

ANSWERING REVIEWERS



December 28, 2013

Dear Editor In Chief of World Journal of Gastroenterology

Please find enclosed the revised manuscript in Word format (file name: 7070-Review.doc).

Title: Allele and haplotype frequencies for HLA-DQ in Iranian celiac disease patients

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Name of Journal: *World Journal of Gastroenterology*

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First of all, we would like to thank all the reviewers for their valuable comments.

The manuscript has been revised and improved following the reviewers' suggestions:

1. The format has been updated

- (1) Regarding the language certificate, Prof. Wijmenga's department employs a full-time professional editor to help international researchers with their papers and other texts written in English. You can refer to <http://www.rug.nl/research/genetics/staff/jackie-senior>

2. The manuscript has been revised to address reviewers' comments as follows:

- (2) Reviewer 00188820: "The tagging method of SNP analysis showed less sensitivity and specificity. Instead of this method, which one is recommended for screening also in Iranian population?"

REPLY: Although HLA DQ8 did not work as well in the TagSNP method, we still recommended this method for screening in Iranian population but for the results of DQ8 to be interpreted cautiously with TagSNP in future work. TagSNP works very well for the other measures, it's just less sensitive for DQ8.

- (3) Reviewer 00188820: "The authors discussed the interesting point of correlation of HLA risk alleles and Marsh classification, however the method of statistical analysis (correlation) was not described in statistical section."

REPLY: This has been corrected and described as below:

"The correlation between HLA risk alleles and Marsh classification was also investigated"

- (4) Reviewer 00188820: "As a result of HLA mapping, is there a method or combination on non- or less-invasive methods to bypass the endoscopy and biopsy sampling in the diagnose of celiac disease?"

REPLY: Carrying HLA risk alleles can be a predictor of susceptibility to celiac disease but it is not enough for diagnosis of CD. Serology with high titer 10x above normal has a very high

sensitivity and specificity for CD on its own. HLA-DQ2 and -DQ8 determination is useful in excluding, probably lifelong, celiac disease in individuals with an equivocal small bowel histological finding. We therefore suggest that performing readily available serological tests, in combination with HLA typing, will significantly reduce the burden of celiac disease in the at-risk population by providing more accurate diagnoses and enabling timely treatment with a gluten-free diet.

- (5) Reviewer 02548945: "Although, the information on HLA allele distribution in Iranian Celiac disease patients is important given their critical role in predisposing the individuals to gluten insensitivity, but small number of patients limits the statistical conclusions that can be derived from this study"

REPLY: we agree with reviewer comment but as we mentioned in the discussion, despite our small cohort, this pilot study has provided information on the genetic background of CD in Iranians and the data of this study is useful to other researchers and to future work on this disease. Also this study provides information that can be used in family screening.

3. References and typesetting were corrected.

Thank you again for accepting our manuscript for publication in the *World Journal of Gastroenterology*.

Sincerely yours,

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