STEM CELLS AND TISSUE REGENERATION

(Innovative Orthopaedic Biomaterial and Drug Translational Research)

Principal Investigator

Professor Ling Qin

Team

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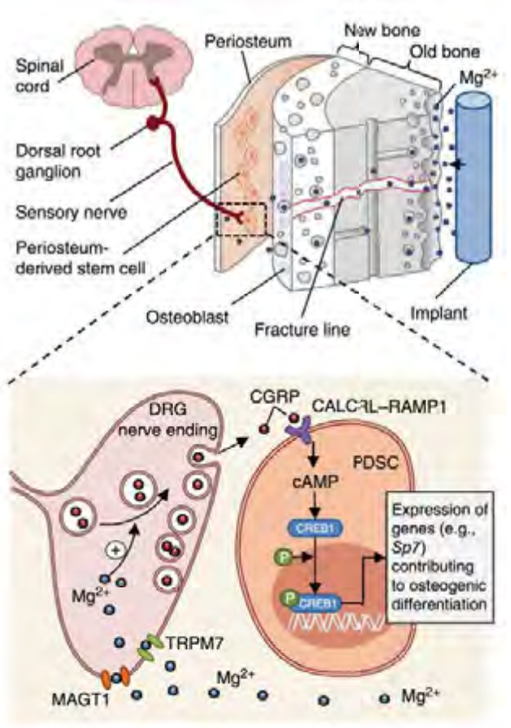
Research Progress Summary

The elderly population in Hong Kong will reach 26.4% by 2036 and will keep increasing. Ageing is closely associated with an increase of occurrences of osteoporotic fracture, osteoarthritis, osteonecrosis and bone cancer. These severe musculoskeletal conditions and their associated morbidities and mortalities impose huge socioeconomic and healthcare burden to patients, their families and the society. This leads to a high demand of new surgical interventions for orthopaedic surgeries, including fracture fixation and joint replacement that require various types of bone grafts and implants. The current global market for orthopaedic implants worth approximately US$ 46.5 billion. The World Health Organization (WHO) announced year 2000 to 2010 as the Bone Joint Decade and has subsequently extended it to 2020. This implies that musculoskeletal diseases are a big challenge for our modern yet ageing society. Therefore, there is an urgent need for further development and improvement of orthopaedic implants to accelerate musculoskeletal regeneration.

The research team led by Professor Ling Qin focuses on the research and development of innovative orthopaedic implants and drugs for the treatment of skeletal disorders, injuries with limited healing potential including patients with impaired healing capacity, large bone defects and healing at different tissue types such as the bone-tendon / bone-cartilage interface. The team has been developing innovative biomedical and tissue engineering products, clinical indication-orientated treatment regimens and protocols that utilise stem cells, bioactive and biodegradable materials, endogenous and exogenous growth factors, and external biophysical stimuli to enhance musculoskeletal tissue regeneration. The goal of the team's research is to facilitate not only anatomical but more importantly the functional restoration to achieve early rehabilitation and reduce disease associated morbidity and mortality.

Recently, the development of biodegradable orthopaedic implants using Magnesium (Mg) is a major focus of the team. Mg has properties similar to that of cortical bone and can be degraded in the human body with no adverse reactions. The comparable material properties between Mg and bone limits the shielding effect that is often generated by conventional implant materials, such as stainless steel and titanium. These implants with high stiffness could weaken the implanted bone. Furthermore, Mg induces bone formation and enhances osteogenesis in fracture healing. The team has identified that Mg-induced osteogenesis has a neuronal origin and is related to the expression of Calcitonin gene-related peptide (CGRP) in the dorsal root ganglion (Zhang Y et al., *Nat Med.* 2016; 22(10): 1160-9.).



Zhang Y et al., *Nat Med.* 2016; 22(10):1160-9.

Schematic diagram showing diffusion of implant-derived Mg^{2+} across the bone toward the periosteum that is innervated by DRG sensory neurons and enriched with PDSCs undergoing osteogenic differentiation into new bone (top). Inset (shown enlarged at bottom), the released Mg^{2+} enters DRG neurons via Mg^{2+} transporters or channels (i.e., MAGT1 and TRPM7) and promotes CGRP-vesicles accumulation and exocytosis. The DRG-released CGRP, in turn, activates the CGRP receptor (consisting of CALCRL and RAMP1) in PDSCs, which triggers phosphorylation of CREB1 via cAMP and promotes the expression of genes contributing to osteogenic differentiation.

Recognitions

Awards and Fellowships

Member's Full Name	Details
Ling Qin, Dick Chow, Jiali Wang	Gold medal with congratulations of jury by The 44th edition of the International Exhibition of Inventions of Geneva (April 2016)
Li Tian, Jiali Wang, Jiankun Xu, Bing Chen, Le Huang	Best Paper Recognition Awards by 2016 International Combined Meeting of Orthopaedic Research Societies (ICORS) (September 2016)
Wenxue Tong	Best Poster Awards by 2016 International Combined Meeting of Orthopaedic Research Societies (ICORS) (September 2016)
Wing Ho Chau, Jiankun Xu, Li Tian, Jiali Wang	Bronze Award in the BES-SEC Students' Design Competition at the 16th International Conference on Biomedical Engineering by The Biomedical Engineering Society (Singapore) and The Society of Engineers for the Community (December 2016)

Grants and Consultancy

Full Name of PI	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ling Qin	Joint R&D of Biometals as Orthopaedic Implants	Research Grants Council - Collaborative Research Fund	01/03/2015	28/02/2018	6,190,000
Ling Qin	Magnesium as a Promising Biodegradable Metal for Fixation of Bone Fracture	Chinese Academy of Sciences - Croucher Funding Scheme for Joint Laboratories	01/07/2014	30/06/2017	1,116,600
Ling Qin	A Novel Bioactive and Degradable Magnesium Screw with Polymer Coating Developed for Osteoporotic Fracture Fixation	Innovation and Technology Fund - Innovation and Technology Support Programme	01/09/2014	29/02/2016	1,043,400
Ling Qin	Design and Biological Response of Biodegradable Mg-Sr-Zn Alloy for Ligament / tendon-bone Reconstruction	National Natural Science Foundation of China - Research Grants Council Joint Research Scheme	01/01/2014	31/12/2017	750,000
Ling Qin	An Innovative Intramedullary Nail Containing Biodegradable Osteogenic Magnesium (Mg) Designed for Fracture Repair Enhancement-From Mechanisms to Translation	Research Grants Council - General Research Fund	01/01/2015	31/12/2017	647,399

Full Name of PI	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK$)
Ling Qin	Volumetric Bone Mineral Density and Bone Microarchitecture: A New Population-based Reference Study with High Resolution peripheral Quantitative Computer Tomography	Food and Health Bureau - Health and Medical Research Fund	01/03/2015	28/02/2017	996,216
Ling Qin	R&D of a Novel Bone Targeting Delivery System Carrying Bone-forming Phytomolecule Icaritin for Prevention of Osteonecrosis	Food and Health Bureau - Health and Medical Research Fund	01/04/2015	31/03/2017	997,540
Ling Qin	An Innovative Bio-intramedullary Nail with Osteogenic Mg-ions for Accelerating Bone Defect Repair – A Proof-of-Concept Study	Research Grants Council - General Research Fund	01/01/2017	31/12/2019	929,880

Publications

A. Journal Papers

1. Zhang Y, Xu J, Ruan YC, Yu MK, O'Laughlin M, Wise H, Chen D, Tian L, Shi D, Wang J, Chen S, Feng JQ, Chow DH, Xie X, Zheng L, Huang L, Huang S, Leung K, Lu N, Zhao L, Li H, Zhao D, Guo X, Chan K, Witte F, Chan HC, Zheng Y, Qin L. Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats. *Nature Medicine*. 2016; 22(10):1160-9.
2. Zheng NY, Tang N, Qin L. Atypical femoral fractures and current management. *Journal of Orthopaedic Translation*. 2016; 7:7-22.

B. Book Chapters

1. 許建坤、張翼峰、秦嶺。可降解金屬的研究方法。頁36-71。可降解金屬。鄭玉峰（主編）、秦嶺、楊柯（副主編）。科學出版社，北京，2016（ISBN: 9787030503947）。
2. 許建坤、張翼峰、秦嶺。可降解金屬的生理學作用——鎂與骨組織、元素Fe。頁72-84。可降解金屬。鄭玉峰（主編）、秦嶺、楊柯（副主編）。科學出版社，北京，2016（ISBN: 9787030503947）。
3. 王佳力、楊智均、秦嶺。鎂營養添加劑與相關疾病的防治與治療。頁343-347。可降解金屬。鄭玉峰（主編）、秦嶺、楊柯（副主編）。科學出版社，北京，2016（ISBN: 9787030503947）。
4. 秦嶺。含可降解鎂金屬粉末的多孔活性複合骨修復支架材料的設計與評價。頁349-369。可降解金屬。鄭玉峰（主編）、秦嶺、楊柯（副主編）。科學出版社，北京，2016（ISBN: 9787030503947）。

C. Conference Papers

1. Xu JK, Zhang YF, Wang JL, Zheng YF, Qin L. Linking CGRP and Periosteum-derived stem cells (PDSCs) to Magnesium-improved fracture healing in rats. In: *8th International Conference on Osteoporosis and Bone Research*; Chongqing, China; 2016 Oct 19-22.
2. Xu JK, Zhang YF, Wang JL, Zheng YF, Qin L. Unique role of Periosteum in Magnesium-augmented healing of long-bone fracture. In: *17th International Union of Materials Research Societies (IUMRS) International Conference in Asia*; Qing Dao, China; 2016 Oct 20-24.
3. Zheng LZ, Wang XL, Wang JL, Qin L. Establishment of a cost-effective steroid associated osteonecrosis in rats. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
4. Chow DH, Zheng LZ, Tian L, Ho KS, Qin L, Guo X. Application of ultrasound shortened the decalcification duration of human cortical bone sample. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
5. Tian L, Sheng YF, Chow DH, Huang L, Wu C, Ngai T, Tang N, Leung KS, Qin L. A novel bioactive and degradable magnesium screw with polymer coating developed for osteoporotic fracture fixation. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
6. Wang J-L, Xu JK, Yung PS, Chan KM, Qin L. Biodegradable magnesium interference screws accelerate mineralization of fibrous tissue at the tendon–bone insertion in anterior cruciate ligament reconstruction model of rabbit. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
7. Li H, Xie X, Zheng Y, Qin L. Zn-based biodegradable alloys in orthopaedics. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
8. Tong W, Mak KK, Qin L. Introducing Wnt16 attenuates the severity of osteoarthritis. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.
9. Chau WH, Cheng YS, Mak FT, Cheung KS, Qin L, Ng BKW. A unique multi-planar external fixator developed for hip distraction. In: *1st International Combined Meeting of Orthopaedic Research Societies*; Xian, China; 2016 Sep 21-25.