Dear Editor,

Please find the enclosed revised manuscript in Word Format.

Title: Genetic Polymorphism in the pathogenesis of irritable bowel syndrome

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The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated

2. Revision has been made according to the suggestions of the reviewer

Reviewer 1

- Revision had been made in the introduction empathizing the actual contributions of genetic polymorphism (1%-5%) to manifestation of functional GI disorders

  Although a number of IBS- related genes have been identified, the majority of them required further validation. Besides, each of them may only contribute to the pathophysiology in 1%-5% in patients with functional gastrointestinal disorders.[4,5] This review will summarize how genetic determinations may possibly regulate the putative mechanisms mentioned. (page 4, line 1-5)

- More up-to date references are added

  While the L/L genotype was significantly associated with IBS, IBS-C and IBS-M patients in Korean population. (page 5, line 10-12)

  Voltage-gated sodium channel (Na_v) are present in gastrointestinal smooth muscles. These missense mutations were found in tetrodotoxin-resistant sodium channel (SCN5A) in 13 out of 584 patients with irritable bowel syndrome. It was more prevalent in Diarrhea –predominant IBS patients. And these mutations showed disruption in Na_v 1.5 function with decreased peak currents and mechanosensitivity. (page 8, line 17 to page 9, line 4)

- English syntax errors had been rectified in the passage.

Reviewer 2

- Implementation of Genetic polymorphism identification in clinical diagnostic workup of IBS

  Further studies should be required. A combination of gene expression profiling and biomarkers should be implemented for better prediction of specific subset of IBS patients. (page 12, line 9-11)

- The relationship between genetic information and stress induced symptoms in IBS

  Research has implicated that a combination of genetic and environmental risk factors(eg. Early life adversity, traumatic experiences) in the pathogenesis of mood disorders such as depression. While strong association was established between psychological distress and functional gastrointestinal diseases, an established biopsychosocial model was suggested where early life stress may predispose HPA axis dysfunction and develop functional gastrointestinal symptoms. (Page 9, line 1-4)

3. References and typesetting were corrected

Thank you again for considering my manuscript in the World Journal of Gastroenterology.