Reviewer's report

Title: 25(OH) D3 alleviate liver NK cytotoxicity in acute but not in chronic fibrosis model of BALB/c mice due to modulations in vitamin D receptor

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Reviewer: Lindsey Kennedy

Reviewer's report:

In this manuscript, the authors claim that vitamin D treatment is able to reduced NK cell cytotoxicity in the acute, but not chronic, model of liver fibrosis. Mainly, they believe that during the acute fibrosis setting the vitamin D increase in NK cell cytotoxicity leads to decreased hepatic stellate cell (HSC) activation. However, during chronic fibrosis vitamin D worsens the fibrotic effect. The conclusions from the paper are not fully supported by the work.

1. Staining for NK cells should have been performed.

2. Appropriate markers of NK cell cytotoxicity and activation were not used. Better characterization of the NK cells should have been performed.

3. Staining for VDR should have been performed in the liver. It is unclear where the vitamin D/VDR interaction is occurring.

4. The authors did not fully evaluate VDR downstream signaling to show changes in activation.

5. Vitamin D strongly regulates intestinal function and this may be a reason the authors have different outcomes in acute versus chronic settings.

6. The reasoning as to why there are worse conditions for vitamin D in the chronic fibrosis setting is unclear and was not fully explored or explained.
7. The authors only looked at alpha-SMA as a fibrotic marker, but other factors should have been evaluated.

8. HSCs should have been stained in the model.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
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Quality of written English
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