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Column: Review

Title: Role of Spleen Tyrosine Kinase in Liver Diseases

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The authors would like to thank the reviewers for appreciating the work and for their valuable comments. Below are the point-to-point answers and explanation to the changes that have been made in the revised manuscript. All the modifications made are highlighted in the revised version of the manuscript.

Reviewer #1:

This manuscript provides the review of the role of tyrosine kinase, Syk, in the pathogenesis of liver diseases, including liver fibrosis, viral hepatitis, ALD, NASH, and HCC. Moreover, the section on Syk inhibitors provides some insights into the possible therapeutic intervention in Syk activation associated with inflammatory and autoimmune disorders.

We thank the reviewer for the kind words and highlighting the important sections of this review. However, it should be noted that the section on Syk signaling mechanism provides the outdated picture of the kinase activation. This is particularly striking, since recent literature data on Syk clearly point to the role of Syk phosphorylation on Tyr as well as Ser in affecting the kinase signaling potential. Hence, before any further consideration the authors should review and discuss the following papers (J. Biosci. Med.2018, 6(3):70-85; Inflammopharmacology 2018, 26:805-815. Moreover, the current model of Syk signaling mechanism is provided in Fig. 3, of the recent paper (Inflammopharmacology 2019, 27: 203-211.

We thank the reviewer for this critical comment. We have now incorporated the suggested references and have updated the SYK signaling mechanism based on the recent suggested papers.

Reviewer #2:

1. Add the unique of this study compared to other studies discuss the same issue.

As suggested by the other reviewer, this manuscript provides the review of the role of tyrosine kinase, Syk, in the pathogenesis of liver diseases, including liver fibrosis, viral hepatitis, ALD, NASH, and HCC. Moreover, the section on Syk inhibitors provides some insights into the possible therapeutic intervention in Syk activation associated with inflammatory and autoimmune disorders. This is a unique review highlighting the role of the SYK in liver diseases.

2. Add more on the basic of this disease in the introduction.

Thank you for this comment. Since this review is focused on SYK pathway, we have provided sufficient information about the liver diseases as required in the context to this review.

3. Discuss role of imaging using these ref -Razek AA, Massoud SM, Azziz MR,et al. Prediction of esophageal varices in cirrhotic patients with apparent diffusion coefficient of the spleen. Abdom Imaging 2015;40:1465-9. -Razek AA, Khashaba M, Abdalla A, et al. Apparent diffusion coefficient value of hepatic fibrosis and inflammation in children with chronic hepatitis. Radiol Med 2014;119:903-9. -Razek AA, Abdalla A, Omran E, et al. Diagnosis and quantification of hepatic fibrosis in children with diffusion weighted MR imaging. Eur J Radiol 2011;78:129-34.

We thank the reviewer for this comment. However, we do not agree with this comment and incorporation of the suggested references as these references are beyond the scope of the focus of this review.

4. English language correction through the manuscript.

We have proof-read the manuscript and have made the corrections wherever possible.

5. Update of references as most of references are old using these ref Besheer T, Elalfy H, Abd El-Maksoud M, et al. Diffusion-weighted magnetic resonance imaging and micro-RNA in the diagnosis of hepatic fibrosis in chronic hepatitis C virus. World J Gastroenterol 2019;25:1366-1377.

We thank the reviewer for this comment. However, we do not agree with this comment and incorporation of the suggested references as these references are beyond the scope of the focus of this review.