

ANSWERING REVIEWERS

Padova, December 2, 2013

Liang-Sheng Ma
Editor in Chief
World Journal of Gastroenterology



Dear Editor,

Enclosed, please find the edited manuscript in Word format (file name: 5753-review.docx).

Title: Telomeres, telomerase and colorectal cancer

Authors: Roberta Bertorelle , Enrica Rampazzo, Salvatore Pucciarelli, Donato Nitti, Anita De Rossi

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5753

The revised manuscript has been improved according to the reviewers' suggestions. A point-by-point response to the reviewers' comments is provided below. The changes made in the revised manuscript are in bold.

The format has been updated

The references and typesetting were corrected

The final version of the manuscript has been revised by native English speakers

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

Yours sincerely,
Anita De Rossi

A handwritten signature in black ink that reads 'Anita De Rossi'.

Address for correspondence

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Reply to Reviewers' Comments

Reviewer 1

The manuscript 'Telomeres, telomerase and colorectal cancers' by Bertorelle et al reviews the role of telomere/telomerase in colorectal carcinogenesis, diagnosis and prognosis. It is an

interesting review and has covered most of the updated information/progress in the field. I only have a couple of suggestions. 1. Abstract is a bit too long and could be more concise.

In agreement with the reviewer's suggestions, we shortened the abstract.

2. It might better to include the most recent findings (Pucci et al 2013, Cell Stem Cell 12:479) that short telomeres may affect genome-wide DNA methylation and epigenetic landscape in cells/tissues, which may play a role in regulation of oncogene expression as well as tumor suppressor silencing.

We thanks the reviewer for mentioning this important article, and we have included it in the revised manuscript (Page 5, Reference 13).

3. Page 5: codes for an mRNA composed of 16 exons and 15 introns': mRNA should not composed of introns.

Indeed, mRNA is composed only of exons; only the premature RNA contains exons and introns. The incorrect information was the result of a typing error; we thank the reviewer for finding this error and we have corrected it.

4. Page 5, in the same paragraph as above. Please provide references for each finding you mentioned.

The findings listed in this paragraph have been reviewed in detail in Reference 17 (Dolcetti and De Rossi, 2012). For clarity, we have now identified this point as follows: reviewed in 17.

5. Please spell out MMR in the text, not just in the figure legends. Minor points: please check spellings and grammars

MMR is specified in the text (Page 7). The final version of the manuscript has been revised by native English speakers.

Reviewer 2

In this review paper, the authors reported several issues just known in literature. Some sections of the manuscript are redundant and overall the manuscript should be shortened

The abstract has been shortened, and a few redundant sentences throughout the manuscript have been deleted. We would like to pointed out that the purpose of this specific review is to accurately describe the literature data (including ours) in the field of telomeres, telomerase and colorectal cancer. We advance a model for the kinetics of telomere shortening and telomerase activation in colorectal cancer (Figure 1).

Reviewer 3

This is a very interesting review about telomeres and telomerase in colorectal cancers. The manuscript is well written. I have only some minor suggestions.

1) In the Abstract and 1st paragraph of the Introduction, I would delete “this molecular heterogeneity also accounts for the great clinical variability of the disease”. Delete “the” after “Besides”.

According to the reviewer's suggestions, the sentence has been modified and "the " has been deleted.

2) All gene names should be in italic.

All gene names are now presented in italic.

3) In Page 6, I would delete the 1st sentence of the last paragraph. In the same paragraph, please delete “high-grade” from “high-grade microsatellite instability”. In the end of the same paragraph (Page 7), I would add a sentence like “While significance of telomere alterations in MSI CRC is unclear, telomere dysfunction is considered to be a major driving force in the generation of CIN.”

We revised the text according to the reviewer's suggestions (Page 7).

4) In the second paragraph of Page 7 (Line 8-9), I would change “colorectal polyps” to “colorectal adenomas from patients with familial adenomatous polyposis (FAP). Please change “familial APC” to “familial FAP”.

The text has been changed according to the reviewer's suggestions (Page 7).

5) Please rephrase the 1st paragraph in the Concluding remarks. There is nothing wrong, but I don't like that “according to the majority of studies” and “according to most studies” appear in one short paragraph.

The first paragraph has been rephrased.