ANSWERING REVIEWERS

March 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8247-review.doc).

Title: Animal models of atherosclerosis.

Author: Fatemeh Ramezani Kapourchali, Gangadaran Surendiran, Li Chen, Elizabeth Uitz, Babak Bahadiri, Mohammed H. Moghadasian.

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

ESPS Manuscript NO: 8247

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

Responses to the comments of Editor
Comments:

Please highlight the changes made to the manuscript according to the peer-reviewers' comments
Thank you for your careful review of our manuscript. Please be informed that the reviewers' comments were well taken and accordingly the manuscript has been revised to include all of the reviewers' points. The changes are made using "Track change" of Microsoft word, in order to highlight the changes in the revised manuscript.

1. Please provide a running title for this paper. no more than 6 words
Running title is provided in the revised manuscript.

2. Please describe every author's contribution to this paper. You may refer to the format.
Author's contribution has been included in the revised manuscript.

3. Please provide Corresponding author's title (Professor, MD, PhD),
Title of the corresponding author is provided in the revised manuscript.

1. An informative, unstructured abstracts of no less than 200 words should accompany each manuscript.
   Abstract has been modified in the revised manuscript based on the comment.

2. **Pleased provide PubMed citation numbers for the reference list, e.g. PMID and DOI, which can be found at http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed and http://www.crossref.org/SimpleTextQuery/, respectively. The numbers will be used in the E-version of this journal. Thanks very much for your co-operation.**

Pub med citation number for the references has been provided in the revised manuscript.

Responses to the comments of Reviewer

Reviewer 1: 00631850
Comments:
This is good short review exposing the different animal models of atherosclerosis. It is clear and well written, covering briefly a wide number of models, indicating its advantages and disadvantages. I have no further comments.
Thank you for your careful review of our manuscript. Your comments are really encouraging.

Reviewer 2: 00503094

Comments: This is a reasonably good mini review.
Thank you for your careful review of our manuscript. Your comments were well taken and accordingly the manuscript was revised to include all of your points. Please see below, our specific responses to your comments. All corrections are high lightened by "Track changes" in the revised manuscript as suggested by the Editor.

1. For section on mice regarding differences, it is important that differences in the immune and inflammatory responses are mentioned given that atherosclerosis is an inflammatory disorder.
The suggested point is included in the revised manuscript, under the section "Mice" and highlighted using "Track Change".

2. More details on differences between apoE KO and LDL-r KO would be desirable.
More details on the difference between apoE KO and LDLr –KO mice have been included; further, Figure 1 entitled: "Representative photomicrographs taken at aortic root from apo E-KO (Panel A), LDL-r-KO (Panel B) and their wild-type background C57BL/6J (Panel C) mice" has been included in the revised manuscript.

3. Some mention is required on the bone marrow transplantation approach along with how current models can be adapted to study aneurysms and plaque regression.
The suggested point is included in the revised manuscript, under the section "Mice" and highlighted using "Track Change", at least 2 additional references in this regard have been included and discussed.

4. "Tow strains of rabbits"? What are these rabbits "naturally defective " in? Some mention is required.
"Tow strains of rabbits" corrected to "Two strains of rabbits" and explained in detail about those two rabbit models in the revised manuscript.

5. Some mention on how the rabbit models compare with human atherosclerotic lesions would be desirable.
The suggested point is included in the revised manuscript, under the section "Rabbits" and highlighted using "Track Change".

Reviewer 3: 00504522

Comments: This is a brief but informative review describing the main animal models used in atherosclerosis research. The article contains all the necessary information for a researcher to choose which animal model fits to his research. All, authors, especially the corresponding author, have a strong background on this field which guarantee for the validity of the information presented in this article. I do not have any major comments just two friendly recommendations:
Thank you for your careful review of our manuscript. Your comments were well taken and accordingly the manuscript was revised to include all of your points. Please see below, our specific responses to your comments. All corrections are high lightened by "Track changes" in the revised manuscript as suggested by the Editor.

1) A table depicting all the animal models with their characteristics, advantages and shortcomings could be very informative of the reader
As per suggestion the table entitled "Table 1: Animal models and their features." has been included in the revised manuscript.

2) More data on the histopathological phenotypes of each model could be added.
Figure 1 entitled: "Representative photomicrographs taken at aortic root from apo E-KO (Panel A), LDL-r-KO (Panel B) and their wild-type background C57BL/6J (Panel C) mice" has been included in the revised manuscript.

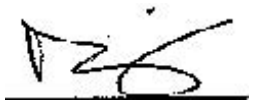
Reviewer 4: 00571492 Comments: The review entitled "Animal models of atherosclerosis" is very timely and one in which is beneficial to all in the field of cardiovascular research. I found the manuscript well planned, however believe it could be enhanced significantly with some revision, namely by:
Thank you for your careful review of our manuscript. Your comments were well taken and accordingly the manuscript was revised to include all of your points. Please see below, our specific responses to your comments. All corrections are high lightened by "Track changes" in the revised manuscript as suggested by the Editor.

1) Being edited significantly by a native English speaker, and one that has some experience writing journal articles as it currently lacks maturity. For example, quotes such as "However, it is impossible to have such an animal model..." should not be included. Rather, something like "Efforts are being made to develop animal models that replicate human atherosclerosis, however currently each have some limitations". This style of writing is unscientific and needs editing throughout the manuscript.
The manuscript has been revised and edited thoroughly for correctness and maturity as suggested. The suggested sentence has been included.

2) Reviewing the current literature in more detail to include new models of atherosclerosis that have recently been developed but are not currently included in the manuscript. Primarily mouse models such as the diabetic ApoE/GPx1, and the surgically induced ApoE model (Chen YC et al 2013).
Several new models have been discussed and included; these changes have been high lightened by "Track changes" in the revised manuscript.

3) The manuscript should only describe the positives and negatives of the different animal models and avoid describing previous experimental findings such as "We have reported that hypercholesterolemia and atherosclerosis can be prevented by dietary plant sterols...". It does not add to the discussion. Overall the manuscript is well planned and will be of significant benefit to those in the field of cardiovascular research.

Changes have been made to include your comments. The suggested point is incorporated and high lightened by “Track changes” in the revised manuscript. Thank you again for publishing our manuscript in the *World Journal of Clinical Cases*. Sincerely yours,



Mohammed H. Moghadasian, Ph. D. Professor Department of Human Nutritional Sciences University of Manitoba 351 Tache Avenue, Winnipeg, Manitoba Canada R2H 2A6 Phone: 204-235-3934 Email: mmoghadasian@sbrc.ca