

June 20, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16669-review.doc).



**Title:** Novel antigen delivery systems

**Author:** Maria Trovato, Piergiuseppe De Berardinis

**Name of Journal:** *World Journal of Virology*

**ESPS Manuscript NO:** 16669

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

(1) Reviewer # 00504174: In this review, Trovato and De Berardinis reviewed the main current strategies used of live attenuated and inactivated vaccines, DNA vaccines, viral vectors, lipid-based carrier systems (liposomes and virosomes) and polymeric nanoparticle vaccines and virus-like particles. Moreover, they are mentioned additional new insight on regard of their work on a the new delivery system based on a non-pathogenic prokaryotic organism: the "E2 scaffold". The issues is of great interest and the authors showed the main topics on the evolution of vaccine strategies. However, several aspects should be revised to give a more complete scenario to the reader. In particular: 1- page 3: the author have to include a table that reassume the different type of vaccine mentioned in the paragraph (the inactivated vaccines should include also influenza virus vaccine). 2- page 4: In the section on the DNA vaccines the author have to include a table that shows the main difference or similarities of the nature of the induced immunity (humoral versus cellular immunity) that DNA vaccine produce compared to the inactivated and live vaccine. 3- page 12: in the section that describes the "E2 scaffold" vaccine delivery system the author have to include the FIGURE 1 (A;B;C panels) that it was not included in the manuscript but it is comment in the text. 4- The author at the end of the section describing "E2 scaffold" vaccine delivery system should give a more descriptive main issue of the relevance of this strategies. Is it the best strategie among the main used ? Is the immunity induced by the "E2 scaffold" similar to the other in the type of humoral versus cellular responses?

*According to Reviewer's suggestions, we provided Table 1 that summarizes the different type of vaccines mentioned in the manuscript and also reports the type of the induced immune response. We also included (at the end of the text) the Figure 1 (A; B; C panels) that unfortunately was not uploaded in the previous submission. At the end of section describing "E2 scaffold", we gave a more descriptive main issue of the relevance of this strategy.*

(2) Reviewer # 00504253: This review is an update on current strategies with respect to live attenuated and inactivated vaccines, DNA vaccines, viral vectors, lipid-based carrier systems such as liposomes and virosomes as well as polymeric nanoparticle vaccines and virus-like particles. The manuscript is well written and informative and basically acceptable with major changes. Major points 1: I cannot find Figure 1 in the manuscript. Please show figure 1. 2: Author wrote that E2 scaffold was shown to be a versatile and immunogenic delivery system, being able to display in a properly configuration antigenic/therapeutic peptides or proteins and to elicit humoral and cellular immune responses upon different ways of administrations. I understand the benefit of E2 scaffold, but please write the possible negative side effects of the E2 scaffold vaccine delivery system. 3: Present the list of the delivery systems in Table form comparing

advantages and disadvantages of each method. It would help readers to understand the manuscript better.

*According to Reviewer's suggestions, we added Figure 1 in the manuscript, at the end of the text. We also described the possible negative side effects on the E2 scaffold vaccine delivery system. Moreover, we provided in Table 1 an overview of the advantages and disadvantages of the different formulations described in this review.*

(3) Reviewer # 00504884: This is a comprehensive review recent advances in vaccine technology focusing on delivery systems. Overall, the content is well presented. The detailed listing of the different approaches should provide a useful resource for scientist in this filed, although it could be helpful to get some critical evaluation of some of the presented systems (safety, efficiency, reliability, feasibility). It would be good if the authors could provide a short critical evaluation or comment at the end of each section. Minor corrections, suggestions and comments have been made on the text using the tracking system (document attached)

*According to Reviewer's suggestions, we provided a short critical evaluation of some of the presented systems at the end of each section. Finally, we accepted minor corrections and suggestions made on the text.*

3 References and typesetting were corrected

Sincerely yours,

A handwritten signature in dark ink, reading "Piergiuseppe De Berardinis". The signature is fluid and cursive, with the last name "Berardinis" having a prominent flourish at the end.

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