

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; Mr. Jimmy Cheng; Dr. Xu Liangliang; Ms. Li Nan; Ms. Liu Yang; Mr. Wang Kuixing; Mr. Lin Sien; Mr. Huang Shuo; Mr. Cheng Yuanfeng; Mr. Wu Tainyi; Mr. Sun Yixin; Mr. Wang Bin; Dr. Zou Liyi.

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 novel genes regulating circulating mesenchymal stem cells (MSCs); musculoskeletal tissue engineering and gene therapy using bone marrow derived MSCs as vehicles. The team has published 11 research papers and generated over HK\$5.0 M new research grants in the period of 2013. Prof. Li has successfully organized the 3rd CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in Hong Kong, 11-12 November 2013, with more than 30 overseas invited speakers and over 300 attendants and overwhelming good feedback.

Chinese version (less than 100 words):

李剛教授實驗室的主要研究興趣是調控迴圈間充質幹細胞的新基因功能；利用骨髓來源的間充質幹細胞進行骨骼肌肉系統的組織工程學和基於幹細胞為載體的基因療法的科研工作。本研究組在 2013 年共發表 11 篇研究論文並獲得了超過五百萬港幣的新的研究經費。李教授于 2013 年 11 月 11-12 日在香港中文大學威爾士醫院成功主辦了第三屆香港中文大學幹細胞與再生醫學國際研討會，共有 30 多位海外嘉賓和 300 多人參加，收到一致的好評。

Research Progress Summary:

In 2013, the research team has 13 members (1 Postdoc RA, 1 Senior technician, 1 Research Associate, 1 RA, 8 PhD students and 1 academic visitors) 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) MSCs as anti-cancer vehicles 利用幹細胞治療腫瘤的研究。(3) 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。(4) 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 121 papers have been published from the research work and over HK\$5.0 Million research grants have been secured by this PI over the period. The PI also successfully organized the 3rd CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in CUHK PWH campus, 11-12 November 2013, with more than 30 overseas invited speakers and over 300 attendants, the symposium received many feedback and became an icon for Hong Kong in the field of stem cell biology and regenerative medicine. The PI has been invited to give keynote

speeches and lectures at various national and international conferences and meetings for 11 times in 2013. 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.

Recognitions:

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

Member' s Name	Details
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 Orthopadeic 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	Hon. Consultant, Beijing Institute of External Fixation Technology, Beijing, China.
Gang Li	Member of Editorial Board, Orthopaedics Journal of China
Gang Li	Member of Editorial Board, Journal of Orthopaedic Surgery and Research
Gang Li	Member of Editorial Board, Calcified Tissue International
Gang Li	Member of Editorial Board, Chinese Journal of Orthopaedic Trauma
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	Start/End dates (dd/mm/yy)	Amount (HK\$)
Gang Li	Functional characterizations of peripheral blood derived mesenchymal stem cells [CUHK471110]	Research Grant Council, Hong Kong Government	01/01/2011 -31/12/2013	\$986,000
Gang Li	Promote fracture healing by administration of allogenic mesenchymal stem cells (MSCs) [CUHK470813]	Research Grant Council, Hong Kong Government	01/01/2014 -31/12/2016	\$779,429
Gang Li	Rat spinal fusion studies [CUHK Cost Centre Code: 7010124]	Eli Lily Co., USA	01/02/2011 -31/05/2014	\$2,099,060
Gang Li	Effect of Sclerostin antibody on osteoporotic fracture healing in rats and underline mechanisms [CUHK	Amgen Company USA	01/05/2011 -30/10/2013	\$1,414,136

	Cost Centre Code: 7010149]			
Gang Li	用胸腺嘧啶激酶基因修饰的间充质干细胞治疗肿瘤的研究 [81172177]	国家自然科学基金	01/01/2012 31/12/2015	RMB550,000
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 [81371946]	国家自然科学基金	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 [JCYJ20130401171935811]	深圳市科技创新委员会	01/10/2013 -31/09/2015	RMB150,000
Gang Li	Does the growth factor and mechanical influence tenocyte differentiation through miRNAs? [CUHK cost centre code: 8303207]	Lui Che Woo Institute of Innovation Medicine, SMART Program Seeding fund	01/09/2013 -31/08/2015	\$250,000

Publications:

To avoid duplication of outputs between years, only published (online or in print form) publications within the period of 1 January 2013 – 31 December 2013 with **the Li Ka Shing Institute of Health Sciences acknowledged** should be counted. Papers ahead of printing, or published after 31 December 2013 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)

1. 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 β -catenin. *Stem Cells and Development* (In press) doi: 10.1089/scd.2013.0185. Epub 2013 Sep 27.
2. Lee WYW, Zhang T, Lau CPY, Wang CC, Chan KM, Li G. Immortalized human fetal bone marrow-derived mesenchymal stem cell expressing anti-tumor suicide gene for anti-tumor therapy in vitro and in vivo. *Cytotherapy*, 2013; 15: 1484-1497.
3. Luo KW, Ko CH, Yue GG, Lee MY, Siu WS, Lee JK, Shum WT, Fung KP, Leung PC, Li G, Evdokiou A, Lau CB. Anti-tumor and anti-osteolysis effects of the metronomic use of zoledronic acid in primary and metastatic breast cancer mouse models. *Cancer Lett.* 2013; 339 (1): 42-8.
4. Zhang T, Lee YW, Rui YF, Cheng TY, Li G. Bone marrow-derived mesenchymal stem cells promote growth and angiogenesis of breast and prostate tumors. *Stem Cell Research & Therapy*, 2013, 4:70 doi:10.1186/scrt221.
5. Zhao J, Yang C, Su C, Yu M, Zhang X, Hang S, Li G, Yu M, Li X. Reconstruction of orbital defects by implantation of antigen-free bovine cancellous bone scaffold combined with bone marrow mesenchymal stem cells in rats. *Graefe's Archive for Clinical and Experimental Ophthalmology*, 2013; 251:1325-1333.
6. Cui L, Cheng H, Song C, Li CY, Simonet WS, Ke HZ, Li G. Time-dependent effects of Sclerostin antibody on a mouse fracture healing model. *Journal of Musculoskeletal and Neuronal Interactions*, 2013; 13(2):178-184.
7. Meng FB, Liu XY, Li HT, Pang XN and Li G. Regulation of blood glucose by administration of

allogenic bone marrow derived mesenchymal stem cells into diabetic rats through modulating regeneration of both β and δ islet cells. *Journal of Diabetes Research & Clinical Metabolism*, 2013; 2:1 (DOI: <http://dx.doi.org/10.7243/2050-0866-2-7>).

8. Zhang XB, Meng XM, Baylink D, Neises A, Kiroyan J, Su RJ, Kimberly P, Gridley D, Wang J, William KH, Lee W, Li G. Rapid and efficient reprogramming of human fetal and adult blood CD34+ cells into mesenchymal stem cells with a single factor. *Cell Research*, 2013; 23(5):658-72.
9. Ni M, Rui YF, Tan Q, Liu Y, Xu LL, Chan KM, Wang Y, Li G. Engineered scaffold-free tendon tissue produced by tendon-derived stem cells. *Biomaterials*, 2013; 34: 2024-2037.
10. Xu LL, Meng FB, Ni M, Lee YW, Li G. N-cadherin regulates osteogenesis and migration of bone marrow-derived mesenchymal stem cells. *Molecular Biology Report*, 2013; 40(3):2533-2539.
11. Zhang T and Li G. "Use of bone marrow mesenchymal stem cells as tumor specific delivery vehicles" pp 191-201. In M.A. Hayat (ed.), *Stem Cells and Cancer Stem Cells*, Volume 9, 191 © Springer Science + Business Media, Dordrecht 2013.

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 1	Copyright owner and year
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 β -catenin. <i>Stem Cells and Development</i> (In press) doi: 10.1089/scd.2013.0185. Epub 2013 Sep 27.	Gang Li 2013

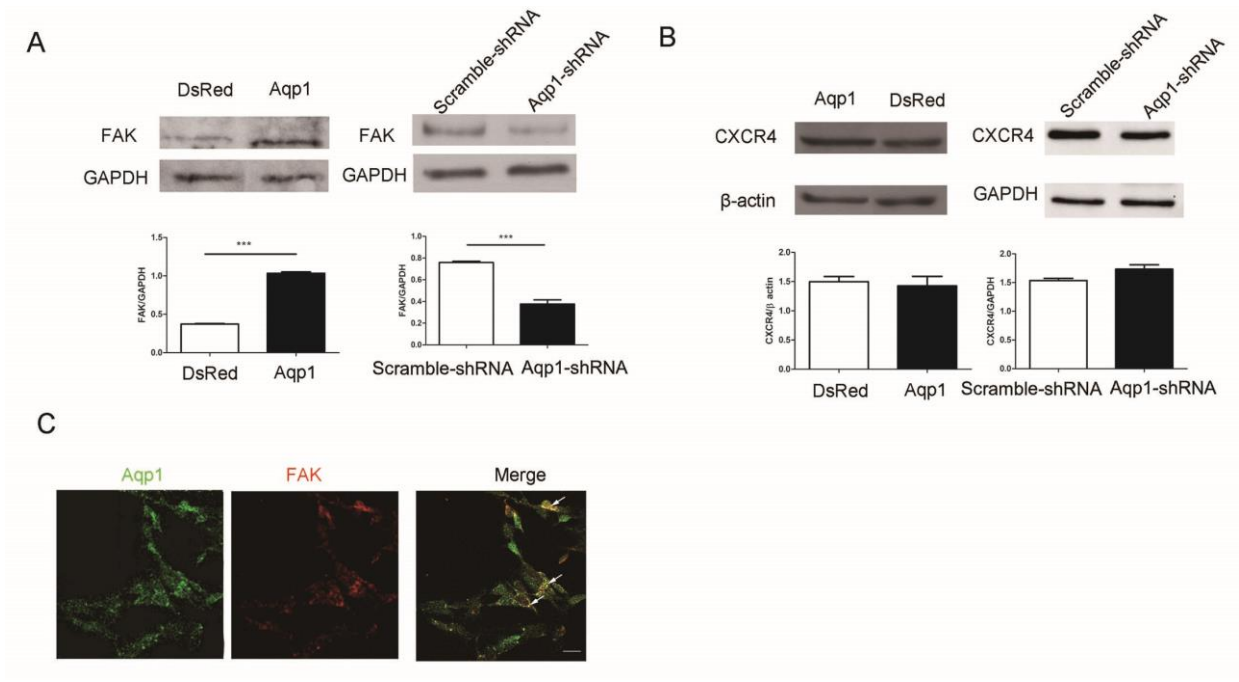


Fig. 1. FAK level was regulated by Aqp1. Western blot showed the expression FAK (A) and CXCR4 (B) in Aqp1 depleted and overexpressing MSCs and quantified by software Image J. The localization of Aqp1 (green) and FAK (red) labeled with fluorescent antibodies was displayed by confocal microscope (C). Co-localization area of Aqp1 and FAK was highlighted (arrow) and analyzed by software Image Pro Plus 6.0 with pearson's correlation $R_r=0.814934$. Scale bar: 100 μ m. All error bars represent SEM (***) $p < 0.001$.

Source of figure 2	Copyright owner and year
Lee WYW, Zhang T, Lau CPY, Wang CC , Chan KM, Li G. Immortalized human fetal bone marrow-derived mesenchymal stem cell expressing anti-tumor suicide gene for anti-tumor therapy in vitro and in vivo. <i>Cytotherapy</i> , 2013; 15: 1484-1497.	Gang Li 2013

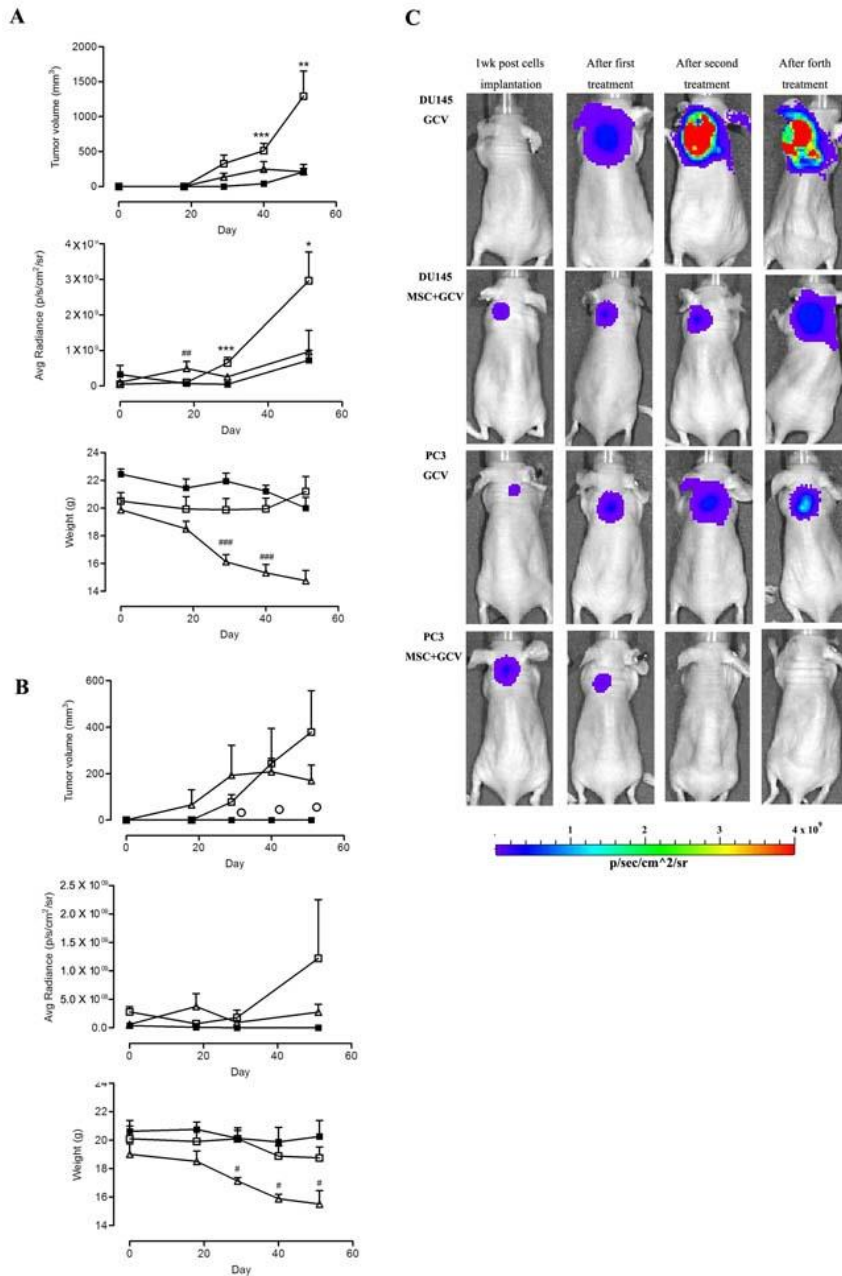


Fig. 2. Anti-tumor effect of SV40-TK-hfBMSCs/GCV treatment in tumor xenograft animal model. Anti-tumor effect in DU145 group (n=7) (A) or in PC3 group (n=5, one outlier is shown as circle) (B) as indicated by tumor volume measurement and in vivo live bioluminescent imaging, and weighting was done to indicate the side effects along. The treatment was as effective as Dox in inhibiting tumor growth, but without rendering side effect on animals' weights. (C) Representative bioluminescent images were acquired by IVIS200.