**Reviewer’s report**

**Title:** Association between polymorphisms of TAS2R16 and susceptibility to colorectal cancer

**Version:** 0 **Date:** 22 Jun 2017

**Reviewer:** Manuela Gariboldi

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Only one SNP (rs1525489) was significantly different, although with low significance, in two of the four populations analyzed. And overall it only showed a p-trend. The fact that the association was found in sub-populations from Lithuania and Spain and not in populations from Czech Republic and Italy, compensating the different origins in both groups, supports the possibility that it is a casual interaction.

A study aimed at evaluating the role of TAS2R16 in the context of colorectal adenomas has already been conducted, although on populations from different ethnicity (Schembre SM et al., Variations in bitter-taste receptor genes, dietary intake, and colorectal adenoma risk. Nutr Cancer. 2013; 65:982-90), and should be mentioned and discussed in the text. This study found non association of the SNP analyzed and presence of adenomas. The sentence "The study was carried out in a large cohort of European individuals and it is the first to evaluate the role of this receptor in the context of CRC carcinogenesis" should be modified accordingly.

The only new result emerging from here is the association of SNP rs1525489 with an increased risk of developing rectal cancer (p=0.007) in the whole series analyzed. Please add its association in each stratified population. To support the significance of rs1525489 SNP between colon and rectum, authors speculate that colon and rectum may have a different expression of TAS2R16. Despite what they say, separate gene expression profiles of rectal and colon cancer are available for example at TCGA portal and should be investigated and results should be added to the text, to confirm what they say.

Nevertheless, it has been reported that there is no overall effect of aspirin on the risk of rectal cancer (Garcia-Albeniz X. and A.T. Chan. Aspirin for the prevention of colorectal cancer. Best Pract Res Clin Gastroenterol. 2011; 25: 461-472).

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.
Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
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Acceptable

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