

São Paulo, June 10st, 2022

Dear Editors-in-Chief Ke-Qin Hu,

World Journal of Hepatology

Please find attached a copy of the manuscript entitled “Revisited Haemochromatosis”, which we would like to submit for publication as a review article or similar type in the *World Journal of Hepatology*. Thanks for the review, all points have been corrected and are in blue in the manuscript.

A working group of the international society for the study of iron in biology and medicine (BIOIRON Society), including Prof. Brissot and I, concluded that the classification based in different molecular subtypes is difficult to be adopted in clinical practice and proposed a new classification approaching clinical questions and molecular complexity. This current evolution of the haemochromatosis classifications was published in the *Blood*, 2021. The aim of the present review is to provide an update on classification, pathophysiology, and therapeutic recommendations.

We hope this information will be interesting to *World Journal of Hepatology*'s readers.

Thank you very much in advance

Best regards,

Prof. Paulo Caleb Santos and Prof. Pierre Brissot.

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University of Rennes1, Rennes, France and French National Academy of Medicine, Paris, France.

Resolution of the points raised by the reviewers

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Authors described the classification, pathophysiology, and therapeutic recommendations of Revisited Haemochromatosis in detail, and they have a good expression, it is very interesting in readers, and will provide a good view.

Author's response: Thank you very much for the points described above.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The submitted review focused on hemochromatosis, in particular summarizing the molecular mechanisms regulating hepcidin gene expression but, above all, redefining the classification and the clinical approach to the different forms of primary iron overload. This new classification and clinical approach are actually simplified compared to the molecular characterization which might also be not immediately available to all the clinics. The review is clear and provides clinical indications that can be easily applied; however, it would be nice to have a figure which summarize the mechanisms regulating hepcidin. This could be useful for the reader that is not very familiar with the pathways modulating hepcidin transcription.

Author's response: We thank you for the points described, about the figure talking about the regulation of hepcidin, we inserted it in the manuscript.

Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Author's response: Thank you very much for the points described above.

Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Hepatology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Author's response: Thank you very much for the points described above. We revised the manuscript and changed some points that are in blue.