

## ANSWERING REVIEWERS

January 10, 2014

Dear Prof. Lian-Sheng Ma,  
President and Editor-in-Chief “*World Journal of Gastroenterology*”

Please find enclosed the edited manuscript in Word format (file name: Manuscript ESPS6777.doc).

**Title:** Cellular Physiological Approach for Treatment of Gastric Cancer

**Author:** Atsushi Shiozaki, Daisuke Ichikawa, Eigo Otsuji, Yoshinori Marunaka

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 6777

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

**Comments from Reviewer:**

1) It would be more helpful if the authors can elaborate more detail about the regulatory volume decrease.

**Response:**

According to the reviewer’s comment, we revised “Regulation of osmolality” part (page 11), as follows.

“RVD occurs after hypotonicity-caused cell swelling. RVD is caused by activation of ion channels and transporters, which cause effluxes of  $K^+$ ,  $Cl^-$ , and  $H_2O$ , leading to cell shrinkage.”

2) Do chloride channels contribute to the regulation of intracellular ion concentration in GC cells?

**Response:**

According to the reviewer’s comment, we revised “Regulation of intracellular ion concentration” part (page 10), as follows. Further, we added the new reference, No.50.

“ $Cl^-$  channels also contribute to the regulation of  $[Cl^-]_i$  which is related to cell volume. When cell shrinkage occurs isosmotically,  $[Cl^-]_i$  decreases because the major membrane-permeable anion is  $Cl^-$  [50].”

3) Is NPPB the CLIC blocker?

**Response:**

According to the reviewer’s comment, we revised “Regulation of osmolality” part (page 11), as follows.

“NPPB is the broad spectrum  $Cl^-$  channel blocker which is fat-soluble and inhibits both  $Cl^-$  channels in cell membrane and CLIC.”

4) Do the NKCC and AQP play some roles in RVD?

**Response:**

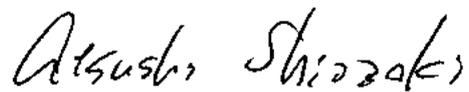
According to the reviewer’s comment, we revised “Regulation of osmolality” part (page 11), as follows. Further, we added the new reference, No.63, 64.

“AQPs also contribute to RVD [63]. On the other hand, NKCC plays some roles in regulatory volume increase (RVI) [64].”

3 References and typesetting were corrected

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

Sincerely yours,

A handwritten signature in black ink that reads "Atsushi Shiozaki". The signature is written in a cursive, slightly slanted style.

Atsushi Shiozaki, MD, PhD

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