Author's response to reviews

Title: The balance between two isoforms of LEF-1 is a regulator in the growth of colon carcinoma

Authors:

Shu-Hong Wang (wsh2003@126.com)
Ke-Jun Nan (nankj@163.com)
Yao-Chun Wang (Tanking@sina.com)
Wen-Juan Wang (Wangwenjuan1983@tom.com)
Tao Tian (Tiantao0607@163.com)

Version: 6 Date: 19 April 2012

Author's response to reviews: see over
Dear Dr Timothy Shipley,

Re: Manuscript reference MS: 6024328605352270

Please find attached a revised version of our manuscript “The balance between two isoforms of LEF-1 regulates colon carcinoma growth”, which we would like to resubmit for publication as an original article in *BMC Gastroenterology*.

Your comments and those of the reviewer were highly insightful and enabled us to greatly improve the quality of our manuscript. In accordance with the reviewer’s suggestion, we changed the title of our manuscript and modified the relevant contents. In the following pages, please find our point-by-point responses to each of the comments of the reviewer as well as responses to your comments.

Revisions in the text are shown using red highlighting for additions, and strikethrough font highlights for deletions. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in *BMC Gastroenterology*.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,
Dr Shu-Hong Wang PhD
Department of Medical Oncology
The First Affiliated Hospital of the School of Medicine of Xi'an Jiaotong University
Xi'an 710061, China
Tel: +86-29-85324086
Email: wsh2003@126.com
Responses to the Reviewer’s comments

Major comment:

1 Question: Previous review: The authors responded that they had quantified the flow cytometry data and observed significant increases in G0/G1. However, my question related to the SUB G0/G1 population that would be expected since it is indicative of apoptosis. Accumulation in G0/G1 alone is more indicative of cell cycle arrest.

The authors now provide a possible explanation that should be included in the discussion.

Response: The possible explanation has been included in the Discussion as the suggestion of reviewer.

2 Question: With respect to Figure 6, I commented that the authors should evaluate whether reduced tumor vascularization observed for cells expressing the LEF-1-ΔL variant is also significantly reduced in tumors of the same size.

The authors did this analysis and found differences that were not statistically significant. This is now stated in the manuscript. However, with this finding, the consequence of changes in expression of Lef-1 variants in vivo remains unclear.

Response: According to our results, colon cell lines expressing LEF-1-ΔL grow much slower than those expressing the full-length both in vitro and in vivo. As is known, rapid proliferation of tumor cells can cause hypoxia of the internal tumor tissues, which can induce the formation of new blood vessels through high level cytokines such as VEGF. Therefore, the significant difference in microvessels between colon tumors formed by different LEF-1 cell lines may be a result of the difference in the ability for cell proliferation. In the early stage of tumor formation, hypoxia caused by both tumor cells was at a low level, which could not induce statistical differences in the observed microvessels. Therefore, the reduction in tumor vascularization of HT29-LEF-1-ΔL formed gradually during the process of tumor growth, rather than in the initial stages of tumor formation. Though there are many details of tumor formation in colon cell lines with LEF-1 variants to be further understood, the proliferating capability of these cells may be one of the most important inherent initiating agents that can influence tumor growth.

3 Question: The title was changed but is not readily understandable as is. The balance between two isoforms of LEF-1 is a regulator in the growth of colon carcinoma. Should perhaps be changed to The balance between two isoforms of LEF-1 regulates colon carcinoma growth.

Response: The title “Truncated LEF-1 is one key regulator in the growth of colon carcinoma” has been changed into “The balance between two isoforms of LEF-1 regulates colon carcinoma growth” as the suggestion of reviewer.
4 **Question:** Sections added to this manuscript need to be revised by a native English speaker.

**Response:** According to editor’s suggestion, sections added have been edited by an Edanz editor.