BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells
ESPS manuscript NO: 20084
Title: Induction of CXC chemokines in human mesenchymal stem cells by stimulation with secreted frizzled-related proteins through non-canonical Wnt signaling
Reviewer's code: 00110885
Reviewer's country: United States
Science editor: Fang-Fang Ji
Date sent for review: 2015-06-01 14:13
Date reviewed: 2015-08-31 21:17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In their manuscript "Induction of CXC Chemokines in Human Mesenchymal Stem Cells by Stimulation with Secreted Frizzled-Related Proteins through Non-Canonical Wnt Signaling" Bischoff et al. investigate how MSC respond to canonical and non-canonical Wnt signaling. They show that non-canonical Wnt5a protein and frizzled-related proteins (sFRPs) that are known inhibitors of both canonical and non-canonical Wnt signaling stimulate the p44/42 ERK and phospholipase C pathways operating through the non-canonical frizzled (Fzd) receptors 2 and 5 in MSC. A number of published reports had previously shown that SFRP1 is not only a suppressor but also an activator of wnt signaling, which somewhat limits the novelty of the study.The authors provide evidence that this signaling results in elevated expression of CXCL5 and CXCL8 by MSC and speculate that these chemokines contribute to blood vessel formation during osteogenesis in bone repair. The manuscript is well written and may have important implications for the field of MSC biology. However, not all conclusions are supported by results. The core of the manuscript is Wnt signaling. It is not clear what the chemokines regulated by it do, if anything. Cherry picking two chemokines out

of all the soluble factors that could be regulated by the Wnt pathway seems unfounded. For instance, VEGF, the bona fide angiogenesis regulator, is induced by Wnt signaling http://cancerres.aacrjournals.org/content/61/16/6050.long What is the direct evidence that CXCL5 and CXCL8 functionally adds to bone formation through angiogenesis? Could previously reported bone development defect in CXCR-null mice be due to the lack of MSC proliferation / migration / differentiation defect? And could the vascular bone phenotype of these mice be a consequence, rather than the cause, of MSC function deficiency? The study is incomplete without an assay measuring a functional change in MSC properties in the context of their speculated angiogenesis/osteogenesis implication. If CXCL5 and CXCL8 do promote angiogenesis, how do they do that? By signaling through CXCR1 and/or CXCR2? In what cells? Endothelial? Or MSC themselves? Are these receptors expressed on MSC? These are some of the questions that the authors should try to answer. Unless the data on CXCL5 and CXCL8 expression relevance are provided, the title and the conclusions should be restricted to the observations on Wnt signaling and the chemokine data – grouped in one figure and discussed with reservation. Other comments: There are too many figures with too little data. Group them in to panels. Secreted CXCL8 protein needs to be measured. VEGF and other angiogenic factors should be measured along as controls. P44/42 p and PLC pathways are not a specific readout of Wnt signaling. The authors make it sound like there is only one murine CXCR receptor. However, mouse CXCR1 has also been cloned.

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells
ESPS manuscript NO: 20084
Title: Induction of CXC chemokines in human mesenchymal stem cells by stimulation with secreted frizzled-related proteins through non-canonical Wnt signaling
Reviewer's code: 00031627
Reviewer's country: Italy
Science editor: Fang-Fang Ji
Date sent for review: 2015-06-01 14:13
Date reviewed: 2015-09-02 18:47

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The paper found that CXC chemokine expression in hMSC is controlled in part by cFRPs signalling trough non-canonical Wnt involving Fzd2/5 and the ERK and PLC pathways. The results are interesting. As minor point it could be interesting to know if Authors have evaluated CXCL10. If not this point could be at least discussed. See: Autoimmun Rev. 2014 Mar;13(3):272-80.