

06th of Mar, 2013

Dear Editor,

Please find enclosed the revised and edited manuscript in Word format (Furi_Sipos_WJG_2013_1995_revised.doc).

Title: Epithelial Toll-like Receptor 9 Signaling in Colorectal Inflammation and Cancer: Clinico-pathogenic Aspects

Authos: István Fűri, Ferenc Sipos, Tiana M. Germann, Alexandra Kalmár, Zsolt Tulassay, Béla Molnár, Györgyi Múzes

ESPS manuscript No: 1995

Unfortunately, our firstly submitted manuscript was electronically edited instead of our previously revised manuscript (send back via email to Professor L.S. Ma /l.s.ma@wjgnet.com/ and esps@wjgnet.com on the 9th of February, 2013). Now we send you back the correct version!

The manuscript has been improved according to the formal requirements of WJG and suggestions of reviewer.

1. At first sight, it seems to be controversial that both TLR9 agonists and antagonists may have beneficial biologic effects in IBD or colorectal cancer. Due to complex signaling of oligodeoxynucleotide binding TLRs (including TLR9) a dynamic regulation of pro- and anti-inflammatory cytokines is present, therefore TLR9 antagonists may have therapeutic potential in these conditions as well. This explanation of the discussion of TLR9 antagonists had been inserted to the text.

2. A new chapter discussing TLR9 polymorphisms' contribution to the development of disease had been inserted to the text.

3. The conclusion part had been edited.

4. A detailed figure legend had been inserted to the text.

5. As concrete scientific data about the role of TLR9 k.o. mice in IBD or colon cancer pathomechanism cannot be found on large scientific search engines, we, the authors, do not think that the discussion of these kind of animal model are necessary for this review. TLR9 k.o. mice had been usually used in infectology researches, which is not topic of our manuscript.

6. The title had been changed from "Epithelial Toll-like Receptor 9 Signaling in Colorectal Inflammation and Cancer: Pathogenic Role and Therapeutic Possibilities" to "Epithelial Toll-like Receptor 9 Signaling in Colorectal Inflammation and Cancer: Clinico-pathogenic Aspects". The latter version contains exactly 12 words.

7. The abstract had been expanded to 209 words.

8. A "Core Tip" section has been inserted.

9. Reference 57 was already re-numbered in the revised form of our article, so this point now has no meaning.

10. The number of the referred articles is 65. Originally, I (Ferenc Sipos) was invited to write an editorial from this topic, later this topic was suggested to be a review. Up-to-date we cannot refer 100 relevant articles in this topic, so I would like to avoid refer irrelevant articles.

11. The source file of Figure 1 had been attached.

12. The manuscript was edited for English language, and we believe that the English language quality of our work reaches at least grade B. (certification attached)

13. All the corrections had been highlighted by yellow colour in the revised manuscript.

We hope that our revised manuscript is acceptable for publishing in Your honoured journal, *World Journal of Gastroenterology*.

Sincerely yours,

István Fűri

István Fűri

Researcher

2nd Dept. of Internal Medicine

Semmelweis University

Budapest, Szentkirályi u. 46

H-1088-Hungary

Fax: +36-1-2660816



Ferenc Sipos MD, PhD

Assistant Professor of Medicine & Gastroenterology

2nd Dept. of Internal Medicine

Semmelweis University

Budapest, Szentkirályi u. 46.

H-1088-Hungary

Fax: +36-1-2660816; E-mail: dr.siposf@gmail.com