

## Format for ANSWERING REVIEWERS

May 27, 2015



Dear Editor Fang-Fang Ji

Please find enclosed the edited manuscript number 14890 in Word format (Manuscript 14890), which was modified according to the issues raised by the reviewers. Please find enclosed.

**Title:** "Purinergic signaling and HIV/AIDS: from viral entry to therapy"

**Author:** Daniela F. Passos, Maria Rosa C. Schetinger and Daniela B. R.

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

**ESPS Manuscript NO:** 14890

All points raised by the referees were considered in detail. We would like to thank the reviewers for their careful reading of the manuscript. Their comments and suggestions improved the quality of the manuscript and we hope that it will now be considered suitable for publication in the **World Journal of Virology**.

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

### **1 Format has been updated**

We have updated the format according to the "Format for Minireview" document.

### **2 Revision has been made according to the suggestions of the reviewer**

Referee 1:

1. In my opinion, I felt the description of this topic is too superficial, most content needs to be discussed more detailed. For example, the section "HIV infection and the immune system", only general immune response was described, no description concerning on the HIV specific immune response.

We believe the HIV specific immune response is not the main point in this paper so we kept the description short.

2. About purinergic signaling, the authors need to discuss the signal transduction crosstalk and networks

The importance of considering cross-talks and networks when talking about pathogenic

mechanisms has been highlighted

3. Some good figures are required for a review paper.

An illustration has been added.

4. Are there any significant data suggest the purinergic receptor, ATP/ adenosine and ATP analogs as potential therapeutic targets? It is difficult convincing readers these molecules could serve as drug candidates.

The findings that suggest that purinergic ATP and purinergic receptors are described in the paper, however this field has just started being exploited and more studies are necessary to corroborate with them.

Referee 2:

1. This is a pretty good review with some good and useful information of the role of purinergic signaling in HIV and how it can be thought of as an area to target HIV. The intro lacks some explanations and definitions so it starts out a little unclear but the bulk of the manuscript is written pretty well. I would suggest improving the intro by defining some things up front: for example describe exactly what the purinergic signaling system is in the intro to make it clear what you will be talking about, also NTPDase is not defined in the intro or what it does which could help the reader as you introduce the system for the first time to the reader.

The text has been changed so the definitions are ahead of all citations.

2. ADA is not defined in intro either but then later is defined as ectoadenosine deaminase on page 6 then redefined on page 12 as adenosine deaminase.

The issue has been addressed.

3. HAND is not defined.

The issue has been addressed.

4. Then little things like it isn't control of "the" HIV infection, it is control of HIV infection. This should be corrected throughout.

These issues have been addressed

Referee 3:

Overall a timely review which covers an important topic. Minor corrections and comments are provided as track changes in the original manuscript.

The changes have been accepted.

3 References and typesetting were corrected

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

Sincerely yours,

Daniela F. Passos

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Dear Editor-in-Chief: Fang-Fang Ji,

Please find enclosed the new version of our manuscript number: 14890 entitled "**Purinergic signaling and HIV/AIDS: from viral entry to therapy**", which was modified according to suggestions by chief editor. We hope that it will now be considered suitable for publication in the **World Journal of Virology**.

Thank you for your attention.

Sincerely yours,

Daniela Passos

#### **CHANGES MADE IN THE MANUSCRIPT**

1. On the "BACKGROUND ON PURINERGIC SIGNALING" section "AP", acronym for alkaline phosphatases, was put between brackets.
2. On the 2<sup>nd</sup> paragraph of the "ECTOENZYMES AND HIV DISEASE PROGRESSION" section, the verb to be was changed from "are" to "is" to correct concordance with "the pool".
3. On the 1<sup>st</sup> paragraph of the "PURINERGIC RECEPTORS, ATP/ADENOSINE AND ATP ANALOGS AS POTENTIAL THERAPEUTIC APPROACHES" section, the verb to have was changed from "have" to "has" to correct concordance with "the study".
4. Finally, a third figure was added as suggested. This figure summarized the involvement of purinergic receptors in different stages of the infection. We are aware that not all the players were shown in this figure (such as the enzymes) but we believe more elements in one single figure could compromise the visual clearness of the figure. Perhaps we could add another figure with these elements if necessary.