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April 17, 2011

Dear Editor

Please find enclosed the edited manuscript in Word format (filename:6803-review.doc)

Title: Rho/ROCK signaling in motility and metastasis of gastric cancer

Author: Tasuku Matsuoka and Masakazu Yashiro

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6803

We greatly appreciate your invitation for us to re-submit our article article "Rho/ROCK signaling in motility and metastasis of gastric cancer". 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

We are most grateful to you and the reviewers for the helpful comments and have addressed each concern with either new data or modification of the manuscript text. A brief overview of changes made has been included below, and we hope that the explanations and revision of our work is satisfactory.

We have carefully considered the referee's comments and have made responses as described below. Also, we highlight all changes in the revised manuscript.

Referee #1:

(1) The authors should separate ROCK into ROCK1 and ROCK2, as they have different functions and also different regulators (e.g. RhoE for ROCK1 and not ROCK2) and possibly different downstream target.

Response: We agree that this information is of value. According to your suggestion, we have now amplified the text in the "OVERVIEW OF RHO/ROCK PATHWAY" section and added information to Table (Characteristics of Rho/ROCK substrates).

Referee #2:

(1) First of all, there is shortage of readability in this review, which should and had better be polished and checked by an English native speaker/editor before submission. For instance, frequent somewhere in the review, it is simply reference-packed rather than informatively-organized and readable.

Response: We greatly appreciate the reviewer's precious comments. Actually, English grammar was already checked by native speaker in writing this paper. However, we carefully checked grammar, spelling and logic errors again and revised

in this manuscript. We edited the text worth to read more persuasive and better informatively-organised.

(2) Secondly, the review seems to be somehow longer than it could be, which was built on two aspects, that is motility and metastasis. To be readable and focus, the paper presented could be dividied into two serial reviews over which deserves your thinking.

Response: We appreciate the point made by the reviewer. In this paper, the main purpose of our review is to clarify the role of Rho/ROCK signaling in metastasis of gastric carcinoma. Gastric carcinoma, especially scirrhous type of this malignancy shows the specific progression pattern which is closely correlated with metastatic activity. Cell movement may be an important process for elucidating this mechanism as shown in this text. One of the things we would like to emphasize in this report is how cell motility contributes to establishment of metastasis. Rho/ROCK pathway has played a critical role in motility of cancer cells which leading to invade to distant organs. Therefore, we would like to mention that story of motility and metastasis is also essential to derive our goal. We apologize for confusing the reviewer due to our insufficient organization of the text. As mentioned above, we edited the manuscript more readable and better organized.

(3) Third, with regards the relevant contents of Rho/ROCK family (RHOA, RHOB and RHOC), it would be better to list in a table rather than in word form.

Response: We agree that this is an area where additional information is useful. We made a new Table (Characteristics of Rho/ROCK substrates) as the reviewer mentioned.

(4) Figure 1 here is not helpful in illustrating the information the authors delievered. It would be suggestion that the figure 1 here should be redone.

Response: We agree that this information is of value. We changed the Figure 1 in accordance with reviewer's comments.

We hope you will seriously consider this report for publication in the *World Journal of Gastroenterology*

Sincerely yours

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