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24th of October 2022

Dear Editor:

Please find enclosed our revised manuscript entitled "Current opinion in the regulation of small-intestinal magnesium absorption," which we request you to consider for publication as a Review article in the *World Journal of Gastroenterology*.

We appreciate the interest that the reviewers have taken in our manuscript and the constructive criticisms they have given. We have addressed all of suggestions and comments of the reviewers. In accordance with the comments and suggestions, we have revised our manuscript.

This revised manuscript has not been published elsewhere and is not under consideration by another journal. We have approved the manuscript and agree with submission to *World Journal of Gastroenterology*. There are no conflicts of interest to declare.

We look forward to hearing from you at your earliest convenience.

Sincerely Yours,

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## Reviewer #2:

1.In paragraph: Mechanism of small intestinal Mg<sup>2+</sup> absorption, the authors mention that "One research group has proposed that transient receptor potential melastatin (TRPM)6 mRNA expression and transcellular Mg<sup>2+</sup> absorption were not present in the small intestine. However, a study from the same group showed positive immunofluorescence staining of TRPM6 protein in the absorptive cells along the brush-border membrane of the villi in the duodenum", That seems contradictory, what is the possible explanation?

Answer; We aim to point out the contradictory report from that group. They could detect TRPM6 protein, but not TPRM6 mRNA, in small intestine. The concluded that "TRPM6 mRNA expression and transcellular Mg<sup>2+</sup> absorption were not present in the small intestine", it was a mistake conclusion.

2.In paragraph: Transcellular Mg<sup>2+</sup> absorption, the sentence"In addition, recent mass spectrometric peptide sequence analysis confirmed the expressions of TRPM6 and TRPM7 in the duodenum and jejunum", seems be superfluous.

Answer; The present of TRPM6 and TRPM7 in small intestine is currently under debate. Mass spectrometric study of TRPM6 and TRPM7 in the duodenum and jejunum can confirm the expression of these protein in small intestine. This sentence is not superfluous.

3.In paragraph: Transcellular Mg<sup>2+</sup> absorption, the sentence"A recent study reported the expression of a heterodimer TRPM6/7 channel in the plasma membrane of duodenal and jejunal epithelium", should be moved before "However"

**Answer.** We have edited our manuscript according to reviewer's comment.

4.In paragraph: Paracellular  $Mg^{2+}$  absorption , In the fifth line, "Currently" should be canceled. In the tenth line," However" is not appropriate here

<u>Answer.</u> We have edited our manuscript according to reviewer's comment. We deleted Currently in fifth line and However in seventh line of the paragraph "Paracellular Mg<sup>2+</sup> absorption".

5.In paragraph: Luminal acidity, In the tenth line," However" is not appropriate here

**Answer.** We have edited our manuscript according to reviewer's comment. We deleted However in tenth line of the paragraph "Luminal acidity".