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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 32393
Title: Effects of CXCR3/HO-1 genes on the modification of bone marrow mesenchymal stem cells in small bowel transplant rejection
Reviewer's code: 03287656
Reviewer's country: United States
Science editor: Ze-Mao Gong
Date sent for review: 2017-02-21
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[Y] 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	[ ] Minor revision
[ ] Grade E: Poor		[ ] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[ ] No	

COMMENTS TO AUTHORS

The authors present data that injection of mesenchymal stem cells transduced with the genes CXCR3 and/or HO-1 appear to improve immunologic tolerance of transplanted allogeneic small bowel tissue in rates. Histologic and immunologic evaluations support the findings that these two proteins can increase the potential immunotolerizing aspects of MSCs. Comments are below. Figure 3 shows that BMMSCs transduces with the adenovirus CXCR3/HO-1 construct express both CSCR3 mRNA and protein. However, the levels of HO-1 mRNA and protein do not appear to have been evaluated. Concurrent evaluation of both HO-1 and CSCR3 mRNA and protein levels at this step would be helpful. Figure 4 shows histologic evaluation of small bowel after transplant for each of the experimental groups. The quality of the figure is too poor to properly evaluate the author's conclusions. Further, the materials and methods describe using a histologic method from 1970 to describe "pathologic rejection." If the authors want to make a claim regarding the effect of the modified BMMCSs on acute rejection, a more modern grading

scheme should be used such as "Transplantation. 75(8):1241-1248, April 27, 2003." While I cannot evaluate the histology due to image quality, the description of the pathologic changes does not mention any vascular findings such as arteritis. Nor does the description mention any cytologic changes such as apoptosis (later evaluated by fluorescence, but traditional grading of rejection relies on H&E) or nuclear enlargement and/or hyperchromasia in the epithelium. Are the histologic changes observed due to ischemic issues in the BM group? How patchy or confluent were the described lesions? What type of inflammatory infiltrate is increased (acute or mononuclear cell?)? Figure 6 B shows the same chi-squared and P value for every comparison. Can this be correct? Figure 7 is not clear as to the source of cells or tissue analyzed. Did the authors remove a piece of intestine from the rats on days 1, 3, 7, 10 and 14 and analyze the protein expression on that tissue? If so, the figure caption should reflect that. Does manipulating the transplanted bowel tissue so invasively have any potential to bias the results? Why is this a viable strategy rather than sacrificing rats at a certain time point and comparing the same expression patterns then? Figure 9 shows expression of CXCR3 and HO-1 protein in the small bowel. What cells are likely being stained? Are these actually BMMCSs?