Reviewer’s report

Title: A novel scoring system for prognostic prediction in d-galactosamine/lipopolysaccharide-induced fulminant hepatic failure BALB/c mice

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Reviewer: Martin L Yarmush

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In this manuscript, the authors attempt to develop a scoring system to predict the prognosis of fulminant hepatic failure (FHF). The scoring system was developed in a d-galactosamine/lipopolysaccharide-treated mouse model of FHF. Levels of plasma metabolites were quantified using gas chromatography/time-of-flight mass spectrometry (metabonomics) and data were processed with partial least squares discriminant analysis (PLS-DA). The metabonomic data were used to construct the scoring system by multivariate logistic regression. This study is an extension of the authors’ prior work in which they used the same FHF animal model to identify 5 biomarkers including phosphate, # hydroxybutyrate (HB), urea, glucose, and lactate which may constitute a set of markers for early diagnosis and prognosis of FHF. The results are presented in three figures which are described in the text. The reported findings are: 1) ribitol was not present in the mouse plasma thereby allowing it to be used as an internal standard, 2) loading plots revealed that plasma concentrations of 5 biomarkers (phosphate, #, urea, glucose, and lactate) had the highest weightings on clustering differences at 4, 5, and 6 hour time points, and 3) a death/survival index (DSI) of >0.65 or <-0.65 corresponded to a 93.3% or 6.7% probability of survival, respectively.

In order for this manuscript to be acceptable for publication, the authors would need to address the comments below.

Minor Essential Revisions:

1. In the multivariate logistic regression analysis used to derive the DSI, the authors state that “After 3 steps, lactate and glucose were removed, and the other variables (HB, urea, and phosphate) were used to calculate the nomogram”. The authors should explain why lactate and glucose were removed in calculating the DSI.

2. The scoring system developed in this study was based on the d-galactosamine/lipopolysaccharide-treated mouse model of FHF. Whether this FHF animal model has a direct correlation to an etiology of FHF seen clinically is unknown. In addition, it is unknown whether such a scoring system based on metabonomics and multivariate logistic regression would be applicable to predicting the prognosis FHF seen in clinical practice. The authors should state this as a potential limitation of the study in the Discussion section.
3. There are several grammatical errors throughout the text that should be corrected.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests’ below. If your reply is yes to any, please give details below.