



May 16, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8451-edited.doc).

**Title:** Infectious burden and atherosclerosis: a clinical issue

**Author:** Sessa R, Di Pietro M, Filardo S, Turriziani O

**Name of Journal:** *World Journal of Clinical Cases*

**ESPS Manuscript NO:** 8451

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer 00070481

(1) language should be polished.

We agree with the referee and we reviewed the paper.

3 Revision has been made according to the suggestions of the reviewer 00503099

(1) This is a very well written and comprehensive review with viewpoint on an area of interest. The manuscript is fully up-to-date, is very good in distinguishing between live bacteria and DNA signatures in plaques; it is very good on delineating direct and indirect effects of infection/inflammation on the development of atherosclerosis. It picks up controversy. It has a very good section on limitations of serology. The diagram is useful; oral pathogens are included. I would still like to see mention of "foam cell" formation, which is a relevant morphological change of macrophages when exposed to microorganisms/PAMPs.

We agree with the referee and we inserted the statement "In vitro studies have demonstrated that periodontal pathogens are able to infect endothelial cells, SMCs and macrophages, eliciting the production of proinflammatory cytokines and chemokines (e.g. IL-6 and monocyte chemoattractant protein (MCP)-1) and the formation of foam cells, hence contributing to atherosclerosis (41,42) ". See page 7.

(2) Lastly, I find the title suboptimal: while this thought (underestimated issue) fits very well in the discussion (1st paragraph), where it is meant in a clinical treatment sense, in the title it implies that not much is thought about it- but this is contradicted by the immense literature list!

We agree with the referee and we modified the title.

4 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Clinical Cases*.

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Peter LAKATOS', written in a cursive style.

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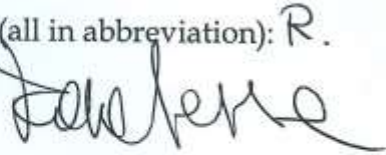
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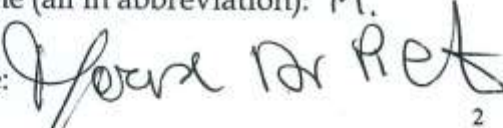
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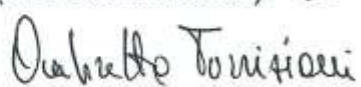
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