

Name of journal: World Journal of Gastroenterology

Manuscript NO.: 19051

Column: Topic Highlights

Title: Epigenetic Regulation of Insulin-like Growth Factor Axis in Hepatocellular Carcinoma

Authors: Hend Mohamed El Tayebi and Ahmed Ihab Abdelaziz

Dear Editor,

Please find enclosed the resubmitted revised manuscript for the mini-review titled;

Epigenetic Regulation of Insulin-like Growth Factor Axis in Hepatocellular Carcinoma; Manuscript NO.: 19051.

We have read thoroughly all the reviewer comments with the constructive criticism which I do respect for the perfection of the manuscript.

We have taken all comments into consideration and we answered the questions and revised the text accordingly (all changes are highlighted in bold).

I am herewith attaching the revised manuscript and the point to point replies to the reviewers.

I always do appreciate very much your support.

With my best regards,

Sincerely,

Ahmed Ihab

Reply to reviewers:

1. Please add figures and tables in this paper!

According to your recommendation, a table and a figure has been added to the mini-review and cited in the text. The table and figure titles are: "Table 1: microRNAs regulating the key players of the IGF axis in HCC" and "Figure 1: Regulation of IGF signaling pathway by microRNAs in HCC", respectively.

The figure as well as figure legend has been inserted at the end (pages 15 and 16) of the manuscript before the References section. The table is submitted as a separate word file.

2. You'd better offer us one paper with word format next (such as, .doc or .docx), which is easy to be edited and helpful to publish earlier. Thank you very much!

Based on your request, the revised manuscript will be submitted as a word file.

3. **Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B). For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies mentioned in ‘The Revision Policies of BPG for Article’.**

According to your request, the manuscript has been revised thoroughly and edited by an English native speaker in the English center, German University in Cairo (GUC). The English department is acknowledged in the acknowledgment section in the revised manuscript.

4. **Running title: (Less than 6 words)**

A running title has been added as follows: El Tayebi HM *et al microRNAs and Insulin-like growth factor pathway*

5. **Please rearrange all the authors’ affiliations with Department, University or Institute, City, Postcode, Country, etc. (without any symbol or figure like * or ¹, postcode must be there) Such as: full name, address**

According to your request, the author affiliations have been rearranged as follows:
El Tayebi H.M

The Molecular Pathology Research Group, Department of Pharmacology and Toxicology, Faculty of Pharmacy and Biotechnology, German University in Cairo, Cairo,11835, Egypt

Abdelaziz A.I.

The Molecular Pathology Research Group, Department of Pharmacology and Toxicology, Faculty of Pharmacy and Biotechnology, German University in Cairo, Cairo,11835, Egypt

6. **Please provide the author contributions. Authors must indicate their specific contributions to the published work. This information will be published as a footnote to the paper. See the format in the attachment file-revision policies. The format of this section should be like this: Author contributions: XXX (family name should be put first in full, followed by middle names and first name in abbreviation with first letter in capital) designed research; XXX performed research; XXX contributed new reagents or analytic tools; XXX analyzed data; XXX wrote the paper. An author may list more than one contribution, and more than one author may have contributed to the same aspect.**

The author contribution has been added in the front page of the manuscript as follows:

Author contribution: El Tayebi H M contributed in literature reviewing, manuscript writing and editing, **Abdelaziz A I** contributed in designation, revision and correction of the manuscript

**7. Supported by
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2. Please provide all authors abbreviation names and manuscript title here. World J Gastroenterol 2015; In press

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3. Some files [Conflict-of-Interest Statement (COI), Copyright (need signature of all authors) and language Certificate (.pdf)] and Audio core tip (.mp3)

All these required documents and files are either attached in the manuscript or submitted with the manuscript in the online submission.

9. Please distinguish the title level, level I used all capital letters and bold, level II used Italic effect and bold, level III was just bold.

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All references are edited with the addition of the PubMed citation numbers and DOI citation as well as the required reference style.

11. Google Scholar :

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Abstract One of the highly important signaling pathways that contribute to hepatocarcinogenesis is the Insulin-like Growth Factor (IGF) signaling pathway. IGF network dysregulation is clear essential evidence in many cancers and developmental abnormalities. In hepatocellular carcinoma (HCC), minority of patients are eligible for curative treatments such as tumor resection or liver transplant. Nevertheless, unfortunately, there is a high recurrence of HCC after surgical tumor removal. Recent researches are focusing on targeting IGF axis members in an attempt to find therapeutic means for many health problems. In this review, we are shedding the lights on the regulation of the IGF axis member mainly by microRNAs in HCC where microRNAs are trying desperately to halt the aberrantly expressed IGF network by the fact that single microRNA can have multiple downstream targets in one or more signaling pathways. This is an approach in an attempt to find an efficient radical cure for HCC. Keywords Hepatocellular carcinoma, Insulin-like Growth Factors, Insulin-like growth factor receptors, epigenetics, microRNAs Introduction Insulin-like growth factor (IGF) axis is a highly conserved signaling pathway throughout evolution and has a crucial role in cellular and tissue regeneration through its proliferative and anti-apoptotic activities and its dysregulation is evidenced in many diseases [1]. IGF network possess important key players; IGF-I and IGF-II ligands that bind to their

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