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

PI: Li Gang (Department of Orthopaedics and Traumatology)

Team: Dr. Wayne Lee (Research Assistant Professor); Dr. Zhang Jinfang (Research Assistant Professor); Dr. Xu Liangliang (Postdoctoral Fellow); Dr. Guo Jia (RA); Dr. Lin Sien (RA); Ms. Liu Yang (PhD student); Mr. Cheng Yuanfeng (PhD student); Mr. Wu Tainyi (PhD student); Mr. Sun Yixin (PhD student); Mr. Wang Bin (PhD student); Mr. Shi Liu (PhD student); Mr. Xu Jia (Visiting Fellow).

Non-technical Summary (in layman language, i.e. a short paragraph of less than 100 words in <u>both</u> 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 14 research papers, 12 China national invention patents and generated over HK\$4.0 M research grants in 2015. Prof. Li has been elected as the Chairman of China Branch, International Limb Lengthening and Reconstruction Societies (ILLRS) and Association from Study and Application of the Methods of Ilizarov (ASAMI) and members of several national orthopaedic research societies. Prof. Li has successfully organized the 5th CUHK International Symposium on Stem Cell Biology and Regenerative Medicine in Hong Kong, 12 November 2015, with more than 20 overseas invited speakers and over 150 attendants; Mainland, Taiwan, Hong Kong and Macau Forum on Tissue Regeneration Innovation and Translation (Chinese Academy of Engineering Forum), 13-14 November 2015, Shenzhen, China, with 7 academicians of CAE and over 20 invited speakers from USA, Australia, Europe and over 300 people including our VC Prof. Joseph Sung attended the meeting; the two meetings 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组织来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 2015 年共發 14 篇研究論文, 12 个中国发明专利並獲得 了超過四百萬港幣的新的研究經費。李教授于 2015 年 9 月被选为国际肢体延长和重建学会 和 Ilizarov 方法研究和应用协会中国部主席。李教授与 2015 年 11 月 12 日在香港中文大學威 爾士醫院成功主辦了第五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 嘉賓参会; 2015 年 11 月 13-14 日在中国深圳成功举办了海峡两岸及香港, 澳门地区创伤修 复 (愈合)与组织再生创新成果及转化应用论坛 (暨中国工程院院士论坛), 共有 7 位中国 工程院院士和 20 多位来自美国和欧洲等特邀嘉宾和超过 300 多人参会, 两个大会受到参会人 员的一致的好評。

Research Progress Summary:

In 2015, the research team has 12 members (2 RAPs; 1 Postdoc Research Assistant, 2 Research Assistants, 1 Visiting Fellow, 6 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 14 papers have been published from the research work and over HK\$4.0 Million research grants have been secured by this PI in 2015. The PI has been invited to give keynote speeches and lectures at various national and international conferences and meetings for 10 times in 2015, and served as visiting professors in 4 Chinese universities and council members of more than 8 national and international research societies. 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 co-inventor for 12 China national invention patients in 2015. 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 Heath Maintenance, and successfully organized 2 international and national symposiums on stem cells biology and regenerative medicine in 2015.

Recognitions:

<u>Twards and Tenowships</u> (Trease provide relevant document, e.g. copy of notification letter)	Awards and Fellowships (P	ease provide relevant document,	e.g. copy of notification letter)
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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	Visiting Professor, Xijing Orthopadeic Hospital, The Fourth Military Medical		
	University, Xian, China.		
Gang Li	Visiting Professor, South Eastern University Medical School, Nanjing, China.		
Gang Li	Member of Member of Advisory Board, Shanghai Key Laboratory of		
	Orthopaedic Implant, Shanghai Jiaotong University, China.		
Gang Li	Associate Editor, Journal of Orthopaedic Translation		
Gang Li	Member of Editorial Board, Calcified Tissue International		
Gang Li	Council member, Chinese Orthopaedic Research Society, Chinese Orthopaedic		
	Association 中國骨科醫學會基礎醫學組委員		
Gang Li	Council Member, Tissue Engineering and Regenerative Medicine Division,		
-	Chinese Association of Biomedical Engineering 中國生物醫學工程學會組		
	織工程與再生醫學分會 理事會委員		
Gang Li	Member, Division of Orthopaedic Research, Chinese Association of		
	Orthopaedic Surgeons		
Gang Li	General Secretary, Division of Limb Deformity Correction and		
	Reconstruction, Chinese Association of Orthopaedic Surgeons		
Gang Li	Council member, Orthopaedic Committee, Chinese Association of Combined		

	Traditional and Western Medicine (中国中西医结合学会第7届骨伤科专业			
	委员会委员)			
Gang Li	Chairman of China Branch, International Limb Lengthening and			
	Reconstruction Societies (ILLRS) and Association from Study and Application			
	of the Methods of Ilizarov (ASAMI) (国际肢体延长和重建学会, Ilizarov			
	方法研究和应用协会 中国部主席)			
Gang Li	Standing Committee Member, The First Committee of Orthopaedic Research			
	Society, SICOT China Chapter (SICOT 中国部骨科基础学会第一届委员会			
	常务委员)			
Gang Li	Vice Chairman, Orthopaedic Committee of Guangdong, Hong Kong and			
	Macau, Association of Biomedical Engineering of Guangdong Province (广东			
	省生物医学工程学会粤港澳骨科专业委员会 副主任委员)			

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

Name of	Project Title	Funding	Grant	Start/End dates	Amount
PI		Source	Reference	(dd/mm/yy)	(HK\$)
Gang Li	Promote fracture healing	Research	CUHK	01/01/2014	\$779,429
	by administration of	Grant Council,	170010	-31/12/2016	
	allogenic mesenchymal	Hong Kong	470813		
	stem cells (MSCs)	Government			
Gang Li	Is Smad7 a potential	Research	СШНК	01/01/2016-	\$821,097
C	therapeutic target for	Grant Council,	com	31/12/2018	
	preventing osteoporotic	Hong Kong	14119115		
	bone loss?	Government			
Gang Li	SOX11 调控骨髓间充	国家自然科	81371946	01/01/2014-	RMB
	质于细胞分化与迁移的	学基金	010/19/10	31/12/2017	700,000
	研究及甘在丹/软丹百				
	小儿及关任有/扒有丹				
C L	土中的应用 乏体》的同社日佳国睦			01/10/2012	DMD
Gang Li	系统汪射问种异体官随	深圳巾科技	JCYJ20130	01/10/2013-	RMB
	间充质干细胞促进骨折	创新委员会	401171935	31/09/2015	150,000
	愈合的研究		011		
			811		
Gang Li	血管和神经化促进组织	国家自然科	81374568	01/03/2015-	RMB
	工程骨形成的机制研究	学基金		31/12/2019	600,000
Gang Li	Study the effects of	Shenyang	СШНК	01/09/2014-	\$800,000
C	Super-antigens on stem	Xiehe Pharma	eenne	31/08/2017	
	cells functions and their	Company,	7104942		
	applications	China			
Sub-				Approx. HK\$4.0M	[
Total					

Publications:

To avoid duplication of outputs between years, only published (online or in print form) publications within the period of <u>1 January 2015 – 31 December 2015</u> with <u>the Li Ka Shing Institute of Health</u> <u>Sciences acknowledged</u> 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 <u>APA style</u> and <u>relevant document</u>, e.g. first page of papers or conference abstracts)

Journal Papers

- Huang S, Xu LL, Sun YX, Zhang YF, Li G. The fate of systemically administrated allogeneic mesenchymal stem cells (MSCs) in mouse femoral fracture healing. Stem Cell Research and Therapy, 2015; 6: 206.
- 2. Yu LM, Huang JP, Wang J, Cui L, Sun YX, Chen LY, Su YJ, Lin S, Li G. Antler collagen/chitosan scaffolds improve critical calvarial defect healing in rats. Journal of Biomaterials and Tissue Engineering, 2015; 5:1-6.
- Fu WM, Zhu X, Wang WM, Lu YF, Hu BG, Wang H, Liang WC, Wang SS, Ko CH, Waye MMY, Kung HF, Li G, Zhang JF. Hotair mediates hepatocarcinogenesis through suppressing MiRNA-218 expression and activating P14 and P16 signaling. Journal of Hepatology; 2015 Oct; 63(4): 886-95.
- 4. Chen YF, Sun YX, Pan XH, Ho KW, Li G. Joint distraction attenuates osteoarthritis by reducing secondary inflammation, cartilage degeneration and subchondral bone aberrant change. Osteoarthritis and Cartilage; 2015; 23 (10): 1728-1735.
- Rui YF, Xu LL, Chen R, Zhang T, Lin S, Hou YH, Liu Y, Meng FB, Liu ZQ, Ni M, Tsang KZ, Yang FY, Wang C, Chan HC, Jiang XH, Li G. Epigenetic memory gained by priming with osteogenic induction medium improves osteogenesis and other properties of mesenchymal stem cells. Scientific Reports, 2015; 5:11056.
- Lin SE, Huang JP, Fu ZW, Liang YL, Wu HY, Xu LL, Sun YX, Lee WYW, Wu T, Qin L, Cui L, Li G. The effects of atorvastatin on the prevention of osteoporosis and dyslipidemia in the high-fat-fed ovariectomized rats. Calcified Tissue International, 2015 Jun; 96(6):541-51.
- Sun YX, Xu LL, Huang S, Liu Y, Hou YH, Chan KM, Pan XH, Li G. Mir-21 overexpressing mesenchymal stem cells accelerate fracture healing in a rat closed femur fracture model. BioMed Research International, 2015:412327.
- 8. Wang KX, Xu LL, Rui YF, Huang S, Lin SE, Xiong JH, Li YH, Lee WYW, Li G. The effects of secretion factors from umbilical cord derived mesenchymal stem cells on osteogenic differentiation of mesenchymal stem cells. PLoS One, 2015; 10(3): e0120593.
- 9. Huang B, Li G, Jiang XH. Fate determination in mesenchymal stem cells: A perspective from histone modifying enzymes. Stem Cell Research & Therapy, 2015; 6(1): 35.
- 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 l diabetes. Cell Transplantation, Cell Transplantation, 2015; 24: 891-907.
- 11. Nadeem D, Smith CA, Dalby MJ, Meek RMD, Lin S, Li G, Su B. Three-dimensional CaP/gelatin lattice scaffolds with integrated osteoinductive surface topographies for bone tissue engineering. Biofabrication, 2015; 7(1):015005.
- 12. Xu LL, Huang S, Hou YH, Liu Y, Ni M, Meng FB, Wang KX, Rui YF, Jiang XH, Li G. Sox11-modified mesenchymal stem cells (MSCs) accelerate bone fracture healing: Sox11

regulates differentiation and migration of MSCs. FASEB Journal, 2015; 29(4):1143-52.

- 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, 2015; 359(2): 537-545.
- 14. Huang S, Xu LL, Sun YX, Wu TY, Wang KX, Li G. An improved protocol for isolation and culture of mesenchymal stem cells from mouse bone marrow. Journal of Orthopaedic Translation; 2015; 3: 26-33.

Book Chapters

张涛,王喜良,李刚。"肢体再生的生物学基础和再生医学" pp 185-191。干细胞与再生医学 习题集。庞希宁, 付小兵。人民衛生出版社,北京,2015 (ISBN 978-7-117-20957-1/ R.20958).

Others (Patents)

- 1. 踝关节冠状面畸形调控矫形器。夏和桃,李剛,彭爱民,王坤正, 唐海, 夏洪箐。中 國發明專利 ZL 2013 1 0400836.6。授權證書號 1685211.
- 2. 踝关节多维调控矫形器。夏和桃,李剛,彭爱民,夏洪箐,刘利民。中國發明專利 ZL 2013 1 0400817.3。授權證書號 1684956.
- 3. 肘关节动静结合调控外固定器。夏和桃,李剛,彭爱民,夏洪箐,刘利民。中國發明專利 ZL 2013 1 0400954.7。授權證書號 1661159.
- 4. 膝关节动静结合调控外固定器。夏和桃,李剛,彭爱民,夏洪箐,杨华清,刘利民。中 國發明專利 ZL 2013 1 0400953.2。授權證書號 1660045.
- 5. 快速牵伸延长杆。夏和桃,李剛,唐佩福,彭爱民,王坤正,夏洪箐。中國發明專利 ZL 2013 1 0400851.0。授權證書號 1660706.
- 6. 肩关节动静结合调控外固定器。夏和桃,李剛,彭爱民,唐佩福,刘利民,夏洪箐。中 國發明專利 ZL 2013 1 0400834.7。授權證書號 1659033.
- 肱骨近端 T 型外固定器。夏和桃,唐海, 唐佩福,彭爱民,李剛,杨华清,夏洪箐。
 中國發明專利 ZL 2013 1 0400794.6。授權證書號 1684697.
- 马蹄足矫形器。夏和桃,李剛,唐海,彭爱民,夏洪箐,刘利民。中國發明專利 ZL 2013 1 0400853.X。授權證書號 1659597.
- 9. 管状牵伸加压连接杆控制装置及骨外固定器。夏和桃,李剛,唐海,彭爱民,夏洪箐, 刘利民。中國發明專利 ZL 2013 1 0400810.1。授權證書號 1659055.
- 10. 髋关节矫形与股骨延长器。夏和桃,李剛,彭爱民,刘利民,王坤正,夏洪箐。中國發明專利 ZL 2013 1 0400852.5。授權證書號 1659311.
- 11. 跟足多功能调控外固定器。夏和桃,李剛,彭爱民,夏洪箐,刘利民,杨华清。中國發明專利 ZL 2013 1 0400828.1。授權證書號 1660513.
- 12. 踝关节冠状面复合畸形调控矫形器。夏和桃,李剛,彭爱民,唐佩福,夏洪箐,刘利民。 中國發明專利 ZL 2013 1 0400826.2。授權證書號 168833.

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 <u>attach the figure(s) in graphic format</u>, e.g. jpg, and provide <u>supporting document for copyright permission</u> for using the figure(s)):

Source of figure	Legend of figure	Copyright owner and year
Fig.1 Rui YF, Xu LL, Chen R, Zhang T, Lin S, Hou YH, Liu Y, Meng FB, Liu ZQ, Ni M, Tsang KZ, Yang FY, Wang C, Chan HC, Jiang XH, Li G . Epigenetic memory gained by priming with osteogenic induction medium improves osteogenesis and other properties of mesenchymal stem cells. Scientific Reports, 2015; 5:11056.	Fig. 1. The schematic outlines of the procedure for de-osteogenic differentiation of MSCs and involvement of Nanog/Oct4 in this process.	Gang Li 2015
Fig. 2 Xu LL, Huang S, Hou YH, Liu Y, Ni M, Meng FB, Wang KX, Rui YF, Jiang XH, Li G. Sox11-modified mesenchymal stem cells (MSCs) accelerate bone fracture healing: Sox11 regulates differentiation and migration of MSCs. FASEB Journal, 2015; 29(4):1143-52.	Figure 6. Histological analysis of fracture calluses. At 5-week after cell transplantation, the femurs were collected for histological analysis. (A) Longitudinal sections of calluses were subjected to HE and Safranin O staining and immunohistochemical analysis with GFP and OCN antibodies. (B) The region of interest was 3 mm below and above the fracture line identified in the sections. (C&D) The percentage of bone in callus and chondrocytes in the uncalcified callus was calculated using Image J software according to histological staining. Sections were obtained from at least 4 rats from each group. *p<0.05.	Gang Li 2015



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)