FACULDADE DE MEDICINA DE RIBEIRÃO PRETO
DA UNIVERSIDADE DE SÃO PAULO

Ribeirão Preto, January 17, 2019.

Response to reviewers

Name of Journal: World Journal of Hepatology

Manuscript NO.: 45045.

Manuscript Type: CASE CONTROL STUDY.

Title: "COMPREHENSIVE ANALYSIS OF THE HFE GENE IN HEREDITARY HEMOCHROMATOSIS AND ACQUIRED IRON OVERLOAD".

Authors: Wagner Narciso de Campos*, Juliana Doblas Massaro*, Eduardo Luiz Rachid Cançado, Cláudia Emília Vieira Wiezel, Aguinaldo Luiz Simões, Andreza Correa Teixeira, Fernanda Fernandes de Souza, Celso Teixeira Mendes-Junior, Ana de Lourdes Candolo Martinelli, Eduardo Antônio Donadi. *These authors contributed equally in the production of the paper.

Dear Editor,

We would like to thank you for the opportunity to present our research work to the World Journal of Hepatology. Find enclosed the answers to the reviewers, particularly to Reviewer 02444752, who made suggestions regarding the abstract and the title of the manuscript. Although the modifications made in the abstract section are within the rules of the Journal, the title modification would imply in an excess of words, from 12 to 16, a decision that the Editor should take into account. The manuscript was completely revised regarding the English style. In the text archive the alterations are marked in red.

Looking forward to hearing from you in the near future,

Best regards!

EDUARDO ANTÔNIO DONADI, MD, PhD

Mailing Address: Ribeirão Preto Medical School, University of São Paulo
Division of Clinical Immunology, Department of Medicine
Avenida Bandeirantes 3900, Monte Alegre
14049-900, Ribeirão Preto, SP, Brazil
Phone: +55 16 3602 2566
Fax: +55 16 3602 0229
Email: eadonadi@fmrp.usp.br

Response to Reviewer 00046378:

Dear Reviewer,

Thank you for the evaluation of our manuscript and for the your suggestion that the article is acceptable for publication.

Response to Reviewer 02444752:

Dear Reviewer,

Thank you for the evaluation of our manuscript. As per your suggestion, we rephrased the aims and the conclusion, and added the background topic in the manuscript abstract as follows:

BACKGROUND: Patients with hepatitis C virus (HCV) and hepatocellular carcinoma (HCC) may or not develop iron overload (IO), which is associated with worst prognosis, because can cause serious damage to organs. *HFE* gene controls the iron uptake from gut, particularly in patients with hereditary hemochromatosis (HH).

AIMS: To identify associations between HFE coding region in patients exhibiting hereditary hemochromatosis and in diseases associated with acquired IO.

CONCLUSION: A differential *HFE* association was observed for HH and for diseases associated with acquired IO (HCV, HCC). Since *HFE* is very distant from other histocompatibility loci, only weak associations were observed with these alleles.

Regarding the title: To change the title and make it more consistent with the purpose of the manuscript, it will be necessary to exceed the number of words permitted by the Journal. The new title would be **"Comprehensive analysis of *HFE* gene in hereditary hemochromatosis and in diseases associated with acquired iron overload"**. We left the decision to the Editor of the Journal.

Short Title: Campos WN and Massaro JD et al. HFE in HH and IO.