

Format for ANSWERING REVIEWERS



December 30, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6531-review.doc).

Title: Expression of Alpha Smooth Muscle Actin in Living Donor Liver Transplant Recipients

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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

Reviewer 1 (00039518)

(1) The Authors should specify in Materials and Methods which was the etiology of liver disease in the 2 pediatric patients who had immunosuppression withdrawal. I suppose it was biliary atresia according to the abbreviation BA reported in Table 1. Furthermore, the reason why the immunosuppressant medication was withdrawn in these 2 cases should be explained

Answer: We added the sentences in Page 7, line 5 to 10. "One patient was an 18-year-old male who underwent LDLT for biliary atresia (BA) at 5- years of age. In this case, immunosuppression (IS) was stopped according to the weaning protocol because of his good condition 68 months after the LDLT. Another patient was an 11-year-old female who underwent LDLT for BA at 11- months of age. Her IS was stopped non-electively because of EBV infection 3 months after the LDLT."

(2) According to figures 2 and 3, the increased number of α -SMA positive cells in 2 transplanted pediatric patients without immunosuppression compared to 4 pediatric patients transplanted and immunosuppressed does not seem to translate into a significantly worse course of fibrosis progression as the 2 immunotolerant patients show staging 0 and 1 at 7 and 9 years from transplant, respectively. This counteracts the statement " α -SMA appears to be a potential marker predicting the progression of fibrosis" (Discussion section). The Authors should comment and discuss this point.

Answer: We added the sentence, in *Discussion* Page 10, line 20 to Page 11, line 1. "In the current study, in two cases of tolerance, the progression of fibrosis remained low, although the ratio of α -SMA-positive areas remained high in both cases. However, Yoshitomi *et al.* reported that liver fibrosis progression in tolerant patients was higher than that in non-tolerant patients [21]. Therefore, we propose that α -SMA may be a potential marker of the progression of liver fibrosis. Thus, we should continue to follow these two cases carefully to ensure that the progression of fibrosis is not missed."

(3) The abbreviation α -SMA must be substituted with the extended expression "smooth muscle actin"

in the title and in the abstract at first citation.

Answer: In the title and abstract, α -SMA was changed to "alpha smooth muscle actin".

(4) Abstract, line 2: change immunosuppressant with immunosuppression; line 5: change ...two patients...with ...two pediatric patients; line 8: change ...to the cases...with...to four transplanted pediatric patients...; line 9: change ...in these adult cases...with ...in three adult transplant patients...; line 11: change ...may...with...could...

Answer: We have changed the sentences according to the suggestions of the reviewer, respectively.

(5) Introduction, page 4, line 16: change...such as infection... withsuch as in the case of infection....

Answer: We have changed the sentence according to the suggestion of the reviewer.

(6) Introduction, page 4, line 24: change ...induced by immunosuppression... with ...induced by withdrawal of immunosuppression....

Answer: We have changed the sentence according to the suggestion of the reviewer.

(7) Discussion, page 10, line 15: change ...imagined that... withsupposed that....

Answer: We have changed the sentence according to the suggestion of the reviewer.

(8) Discussion, pages 10-11: I do not understand well the meaning of the phrase...an increase in α -SMA might have been observed in patients who did not have an increase in α -SMA at the prefibrotic stage if the time of the biopsy had been different. Please clarify.

Answer: We have changed the sentence including this phrase, in *Discussion* Page 11, line 2 to 3. "periodic follow-up examination will be required to evaluate and support this hypothesis."

(9) Discussion, page 11, line 18: change ...reports in mice that T cells... with... reports in mice showing that T cells...

Answer: We have changed the sentence according to the suggestion of the reviewer.

(10) Discussion, page 12, lines 3-4: change the phrase "Therefore, we currently confirm the presence of fibrosis by liver biopsy to decide on the course of treatment" as follows: Therefore, we confirm that the liver fibrosis staging assessed by biopsy is the main parameter influencing the course of treatment.

Answer: We have changed the sentence according to the suggestion of the reviewer.

Reviewer 2 (00502871)

(1) The number of index patients is small (N of 2) limiting the robustness of the conclusions.

Collaboration with other centers for confirmation with a larger sample may be possible.

Answer: Yes, we agree the suggestion of the reviewer. However, present study is "Case report", we would like to report when larger sample is collected in the future.

3 References and typesetting were corrected

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

Sincerely yours,



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