

Answering Reviewers/Response letter

Comment 1: Revise the whole manuscript according to the peer-reviewers' comments.

The manuscript is revised and edited according to the peer-reviewers' comment.

Comment 2: Correct the title with no abbreviations and max of 12 words.

The title is modified as requested to be:

Interplay between microRNA-17-5p, Insulin-like Growth Factor-II through Binding Protein-3 in Hepatocellular Carcinoma

Comment 3: Finish the data sharing statement.

All liver biopsy specimens from patients and healthy donors were taken after informed consent was obtained for participation in the study. Any clinical data stated in the manuscript is anonymous. A patients' consent is uploaded as pdf file.

Comment 4: Define abbreviations and acronyms the first time they are used within the main text and then to use abbreviations throughout the remainder of the manuscript.

The whole manuscript was revised and modified as requested.

Comment 5: Make all the in text citation as superscript

All the in text citation was changed as superscript.

Comment 6: Check if there is any repeated reference, add PMID and DOI citations in the reference list and list all authors.

All the references were checked for any repetition. PMID and DOI were added and all the authors are listed in the reference list (Pages 15 & 16 in the manuscript).

Report Comments:

1-Why author have not performed the in situ expression of the different proteins in liver tissues samples using IHC techniques?

In response to the reviewers' inquiry it is worth mentioning that our main concern in this study is to study the transcriptional regulation of IGFBP-3 by miR-17-5p for the first time and hence the bioavailability of IGF-II which might pave the way for understanding the epigenetic regulation of IGFBP-3 transcriptome. However, in this and previous study (*El Tayebi HM et.al. FEBS Lett, 2012*), we screened both IGFBP-3 and IGF-II on the mRNA level in HCC tissues that showed a significant change which would favorably alter the protein expression.

2- Why patients with non-metastatic, no extrahepatic manifestations and no vascular invasion chosen for the study?

In our case, we were just able to obtain biopsies from liver transplanted patients and their donors with a written consent. As it was not possible to obtain biopsies from metastatic inoperable patients that would aggravate and worsen their condition. So, that was the only possible source of liver biopsies.

3-English language editing and proper reference check required.

English language editing was done by an English instructor at the German University in Cairo and a language certificate was uploaded as a pdf file.

References were checked and corrected as indicated.