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Name of journal: **World Journal of Biological Chemistry**
Manuscript NO.: **29651**
Column: **Review**
Title: **Small non-coding RNAs in translation and cancer**
Authors: **Stefania Oliveto, Marilena Mancino, Nicola Manfrini and Stefano Biffo**
Correspondence to: Stefano Biffo, Ph.D. INGM, National Institute of Molecular Genetics "Romeo ed Enrica Invernizzi", 20122, Milano, Italy and Department of Biosciences, University of Milan, 20133, Milano, Italy
Reviewer code: 00211926 and 02608938
First decision: 2016-09-27 17:15
Scientific editor: Jin-Xin Kong

Milan, 18th October 2016

Dear Editor,

Thank you very much for your interest in our work and for giving us the opportunity to revise our manuscript entitled "*Small non-coding RNAs in translation and cancer*" for publication in *World Journal of Biological Chemistry*.

The manuscript has been reviewed according to the reviewers'suggestions. Below is a detailed report of responses to reviewers.

We hope that the revised manuscript fully addresses the reviewers' requests.

We are looking forward to hear from you.

Best regards,
On behalf of the authors,

Stefano Biffo

Stefania Oliveto

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Step 1. Please revise your manuscript according to the reviewers' comments

Answering reviewers

Reviewer's code: 00211926

COMMENTS TO AUTHORS

Although this article is excellently reviewing the roles of RNAs in Cancer essential research results in this field such as Spadafora C. A LINE-1-encoded reverse transcriptase-dependent regulatory mechanism is active in embryogenesis and tumorigenesis. Ann N Y Acad Sci. 2015 Apr;1341:164-71 are not mentioned. It is suggested to add this.

A: Thanks for your appreciation. The suggested work was cited in the introduction of the manuscript.

Reviewer's code: 02608938

COMMENTS TO AUTHORS

In this manuscript, Oliverto et al nicely reviewed and discussed the updated information of miRNA in protein translation and cancer. Information provided is timingly important, particularly the possible mechanisms how miRNAs regulate mRNA translation and expression of cancer-specific miRNAs. However, some issues should be clarified and taken care of before it can be published. 1. There are two issues about the title of "Small non-coding RNAs in translation and cancer". First, this review is really discussing microRNA (miRNA) instead of ncRNA in protein translation and cancer. Another small ncRNA, piwiRNA, is briefly mentioned even though there are several other small ncRNAs including circRNA (endogenous inhibitor of miRNA) and antigene RNA (agRNA). I prefer only to use miRNA being more specific.

A: The title was corrected according to the above suggestion.

Second, it is better to use "protein translation" or "translation regulation" since the word of translation is nowadays widely used for translational medicine and this title contains "cancer" relevant to clinic issue, potentially confusing readers.

A: We appreciated this comment and we made the title less confusing.

2. The same notion of miRNA vs ncRNA and their roles in protein translation should be applied to abstract structure, particularly for the beginning and ending. Current description is too broad.

A: Since the entire text of this manuscript is focused on microRNA and their role in protein translation and cancer, we deleted in the abstract the concept of non-coding RNAs and we have cited only miRNA.

3. The abstract mentions that the number of miRNA is increasing, but this review body does not further discuss it. It is better to briefly review it since first, some unusual functions of miRNA only occur in a few miRNAs; second, a large number of newly discovered miRNAs are species or human specific such as activation role in gene regulation, binding to 5'UTR or ORF. This point should be mentioned in relevant paragraph.

A: Thanks for the suggestion. The text was modified: we briefly reviewed the concept of miRNA families and we correlated miRNAs function to their tissue specificity. We added the text accordingly at page 8, lines 235-246. Related references were added.

4. In the middle of the first paragraph of miRNA biogenesis and function, miRNA nomenclature should follow definition listed in miRBase (http://www.mirbase.org/index.shtml) or Griffiths-Jones et al (N.A.Res, 34:D140, 2006) for miRNA* and -3p or -5p. Please note that either miRNA* or -3p/-5p is applied only for some miRNAs.

A: We agree with your suggestion and we removed the confusing sentence, making the text more fluid.

5. The concept of tissue specific expression of miRNA due to their promoters are type II regulated by RNA polymerase II should be discussed since a given miRNA(s) must be expressed within the same cell at the same time with its target mRNAs and then it can be functional or meaningful.

A: Discussion of the suggested topic was added at page 7 lines 215-220 and page 8 lines 221-226 . The statement was amplified introducing the concept of miRNA expression related to host gene promoter. References were also added.

6. Writing should be consistency and not exaggerated. Examples include: miRNA or microRNA;

A: Corrections were made throughout the text. In the revised manuscript we used only "miRNA" term.

some tumor type vs "Each tumor type ..." in the abstract since only specific mRNA expression pattern are

presented only for a number of tumor types in table 1;

A: The text was corrected according to the above suggestion.

their potential role … vs "… their relevant role …" in the core tip;

A: Suggested correction was added in the core tip.

was focused largely on vs "… was focused only on …" in the paragraph of A brief history;

A: The statement was corrected according to your suggestion.

missed explanation of lin-14 in the paragraph of A brief history;

A: The point in the paragraph you referred to was better clarified and the reference work was cited.

inappropriate word of "nowadays" with a publication in year 2004 (reference 46);

A: The sentence was rephrased as suggested.

last year with reference in year 2014 (reference 80, 81)

A: Rephrased.

oncomiRs vs Oncomirs;

A: Done

the ORF of the lin-4 or lin-14 on the top page with miRNA biogenesis and function

A: We added "putative".

(No page number was provided making hard to read and cite).

A: We added page and line numbers in the revised manuscript.

Please also take care of typos.

A: Done

Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Review

A: We updated the manuscript according to the above-mentioned guidelines and requirements for Manuscript Revision-Topic Highlight.

Step 3. Please provide an Audio Core Tip

An Audio (.mp3) of the Core Tip was recorded and uploaded.

Step 4. Please subject the manuscript to CrossCheck analysis and the final title to Google Scholar search, and store screenshot images of the results

We performed a Google Scholar search for the title as requested. We performed also CrossCheck analysis using a different anti-plagiarism software from the one you suggested (we don't have iThenticate subscription). The screenshots are uploaded.

Step 5. Please provide the files related to academic rules and norms.

Authors declare no conflict of interests for this article. No file was uploaded.

Step 6. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s)

We indicate here the identification code for "Fondazione BUZZI Unicem": identificativo P23-4.

Step 7. Please revise the language of your manuscript.

The manuscript was proofread by our co-author Nicola Manfrini who is a native speaker.

Step 8. Please sign the Copyright Assignment form

Copyright Assignment form was uploaded, as requested.