

Format for ANSWERING REVIEWERS



January 27, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: **6169-edited.doc**).

Title: Targeted therapy in advanced metastatic colorectal cancer; current concepts and perspectives

Author: Florian Hohla, Thomas Winder, Richard Greil, Ferenc G Rick, Norman L Block, Andrew V Schally

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6169

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

1 The manuscript was written and corrected by two native speakers of English Dr. A.V. Schally and Dr. Norman Block. Dr. A.V. Schally and Dr. Norman Block also made the final revisions for English language proficiency, therefore we do not feel that there is a need for a English language Grade A certificate.

2 Changes made to the manuscript have been highlighted.

3 A Running title was provided: Targeted treatment strategies in colorectal cancer

4 Zip code for Zurich was provided:

5 Affiliations were corrected according to recent changes.

6 Authors contributions have been added.

7 Corresponding authors title was provided.

8 Core tip was added.

9 Citations and references were adapted according to the journal style by endnote program.

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

Reply to reviewer 02461109:

1. If the authors want to emphasize the use of cytotoxic LHRH analogs for future human trials against CRC, it would be better to describe the percentage of CRC that overexpress LHRH receptors in advanced CRC in the text.

We inserted our reply to reviewer **02461109** on page 13 line 10 from the bottom:

In our experimental studies, all 5 human CRC cell lines evaluated expressed LHRH receptors (reference

79, Szepeshazi et al 2007 int J Oncol 30:1485-1492). Currently, there are no clinical data on the expression of LBHRH receptors in CRC. However, a common practice in clinical trials with cytotoxic LHRH analog AN-152 on prostatic, bladder, ovarian and endometrial cancers is to first evaluate the expression of the LHRH receptor in the tumors of patients by immunohistochemistry.

2. The information of LHRH receptor gene mutation in CRC is not described in the text. If available, this point should be added to the text.

We are not aware of any published data on LHRH receptor gene mutation in CRC up to date.

12. Tables were formatted according to editors suggestions.

13. Reference 22 (Cunningham et al NEJM 2004) was added, as it was missing (BOND-study).

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

Sincerely yours,

Florian Hohla, MD

IIIrd Medical Department

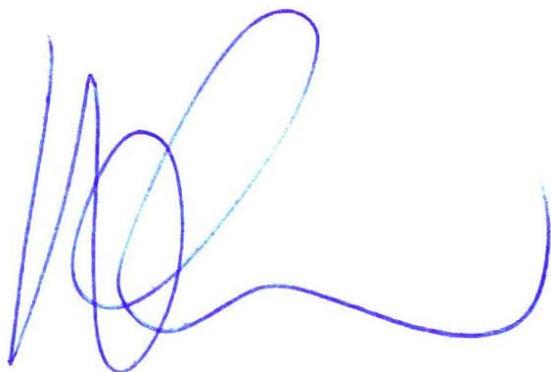
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A handwritten signature in blue ink, consisting of several overlapping loops and a long horizontal stroke at the end.