Reviewer’s report

Title: Comparative Analysis of Blood and Saliva Expression Profiles in Chronic and Refractory Periodontitis Patients

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Reviewer: Koichi Tabeta

Reviewer's report:

The paper (OHEA-D-15-0043) describes identification of characteristic representative genes in blood and saliva samples through a comparative analysis of gene expression profiles in chronic periodontitis (CP) and refractory periodontitis (RP) using GEO database.

The authors obtained GEO data (GSE4325) consisting of 13 samples which were from blood including 4 controls, 4 CP and 5 RP and the rest ten samples from saliva including 3 controls, 4 CP and 3 RP. A comparison between CP and RP samples was performed to differentially expressed genes (DEGs). Then the significantly associated miRNAs in CP were searched based on functional and pathway analysis.

In results, total 213 DEGs in CP including 170 up-regulated and 45 down-regulated DEGs were identified, while 45 DEGs including 23 up-regulated and 22 down-regulated DEGs were identified in RP. In functional enrichment analysis DEGs of CP were mainly enriched in ribosome and regulation of apoptosis related pathways in blood and saliva, while DEGs of RP were significantly enriched in immune response and response to organic substance related pathways.

Several miRNA and genes are listed as potential to be targets for treatment of periodontitis in conclusion.

I truly appreciate the approach and good challenge the author performed to identify the critical genes or miRNA in periodontitis patients or refractory periodontitis patients using the GEO database. However, I have some critical concerns in the paper as following.

Critical comments

Most importantly, I would say the data is no more than the result of screening by the authors, because generally the positivity of data in array analysis should be reanalyzed in the original data to confirm the positivity. We know positive results turn out negative in many case, especially in this small number of comparison.
In another point of view, analyses of GO and DAVID using a large number of array data from clinical samples may figure characteristics of diseases by itself, but in this small number of clinical samples, GO and DAVID analyses are of no use, since we already know how the diseases are complexed and divergently affected by multiple factors. The genes are candidates of further analysis for the authors but not for other researchers.

Of course I admit the data may contain the treasure of gene or miRNA to characterize CP or RP. However, the possibility is extremely too small and unlikely. I see the data GSE4325 was from neutrophil in blood and saliva of patients, which the authors don't mention. I suggest the authors plan extensive analysis in some way for the candidate genes using other samples taking the source into account.

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

No

**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.

No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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