



Università degli Studi di Firenze
Dipartimento di Medicina Sperimentale e Clinica

**CENTRO MANIFESTAZIONI SISTEMICHE DA VIRUS EPATITICI
(MASVE)**

Direttore: Prof.ssa Anna Linda Zignego



Firenze, 12th February 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name:15706-revised.doc). For your convenience, we highlighted all the changes in yellow color.

Title: MicroRNA expression in Hepatitis C Virus-related malignancies: a brief review of the available literature.

Author: Laura Gragnani, Alessia Piluso, Elisa Fognani and Anna Linda Zignego

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15706

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

1 Format has been updated.

2 Revision has been made according to the suggestions of the reviewer:

Reviewer # 02518868

R - The manuscript really needs to edit English. In addition, it needs to describe the novelty of the subject. Because there are some articles on this subject and I did not find further novelty in this manuscript.

A - The English language has been revised as suggested. A certification letter of the editing has been provided. Moreover, regarding the observation on the novelty of the subject, at present, there are no reviews focused on the role of miRNAs in HCC related to HCV infection. In this light, our review aims to select and describe the literature currently available about the role of



miRNAs in the context of HCV-related malignancy (hepatic and lymphatic). Since the reviewer raised this point, we tried to specify this issue in this revised version.

Reviewer # 02680116

R - Minor typos in pages 9 (have been showed) and 17 (sensivity) should be corrected.

A - We thank the reviewer for his appreciation and suggestions; minor typing mistakes have been corrected.

Reviewer # 02943392

R - In this review, Gragnani et al describe studies linking miRNA expression with HCV-associated tumorigenesis in the context of hepatocellular carcinoma and lymphoma. This is a very important topic and of interest to a large audience.

We are very grateful to this reviewer for his/her accurate comments which allowed to improve the quality of the paper.

Specific comments:

R- There seem to be some prominent publications on this topic that were not cited or discussed. For example, *Hepatology*, 49: 1098–1112 and *Oncogene* 25:2537–2545.

A- As suggested by the reviewer we did add a paragraph describing the results reported by these important papers; we actually did know these studies but decided to not include them in the first manuscript version because Murakami et al. and Ura et al. described HCC of different etiology without distinguish HBV-related cancers from HCV-related ones. For this reason, as suggested by the reviewer, we mentioned both the articles in the text but it was not possible to include them in Table 1.

R- Some discussion of technologies used for miRNA profiling and their respective advantages/disadvantages would enhance this and help potentially explain reasons for conflicting reports.



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A- We think that this point raised by the reviewer is very important to clarify the conflicting results reported by different papers. For this reason we better discussed this issue in the conclusion section and also introduced some references about methodological biases.

R- The vast majority of miRNAs are 21-23 nt rather than 19-25 nt as indicated in the review.

A- We changed the information about the median length of microRNAs according to the reviewer suggestion.

R- "microRNA" should be consistently abbreviated to "miRNA" throughout the review.

A- We checked throughout the text and we used the abbreviated form "miRNA".

R- This review would benefit considerably from editing for proper English.

A- The English language has been revised by a professional science editor native-English speaker as certified by the attached letter.

3 References and typesetting were corrected.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

Laura Gragnani, PhD

Centro Manifestazioni Sistemiche da Virus Epatitici
(MASVE)