

Format for ANSWERING REVIEWERS



February 14, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 7220-review.doc).

Title: Intervention on Toll-like receptors in pancreatic cancer

Author: Juan Vaz , Roland Andersson

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 7220

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

(1) Reviewer No. 00057875

In the review by Vaz and Andersson entitled "Intervention on Toll-Like Receptors in Pancreatic Cancer", the authors present evidence that TLRs contribute to the pathophysiology of pancreatic cancer and may be promising therapeutic targets. Five TLRs are discussed, including TLR2, TLR3, TLR4, TLR7 and TLR9, as well as respective agonists and inhibitors.

General Comments: Review is of interest. The paper needs to be carefully edited and corrected (grammar/diction).

Specific comments: 1. Please clearly indicate whether each TLR has been reported to be expressed in primary human pancreatic cancer tissue, pancreatic cancer cell lines, or in mouse models.

Although in some cases this was explained, in others it was not clear. Evidence of expression in primary PDA would of course be most clinically relevant. Also please clarify if expression was localized to epithelial and/or stromal cells. 2. Has TLR expression been associated with poor survival of patients with pancreatic cancer? 3. Mention and additional discussion of Figure 1 and Table 1 & 2 should occur earlier in the paper, not in the Concluding Remarks.

Answer

General changes: The manuscript has been carefully edited and corrected. A brief discussion of FOLFIRINOX treatment has been added to the manuscript (page 4, last line – page 5, lines 1-6)

Comment 1: The species is now clearly indicated when relevant. New abbreviations implemented are: mPDA (murine PDA) and hPDA (human PDA). PDA refers to general knowledge or hypothesis than may be actual in all pancreatic ductal adenocarcinoma, undependently of the carrier species.

A new table (table 1) has been created. Here, the hPDA cell lines expressing TLRs are presented. Their original source and phenotype is also showed.

Specific discussion for each TLR has been placed at the end of each section. TLR2 (page 8, line 10-18), TLR3 (page 9, line 10-13), TLR4 (page 11, line 3-17), TLR7 (page 12, line 19-27), TLR9 (page 14, line 4-6). Clinical aspects for each TLR may be found here.

Comment 2: TLR4 (page 11, line 1-4).

Comment 3: All tables and figure 1 are now introduced at the end of the introduction (page 5, line 15-17). The closing remarks section has been modified. A more general discussion is now presented since specific discussion for each TLR has been relocated as described above. Note that the manuscript include now three tables and one figure. The previous Table 1 and Table 2 are now Table 2 and Table 3, respectively.

(2) Reviewer No. 00068107

Answer: The language has been carefully polished.

3 References and typesetting have been carefully gone through.

Thank you for considering publishing our review in the *World Journal of Gastroenterology*.

Sincerely yours,

Roland Andersson

Roland Andersson, MD, PhD
Professor of Surgery
Dept of Surgery, Clinical Sciences Lund
Lund University
SE-221 85 Lund, Sweden
Tel +46-46 172359
E-mail: roland.andersson@med.lu.se