

Xiang Li, Assistant Editor
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Dear Editor,

Thank you very much for handling the reviewing process of our manuscript 36923, entitled "**Metabolomics: from liver chiromancy to personalized precision medicine in advanced chronic liver disease**". We also would like to thank the reviewers for their time and helpful.

Regarding the concerns raised by the reviewers, please find below a point by point response:

1. The actual version of the manuscript is the final one, as far as we are concerned. If, by any chance, there are additional comments in the document, these must belong to the Editorial Office itself.
2. This review did not aim to overview ALL the biomarkers available in each liver disease, but only the few metabolomic ones that were previously studied. This is why we did not go into detail concerning novel findings in genomic, epigenomic, transcriptomic or proteomic field, including the circulating DNA methylation markers for early HCC.
3. We agree with the reviewer when stating that in ACLF mortality is dependent by liver and extrahepatic organ failure(s). Applying metabolomics into this field is extremely challenging, therefore we focused in our review on findings regarding infections in cirrhosis and alcoholic hepatitis, knowing that infection and alcohol are the most frequent precipitating factors for ACLF.
4. We have the strong impression that by this review and through our conclusions, we managed to identify the most important unmet needs, gaps in knowledge and future perspectives for the use of metabolomics in advanced liver diseases.

Again, we would like to thank the Editor and all the Reviewers for their contribution towards the improvement of the manuscript.

Kind regards,

Horia Stefanescu, MD, PhD

Regional Institute of Gastroenterology and Hepatology

Croitorilor 19-21, 400186
Cluj-Napoca, Romania

004 0766 318283
horia.stefanescu@irgh.ro