

November 22, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 14537-Review.docx).

Title: Extending the functions of the homeotic intestinal-specific transcription factor Cdx2 through nontranscriptional activities

Author: Jean-Noël Freund, Isabelle Duluc, Jean-Marie Reimund, Isabelle Gross, Claire Domon-Dell

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 14537

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

1. Reviewer 69641

This is a very interesting Review that is pointing up the role of Cdx2 as a factor able to exert a wide array of effects in a way that is not due to its activity as transcription factor. It is of great interest the cytoplasmic localization of Cdx2 in colon cancer. The discussion about this point may be implemented.

Reply

The authors thank the Reviewer for his very positive comments.

We agree with him that the cytoplasmic localization of the Cdx2 protein observed in some human colon cancers is of great interest since, as we mention in the text, this factor may then meet new partners and therefore have new effects under its abnormal location in malignant cells.

According to the suggestion of the Reviewer, we have now added one new sentence (last sentence of the last paragraph in Page 9). Here we emphasize that this issue, although interesting, might be particularly difficult to address at the mechanistic level since appropriate in vitro cellular models with this cytoplasmic localization of Cdx2 are still missing.

2. Reviewer 70758

The paper by Jean-Noel Freund et al., named: "Extending the functions of the homeotic intestinal-specific transcription factor Cdx2 through nontranscriptional activities" is a minireview paper, aiming to present some of the characteristics of the Cdx2 homeoprotein and especially its role as a tumor suppressor in gut and especially in colorectal cancer (CRC). It's a nice and interesting paper. My only comment is concerning the section "OPEN QUESTIONS AND PERSPECTIVES". In this last section the authors must be concentrated into the extraction of possible conclusions and open questions and not to present foreign data and new citations. I would suggest authors to rewrite this part of the paper. Following revisions and resubmission, this article is potentially suitable for publication.

Reply

The authors appreciate the general comment of the Reviewer who considers this contribution as "a nice and interesting paper".

As recommended by the Reviewer, we have modified the section "Open Questions and Perspectives" which is now split and rearranged into two sections: "Open Questions" and "Conclusion".

In "Open Questions", we discuss the new issues that are and/or might be experimentally investigated

based on the findings on the nontranscriptional functions of Cdx2. We put them in the perspective of what is known for other systems and therefore, we have incorporated the corresponding citations. In the section "Conclusion", we focus on the "take-home message" of this minireview, without references.

3 Typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink, appearing to read 'JN Freund', with a long, sweeping horizontal stroke extending to the right.

Jean-Noel Freund, PhD
Inserm Unit UMR_S1113
University of Strasbourg
67200 Strasbourg
France
E-mail: jean-noel.freund@inserm.fr