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

PI: Prof. Gang Li (Orthopaedics & Traumatology)

Team: Stem Cell and Regenerative Medicine Laboratory (LiKS 501 Lab): Dr. Wayne Lee; Mr. Jimmy Cheng; Dr. Xu Liangliang; Mr. Meng Fanbiao; Ms. Li Nan; Ms. Zhang Ting; Ms. Liu Yang; Mr. Wang Kuixing; Mr. Lin Sien; Mr. Zhang Haixiang; Dr. Xu Daohua.

Non-technical Summary (in layman language for the donor to read (i.e. a short paragraph of <100 words in **both English and Chinese** characters will do):

The main research interests of this team are to on musculoskeletal tissue engineering and gene therapy using bone marrow derived mesenchymal stem cells as vehicles. The team has published more than 12 research papers and generated over HK\$7.3 M research grants in the period of 2012 as PI. Prof. Li has successfully organized the 2nd CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in Shenzhen and Hong Kong, 19-20 November 2012, with more than 20 overseas invited speakers and over 200 attendants.

李剛教授實驗室的主要研究興趣是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 2012 年共發表 12 餘篇研究論文並獲得了超過 七百萬港幣的研究經費。李教授于 2012 年 11 月 19-20 日分別在香港中文大學深圳研究院和威爾士醫 院成功主辦了第二屆香港中文大學幹細胞與再生醫學國際研討會, 共有 20 多位海外嘉賓和 200 多人 參加。

Research Progress Summary:

In 2012, the research team has 11 members (1 Postdoc RA, 1 RA, 1 Senior technician. 6 PhD students and 2 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 well, with 12 papers have been published from the research work and over HK\$7.3 Million research grants have been secured by this PI as over the period. The PI also spent his time in managing the GMP-standard human cell culture laboratory at LiKS Institute, and successfully organized the 2nd CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in CUHK Shenzhen Research Institute and PWH, 19-20 November 2012, with more than 20 overseas invited speakers and over 200 attendants. The PI has been invited to give keynote speeches and lectures at various national and international conferences and meetings for 10 times in 2012. The PI also engaged in knowledge transfer and provided advice/consultation service for Hong Kong Science Park, local and international healthcare related industries, etc.

Recognitions:

Awards and Fellowships

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, 1 st Affiliated		
	Hospital, Shuzhou University Medical School, Shuzhou, China.		
Gang Li	Visiting Professor, South Eastern University Medical School, Nanjing,		
	China.		
Gang Li	Hon. Consultant, Beijing International Orthopaedic Research Centre		
Gang Li	Hon. Consultant, Beijing Institute of External Fixation Technology,		
	Beijing, China.		
Gang Li	Member of Editorial Board, NeuroImage		
Gang Li	Member of Editorial Board, Word Journal of Stem Cells		
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	Consultant, Beijing International Orthopaedic Research Centre		
Gang Li	Member of Editorial Board, Chinese Journal of Orthopaedic Trauma		

Grants and Consultancy

Name of PI	Project Title	Funding Source	Start/End dates (dd/mm/yy)	Amount (HK\$)
Gang Li	Animal studies of proprietary bioproduct or small molecules with potential osteogenesis stimulation effect	Eli Lily Co., USA	01/03/2010 -31/12/2012	\$1,337,000
Gang Li	Functional characterizations of peripheral blood derived mesenchymal stem cells	Research Grant Council, Hong Kong Government	01/01/2011 -31/12/2013	\$986,000
Gang Li	Spinal fusion studies	Eli Lily Co., USA	01/02/2011 -31/05/2013	\$1,099,060
Gang Li	Effect of Sclerostin antibody on osteoporotic fracture healing in rats and underline mechanisms	Amgen Company USA	01/05/2011 -30/10/2013	\$1,928,103
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	国家自然科学基金	2012. 01 -2015. 12	\$616,000 (RMB 550,000)
Gang Li	Assessment of the antiangiogenic effect of an antibody on retinopathy associated neovascularization	Amgen Company USA	01/05/2011 -30/08/2013	\$1,125,800
Gang Li	Development of a center for	Focused Investment	01/03/2011	\$387,360

	research inflammatory diseases (Allocated to ORT)	Scheme B, CUHK Central Fund	-31/12/2013	
Gang Li	Studies of stem cells secretions	0 0	01/04/2012 -31/03/2015	\$300,000
Sub-total				Approx. \$7.3M

Publications:

To avoid duplication of outputs between years, only published (online or in print form) publications within the period of <u>1 January 2012 – 31 December 2012</u> with LiHS acknowledged should be counted. (Please provide details of the publications in APA style and <u>attach</u> relevant documentary proof, viz. copy of publication/letter of acceptance/conference abstract)

- 1. Luo ZH, Zhang LY, Li Z, Li XY, Li G, Yu HB, Jiang C, Dai YF, Guo XF, Xiang JJ, **Li G.** An in silico analysis of dynamic changes in microRNA expression profiles in stepwise development of nasopharyngeal carcinoma. BMC Medical Genomics, 2012; 5:3. (IF: 3.77, Co-author).
- Ni M, Cheng TY, Rui YF, Chan KM, Kuhstoss S, Ma YF, Sato M, Wang, Y, Li G. Dose-dependent enhancement of spinal fusion in rats with Teriparatide [PTH(1-34)]. Spine, 2012; 37(15):1275-1282. (IF: 2.79, Correspondence author)
- 3. Fan QM, Yue B, Bian ZY, Xu WT, Tu B, Dai KR, Li G, Tang TT. The CREB–Smad6–Runx2 axis contributes to the impaired osteogenesis potential of bone marrow stromal cells in fibrous dysplasia of bone. Journal of Pathology, 2012; 228(1):45-55 (IF: 7.25, Co-correspondence author).
- Tang JQ, Zhang LY, She XL, Zhou GQ, Yu FL, Xiang JJ, Li G. Inhibiting CD164 expression in colon cancer cell line HCT116 leads to reduced cancer cell proliferation, mobility and metastasis in vitro and in vivo. Cancer Investigation 2012; 30(5): 380-9. (IF: 2.11, Correspondence author).
- Ma LL, Meng FB, Shi P, Li G, Pang XN. Quantity and proliferation rate of mesenchymal stem cells in human cord blood during gestation. Cell Biology International, 2012; 36:415-418. (IF: 1.75, Co-correspondence author)
- Xu LL, Song C, Ni M, Meng, FB, Xie HQ, Li G. Cellular retinol-binding protein 1 (CRBP-1) regulates osteogenenesis and adipogenesis of mesenchymal stem cells through inhibiting RXR-a-induced ß-catenin degradation. The International Journal of Biochemistry & Cell Biology, 2012; 44:612-619. (IF: 4.96, Correspondence author).
- Shen B, Chu ES, Zhao G, Man K, Wu CW, Cheng JT, Li G, Nie Y, Lo CM, Teoh N, Farrell GC, Sung JJ, Yu J. PPARgamma inhibits hepatocellular carcinoma metastases in vitro and in mice. British Journal of Cancer, 2012;106 (9):1486-94. (IF: 4.83; Co-author)
- Wang CC, Xu H, Man GCW, Zhang T, Chu KO, Chu CY, Cheng JTY, Li G, He YX, Qin L, Chan TH. Prodrug of green tea epigallocatchin-3-gallate (Pro-EGCG) as a potent anti-angiogenesis agent for endometriosis in mice. Angiogenesis, 2012; 16:59–69. (IF:6.06, Co-author)

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 also supporting document for copyright permission for using the figure(s):

Source of figure	Legend of figure	Copyright owner and year
Source of figure Fig. 1 TIFF	Legend of figure CRBP1 promoted osteogenic differentiation of BM-MSCs through regulating —	
	OPN was significantly upregulated. The protein level was normalized to actin (C). (D and E) CRBP1 knockdown impaired osteogenesis of MSCs. Relative expression of OPN, Col12, ALP, OCN and Runx2 in MSC-CRBP1 was checked using real time PCR (D); MSCs transduced with shCRBP1-1 or scrambled shRNA were treated with OIM for 19 days, then calcium nodules were stained by Alizarin Red S (E). (F) MSC-dsRed and MSC-CRBP1 were treated with OIM for 7 days, and then protein extracts were prepared for western blot analysis with anticatenin and anti-pERK1/2 antibodies. The blot was probed with anti-GAPDH antibody to confirm equal loading. Quantification of the band intensity showed that the level of catenin and pERK1/2 was significantly upregulated. The	
	protein levels were normalized to GAPDH. The experiments were repeated three times.	
Fig. 2 JEPG	Representative micro-computed tomographic 3-dimensional reconstructive images of the L5–L6 fusion mass from the 3 groups. There	Gang Li 2012

was increased new bone formation in a dose-dependent manner in the 3 groups. The Vehicle group had less callus volume, PTH4 group had moderate callus volume, and PTH23 group had the maximum callus volume

compared with Vehicle and PTH4 groups. There were still visible gaps in the fusion sites in both Vehicle and PTH4 groups (arrows) suggesting pseudarthrosis formation, whereas no gap was seen in the fusion site in PTH23 group. PTH indicates parathyroid hormone.

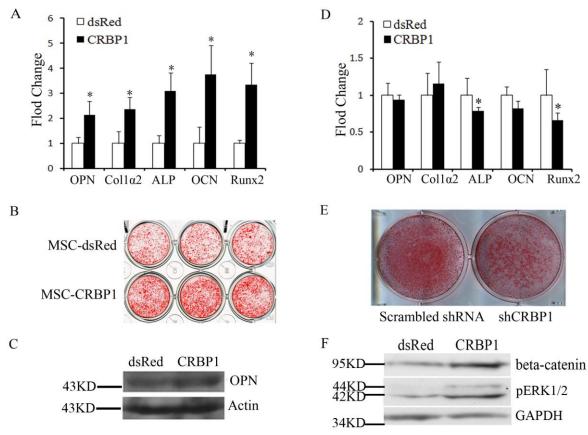


Fig. 1.

Fig. 2

Gropu A: Control

Group B: Low PTH Group C: High PTH

