Reviewer’s report

Title: A proteomic strategy to identify novel serum biomarkers for liver cirrhosis and hepatocellular cancer in individuals with fatty liver disease.

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Reviewer: Kaichun Wu

Reviewer’s report:

The manuscript authored by Gray et al. utilized proteomic approaches to identify novel serum candidate biomarkers to discriminate liver cirrhosis and hepatocellular Cancer in fatty Liver Disease. Five candidate biomarkers were identified, capable of discriminating at least one or other of the patient groups. One novel serum protein, CD5L, was selected for further characterisation in a larger patient group. They concluded that CD5L is an independent predictor of cirrhosis in NAFLD, and it may also identify individuals at greater risk of HCC development.

Overall this manuscript provided new information about serum biomarkers for chronic fatty liver disease and CD5L may yet become available as surveillance, diagnostic and prognostic tools after further validation in larger patient populations. However, before it is found acceptable, the authors should consider the following points:

Major points

1. In the result part of spot identification, the authors should show the MALDI-TOF MS spectra, especially that for spot 5. Spectra, signal/noise ratio as well as more information on the peaks should be given to strengthen the results. Additionally, the Mascot scores for the identified proteins to judge the quality of the protein identification procedure should be given.

2. In Figure 2, data from patient group of pre-cirrhotic NAFLD should be added to make the conclusion more convincing.

3. In Figure 3, sample number seemed too limited to make the conclusion that CD5L does not increase incrementally with the level or stage of fibrosis. More cases should be included to make the conclusion more solid.

Minor point

1. The form of Table1 should be changed according to the standard pattern.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:

I declare that I have no competing interests.