ying TSANG obtained her Ph.D. degree from the Chinese University of Hong Kong. She obtained the postdoctoral training at the Johns Hopkins University and the University of California. She is now an Associate Professor at the Chinese University of Hong Kong. She is the investigator in the State Key Laboratory of Agrobiotechnology, the Ministry of Education Key Laboratories for Regenerative Medicine and the Institute for Tissue Engineering and Regenerative Medicine (ITERM) of the Chinese University of Hong Kong. Her research interest is i) the biology of embryonic stem cells and their cardiac derivatives; ii) ion channels and cardiovascular physiology; and iii) the biology of cancer stem cells. She serves as the editorial board member for several journals in the above research area and has published more than 70 papers and several book chapters.

# Long noncoding RNA SAM promotes myoblast proliferation and skeletal muscle regeneration through stabilizing Sugt1 and facilitating kinetochore assembly

#### **Prof: Hua-ting Wang**

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Long non-coding RNAs (lncRNAs) are novel family of gene regulators but the functional study of lncRNAs in skeletal muscle satellite cells remains at the infancy stage. Here we identified one lncRNA SAM that was enriched in the proliferating myoblast cells and down-regulated as the cells progressed to differentiation. Gain- or loss- of function of SAM in muscle satellite cells altered myogenic proliferation and differentiation. Global deletion of SAM based on the KO-first strategy had no overt effect on mice but impaired adult muscle regeneration following acute damage; the loss also exacerbated the chronic injury induced dystrophic phenotype in the mdx mouse model. Consistently, inducible deletion of SAM in adult satellite cells led to deficiency in acute injury-induced muscle regeneration. Further examination of SCs revealed that SAM loss resulted in cell autonomous defect in cell proliferation and promoted precocious differentiation of myoblasts. Mechanistically, we found SAM interacts and stabilizes Sug1 (suppressor of G2 allele of SKP1) protein, a co-chaperon protein key to kinetochore assembly during cell division. Loss of SAM or Sugt1 both caused disruptive kinetochore assembly and microtubule attachment in mitotic cells due to mis-localization of key component Hec1 protein. Altogether, our findings identified SAM as a regulator of skeletal muscle regeneration and SC proliferation through facilitating Sugt1 mediated kinetochore assembly during cell division.



Dr. Wang is currently an Associate Professor at Li Ka Shing Institute of Health Sciences, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong. She received her B.S degree in 1996 from Nanjing University, China and majored in Environmental Chemistry. In 1998 she moved to USA to pursue her PhD degree at the Ohio State University (OSU) with the award of a Research Assistantship. She studied Molecular Virology under the mentorship of Dr. Louis Mansky and obtained her PhD in 2004. She then remained at OSU since 2004 for her Postdoctoral training under the mentorship of Dr. Denis Guttridge with the support of a Postdoctoral Researcher Fellowship from The Comprehensive Cancer Center, OSU and later a F32 Postdoctoral Fellowship Award from National Institute of Health, USA. In 2009, after a successful Postdoctoral training, she moved to Hong Kong for an Assistant Professor position at Department of Obstetrics and Gynaecology, Faculty of Medicine, the Chinese University of Hong Kong. She then moved to Department of ORT and was soon promoted to Associate Professor in 2015. Since 2004, she has developed life-long interest in studying gene regulatory mechanisms using skeletal muscle cells and cancer cells as model systems. Currently the main focus of her group is to study the functional roles of non-coding RNAs in regulating gene expression in skeletal muscle stem cells and muscle regeneration.

## Stem cell-based blood-vessel-on-a-chip for drug testing and disease modeling

#### Prof. Hon Fai Chan

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Tissue-engineered blood vessels (TEBV) can serve as vascular grafts and also play an important role in the development of organs-on-a-chip. We have developed a microphysiological three-dimensional tissue-engineered blood vessel (TEBV) using stem/progenitor cells such as human mesenchymal stem cells and endothelial progenitor cells. The TEBV exhibited flow-mediated vasodilation, vasoconstriction after exposure to 1 µM phenylephrine and released nitric oxide in a manner similar to that of porcine femoral vein, showing its potential for drug screening. We have also engineered a TBEV model of Hutchison-Gilford Progeria Syndrome (HGPS), which is a rare, accelerated aging disorder caused by nuclear accumulation of progerin, based on using induced pluripotent stem cell (iPSC)-derived SMCs from an HGPS patient. TEBVs fabricated from HGPS iSMCs showed reduced vasoactivity, increased medial wall thickness, increased calcification and apoptosis relative to TEBVs fabricated from normal iSMCs or primary MSCs. Additionally, treatment of HGPS TEBVs with the proposed therapeutic Everolimus increased HGPS TEBV vasoactivity and increased iSMC differentiation in the TEBVs. These results show the ability of this iPSC-derived TEBV to reproduce key features of HGPS for drug screening.



Prof. Hon Fai Chan is an Assistant Professor at the Institute for Tissue Engineering and Regenerative Medicine and School of Biomedical Sciences at The Chinese University of Hong Kong (CUHK). He received his B.Eng. in 2010 from The University of Hong Kong. He then pursued his M.S. and Ph.D. degree at Duke University with the support of the Sir Edward Youde Memorial Fellowships for Overseas Studies. During his Ph.D. training, he focused on developing several microfluidic technologies to perform 3D spheroid culture of mesenchymal stem cells and hepatocytes, and investigated the effect of supplementing extracellular matrix cues on spheroid functions. After graduation in 2015, Hon Fai spent one year at Columbia University as a postdoctoral researcher. He performed highthroughput screening of synthetic genes for optimization of protein expression using microfluidic droplets. In 2016, Hon Fai joined Massachusetts Institute of Technology as a postdoctoral associate. There he conducted organ-on-a-chip research and develop biomechanics-guided folded hydrogel to recapitulate morphogenesis of mucosal folding which is observed in many hollow or tubular organs in human body.

## Staphylococcal Enterotoxin C2 alleviates ovariectomy-induced bone loss via modulating T cells in mice

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Staphylococcal Enterotoxin C2 (SEC2) is a kind of heat-stable enterotoxin that can stimulate T cells and induce various cytokines which suppress tumor cell growth. Intriguingly, as a potent modulator of T cells, SEC2 also exhibits remarkable effects on modulation of bone metabolism. Our previous study demonstrated that SEC2 expedited bone consolidation in distraction osteogenesis model, while fracture healing was also accelerated through local administration of SEC2 in rat. Based on the above findings, we further hypothesized that SEC2 may also retard osteoporosis development via its immune-regulatory effects. In this study, we use C57BL/6 mouse ovariectomized model to investigate the effect of SEC2 on osteoporosis development. We found that SEC2 treatment significantly alleviated the trabecular bone loss at distal femur after OVX surgery. Serum markers showed that SEC2 treatment could enhance bone formation dramatically in vivo, while bone resorption marker Trap-5b was not significantly influenced. However, the enhanced serum RANKL/OPG ratio 3 weeks after OVX surgery was reversed by SEC2 treatment, indicating SEC2 may potentially suppress the abnormal activation of bone resorption after OVX surgery. Furthermore, we repeated the SEC2 treatment in nude mice and found that the beneficial effect was absent, which determined the essential role of T cells in the enhancing effect of SEC2 on trabecular bone. In vitro coculture assay also showed that SEC2 could significantly promote osteogenesis and suppress osteoclastogenesis when lymphocytes were present. We further found that SEC2 treatment could enhance T regulatory cells percent both in vitro and in vivo. Whether this modulating effect is associated with the beneficial effect of SEC2 on trabecular bone still needs further investigation. Overall, our study demonstrated that SEC2 can alleviate trabecular bone loss in OVX model and may be a candidate for osteoporosis treatment.

### A KGN-containing Bilayer Scaffold for Osteochondral Defect Regeneration Based on digital light process(DLP)

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Knee joint injuries are common and difficult to self-repair. Because cartilage and bone are physically linked and have very different biological properties, it is challenging to fabricate a single scaffold that can structurally and biologically fulfill the requirements simultaneously for osteochondral defects regeneration. Here, We used gelatin methacrylate (GelMA) hydrogel to completely bioprint a bilayer scaffold with different structures via digital light process (DLP) technology in one step. The lower layer hydrogel has lotus-like holes to direct BMSCs cells migrate to upper space, while the upper layer hydrogel has both lotus- and radiation-like holes that can help chondrocytes migration and distribution. Additionally, in bioprinting groups, the counts of migration cells are seven folds more than those in column hydrogel without bioprinting in vitro. Besides, the upper layer hydrogel contains kartogenin (KGN), a small molecule that has been proved to accelerate chondrogenic differentiation of BMSCs in other studies. Meanwhile, the bilayer hydrogel showed good performance in osteochondral defect of rabbit, indicating our bilayer hydrogel can promote the regeneration of repaired osteochondral defect. Collectively, these results showed us the mechanical property can be tuned by changing the structure and size of hoes via DLP bioprinting. Additionally, compared to the blank group, our study illustrated that KGN-containing bilayer scaffold can significantly promote the regeneration of bone and cartilage at the same time. Bilayer scaffold fabricated by DLP bioprinting is an effective strategy for osteochodral regeneration and would be applied widely in the future for regeneration of soft-hard connections.

## The effect and underlying mechanism of blood on articular cartilage explored by High-throughput sequencing and Single-cell QPCR

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Intra-articular hemorrhage is a common clinical symptom that can be caused by trauma, surgery or coagulation disorder. It has been confirmed that blood induced joint damage (BIJD) can lead to joint degenerative disease. However, the molecular mechanism of BIJD is still unclear. This project intends to establish an in vivo and in vitro model to detect the changes of chondrocytes and cartilage tissues after blood exposure. Firstly, we proved that in vitro exposure to blood at a low concentration can affecting the normal physiological metabolism of chondrocytes. Then the RNAsequencing (RNA-seq) result illuminate the molecular mechanisms of BIJD. Here, we found the prolonged activation of PI3K-Akt signaling pathway and inhibition of ECM-receptor interaction were the greatest variation in chondrocytes subjected to blood treatment, which lead to a permanent disturbance in cartilage matrix turnover. Finally, we build a mouse knee joint hemorrhage model and the histological results show cartilage surface is rough and less collagen II content. Single cell QPCR result reveal the expression of Igf2, Col2a1, Acan, Clec3a, Col6a2, etc. downregulated significantly among differential genes obtained by RNA-seq after blood treatment in 3 weeks, these genes are closely related to the synthesis of cartilage matrix, suggesting that blood can cause long-term disturbance of cartilage matrix synthesis. This study explored the pathogenesis of BIJD in more depth and provided a new theoretical basis and treatment ideas for clinical treatment of BIJD.

### An injectable continuous stratified structurally and functionally biomimetic construct for enhancing osteochondral regeneration

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Osteochondral regeneration with the formation of hyaline cartilage and subchondral bone as well as the integration between the newly formed tissues with the host tissue still remains a great challenge. In this study, a construct containing an injectable continuous stratified scaffold and multiple cell systems was designed for enhancing osteochondral regeneration. Briefly, an injectable sodium alginate(SA)/bioglass (BG) composite hydrogel containing bone marrow stem cells (BMSCs) (SA/BG + BMSCs) was used for subchondral bone regeneration and an injectable thermosensitive SA/agarose (AG) composite hydrogel with co-culture of BMSCs and articular chondrocytes (ACs) (SA/AG + ACs/BMSCs) was applied for articular cartilage regeneration. The continuous SA phase and the stratified structure enable the scaffold to mimic the natural osteochondral structure. In addition, the SA/BG + BMSCs hydrogel could enhance the osteoblast differentiation of BMSCs by up- regulating their alkaline phosphatase and collagen I gene expressions, and the SA/AG + ACs/BMSCs hydrogel could promote the chondrocyte differentiation of BMSCs by upregulating their Acan and collagen II gene expressions, which indicated that this stratified scaffold could mimic the natural osteochondral function. Furthermore, after the stratified construct was injected into a rat osteochondral defect model, obvious neonatal articular cartilage tissues and subchondral bone tissues with regular surface and highly integration with normal tissues could be observed. This structural and functional biomimetic construct, together with its proper swelling ratio, could not only stimulate the hyaline cartilage and subchondral bone regeneration in an entire osteochondral unit but also promote the integration between the newly formed tissues and the host tissue.

#### TJmjd1a, A Novel Metabolism Regulator in Neural Stem Cells and Aging

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Brain aging is of utmost importance in higher animals and in human beings, especially because many neurodegenerative disorders including Parkinson's disease (PD) and Alzheimer's disease (AD) are closely associated with brain aging. A loss or decline of neural stem/progenitor cells (NSPCs), which are responsible for the maintenance of regenerative potential of the central nervous system (CNS) in adult vertebrate, has been implicated in the brain aging. Jmjd1a, a H3K9 demethylase, is involved in the maintenance of ESC self-renewal and pluripotency. We have previously revealed that Jmjd1a regulates MSC senescence and bone aging via promoting heterochromatin remodeling. The overall objective of this project is to gain novel insights into the role of Jmjd1a in NSPC function and adult neurogenesis during brain aging. We have found that during brain aging, Jmjd1a is dramatically downregulated in brain and NSPC population. Loss of Jmjd1a in mice leads to a reduction in NSPC along with an increase in glial cells, implying Jmjd1a's role in NSPC regulation. We also found that knocking down/ out Jmjd1a in NSPC in vitro promotes glial differentiation while suppressing neuronal differentiation and concurrently reduces NSC self-renewal and proliferation capacity. Through RNA-seq analysis we have identified several genes associated with metabolism regulation that are differentially regulated in Jmjd1a KO NSPCs. To understand whether the loss of Jmjd1a affects brain function, Jmjd1a WT and KO mice were subjected to Morris Water Maze and Novel Object Recognition tests. Jmjd1a KO mice demonstrated a deterioration in learning capability along with age. In all, our study indicates that the age -associated loss of Jmjd1a impacts NSC function and fate regulation by promoting glial and suppressing neuronal differentiation, potentially through the deregulation of metabolic regulatory genes, that subsequently lead to a loss in cognitive function in aged brains.

#### Establishment of Human Endometrium Organoid Based on 3D Bio-printing

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Irreversible endometrial injury caused by uterine curettage, myomectomy and surgical infection may result in scar formation, intrauterine adhesions (IUAs) and other pathological conditions, which can finally lead to infertility and abortion. Although many approaches have been used to treat these disease, high recurrence rates and endometrial thinning have limited therapeutic efficiency and the function of the endometrium can't be restored. Therefore, it is necessary to establish endometrial organoid to repair endometrium and promote endometrial regeneration. Moreover, emerging additive manufacturing techniques enable fabrication of living organs and organoids. In this study, human endometrium organoid with human umbilical vein endothelial cells (HUVECs), human endometrial stem cells (hEnSCs) and human endometrial epithelium cells (HEECs) will be fabricated by 3D bio-printing. And this engineered organoid becomes more close to the structure and function of normal endometrium. In structural aspect, the organoid has two layers, the upper layer is the epithelial layer and the lower layer is composed of stromal cells and HUVEC. What's more, in terms of function, the organoid will replicate the menstrual cycle under hormonal treatment *in vitro* and promote the regeneration of endometrium and vascularization and improved pregnancy outcomes when transplanted in vivo. Thus, the bio-printed human endometrium organoid with multiple cell types may be a practical solution for the treatment of severe endometrium damages and a powerful research model and drug screening tool.

## Functional characterization of Linc-p27 in skeletal muscle satellite cells and muscle regeneration

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Adult muscle stem cells, satellite cells (SCs), as one of most important cell populations in the muscle tissue, contribute to muscle growth, maintenance and regeneration. Normally located in the niche beneath the basal lamina of myofibers in a quiescent stage, they will quickly activate to undergo proliferative expansion and differentiate to myotubes which fuse with each other to form mature myofibers upon injury or exercise. Meanwhile, a portion of activated SCs will return to quiescent stage to replenish the SCs pool.

Here we identified a long non-coding RNA (lncRNA), *Linc-p27* which is induced in activated satellite cell (ASC) then downregulated in differentiated satellite cell (DSC). Functionally, *Linc-p27* knock out (KO) and knock in (KI) C2C12 myoblast cells showed significantly decreased proliferation due to arrest on  $G_0/G_1$  phase of cell cycle. In the BaCl<sub>2</sub> induced acute injury model, knockdown of *Linc-p27* by siRNA injection led to delayed muscle regeneration *in vivo*. Mechanistically, we conducted RNA-pull down followed with mass spectrometry to define the possible binding proteins with *Linc-p27*, which led to the identification of Dhx36, a DNA/RNA helicase to specifically unwind G-quadruplex (G4). Multiple assays demonstrated the specific direct interaction between Dhx36 and *Linc-p27*. Consistently, SC specific deletion of Dhx36 in mouse severally inhibited muscle regeneration in vivo. Furthermore, by overlapping rG4-seq and Dhx36 Cross-Linking Immunoprecipitation followed by sequencing (CLIP-seq) datasets, we found Anp32e is bound by Dhx36 at a rG4 site of its 5'UTR region and it promotes myoblast proliferation. We further showed *Linc-p27* or Dhx36 significantly enhanced the translation of *Anp32e* through unwind rG4 structure in 5' UTR of *Anp32e* to facilitate its translation and promotes myoblast proliferation.

## Linc-ROR promotes chondrogenesis differentiation of mesenchymal stem cells through activating SOX9 expression

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Long noncoding RNAs (lncRNAs) have gained widespread attention in recent years, which serve as important and powerful regulators of various biological activities and play critical roles in a variety of disease progression. Emerging evidences have shown that some lncRNAs play important regulatory roles in chondrogenesis differentiation of mesenchymal stem cell (MSCs), suggesting a potential therapeutic strategy for cartilage repair and osteoarthritis treatment. As a recently identified lncRNA, human linc-ROR was reported to mediate the reprogramming ability of differentiated cells into induced pluripotent stem cells (iPSCs) and human embryonic stem cells (ESCs) self-renewal. However, other functions of linc-ROR remain little known. In this study, linc-ROR was found to be upregulated during chondrogenesis of human bone marrow-derived MSCs. Ectopic expression of linc-ROR significantly accelerated MSC chondrogenesis differentiation. Using bioinformatic prediction and luciferase reporter assays, we demonstrated that linc-ROR functioned as a miRNA sponge for miR-138 and miR-145, both of which were negative regulators of chondrogenesis key factor SOX9. Further investigations revealed that both miR-138 and miR-145 could suppress MSC chondrogenesis activity while co-expression of linc-ROR revealed a rescuing effect. Taken together, linc-ROR modulated chondrogenesis differentiation by acting as a competing endogenous RNA (ceRNA), which may shed light on the functional characterization of lncRNAs in coordinating chondrogenesis.

#### The potential role of RSPO3 in oligodendrogenesis

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Oligodendrocytes play significant role in providing support and insulation to axons via myelination in the central nervous system (CNS). The malfunction of oligodendrogenesis or myelin loss results in neurological disorders, such as multiple sclerosis, leukodystrophies, etc. However, the molecular mechanisms underlying oligodendrogenesis and myelination in CNS development and diseases are still elusive. The R-spondin (RSPO) family of four proteins represents a new group of secreted factors that enhance β-catenin signaling. Like WNTs, RSPOs have important roles in development and act as powerful stem cell growth factors. In this study, we aim to investigate the role of R-Spondin3 (RSPO3) in Oligodendrogenesis. We found that the expression of RSPO3 increased along with postnatal development. RSPO3 was expressed mainly at hippocampus, subventricular zone, corpus callosum, striatum and cerebellum at postnatal stage (PN1-PN30) in mice. Of note, the expression of RSPO3 emerged at postnatal day 7 and peaked at postnatal day 30, overlaying with oligodendrocyte lineage markers, O4 and MBP. These results indicate a potential role of RSPO3 in oligodendrogenesis. In line with this, the *in vitro*differentiation assay of neural progenitor cells (NPC) showed that RSPO3 increased along with the oligodendrocyte differentiation. Moreover, addition of recombinant RSPO3 in NPC enhanced the oligodendrocyte differentiation whereas had no effect on neurons or glia. We also isolated primary OPC from newborn mice and rat and found that RSPO3 enhanced the proliferation and differentiation potentiation of the OPC, but had no effect on neurons or mesenchymal stem cells. This study will not only reveal previously undefined role of RSPO3 in oligodendrogenesis and brain development, but also provide important insights into the underlying mechanism and potential therapeutic target of demyelinating diseases.

# Bioreactor based human fetal mesenchymal stem cell secretome promote diabetic skin wound healing through vascularization

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Fetal tissue usually heals in a scar-less manner. Our study makes use of bioreactor expended human fetal mesenchymal stem cell (FMSC) to produce MSC secretome (HFS) in large scale. We prove the promoting effect of HFS encapsulated poly (lactic-co-glycolic acid) particle (HEP) particle on the healing of diabetic skin wound which is considered as a refractory defect in clinical.

FMSC is mixed with microcarrier and cultured under stirring within bioreactor for 14days. Alamar blue test shows that 50ng/mL HFS promote human fibroblast and keratinocyte viability (n=3, P<0.05). HFS also promote cell migration of two types of human cells, fibroblast, and keratinocyte, after treatment for 3days (n=3, P<0.05). Simultaneously, HFS prohibit FPCL contraction and promote keratinocyte differentiation in the OKC model after 7days treatment (n=3, P<0.05). Then HFS was encapsulated in PLGA particle by double emulation method. ELSA data shows that HFS contains PDGF-BB. The promoting effect has also been observed on the diabetic rat model (n=6, P<0.05).

In summary, HEP may slow release encapsulated HFS to promote skin defect healing on the diabetic rat model. PDGF-BB and lysosome are highly contained in the HFS. IHC and IF staining result shown that the HFS may enhance the healing speed of skin wound through promoting vascularization.

#### Cytosolic interactome of KDM3A and its implication in bone aging

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KDM3A is a crucial histone lysine demethylase which has been found to regulate numerous biological processes. Previous studies from other groups and our lab have found that KDM3A not only exists in the nucleus but also in the cytosol of multiple cell lines. However, the biological function of cytosolic KDM3A is largely unknown. In this study, we have found that kdm3a-/- mice exhibit osteoporosis phenotype in their femur and tibia confirmed by DEXA scan and micro CT. In addition, the isolated bone marrow-derived MSCs from kdm3a-/- mice display compromised cell proliferation, and differentiation capacities. In addition, kdm3a-/- MSCs are more susceptible to DNA damage. Subsequently, we verified the existence of KDM3A in multiple human primary cells and established cell lines and mapped its cytosolic interactome with Virotrap to decipher KDM3A's interacting proteins and possible involvement in MSCs' function. According to the proteomic analysis of the Virotrap data, the most enriched proteins are involved in metabolic PI3K/Akt/mTOR pathways. Altogether, these findings indicate that besides histone modification, non-chromatin-linked roles may underlie the regulatory role of KDM3A in MSC function and osteoporosis.

#### A novel 3D bio-printed cell-laden bilayer scaffolds for uterine regeneration

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Serious injury followed by dilation and curettage (D & C) often lead to uterine scar formation, which may result in infertility in reproductive age women. Tissue engineering has emerged as one of the promising approaches for uterus regeneration. Proper biomimetic-engineered scaffolds are crucial in allowing functional regeneration of uterine, which contains multilayer complex endometrium, myometrium, and serosa. This study demonstrated a 3D bio-printed, bi-layer, cell-laden scaffold for functional uterine regeneration. 3D bio-printed functional layer (endometrial stromal layer) and a basal layer (monolayer epithelium) were composited to build bi-layer biomimetic scaffold. We used two natural polymers, Sodium alginate and Hyaluronic acid, to form the bio-ink for printing. This new-type scaffold showed superior elastic mechanical properties (mechanical strength=191.5±14.98 MPa) and good biocompatibility. We then investigated the therapeutic effect of this novel scaffold on severe uterine injury (bulk full thickness uterine excision) of 41 female SD rats. Nighty days after implantation, rats which received 3D printed bi-layer scaffolds showed thicker endometrium regeneration than endometrium in rats receiving simple scaffolds or in spontaneous regeneration group (one-way ANOVA analysis, P < 0.001), it improved uterine endometrial and muscular regeneration, facilitated microvasculature regeneration. Moreover, rats receiving 3D scaffolds restored the ability of endometrium for embryo implantation and development, and showed higher pregnancy rates (x2 test, P < 0.001). These results indicated that this novel bi-layer cell-laden scaffold could be a promising strategy for human endometrium regeneration and provide perspective for other applications.

#### Influence of calcium phosphate nanoparticles on the hemopoietic system

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Calcium phosphate nanoparticles are widely developed and utilized in medical applications such as bone regeneration, drug loading, controlled drug releasing and targeted accumulation. However, the side effect of nanoparticles infiltration to the hemopoiesis is still unclear. In this study, we used the calcium phosphate polymer-induced liquid-precursor (CaP-PILP) to study the transcriptomic response of hemopoietic system to nanoparticles. The CaP-PILP with a cluster size of 20 nm, which is reported previously by our group, was cultured with hematopoietic stem cells *in vitro* and given an intrabone marrow injection / tail vein injection *in vivo*. The intracellular and whole body biodistribution of the nanoparticles were showed with the help of indocyanine green. Transcriptomic changes of the cells and the main organs such as bone marrow, spleen and liver were demonstrated by the RNA-seq. The blood cell numbers were reflected by the routine blood test and the immune cell subpopulations were enumerated as enrichment scores by xCell from RNA-seq data. This study showed the hemopoietic system response to the CaP-PILP at cell and transcriptional level, and further revealed the signal pathway under high risk. It also optimized a better way for nanoparticle-drug delivery which may help researchers in nanoparticle application in the future.

# Targeted pathological collagen delivery of control-released rapamycin to prevent heterotopic ossification

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The formation of heterotopic ossification (HO) in connective tissues, such as tendons and ligaments, severely damages tissue structure and worsens patients' symptoms. However, no prevention methods currently exist, because concrete pathogenesis of HO remains unclear. In this study, we found that without the activation of mTOR signaling, tendon stem/progenitor cells (TSPCs) would not undergo osteochondrogenic differentiation. Moreover, no newly-formed bone in tendon formed post-injury. As tendinopathy is a tendon's local lesion and mTOR possesses multiple functions in normal tendon cells, it is necessary to deliver rapamycin (RAPA) to the injured sites and avoid disturbing normal tendon. To achieve this, we developed a pathological collagen-oriented drug delivery system. Specifically, we use collagen hybridizing peptide (CHP) to anchor onto the surface of poly (lactic-co-glycolic acid) (PLGA) nanoparticles (CHP-PLGA-RAPA) to carry RAPA to the pathological tendon collagen. CHP-PLGA-RAPA nanoparticles exhibited excellent pathological collagen affinity, controlled-release ability, and bioactivity. CHP-PLGA nanoparticles could specifically bind to pathological tendon and almost completely prevent the progression of HO in tendon injury mice with the effect of RAPA modulating TSPCs' differentiation. Our study points to the mTOR signaling pathway as a viable therapeutic target for tendon HO, and CHP-PLGA could be applied in the treatment of tendon-related disease.

## High-throughput Screening Small Molecules for Stem Cells Phenotype Maintenance and Stepwise Tenogenic Induction

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Tendon stem/progenitor cells (TSPCs) are potential seed cells in tendon tissue engineering and regeneration, but cultured-expanded TSPCs are prone to lose their phenotype. Here, we used the SCX-GFP report system by visualization to conduct a high-throughput screening of 1104 small molecules from FDA approved drug library and 122 small molecules from bioactive libraries, and obtained candidate molecules for mTSPCs phenotypic maintenance. Then, we further verified eight positive small molecules by secondary screening. Furthermore, we performed combinational screening by removing the small molecules one by one, optimized the concentration of each molecule and obtained the most effective small molecule cocktail for phenotypic maintenance of mTSPCs. However, we found that the small molecule cocktail cannot promote proliferation while maintaining the phenotype of mTSPCs. So, in the meanwhile, we also screened and got small molecules which can promote stem cells proliferation by cell counting and CCK8. Finally, we developed an effective stepwise tenogenic induction strategy using small molecules to promote TSPCs proliferate first and then maintain their phenotype. Most importantly, the stepwise induced mTSPCs combined with hydrogel by 3D printing retained the ability to accelerate tendon regeneration in vivo. Thus, we developed the strategy of stepwise inducing TSPCs differentiation, and proved the feasibility and efficacy of the small molecule cocktail in the application of tendon repair.

### **3D Microcarriers as a Large-Scale Culture Platform for Human Tendon Stem/** progenitor Cell Expansion

#### <u>Hong Zhang</u>, Ri-chun Liu, Yang-wu Chen, Chen-qi Tang, Jia-yun Huang, Meng-yan Wang, Yuanhao Xie, Zi Yin, Ya-nan Du, Xiao Chen

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Tendon injuries are common musculoskeletal system disorders. About 30% of the clinical consultations related to the musculoskeletal pain are caused by tendon disorders, but the current treatment of tendon injury is not effective. Tendon tissue engineering is a promising treatment for tendon injury, and tendon stem/progenitor cells are ideal seed cells. Currently, 2D culture dishes or flasks are widely used for culturing human tendon stem/progenitor cells (hTSPCs); however, this method has many disadvantages, such as high material costs, the risk of contamination with repeated passaging, the small number and unstable quality of cells obtained, as well as the risk of cell phenotypic loss. Thus, 2D culture cannot meet the cell number and quality requirements needed for clinical cell therapy. Studies have shown that hTSPCs are more likely to maintain their tenogenic phenotype under 3D culture conditions. 3D microcarriers culture system can not only provide stable 3D culture environment for cells, but also have the advantages of easy to operate, reasonable price, no need for repeated trypsin digestion and passage, large-scale acquisition of cells, etc., and it has the potential to achieve high-efficiency expansion of hTSPCs in vitro. Therefore, this study explored a 3D microcarrier suitable for hTSPCs culture to achieve safe, tenogenic phenotypic maintenance and large-scale expansion of hTSPCs in vitro, providing the foundation for clinical application for hTSPCs.

## MicroRNA-132 directs human periodontal ligament-derived neural crest stem cell neural differentiation

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Purpose: Neurogenesis is the basis of stem cell tissue engineering and regenerative medicine for central nervous system (CNS) disorders. We have established differentiation protocols to direct human periodontal ligament-derived stem cells (PDLSCs) into neuronal lineage, and we recently isolated the neural crest subpopulation from PDLSCs, which are pluripotent in nature. Here, we report the neural differentiation potential of these periodontal ligament-derived neural crest stem cells (NCSCs) as well as its microRNA (miRNA) regulatory mechanism and function in NCSC neural differentiation.

Methods: NCSCs, treated with basic fibroblast growth factor and epidermal growth factor-based differentiation medium for 24 days, expressed neuronal and glial markers ( $\beta$ III-tubulin, neurofilament, NeuN, neuron-specific enolase, GFAP, and S100) and exhibited glutamate-induced calcium responses.

Results: The global miRNA expression profiling identified 60 upregulated and 19 downregulated human miRNAs after neural differentiation, and the gene ontology analysis of the miRNA target genes confirmed the neuronal differentiation-related biological functions. In addition, over expression of miR-132 in NCSCs promoted the expression of neuronal markers and downregulated ZEB2 protein expression. Conclusions: Our results suggested that the pluripotent NCSCs from human periodontal ligament can be directed into neural lineage, which demonstrate its potential in tissue engineering and regenerative medicine for CNS disorders.

# Utilizing Human iPSCs and CRISPR/Cas9 to Study Early Chondrogenesis in the context of SOX9 Haploinsufficiency

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SOX9, as a master regulatory gene in chondrocyte development, involves not only in early bone development, but also in differentiation of the 3 germ layers. Haploinsufficiency (HI) of SOX9 results in Campomelic Dysplasia (CD), which patients suffer from bent long bones and many of them die shortly after birth due to respiratory failure. Our study attempt to create a SOX9 HI human induced pluripotent stem cells (hiPSCs) model for studying early chondrogenesis in the context of SOX9 haploinsufficiency. For generation of our desired SOX9 HI model, CRISPR/Cas9 was used to generate a single nucleotide polymorphism (SNP) splice site mutation at the end of exon 2 in SOX9 in hiPSCs. The SNP mutation was validated by Sanger sequencing of PCR fragments and the SOX9 HI hiPSCs were differentiated to chondrocytes using a well-established 14-day protocol. Different experiments, such as RT-qPCR, immunofluorescence and Safranin O staining were performed on day 14. Our results showed that SOX9 HI chondrocytes have decreased expression of SOX9 in terms of mRNA level. Transcriptome analysis had identified about 1400 differentially expressed genes in both WT and HI phenotype and 3 pathways were enriched, including notch signaling, p53 and ribosomal pathways.

To conclude, SOX9 HI hiPSCs were successfully generated and being differentiated to chondrocytes and from the transcriptome analysis results, several pathways were being enriched in SOX9 HI chondrocytes. Our further research would be to inhibit these pathways one by one and try to rescue the SOX9 HI phenotype with different approaches.

### Dextran Sulfate: A Potentiator of Osteogenic Differentiation in Mesenchymal Stem Cell Cultures

#### Christy Wong Wing Tung, Marisa Assunção, Sebastian Beyer, Anna Blocki

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Traditional osteogenic differentiation of human mesenchymal stem cells (MSCs) is variable in culture, resulting in a heterogeneously committed cell population within a limited bone-like microenvironment. Often times, *in vitro* terminal and functional differentiation of MSCs is thus difficult to achieve in an efficient and timely manner. Hence, approaches that enhance osteogenic differentiation and amplify an osteo-specific microenvironment are needed.

Here we show that supplementation of dextran sulfate (DxS, 500 kDa) drastically increased osteogenic calcification in induced bone marrow MSC cultures, as revealed by Alizarin Red staining. Since hydroxyapatite (HA) is associated with extracellular matrix (ECM), we further investigated the role of DxS in ECM assembly and properties. We found that DxS, which is a negatively charged polyglucose macromolecule, aggregated and co-precipitated ECM components such as fibronectin and collagen I.

The co-presence of DxS within the ECM increased the roughness, as well as the stiffness of the deposited ECM. Of note, an increased substrate roughness and stiffness was shown to promote osteogenic differentiation.

We propose that the amplified cell-specific ECM deposition potentiated the positive feedback between the MSCs and their self-built microenvironment. This combination with increased roughness and stiffness augmented osteogenic differentiation of MSCs.

Hence, supplementation of DxS can advance osteogenic induction cultures by promoting maturation and accumulation of an osteogenic microenvironment.

## Lgr5-overexpressing mesenchymal stem cells augment fracture healing through regulation of Wnt/ERK signaling pathways and mitochondrial dynamics

#### Wei-ping Lin, Liang-liang Xu Wayne Yuk Wai Lee, Dong Sun, and Gang Li

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Fracture remains one of the most common traumatic conditions in orthopedic surgery. The use of mesenchymal stem cells (MSCs) to augment fracture repair is promising. Leucine-rich repeat-containing G protein-coupled receptor 5 (Lgr5), a transmembrane protein, has been identified as a novel adult stem cell marker in various organs and tissues. However, roles of Lgr5 in MSCs are not fully understood. In this study, we investigated cellular functions of Lgr5 in MSCs and its potential implications in treating fracture. Lgr5-overexpressing MSCs (MSC<sup>Lgr5</sup>) were established in murine SV40-promoter-drivenluciferase-reporter MSC cell line through virus transfection. Results of qRT-PCR and Western blot analysis confirmed the increased expression of Lgr5 in MSC<sup>Lgr5</sup>. MSC<sup>Lgr5</sup> exhibited increased osteogenic capacity, which may result from elevated expression of  $\beta$ -catenin and phosphorylated ERK1/2 within the nuclei region of cells. In contrast, inhibition of Lgr5 expression decreased the osteogenic differentiation ability of MSCs, accompanied with increased mitochondrial fragmentation and reduced expression of  $\beta$ -catenin. Local transplantation of MSC<sup>Lgr5</sup> at fracture sites accelerated fracture healing via enhanced osteogenesis and angiogenesis. MSC<sup>Lgr5</sup> stimulated tube formation capacity of HUVEC in Matrigel coculture system in vitro significantly. Taken together, Lgr5 is implicated in the cellular processes of osteogenic differentiation of MSCs through regulation of Wnt/ERK signaling pathways and mitochondrial dynamics in fusion and fission. Inhibition of Lgr5 expression induced increased mitochondrial fragmentation and decreased osteogenic differentiation capacity. MSC<sup>Lgr5</sup> exhibited enhanced therapeutic efficacy for fracture healing, which may serve as a superior cell source for bone tissue repair.

## Psoralen prevents bone loss in ovariectomized mice through targeting NFATc1mediated osteoclastogenesis

#### Yan-yan WANG, Feng-jie ZHANG, Wing Pui TSANG, Chao WAN

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Osteoporosis is the most common metabolic bone disease characterized by a decrease in bone mass and deterioration in bone microarchitecture, leading to bone fragility and high risk of fractures. Discovery of novel therapies remains a significant clinical demand. In recent years, attention is paid to traditional Chinese medicine (TCM) based therapies for osteoporosis. Psoralen (PS), a coumarin derivative compound extracted from *Psoralea croylifolia* L., a widely prescribed herb in TCM formulas, is shown to possess osteoprotective effect. However, the underlying pharmacological mechanisms of PS on regulating bone mass remain unclear. Here, we performed systemic *in vitro* and in *vivo* analyses to examine the cellular and molecular mechanisms of PS on osteoclast function as well as its therapeutic efficacy in ovariectomized (OVX) mice. Our data showed that PS inhibited bone marrow mononuclear cells (BMMNCs) derived osteoclast formation indicated by tartrate-resistant acid phosphatase (TRAP) staining without affecting cell viability. Meanwhile, PS interfered F-actin ring formation and suppressed bone resorption. PS attenuated the expression of osteoclast marker genes including nuclear factor of activated T-cells cytoplasmic1(NFATc1), TRAP, calcitonin receptor, cathepsin K, carbonic anhydrase

II, MMP9 and Fra-2. Mechanistically, PS suppressed RANKL-induced activation of Akt and the levels of transcription factors controlling osteoclast differentiation such as c-Fos, c-Jun and NFATc1. In addition, intraperitoneal delivery of PS prevented bone loss in OVX mice accompanied by decreased osteoclast numbers and the serum level of TRACP5b. Our results suggest that PS may serve as a potential agent for treatment of osteoporosis through targeting NFATc1 mediated osteoclastogenesis.

#### The role of Jmjd1a in neural stem/progenitor cells and adult neurogenesis

#### Lin Gao

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The mammalian hippocampus displays remarkable capacity for neurogenesis throughout life. Newborn neurons, generated by the neural stem/progenitor cells (NSPCs), are important for cognitive functions and mood control. During aging, deterioration of NSPCs leads to compromised neurogenesis and age-related cognitive decline and psychiatric disorders.

Thus, adult hippocampal neurogenesis is of paramount importance since targeting it could be a novel therapeutic strategy against these disorders. Jmjd1a is a histone demethylase that demethylates mono and dimethyl lysine 9 of histone H3. We have demonstrated that deficiency of Jmjd1a impairs the self-renewal capacity of NSPCs and promotes differentiation in vitro. Loss of Jmjd1a in mice leads to a marked reduction of NSPC pool and neuron in the hippocampus of new born and young adult mice. We have also observed that loss of Jmjd1a leads to downregulation of Wnt / $\beta$ -catenin pathway. Given that recent study showed that Wnt signalling is a principal regulator in human adult hippocampal function, we hypothesize that Jmjd1a regulates function of neural stem/progenitor cells and therefore affects adult neurogenesis and homeostasis of the brain via its interaction with the Wnt / $\beta$ -catenin pathway. In this project, we aim to conduct in-depth investigations on the role of Jmjd1a in NSPCs and adult neurogenesis, but also provide important insights into the epigenetic regulatory mechanisms underlying brain aging. In addition, understanding the regulatory mechanisms of neural stem cells and neurogenesis with age will provide important strategies for re-activating neural stem cells to slow down brain aging and promote brain damage repair.

## **Day 1 (Nov 11, 2019)** 1/F Auditorium, Main Clinical Block and Trauma Centre Prince of Wales Hospital, Shatin, Hong Kong

09:00-09:40	Welcome addresses, history of CUHK SCRM meeting, SMART and iTERM program and photo taken	Prof. Rocky Tuan Prof. Patrick Yung Prof. Gang Li
	Session 1: Biomaterials in Regeneration	Moderator: Prof. Ling Qin/ Prof. Raymond Tong
09:40-10:10	Biomimetic materials controlling cellular activity	<b>Prof. Alan Rowan</b> University of Queensland, Australia
10:10-10:40	CaP Micro-/nano-biomimetic scaffolds induce regeneration of interface tissues	<b>Prof. Sheng-min Zhang</b> Huazhong University of Science and Technology, China
10:10-11:05	Injectable bioactive materials for bone regeneration	<b>Prof. Yu-lin Li</b> East China University of Science and Technology, China
11:05-11:30	Tea Break and poster	
	Session 2: New discoveries in musculoskeletal system	Moderator: Prof Gang Li/ Prof. Dong-qing Cai
11:30-11:55	Lineage divergence of synovial joint progenitor cells: Implication to tissue repair	<b>Prof. Danny Chan</b> University of Hong Kong
11:55-12:20	GSDM protein and immunity	<b>Prof. Xiang Gao</b> Nanjing University, China
12:20-12:45	LIM domain proteins Pinch1/2 regulate bone homeostasis	<b>Prof. Guo-zhi Xiao</b> Southern University of Sciences and Technology, China
12:45-13:10	Hippo signaling and skeletal diseases	<b>Prof. Kingston Mak</b> Guangdong Key Laboratory for Regenerative Medicne, China
13:10-13:30	Photocrosslinkable materials for bone regeneration	<b>Prof. Xin Zhao</b> Hong Kong Polytechnic University

## Program Rundown

	Session 3: Stem Cells Biology	Moderator: Prof. Kingston Mak/Prof. Cynthia Jiang
14:30-14:55	Stem cell spheres for therapeutic applications	<b>Prof. Ren-He Xu</b> University of Macau
14:55-15:20	Molecular regulation of muscle stem cell quiescence exit	<b>Prof. Tom H. Cheung</b> Hong Kong University of Science and Technology
15:20-15:45	Adipose-derived stem cell application in reconstructive surgery and musculoskeletal disorder	<b>Prof. Nattawat Onlamoon</b> Mahidol University, Thailand
15:45-16:10	Neuronal intrinsic inhibitors regulating axon regeneration	<b>Prof. Kai Liu</b> Hong Kong University of Science and Technology
16:10-16:35	FoxO3 protects against the paraquat- induced heart injury	<b>Prof. Xu-feng Qi</b> Jianan University, China
16:35-16:55	Tea Break	
	Session 4: Clinical and Translational Research	Moderator: Prof. Louis Cheung/Prof. Samuel Ling
16:55-17:20	Fracture healing and bone Rregeneration: where are we?	<b>Dr. Hua-zhu David Ke</b> Angitia BioPharmaceuticals, China
17:20-17:45	Clinical trial of cartilage defects and osteoarthritis treatment using bone marrow mesenchymal stem cells and infrapatellar fat pad mesenchymal stem cells	<b>Prof. Chih-Hung Chang</b> Far Eastern Memorial Hospital, Taiwan
17:45-18:10	Biological therapies for articular cartilage repair: from basic research to clinical outcome	<b>Dr. Pan Pan Chong</b> University of Malaya
18:10-18:35	The synergistic promoting effect on osteoarthritis chondrocytes regeneration displayed by combined application of both AAV-P65shRNA and AAV-BMP4	<b>Prof. Guang-heng Li</b> Shenzhen 2 <sup>nd</sup> People's Hospital, China
18:35-19:00	Discussion and Remarks	Prof. Gang Li, Prof. Patrick Yung and all
19:00-21:00	Invited Speakers, Guests and Faculty Members Dinner (by invitation)	Bus transport to dinner venue (bus leaves at 18:40 from the meeting venue to the restaurant)

**Day 2 (Nov 12, 2019)** Auditorium, 1/F Main Clinical Block and Trauma Centre Prince of Wales Hospital, Shatin, Hong Kong

	Session 5: Stem Cell Biology 2	Moderator: Prof. Gang Li/ Prof. Anna Blocki
09:00-09:25	<ul><li>Epigenetic and functional</li><li>characterization of histone demethylases</li><li>KDM3A and KDM4C in MSC</li><li>senescence and bone aging</li></ul>	<b>Prof. Cynthia Jiang</b> Chinese University of Hong Kong
09:25-09:50	KIAA1199, a secreted factor of stromal stem cells, promotes bone marrow adipocyte differentiation and inhibits bone densit	<b>Prof. Li Chen</b> University of Southern Denmark
09:50-10:15	Centrosome biology and regenerative potential in striated muscle cells	<b>Prof. David C. Zebrowski</b> Chinese University of Hong Kong
10:15-10:40	Mitochondria-rich human pluripotent stem cell derived-cardiomyocytes with advanced metabolic properties uniquely recapitulate disease phenotype and drug responses	<b>Prof. Ellen Ngar Yun Poon</b> Chinese University of Hong Kong
10:40-11:00	Tea Break and poster	
	Session 6: Hong Kong Cell Biology Society Section	Moderator: Prof Hua-ting Wang/Prof. Bo Gao
11:00-11:25		
11:00-11:25 11:25-11:50	Society Section Two critical checkpoints during early	Wang/Prof. Bo Gao Prof. Zhen-guo Wu Hong Kong University of
	Society SectionTwo critical checkpoints during early activation of adult muscle satellite cellsGenomics technologies for cell	Wang/Prof. Bo Gao Prof. Zhen-guo Wu Hong Kong University of Science and Technology Prof. Alan S.L. Wong
11:25-11:50	Society SectionTwo critical checkpoints during early activation of adult muscle satellite cellsGenomics technologies for cell engineeringTRPV1 channels regulate the electrophysiology of embryonic stem	Wang/Prof. Bo GaoProf. Zhen-guo WuHong Kong University ofScience and TechnologyProf. Alan S.L. WongUniversity of Hong KongProf. Suk Ying TsangChinese University of Hong
11:25-11:50 11:50-12:15	Society SectionTwo critical checkpoints during early activation of adult muscle satellite cellsGenomics technologies for cell engineeringTRPV1 channels regulate the electrophysiology of embryonic stem cells-derived cardiomyocytesLong noncoding RNA SAM promotes myoblast proliferation and skeletal muscle regeneration through stabilizing Sugt1 and facilitating kinetochore	Wang/Prof. Bo GaoProf. Zhen-guo WuHong Kong University ofScience and TechnologyProf. Alan S.L. WongUniversity of Hong KongProf. Suk Ying TsangChinese University of HongKongProf. Hua-ting WangChinese University of Hong

## Program Rundown

	Session 7: Postgraduate Students and Young Researcher Section 1	Moderator: Moderator: Prof. Wayne Lee/Prof. Simon Chow
14:20-14:35	Staphylococcal enterotoxin C2 alleviates ovariectomy-induced bone loss via modulating T cells in mice	Hai-xing Wang CUHK
14:35-14:50	A KGN-containing bilayer scaffold for osteochondral defect regeneration based on digital light process (DLP)	<b>Yi-wei Zou</b> Zhejiang University of Medicine
14:50-15:05	The effect and underlying mechanism of blood on articular cartilage explored by highthroughput sequencing and Single- cell QPCR	<b>Guo Ye</b> Zhejiang Provincial Key Laboratory of TERM
15:05-15:20	An injectable continuous stratified structurally and functionally biomimetic construct for enhancing osteochondral regeneration	<b>Yan-lun Zhu</b> CUHK
15:20-15:35	Jmjd1a, a novel metabolism regulator in neural stem cells and aging	Kin Pong U CUHK
15:35-15:50	Establishment of human endometrium organoid based on 3D bio-printing	Nan-fang Nie Zhejiang University
15:50-16:15	Tea Break	
	Session 8: Postgraduate Students and Young Researchers Section 2	Moderator: Prof. Dick Chow/ Prof. Jerry Xu
16:15-16:30	Functional characterization of Linc-p27 in skeletal muscle satellite cells and muscle regeneration	Guang Xue CUHK
16:30-16:45	Linc-ROR promotes chondrogenesis differentiation of mesenchymal stem cells through activating SOX9	Lu Feng CUHK
16:45-17:00	The potential role of RSPO3 in oligodendrogenesis	Lin-jia Cheng CUHK
17:00-17:15	Bioreactor based human fetal mesenchymal stem cell secretome promote diabetic skin wound healing through vascularization	<b>Bin Wang</b> CUHK
17:15-17:30	Cytosolic interactome of KDM3A and its implication in bone aging	Shao-long Xue CUHK
17:30-17:45	A novel 3D bio-printed cell-laden bilayer scaffolds for uterine regeneration	<b>Yan-shan Liu</b> CUHK
17:45-18:00	Award ceremony for best oral and poster awards for postgraduate students and young researchers	Prof. Gang Li/ Prof. Wayne Lee
18:00-19:00	Meeting Adjourns	Prof. Gang Li
19:00-21:00	Invited Speakers, Guests and Faculty Members Dinner (by invitation)	Bus transport to hotel (bus leaves at 19:00 )

## Special Thanks To:







## **Transportation**

9<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine (SCRM) 1<sup>st</sup> International Chinese Musculoskeletal Research Society (ICMRS) Stem Cells and Regenerative Biology Symposium Joint Hong Kong Society for Cell Biology Symposium

**Location (Site):** 

Auditorium, 1/F, Prince of Wales Hospital 30-32 Ngan Shing St. Shatin, New Territories, Hong Kong

香港新界沙田銀城街30-32號威爾斯親王醫院

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