Answering Reviewers

September 5, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5052-review.doc).

Title: Extravascular use of drug-eluting beads: A promising approach in compartment-based tumor therapy

Author: Simon Binder, Andrew L. Lewis, J.-Matthias Löhr, Michael Keese

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5052

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

1. DEBS IN EXTRAVASCULAR USE should add some prospect of DEBs in intraperitoneal therapy of peritoneal carcinomatosis, which particular emphasis on its clinical application and how to reduce side effects, future research trends etc.

   According information has now been added to the conclusion and is indicated in bold lettering.

2. How can the authors state that these encapsulation devices were able to shield them from the hosts' immune system (ABSTRACT)? Please clarify in "DEBS IN EXTRAVASCULAR USE".

   Encapsulated cells harbouring CYP2B1 is an exciting idea. Based on previous experience with encapsulated insulin-producing cells, it is unclear how long such cells will be left undetected by the immune system. Peri-implant fibrosis and attack by immune-competent cells are common problems and could considerably limit the life span of such implants. Could you please comment on how intratumorally injected cells would escape immune detection?

   We now added explanation of immune-evasion using DEBs verified with new references. A short description of the molecular structure of the DEBs should help to understand the explanation. Changes are indicated in bold lettering.

3. Since peritoneal release of chemotherapeutic drugs is anticipated to have rapid absorption, could you comment on possible off-target effects of these drugs?

   The most common off-target effects are now added in bold lettering.

4. The higher efficacy of free drug vs. encapsulated drugs in vitro as compared with almost equal efficacy in vivo warrants some discussion.

   An explanation of these findings has been added in bold lettering. Since the drugs were administered directly into the compartment, lower dosages could be used to achieve the same or better efficiency. No animals survived treatment with the amount of free drug, which would have been necessary to achieve comparable results.

   A scheme illustrating the function of drug-eluting beads would be of interest to the readers

   Additional information on the drug-eluting beads has now been added and liberation processes have been explained. Changes are indicated by bold lettering.

5. What do the arrows on Fig. 1B indicate?

   The arrows were indicating conglomerates of DOXDEBs (as mentioned in the figure legends). We omitted them, as it is not necessary to have this information in order to understand the concept, and they were rather confusing than explaining.

   Figure 2 A and B are not clear, should update, or add give higher magnification figures to show dox-DEB encapsulated by fibrin and lymphocytes.

   We have replaced the figure 2 A and have changed figure legends of 2 B.

6. There are many small errors in this manuscript, the authors should check carefully and correct them. For example, standard journal abbreviations should be applied in ref.14,43,44,49,50,60,63,66,67,73.

   The MS has been revised to omit all errors in the manuscript. Mistakes were corrected and ISI journal title abbreviations were applied in all references.

   Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B).

   One of our co-authors (Andrew L. Lewis) is a native speaker and corrected all language errors.

7. Please provide the author contributions.

   Authors contributions have been provided

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

Sincerely yours,

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