

## 5. Stem Cells and Tissue Regeneration Research (Part I: Adult Stem Cell Biology and Applications)

**PI:** Gang Li (Department of Orthopaedics and Traumatology)

**Team:** Dr. Wayne Lee (RAP); Dr. Jinfang Zhang (RAP); Dr. Zi Yin (Postdoc); Dr. Xu Liangliang (Research Associate); Dr. Jia Guo (RA); Ms. Liu Yang (PhD student); Mr. Lin Sien (PhD student); Mr. Cheng Yuanfeng (PhD student); Mr. Wu Tainyi (PhD student); Mr. Sun Yixin (PhD student); Mr. Wang Bin (PhD student).

**Non-technical Summary** ([in layman language, i.e. a short paragraph of less than 100 words in both English and Chinese characters](#)):

English version (less than 100 words):

The main research interests of this team are to investigate the use of specific tissue-derived stem cells for musculoskeletal tissue engineering. The team has published 9 research papers and generated over HK\$3.0 M new research grants in 2014. Prof. Li has been awarded a SH Ho Visiting Professorship to visit Stanford University in April 2014. Prof. Li is the recipient of the 1<sup>st</sup> Prize of Natural Science award 2014, Research Awards of High Education Institutions, Ministry of Education, PRC, with a project: “Engineering the vascularized and neurologized bone and their applications in bone regeneration”. Prof. Li has also successfully organized the 4<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in Hong Kong, 17–18 November 2014, with more than 30 overseas invited speakers including Prof. Shinya Yamanaka, Nobel Laureate of 2012 Medicine and Physiology and over 300 attendants; the symposium received overwhelmingly good feedbacks.

Chinese version (less than 100 words):

李剛教授實驗室的主要研究興趣是利用特殊組織來源的間充質幹細胞進行骨骼肌肉系統的組織工程學的科研工作。本研究組在 2014 年共發表 9 篇研究論文並獲得了超過三百萬港幣的新的研究經費。李教授于 2014 年 4 月獲得何善恒訪問教授基金支持訪問美國實體法大學。李教授等的課題“血管神經化組織工程骨構建及其成骨相關機制研究”榮 2014 年中華人民共和國教育部高校科學研究優秀成果獎，自然科學獎(1 等獎)。李教授與 2014 年 11 月 17-18 日在香港中文大學威爾士醫院成功主辦了第四屆香港中文大學幹細胞與再生醫學國際研討會，共有 30 多位海外嘉賓，包括 2012 年諾貝爾醫學何生理學獎得主-山中伸彌教授和 300 多人參加，大會受到一致的好評。

**Research Progress Summary:**

In 2014, the research team has 13 members (2 RAPs; 1 Postdoc RA, 1 Research Associate, 1 RA, 8 PhD students) with the following research projects firmly carried out: (1) Circulating stem cells in diseases and regeneration; their recruitment and homing potentials and underlying biological mechanisms. 循环幹細胞在疾病和組織再生中的作用；他們的調動和募集的生物學機理。 (2) Tendon, cartilage and bone tissue engineering research and new technologies development. 肌腱、軟骨、骨組織工程新技術的研發。 (3) Industry contract research work for new technologies development and developments of preclinical disease animal models. 與公司合作利用前臨床疾病動物模型開發新的治療方法。 These projects all progress as planned, with 9 papers have been published from the research work and over HK\$3.0 Million research grants have been secured by this PI in 2014. Prof. Li has been awarded a SH Ho Visiting Professorship to visit Stanford University in April 2014. Prof. Li is the recipient of the 1<sup>st</sup> Prize of Natural Science award 2014, Research Awards of High Education Institutions, Ministry of Education, PRC, with a project: “Engineering the vascularized and neurologized bone and their applications in bone regeneration”. Prof. Li has also successfully organized the 4<sup>th</sup> CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in Hong Kong, 17–18 November 2014, with more than 30 overseas invited speakers including Prof. Shinya Yamanaka, Nobel Laureate of 2012 Medicine and Physiology and over 300 attendants; the symposium received overwhelmingly good feedbacks. The PI has been invited to give keynote speeches and lectures at various national and international conferences and meetings for 10 times in 2014. The PI also engaged in knowledge transfer and provided advice/consultation service for Hong Kong Science Park, local and international healthcare related industries, etc. The PI also served as chief editor for one book; associated editor for 2 other books in the field of orthopedic surgery and regenerative medicine. The PI has contributed to the CUHK Shenzhen Research Institute serving as a deputy director of the CUHK-ACC Joint Laboratory of Space Medicine and Health Maintenance, and supervised the setup of the research laboratories in SZRI.

### Recognitions:

Awards and Fellowships (Please provide relevant document, e.g. copy of notification letter)

Member's Name	Details
Gang Li	1 <sup>st</sup> Prize of Natural Science award 2014, Research Awards of High Education Institutions, Ministry of Education, PRC. Project: “Engineering the vascularized and neurologized bone and their applications in bone regeneration”.
Gang Li	CUHK the International Partnerships Development Programme Award, to visit University of Oxford (December 2104)
Gang Li	SH Ho Visiting Professorship to visit Stanford University, USA (April 2014)
Gang Li	Visiting Professor, Guang Dong Medical College, Dongguan, China.
Gang Li	Visiting Professor, Key Laboratory of Cell Biology, Ministry of Education of PRC, China Medical University, Shenyang, China.
Gang Li	Member of Member of Advisory Board, Shanghai Key Laboratory of Orthopaedic Implant, Shanghai Jiaotong University, China.
Gang Li	Visiting Professor, Xijing Orthopaedic Hospital, The Fourth Military Medical University, Xian, China.
Gang Li	Visiting Professor, Department of Orthopaedic Surgery, 1st Affiliated

	Hospital, Shuzhou University Medical School, Shuzhou, China.
Gang Li	Visiting Professor, South Eastern University Medical School, Nanjing, China.
Gang Li	Member of Editorial Board, Calcified Tissue International
Gang Li	Associate Editor, Journal of Orthopaedic Translation

**Grants and Consultancy** (Please provide relevant document, e.g. copy of notification letter)

Name of PI	Project Title	Funding Source	Grant Reference	Start/End dates (dd/mm/yy)	Amount (HK\$)
Gang Li	Promote fracture healing by administration of allogenic mesenchymal stem cells (MSCs)	Research Grant Council, Hong Kong Government	CUHK 470813	01/01/2014 -31/12/2016	\$779,429
Gang Li	SOX11 调控骨髓间充质干细胞分化与迁移的研究及其在骨/软骨再生中的应用	国家自然科学基金	81371946	01/01/2014 31/12/2017	RMB700,000
Gang Li	系统注射同种异体骨髓间充质干细胞促进骨折愈合的研究	深圳市科技创新委员会	JCYJ201304 01171935811	01/10/2013 -31/09/2015	RMB150,000
Gang Li	Does the growth factor and mechanical influence tenocyte differentiation through miRNAs?	Lui Che Woo Institute of Innovation Medicine, SMART Program Seeding fund	CUHK 8303207	01/09/2013 -31/08/2015	\$250,000
Gang Li	Phase I clinical trial of autologous bone marrow derived mesenchymal stem cells intra-articular Injection for the treatment of carpal osteoarthritis	Lui Che Woo Institute of Innovation Medicine, SMART Program Seeding fund	CUHK 8303214	01/09/2013 -31/08/2015	\$250,000
Gang Li	Study the effects of Super-antigens on stem cells functions and their applications	Shenyang Xiehe Pharma-therapeutical Company, China	CUHK 7104942	01/09/2014 for 3 years	\$800,000
<b>Sub-Total</b>					<b>Approx. HK\$3.0M</b>

**Publications:**

To avoid duplication of outputs between years, only published (online or in print form) publications within the period of 1 January 2014 – 31 December 2014 **with the Li Ka Shing Institute of Health Sciences acknowledged** should be counted. Papers ahead of printing, or published after 31 December 2014 will be reserved for next year's report. (Please provide details of the publications in APA style and relevant document, e.g. first page of papers or conference abstracts)

## Journal Papers

1. Liu J, Nie H, Xu Z, Niu X, Guo S, Yin J, Guo F, **Li G**, Wang Y, Zhang C. The Effect of 3D Nanofibrous Scaffolds on the Chondrogenesis of Induced Pluripotent Stem Cells and Their Application in Restoration of Cartilage Defects. *PLoS One*. 2014 Nov 12;9(11):e111566.
2. Xu LL, Liu Y, Hou YH, Wang KX, Wong YM, Lin SE, **Li G**. U0126 promotes osteogenesis of rat bone marrow-derived mesenchymal stem cells by activating BMP/Smad signaling pathway. *Cell & Tissue Research*, 2014; in press.
3. Lin SE, Huang JP, Zheng L, Liu YZ, Fu ZW, Xu BL, Wu T, Qin L, **Li G**, Cui L. Glucocorticoid-induced osteoporosis in growing rats. *Calcified Tissue International*, 95:362-373.
4. Li N, Lee YW, Lin SE, Ni M, Zhang T, Huang XR, Lan HY, **Li G**. Partial loss of Smad7 function impairs osteogenesis and enhances osteoclastogenesis in mice. *Bone*, 2014 Jul 3; 67C: 46-55.
5. Wu TY, Liu Y, Wang B, **Li G**. The roles of mesenchymal stem cells in tissue repair and disease modification. *Current Stem Cell Research and Therapy*, 2014; 9: 424-431.
6. Wu CL, Liu FL, Li PD, Zhao GF, Lan SW, Jiang WY, Meng XW, Tian LX, **Li G**, Li YL, Liu JY. Engineered hair follicle mesenchymal stem cells overexpressing controlled-release insulin reverse hyperglycemia in mice with type 1 diabetes. *Cell Transplantation*, 2014; in press (DOI: 10.3727/096368914X681919)
7. Meng FB, Rui YF, Xu LL, Wan C, Jiang XH, **Li G**. Aqp1 enhances migration of bone marrow mesenchymal stem cells through regulation of FAK and  $\beta$ -catenin. *Stem Cells and Development*, 2014; 23(1):66-75. doi: 10.1089/scd.2013.0185.
8. Xu LL, **Li G**. Circulating mesenchymal stem cells and their clinical implications. *Journal of Orthopaedic Translation*, 2014; 2: 1-7. (<http://dx.doi.org/10.1016/j.jot.2013.11.002>)
9. Lin LW, Wang H, Ni M, Rui YF, Cheng TY, Cheng CK, Pan XH, **Li G**, Lin CJ. Enhanced osteo-integration of medical titanium implant with surface modifications in micro-nano scale structures. *Journal of Orthopaedic Translation*, 2014; 2: 35-42.

## Book Chapters

1. 李剛. “肢體再生的生物學基礎與進展” pp 20-37. 實用骨外固定學. 夏和桃主編. 人民衛生出版社, 北京, 2013 (ISBN 978-7-117-17408-4).
2. 李剛. “肢體再生的生物學基礎和再生醫學” pp 33-46. Ilizarov 技術骨科應用進展. 秦泗河, 李剛主編. 人民軍醫出版社, 北京, 2014. 1 (ISBN 978-7-5091-7054-4).
3. 李剛. “夢裡尋他千百度-李剛與 Ilizarov 技術的情緣” pp 592=598. Ilizarov 技術骨科應用進展. 秦泗河, 李剛主編. 人民軍醫出版社, 北京, 2014. 1 (ISBN 978-7-5091-7054-4).

4. 李楠, 王魁星, 李剛。 “間充質幹細胞技術與骨科應用” pp194-206。 骨內科學。 秦嶺 主編。 人民衛生出版社, 北京, 2013 (ISBN 978-7-117-18088-7).

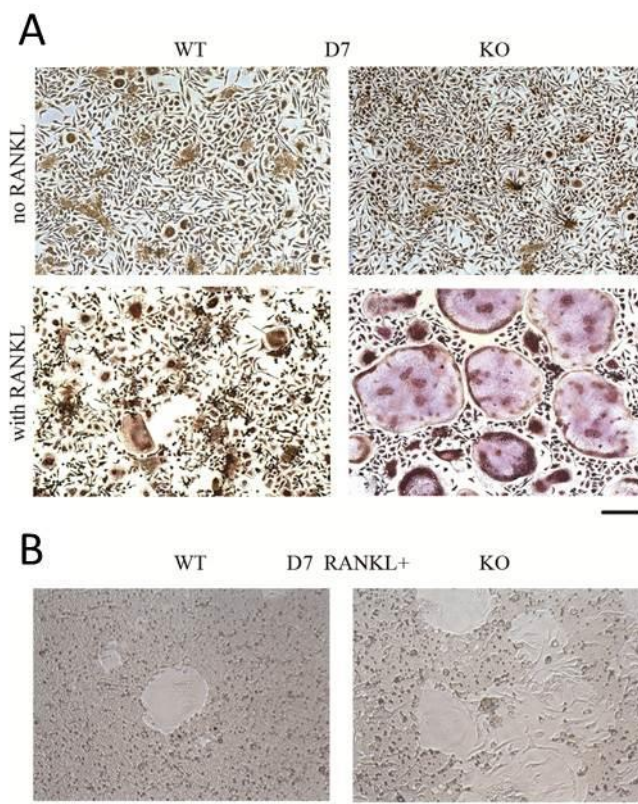
#### Books

1. Ilizarov 技術骨科應用進展。 秦泗河, 李剛主編。 人民軍醫出版社, 北京, 2014. 1 (ISBN 978-7-5091-7054-4) (120 万字) Development and application of Ilizarov technology in orthopaedic surgery. Qin Sihe and Li Gang (Editor). People's Military Medical Press, Beijing, 2014. 01 (ISBN 978-7-5091-7054-4); 120K words.
2. 實用骨外固定學。 夏和桃主編。 彭愛民, 劉利民, 李剛, 秦泗河副主編。 人民衛生出版社, 北京, 2013 (ISBN 978-7-117-17408-4) (202 萬字) Practical Guides for Bone External Technology. Xia He-Tao (Editor). Peng Ai-Min, Liu Li-Min; Li Gang and Qin Si-He (Associate Editor). People's Medical Publishing House, Beijing, PR China, 2013 (ISBN 978-7-117-17408-4), 202K words.

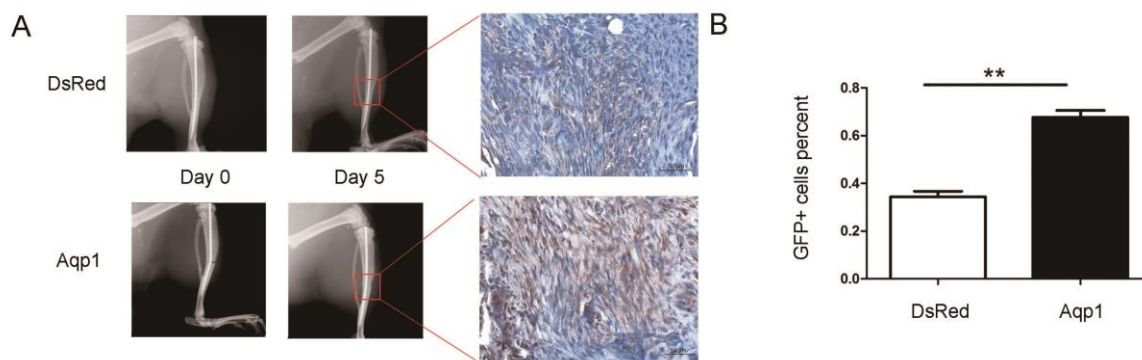
**One to two Symbolic Figure(s)** which can represent your team's research area (aim to emphasize your team's characteristics and help people relate to your area of research) (Please separately attach the figure(s) in graphic format, e.g. jpg, and provide supporting document for copyright permission for using the figure(s)):

Source of figure	Legend of figure	Copyright owner and year
<p><b>Fig.1</b></p> <p>Li N, Lee YW, Lin SE, Ni M, Zhang T, Huang XR, Lan HY, Li G. Partial loss of Smad7 function impairs osteogenesis and enhances osteoclastogenesis in mice. Bone, 2014 Jul 3; 67C: 46-55.</p>	<p><b>Fig. 1.</b> Smad7 KO mice have higher osteoclastogenesis potential and bone resorption ability. (A) Photomicrographs showing the osteoclasts like cells (TRAP staining) formation in the bone marrow derived mononuclear cells after RANKL induction at day 3 of both Smad7 KO and WT mice groups. (B) Photomicrographs showing the bone resorption activity of the osteoclasts using HA-coated plate for both WT and KO mice. All scale bar = 200 μm.</p>	<p>Gang Li 2014</p>
<p><b>Fig. 2</b></p> <p>Meng FB, Rui YF, Xu LL, Wan C, Jiang XH, Li G. Aqp1 enhances migration</p>	<p>Figure 2. Aqp1 Overexpression promoted MSCs homing to fracture sites and healing. Immunohistochemistry of administrated MSCs at the fracture site. X-rays images depicted</p>	<p>Gang Li 2014</p>

<p>of bone marrow mesenchymal stem cells through regulation of FAK and <math>\beta</math>-catenin. <i>Stem Cells and Development</i>, 2014; 23(1):66-75. doi: 10.1089/scd.2013.0185.</p>	<p>tibial fracture after surgery (left, A) and five days later (right, A). There was only soft callus in the fracture gap at five days after fracture and GFP positive cells were seen at the boxed areas, showing more GFP cells in the Aqp1-MSCs group (A). The percentage of GFP positive cells was quantified by the ratio of brown cells (GFP positive) to whole cells (blue cells plus brown cells) auto-selected by software image pro plus 6.0 in the randomly selected fields, showing that there was significantly more GFP-MSCs in the Aqp-1 MSCs group (B, n = 5). Scale bar: 50 <math>\mu</math>m. All error bars represent SEM (**p &lt; 0.01).</p>	
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**Figure 1.**



**Figure 2.**

**Checklist for Report submission**

- ✓ Supporting documents, e.g. copy of notification letter, for Awards and Fellowships
- ☐ Supporting documents, e.g. copy of notification letter, for Grants and Consultancy
- ✓ Supporting documents, e.g. the first page of papers or conference abstracts or the page with affiliation, for Publications
- ✓ Graphic file(s) for one to two symbolic figure(s)
- ☐ Supporting documents for copyright permission for using the above figure(s)