

ESPS Peer-review Report

Name of Journal: World Journal of Virology

ESPS Manuscript NO: 8657

Title: Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission

Reviewer code: 00504484

Science editor: Ling-Ling Wen

Date sent for review: 2014-01-03 13:20

Date reviewed: 2014-01-08 02:51

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Lourenço et al. describe the effect of seminal lactoferrin on the induction of chemokine ligand 20 (CCL20) by the cell line HEC-1A. The results are straight forward and they do support the conclusion that seminal lactoferrin increases the production of CCL20 in their cultures, but this is not new. The statement that this induction is higher by the semen of HIV+ patients is not clearly supported by their results, even if some marginal statistical difference can be claimed between HIV- and HIV+ seminal plasma. In conclusion, I think that this paper does not add significant new information to the field. Minor points: 1.- When HEC-1A cells are stimulated with seminal plasma, are they still maintained in medium supplemented with 10% fetal calf serum? I think that the stimulatory effect should be more evident in serum-free medium. 2.- Could the authors provide an explanation to the multiple peaks of lactoferrin observed in the chromatogram of Fig. 3? Please, add at least some comment in the Discussion. 3.- Fig.3: please indicate which parameter(s) is(are) shown in the ordinates axis.

ESPS Peer-review Report
Name of Journal: World Journal of Virology

ESPS Manuscript NO: 8657

Title: Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission

Reviewer code: 00503963

Science editor: Ling-Ling Wen

Date sent for review: 2014-01-03 13:20

Date reviewed: 2014-01-16 14:18

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The current article described the seminal plasma/ lactoferrin affects the CCL20 production by HEC-1 cells. It is an interesting and important topic. My comments are as below: 1. Page 7, cell culture, I doubt that if too many/crowded cells at a density of 200000 cells per well in 96-well culture plates. 2. Page 8, Measurement of total protein in seminal plasma, "Bradfort" should be "Bradford", please check which one is correct? 3. Fig. 1A, why not include seminal plasma specimens from HIV+ subjects? 4. About the role of lactoferrin, why not fractionate the seminal plasma from HIV+ sample simultaneously? 5. Fig. 3B, why fractions with the higher lactoferrin revealed in discontinuous pattern (fractionations 1, 3-5, 7-9, 10-13)? 6. In Fig. 4, 5 sample revealed a detectable viral load, however, 17 samples with undetectable viral load. How define HIV+ in the current study?

ESPS Peer-review Report**Name of Journal:** World Journal of Virology**ESPS Manuscript NO:** 8657**Title:** Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission**Reviewer code:** 00202286**Science editor:** Ling-Ling Wen**Date sent for review:** 2014-01-03 13:20**Date reviewed:** 2014-02-16 12:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In this paper, the authors suggest that semen lactoferrin promotes CCL20 production by endocervical epithelial cells and propose some relationship with heterosexual HIV-1 transmission. The experiments appear to have been carefully planned and performed, with appropriate controls. The results have been adequately interpreted. The statistical tests have been well chosen. The paper is well written. Abstract The Abstract appears to be a bit long. "HIV?" is not "HIV-". The authors should decide what term they will further on use in the paper. There are some instances where both terms are used. It should be checked all along the MS. Results section First paragraph: What is the CCL20 concentration obtained in the supernatant of HIV+ seminal plasma treated cells? And if not available, why was it not done or expressed? Some abbreviations should be spelled out: i.e., LCs, SIV, to increase the general readership. There are few typos. This reviewer corrected some of them. The edited text is attached.

ESPS Peer-review Report

Name of Journal: World Journal of Virology

ESPS Manuscript NO: 8657

Title: Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission

Reviewer code: 00731613

Science editor: Ling-Ling Wen

Date sent for review: 2014-01-03 13:20

Date reviewed: 2014-02-21 15:01

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The authors need to do the following modifications and submit further consideration. 1) Write the abbreviations in expanded form when used for the first time in the manuscript. Further, usage of abbreviations is acceptable. 2) The role of human IL-1beta as a positive control needs to be elaborated for better understanding 3) Mention the sample size in the methodology sections. 4) Elaborate inclusion and exclusion criteria more clearly. 5) It is necessary to mention in the manuscript on whether aseptic precautions were followed in collecting semen samples and how were they stored? 6) I suggest the authors highlight the clinical significance of their study findings. Overall, the study has significant findings and the manuscript is well written

ESPS Peer-review Report

Name of Journal: World Journal of Virology

ESPS Manuscript NO: 8657

Title: Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission

Reviewer code: 00053556

Science editor: Ling-Ling Wen

Date sent for review: 2014-01-03 13:20

Date reviewed: 2014-02-23 16:25

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Comments to the Editor: Thanks for inviting me to review the review article entitled " Semen lactoferrin promotes CCL20 production by epithelial cells: involvement in HIV transmission ". Minor Comment: ? The editing of the manuscript needs minor revision. ? Language level: B. Minor revision is needed

1. TITLE Reflect the major content of the article.
2. ABSTRACT fulfill the journal requirements however, the following points are better to be considered:
 - o aim is better to be started with an action verb,
 - o HIV? / HIV+: when mentioned for the first time are better to be fully written; HIV seronegative (HIV-) / HIV seropositive (HIV+).
 - o No need to mention the ethical approval in the abstract section.
 - o The technique used in measurement of HIV viral load has to be mentioned.
 - o No need to specify the statistical tests used to evaluate results in the abstract section.
3. INTRODUCTION Well written and the systematic searches through the relative databases were well established. However, the last sentence in the last paragraph concerning the aim of the work needs to be revised and clearly written: " It showed that seminal plasma is able to promote the production of CCL20 by HEC-1A cells and that this secretion is correlated to the amount of lactoferrin present in the specimen."
4. MATERIALS AND METHODS: This section is well covered and statistical analyses were appropriate; however, the following points are better to be considered:
 - Seminal plasmas samples "HIV- men were tested for the absence of other infectious agents." Authors have to specify these agents.
 - Cell culture:
 - o The concentration of antibiotic-antimycotic solution has to be mentioned.
 - o 10% of foetal bovine serum (FBS) is needed for cell growth until confluence, however, for stimulation experiments, much less concentration is needed and this has to be revised.
 - o Using

cell density of 200000 cells/well needs revision or justification as the optimum conc. for cultured until confluence is usually of 100000 cells/well. Viral load in seminal plasma The used technique needs more details in order to be reproducible. Measurement of total protein in seminal plasma The Bradford technique lacks its reference. 5. RESULTS: o Subheadings are well maintained and results were well organized. o The concentration of CCL20 in the supernatants of HEC-1A cells incubated with seminal plasma specimens from 12 HIV- subjects as well as 22 HIV+ subjects were measured, however in results section as well as in figure 1A, the concentration of CCL20 from 12 HIV- subjects only was mentioned, while that of HIV+ subjects were expressed in term of relative CCL20 index only. Furthermore, this index was mentioned as the mean stimulation of CCL20 and this needs revision and correction. o Figure 3: X & Y axes have to be identified. 6. DISCUSSION: It is well organized and an overall theoretical analysis is incompletely given, where, the following items are better to be considered; o Third paragraph: SIV: simian immunodeficiency virus (SIV) o Incomplete analysis of all results where, correlation between viral load in seminal plasma from HIV+ subjects and its ability to stimulate the production of CCL20 by HEC-1A cells were not well covered in this section, where, the discussion is only about the role of seminal plasma lactoferrin in increasing the production of CCL20 by HEC-1A cells. 7. REFERENCES: Finally relevant but insufficient references were cited, especially the most current literatures (3/22 references only were cited from publications \geq 2008). The journal style for writing this section is well maintained.