Reviewer's report


Version: 1 Date: 22 July 2013

Reviewer: Dan Jin

Reviewer's report:

Dear Editors,

Have a nice day!

Thanks very much for giving us an opportunity to review the article entitled “Design and Construction A New Vascularized Tissue-engineered Bone Graft Using Pre-differentiated rADSCs, Arteriovenous Vascular Bundle and Porous Nano-hydroxyapatide/polyamide-66 Scaffold.” by Pei Yang Dr, Xin Huang Dr, Chunsheng Wang Dr, Xiaoqian Dang Prof, Henry J Mankin Prof, Zhenfeng Duan Dr and Kunzheng Wang Prof.

The present study examined the potential of angiogenesis of biomaterial scaffold using the combination of pre-differentiated rADSCs and arteriovenous vascular bundle with the methods of short-term histological techniques and immunohistochemical studies. Since the construction of tissue engineered bone with bone marrow stromal cells and arteriovenous vascular bundle has been studied and reported, this design of this study is not novel. However, what interested me is that the rADSCs chosen as seeding cells and the using of a relatively new biomaterial. At this point, this study seems worth publishing. However, this study seems to be part of a subject. There are several points which the authors should consider:

- Discretionary Revisions#

1. There are several suggestions of figures: 1. In the part of Histological quantitative analysis (Page 14), the description of data could be simplified, which could be well defined by the table. 2. It would be more appropriate if the author could add the bars indicate into the figures (figure3, figure5, figure7, figure8). 3. In the histogram of Figure 10, the order of bars should be adjusted to make a clear contrast in consistent with the order of outcomes of western blot. 4. Group B and Group should be changed into Group B and Group C (line 19 of page 2)

- Minor Essential Revisions#

1. The major problem is that the article title does not reflect this study appropriately. The title of this article is to design and construct tissue engineered bone, but the study is mainly the detection of vascularization without any
relationship with bone. Though important the detection of vascularization, such as blood vessels density of tissue is, it is not appropriate that there is no osteoblastic markers’ evaluation with the title of construction of tissue engineered bone. Otherwise, the author should consider making the article title related to vascularization and so on.

2, In the materials and methods section, the contents of osteoblastic and vascular differentiation were described, why the details of detection of osteoblastic differentiation were not mentioned in the results section?

3, In the detection section (P10), why the tissue in the C group is tested with the muscle?

4, The clearance degree for coatings of new tissue must affect the level of protein extraction and detection. In terms of clearance degree for coatings of new tissue, how to ensure that is consistent among various groups?

5, Part of conclusion seems to be far-fetched, because there is no direct experimental evidence to support it: P15, the sentence “The results revealed that compared with muscular wrapping method, vascular bundle implantation could promote vascularization of the scaffold. ” is not supported by the experiment without the comparing of muscular wrapping method. P17, the sentence “Therefore, angiogenesis of tissue engineered scaffold ultimately depends on the migration and formation of endothelial cells”, which seems to highlight the advantages of rADSCs, is very unexpected without relations with the other part of this section. P18#the sentence “Arteriovenous vascular bundle implantation was used in both Group A and B, but the scaffolds of Group A were composite with rADSCs-Endo which can self-secrete angiogenic growth factors such as VEGF and FGF (the western blot assay demonstrated the increased expression of VEGF and FGF in group A)” is not supported by direct experimental evidence. Though the results of western blot confirmed the increasing of VEGF, there is no direct evidence confirming that the reason is the increasing of rADSCs.

6, There is a little doubt for the experimental groups, when considering whether it is reasonable. If they can add a group of rADSCs + nHA/PA66, this study can be illustrated more reasonable.

7, When introducing the background, the author described the choice of seeding cells in the construction of tissue engineered bone and the methods of vascularization. The relative literature has been cited comprehensively, but the main problem is the lack of analysis. The continuity and novelty of this study compared with the previous studies is no illustrated, which should be added.

8, Both in vivo and vitro experiments, the density of the cells inoculated with the composite biomaterial should be illustrated.

9, Who completed the histological semi-quantitative detection? Was this detection a double-blind trial?

10, In the discussion section, as stated in the background section, the
construction of tissue engineered aims to treating bone defects, so does the vascularization. Considering this, there are three problems: 1, this study was not involved in any detection of bone formation; 2, The new tissue in the second and fourth week was proved to be almost the vessels and fibrosis. There is any bone tissue? This should be illustrated or explained; 3, what is the outcome of implanted rADSCs?

Therefore, we suggest this article could be accepted after the revision based on above reviews.

Thanks again for your invitation!

Kind regards!

Yours sincerely,

Dan Jin, M.D; Ph.D.

Department of Orthopaedics and Traumatology, Nanfang Hospital, Southern Medical University
1838, North Guangzhou Avenue, Guangzhou City, Guangdong Province, PR China 510515

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.