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June 27, 2019

Dr. Subrata Ghosh
Editor-in-Chief, World Journal of Gastroenterology
Baishideng Publishing Group
7041 Koll Center Parkway, Suite 160
Pleasanton, CA 94566 USA

Dear Dr. Ghosh,

On behalf of the co-authors I am pleased to submit for publication in *World Journal of Gastroenterology* a revised version of our manuscript #48781 entitled "The Role of Ion Channels in Gastrointestinal Cancer". We thank the reviewers for their helpful comments. Our point-by-point responses are below.

Response to reviewers

Reviewer #1.

Comment: As the paper was entitled "ion channels in GI cancers", more kinds of ion channels should be discussed here. For example, zinc transporters.

Response: A new section on zinc transporters has been added along with a new Table 5 listing all of the GI cancers in which various Zn transporters are dysregulated.

Reviewer #2

Comment: In general, the authors should address more details about the diagnostic and prognostic implications of ion channels in CONCLUSION or PROPECT, especially targeted therapy should be streamlined and updated.

Response: A revised, updated and more detailed CONCLUSION section has been prepared that focuses on the diagnostic and prognostic implications of ion channels, especially targeted therapy.

Reviewer #3

Comment: Major comment: 1. The authors should prepare 2-3 figures showing the potential molecular mechanisms of the association of ion channels and cancer. Only as a suggestion, it may be a figure with oncogenic ion channels and the other one with channels as tumor suppressors. Another figure may focus either on CFTR or drug repurposing. Minor comments: 1.

It makes more sense to place the section “additional mechanisms of tumor suppression” immediately after the Wnt/beta catenin signaling paragraph. 2. Page 29, last paragraph “it’s up-regulation is” should be “its up-regulation is”.

Response: We have prepared three new figures, following the suggestions of the reviewer. The first two figures describe potential mechanisms and pathways of tumor suppression mediated by CFTR (Fig. 1 and 2). The third figure depicts potential oncogenic and tumor suppression mechanisms of ion channels (Fig.3).

Sincerely,

A handwritten signature in black ink, appearing to read "Patricia Scott", with a stylized flourish at the end.

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