

ANSWERING REVIEWERS

October 17, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name:

Pirola Editorial ID 00011378 R1 edited)

Title: Liver enzymes, metabolomics and GWAS: From systems biology to the personalized medicine

Author: Silvia Sookoian, MD, PhD and Carlos J. Pirola, PhD

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: Editorial: ID (00011378)

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

R1 This article is a well written review on the use of metabolic enzymes in the diagnosis of liver disease. It describes the pros and cons of the the current tests and looks at how new gene discovers could be used as better biomarkers. There are no issues with this manuscript.

Answer: Thank you very much for these encouraging comments, we are glad to know that the reviewer 1 found the paper interesting.

R2 Perhaps you could point out the most, with examples, the potential utility in clinical practice of genomics and metabolomics in defining new risk profiles, such as (genome wide association) demonstration of a correlation between a polymorphism in the vicinity of the IL28B gene, encoding interferon lambda 3, and the response to treatment with ribavirin.

Answer: Examples of utility in clinical practice are given in pages 14-17, the polymorphism in IL28B gene and the response to antiviral treatment is not connected to metabolomics, hence we prefer not to create confusion in the readers.

R3 The paper is novel and original and is well written. It, in my opinion, deserves to be published. Minor comment: Please, insert TM6SF2 among the genes associated with ALT levels.

Answer: Thank you for the encouraging comments, a reference about the putative role of TM6SF2

was added. Please see pages 16, 17 and 25.

R4 This is an interesting and thoughtful review. Authors should briefly add evidence for linkage among body iron stores, transaminase activity and the prevalence of cardiometabolic risk factors, outlighting that iron stores might be investigated as a potentially modifiable risk factor.

Answer: Thank you for the advice, we introduced a comment and a reference about iron stores and cardiometabolic risk factors, please see page 16 and page 25.

3 References and typesetting were corrected

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

4-The paper has been sent for editing for language to an independent provider www.FirstEditing.com.

Sincerely yours,

Carlos J Pirola, PhD, FAHA, FASHG.

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