Reviewer's report

Title: In-vivo generation of bone via endochondral ossification by in-vitro chondrogenic priming of adult human and rat mesenchymal stem cells

Version: 2 Date: 22 August 2010

Reviewer: Toru Ogasawara

Reviewer's report:

The article ‘In-vivo generation of bone via endochondral ossification by in-vitro chondrogenic priming of adult human and rat mesenchymal stem cells’ by Farrell et al. aims to overcome present problem of bone tissue engineering by mesenchymal stem cell(MSC)s. The authors previously reported that bone formation was not observed in 4 weeks in-vivo implantation of chondrogenic primed MSC seeded scaffolds (Farrell E et al. Tissue Eng Part C Methods 2009). However, in this manuscript they showed that chondrogenic primed MSC seeded scaffolds can undergo endochondral ossification by improving the experimental procedures. They also demonstrated that both host and donor cells played a role in bone formation by using transgenic animal model. Though there are several additional experiments that could potentially improve this manuscript, the present study provides new information in this area. Therefore publication on BMC Musculoskeletal Disorders is merited. Minor and discretionary revisions are suggested below.

- Major Compulsory Revisions: None

- Minor Essential Revisions

1. In the second sentence of the first paragraph of the Results, though the authors described “Expression of sox 9, collagen type II, runx2 and collagen type X were significantly elevated compared to monolayer control levels”, no control data was included in Fig. 1A#. The authors should include control data in Fig 1Ai, otherwise, the text should be simply “Expression of sox 9, collagen type II, runx2 and collagen type X were confirmed”.

2. Labels are missing in each panel of Fig 1C (#, #, # and #?).

3. In figure legend, there is no explanation about boxed regions in figure1C (the right upper panel and the left lower panel).

- Discretionary Revisions

1. The manuscript would be improved if the qRT-PCR result of doner3 was included in Fig. 1A#. Also, if there was any difference in the expression patterns of chondrogenic and hypertrophic markers among doner1-3, the authors might be able to discuss about the reason why in a third donor bone formation were
observed only in chondrogenically primed pellets, not chondrogenic primed MSC seeded scaffolds

2. The manuscript would be improved if the representative results of each sample (doner1-3) were included in Fig. 1A#.

3. In the fourth and the fifth sentences of the third paragraph of the Results (beginning “Once again no bone formation was observed…), the authors used “data not shown”, though, the manuscript would be enhanced if the data were presented.

4. The manuscript would be improved if the result of negative control (immunohistochemistry by nonimmune serum etc.) was added in Fig.3.

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.