Reviewer’s report

Title: Effect of a rare genetic variant of TM7SF4 gene on osteoclasts of patients with Paget's disease of bone

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Reviewer: Nerea Alonso

Reviewer's report:

Laurier et al studied the functional consequences of rs62620995 on osteoclasts and bone resorption. This is a rare variant within TM7SF4 gene, which was identified in French-Canadian population showing potential effects in patients with Paget's Disease of Bone (PDB). The authors have performed a good and complete approach to the research question and investigate the role of this SNP at both RNA and protein level, concluding that rs62620995 increases the number of nuclei in osteoclasts and affects DC-STAMP expression during osteoclastogenesis in PDB.

The quality of the experiments and the approach performed show a good standard to be published in this journal. However, some minor changes are suggested to be implemented in order to clarify some sections:

- The authors need to reflect in the text if there is any significant difference in age, gender or extent of disease between the different groups analysed in the study.

- Although the authors claim to follow Bustin et al (Clinical Chemistry 2009 and BMC Mol Biol 2010) for qPCR publication, these papers strongly advise to disclose the probe sequence, which is missing in the present manuscript. The authors also need to clarify the analysis method they followed for the qPCR results (absolute or relative quantification) and the efficiency of the reactions.

- Following the above, on figure 3, does the ratio represented in the figures correspond to fold change? Besides, all figures are normalised by HKG, which is not mentioned in the manuscript. The authors used 3 endogenous controls, are those 3 showing similar results? The results from each of the endogenous control need to be discussed in the paper.

- The definition of PAL in Table 1 needs a better elaboration.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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