

October 06, 2016.

Dear Editor

Please find enclosed the revised manuscript in Word format (file name: 1. 29376- Revised Manuscript.doc).

Title: *CYP1A1*, *CYP2E1* and *EPHX1* polymorphisms in sporadic colorectal neoplasms: A case-control study

Autors: Glaucia Maria de Mendonça Fernandes, Anelise Russo, Marcela Alcântara Proença, Nathalia Fernanda Gazola, Gabriela Helena Rodrigues, Patrícia Matos Biselli-Chicote, Ana Elizabete Silva, João Gomes Netinho, Érika Cristina Pavarino, Eny Maria Goloni-Bertollo.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 29376

We are very thankful for the comprehensive review performed to our manuscript referred above, and the request that we resubmit a revised version of it. As you will see from the resubmitted copy we have addressed the issues raised by the reviewers in a constructive manner and editor's suggestions, clarifying some issues. Attachment we list our responses to each individual point raised by the Referee.

We have uploaded our revised manuscript according and the answers to questions and suggestions from reviewers, hoping that it now reaches the standard for publication in the World Journal of Gastroenterology.

Thanks again for the attention to our manuscript.

Yours sincerely,



Eny Maria Goloni Bertollo, PhD
Corresponding author

Genetics and Molecular Biology Research Unit - UPGEM, Department of Molecular Biology São José do Rio Preto Medical School (FAMERP) - Brazil

Email: eny.goloni@famerp.br

Response to reviewers

Reviewer 02445638

Suggestion of Reviewer 02445638	Response to Reviewer 02445638
Minor corrections are needed: Page 3, line 7 "CYP1A1*5B" should be corrected to CYP1A1*2C	Text was corrected
Page 6, line 15 "timine" should be corrected to thymine	Text was corrected
Page 7, line 3 check date of protocol for accuracy	The number 012/2012 corresponds to the protocol number of the approved research by the Ethics in Research Committee of the Institution. This information was clarified on the text.
Page 7, line 16 "In the present study, it was not any necessary follow-up period of individuals". Should read: In the present study, there was no necessity for a follow-up period of individuals.	Text was corrected
Page 10: Suggestion-this information would be easier to read in Table form: "Frequencies of polymorphic alleles for CYP1A1*2A, CYP1A1*2C, CYP2E1*5B, CYP2E1*6, EPHX1 Tyr113His and EPHX1 His139Arg were 0.15, 0.09, 0.16, 0.23, 0.25 and 0.18 in cases and 0.23, 0.13, 0.06, 0.11, 0.27 and 0.23 in control individuals".	The allele frequencies were described in the Table 2.
Page 10: It might be helpful to the reader to briefly indicate here why the HWE case vs control difference is important (this is addressed appropriately in the discussion).	A sentence was included in the text. "HWE analysis is performed in case-control studies to verify if the allele frequency is similar to the expected throughout the generations, and allows investigate the association between an allele and pathological conditions."
Page 10, line 19 use the word "represented" instead of "representative".	Text was corrected
Page 10: "In the present study, the interaction of the presence of polymorphisms and tobacco or alcohol consumption with the SCRC risk was	The difference between male vs female tobacco/alcohol use and polymorphisms had not been performed. We analyze statistically

not evidenced (Table 4)". Was there a difference between male vs female tobacco/alcohol use and polymorphisms?	this issue. No significant results were found.
Page 12, line 5 use "and" not "e"	Text was corrected
Page 13, lines 2-3 It would be interesting to know a bit about what these study differences are without having to look up the reference.	A sentence was included in the text.
Page 13, line 12 Should read "interestingly" not "interesting"	Text was corrected

Reviewer 00061154

Suggestion of the Reviewer 00061154	Response to Reviewer 00061154
page 6: what is "timine? page 6: what is "timine?	Text was corrected
page 7: how were the numbers of 227 and 400 arrived at	The optimal number of the patients to be included was calculated according to Beigelman (1994), for determining the sample size based on the estimated population proportion given by: $n = \frac{Z^2 \cdot p \cdot q}{E^2}$ Furthermore, all the patients assisted by the Coloproctology Service of the Base Hospital, between 2010 and 2013, were included in the study.
page 7: could some of the controls have as yet undetected sporadic CRC?	The controls are blood donors of Blood bank of Base Hospital - HB / FAMERP. These individuals do not present a history of cancer diagnosis and no family history of cancer. Blood donors are considered healthy individuals because they present negative result for several diseases in the laboratorial tests performed in the Blood bank, according the criteria of the American Association of Blood Donors and the International Society of Blood Transfusion. A sentence was included in the text.
page 7: why were patients with prior radiation/chemotherapy excluded?	The patients treated with radiation/chemotherapy were excluded because these procedures

	can alter the genetic material and interfere in the results.
page 8: why was stage of disease documented?	This information is needed to understand the statistical analysis that we performed to investigate the associate between the disease stage with polymorphisms for the SCRC. As no association was found in these analyzes we do not included a table with the data, but is informed in the results section. Page 12 paragraph 3.
page 11: Discussion is misspelled A table comparing the present study with others would be useful	Text was corrected. It was added a sentence informing the creation of Table 6 containing the information: "A simplified summary of the comparison of this discussion can be visualized in Table 6."