

## Reply To Reviewers for manuscript ID: 37300

Dear Editor,

Thank you for sending us the opinions of the reviewers concerning our ms. ID: 37300. These helped us improve our manuscript. We are replying below point by point to their suggestions. Thank you for reviewing again our manuscript. We hope that now it will correspond to the quality of your journal.

for some articles de DOI code, only the link and PMID or PMC, what should we do ?

Best regards,

Prof.Dr. Dumitrascu Dan

Dr. Popa Stefan

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Reviewer ID : 00036825

While the abdominal pain and its measure is the leading symptom in IBS, the analysis of the association between this symptom and genetic polymorphisms should promote the research of this field. The completion of the study in this aim is required.

**We changed accordingly**

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Reviewer ID : 03261325

Nice review of main studied genetic polymorphism in IBS but with some limitations: • Not all published studies in the field are included in review (ex. Zhang Y et al. Association of the Serotonin Receptor 3E Gene as a Functional Variant in the MicroRNA-510 Target Site with Diarrhea Predominant Irritable Bowel Syndrome in Chinese Women J Neurogastroenterol Motil. 2016 Apr 30;22(2):272-81. doi: 10.5056/jnm15138; Kohen R et al. The serotonin transporter polymorphism rs25531 is associated with irritable bowel syndrome. Dig Dis Sci 2009; 54: 2663-2670 [PMID: 19125330 DOI: 10.1007/s10620-008-0666-3]; Van Kerkhoven LA et al. Meta-analysis: a functional polymorphism in the gene encoding for activity of the serotonin transporter protein is not associated with the irritable bowel syndrome. Aliment Pharmacol Ther 2007; 26: 979-986 [PMID: 17877505 DOI: 10.1111/j.1365-2036.2007.03453.x] • The references are not in the format recommended by WJG

**Thank you for the suggestion, we added accordingly the references.**

Reviewer ID : 02441672

Its a good and relevant review .However, in the discussion I suggest that the biopsychosocial component of functional gastrointestinal tract diseases be highlighted. in addition, I suggest that a commentary be included on the possible role of the interaction between ethnicity, geographic region, specific food consumption and genetic markers.

We included comments on the issues suggested by you.

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Reviewer ID : 00001787

I read with interest the MS "Genetic Studies in Irritable Bowel Syndrome-Status Quo" by Popa S-L and coworkers. It is a well designed and developed review paper on a controversial issue. The Authors should be commended for providing such a relevant review. No suggestions on this side.

The reviewer agreed with our manuscript, we appreciate.

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Reviewer ID : 00009064

Good review of the existing data on genetics of IBS.

The reviewer agreed with our manuscript, we appreciate.

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Reviewer ID : 03478585

1. There are too many grammatical and expressive mistakes. The quality of English needs improving. Such as “We decided not to analyse SNP which were not investigated in less than five papers,”; “between the IBS patients and healthy controls IBS”; “They found an association of SNPs in HTR3A and HTR3E in with IBS-D”; “In a study from 2011”; “The Val alleles leads to”; “The association of this polymorphism with IBS, is demonstrated, recent data shows that alteration of GNB3 825C>T CC type, has a direct effect on gastrointestinal sensation and peristalsis.”;

We reexamined the text by a professional medical English language editor

2. There are some unnecessary repeated contents in the text. Such as “The serotonin transporter (SERT) encoded by the gene SLC6A4 regulates the intensity and duration of serotonin signaling by re-uptaking serotonin from the synaptic cleft” and “The Serotonin transporter (SERT or SLC6A4) has the role of re-uptaking serotonin from the synaptic cleft to the presynaptic neuron, the interstitial space into enterocytes in the gut and also recycles it in a sodium-dependent mode. The solute carrier family 6 member 4 (SLC6A4) gene encodes the serotonin transporter (SERT).”

We changed accordingly

3. According to the Rome IV criteria, IBS can be divided into IBS-C, IBS-D, IBS-M and IBS-U. Why ignore IBS-U and why not explain A-IBS?

We changed Rome III to Rome IV.

4. Please keep consistent in the expression of terms in the text. Such as “IBS-D” or “D-IBS”;

We also modified the inconsistencies in denomination of IBS-D.

5. There are confusions in the use of full name and abbreviation of some terms. Such as “The serotonin transporter (SERT)”; “polymerase chain reaction (PCR)”; 6. There are confusions in the use of the name of protein and gene. Such as “The polymorphisms of the Serotonin transporter (SERT or SLC6A4) gene”.

The sentence on SERT was corrected