Reviewer’s report

Title: Investigation into the controversial association of Streptococcus gallolyticus with colorectal cancer and adenoma

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Reviewer: Guillermo Ignacio Perez-Perez

Reviewer’s report:

The revised manuscript of Abdulamir et al entitled “Investigation into the controversial association of Streptococcus gallolyticus with colorectal cancer and adenoma” has incorporated many of the observations made by the reviewers and modified according to the manuscript. However, I still have several observations and problems with this manuscript.

a. One of my problems is the selection of B. fragilis as a control antigen. B. fragilis is part of the normal flora in most if not all the humans and the possibility of a vigorous immune response to its specific antigens is low. Furthermore, B. fragilis has not been associated with a specific clinical presentation of the lower GI tract. In addition, the explanation of the authors regarding the specific antigenic properties of LPS from B. fragilis came from studies with monoclonal antibodies.

b. I still concern with the amount of mRNA that could be lost during storage and processing of the colonic biopsies, despite the explanation offered by the authors and I feel that at the end is affecting the results.

c. The authors concluded that S. gallolyticus is associated with CRC and colorectal adenoma and they proposed that its is promoting certain inflammatory, anti-apoptotic, and angiogenic factors of transformation like NF#B and IL-8, despite that only 70% of the patients were seropositives. Is there a strong correlation between S. gallolyticus serology and expression of NF#B and IL-8?

d. Mean age of the CRC and adenoma patients are provided but there is not indication of the age of the HV and the 30 control subjects that were referred for colonoscopy.

e. Once again, the authors included in their figure 1, the population used to define the cut off values used in the manuscript. Please remove the group of that figure.

f. The tables repeat several times some of the rows. Authors should minimize in the information in a fewer number of tables. Table 1 and 2 should be combined. At the same time, the information included in tables 3, 4, 5, and 6 is already included on tables 1 and 2. Tables 3 to 6 should be combined.

g. Overall, the information in the tables is difficult to follow up. The parameters for assessing NF#B were different that the used for IL-8.

The paper showed some evidences that a potential association of colorectal
cancer with S. gallolyticus serology but do not confirm the association and the authors need to toner down their conclusions.

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'