Dear Editors and Reviewers,

Thank you for your comments and suggestions. Please see point by point responses below in red.

**Editorial comments:**

The manuscript has been modified by the Science Editor to comply with the JoVE formatting standard. Please maintain the current formatting throughout the manuscript. The updated manuscript (54729\_R2\_033016.docx) is located in your Editorial Manager account. In the revised PDF submission, there is a hyperlink for downloading the .docx file. Please download the .docx file and use this updated version for any future revisions.  
  
Changes made by the Science Editor:  
  
1. There have been edits made to the manuscript.

Thank you for making the edits.   
  
Changes to be made by the Author(s):  
  
1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues. The JoVE editor will not copy-edit your manuscript and any errors in the submitted revision may be present in the published version.  
  
2. There are two minor typos: Introduction, line 138 – Figure 1 does not have panels A-D; and Line 497, “hold” should be “hole.”

Figure 1 and 2 were mislabeled. Figure 1 should be the multipanel figure that was labeled Figure 2 and Figure 2 should be the single panel figure that was labeled Figure 1. They were relabeled and reuploaded on the JoVE submission site.

The typo on line 471 was fixed – “hold,” was changed to, “hole.”

**Reviewers' comments:**

**Reviewer #1:**  
*Manuscript Summary:*  
This manuscript describes a small series of experiments with a rat liver hilar clamp model to study the effect of pegylated-superoxide dismutase (PEG-SOD) in reducing the effects of ischemia-reperfusion injury.  
  
*Major Concerns:*  
No major concerns identified  
  
*Minor Concerns:*  
Minor concerns include:  
1)The experimental groups each utilize a very low "N" which increases concern about the validity of the statistical analyses. The authors should explain why such a low "N" was used and discuss the potential impact this has on their data.

Although a low N was used we were able to demonstrate the significant effect that PEG-SOD has on ameliorating ischemia-reperfusion injury in the liver. There was also low animal intervariability. We have utilized this model with a number of potential molecules in our lab and it is reproducible.

2) The authors should elaborate on their reasons for selecting to evaluate PEG-SOD in these experiments.

We elaborated on our selection of PEG-SOD in a new paragraph in the discussion section of the manuscript.

3) The authors should comment on the impact of PEG-SOD on pathologic changes in the liver tissue. Did it reduce histologic evidence of liver injury?

In our experience using this and similar models the one hour long period of ischemia and two hour long period of reperfusion is not of sufficient duration to produce dramatic histologic changes, although as demonstrated here there is clearly a significant impact on biochemical markers.   
  
*Additional Comments to Authors:*  
N/A  
  
  
**Reviewer #2:**  
*Manuscript Summary:*  
Beal et al present a novel technique of partial portal vein clamping ad cannulation in a rat model. The authors found that injection of PEG-SOD directly into the portal vein branch of the left lobe decrease liver injury after ischemia and reperfusion.  
  
*Major Concerns:*  
No major concerns  
  
*Minor Concerns:*  
The paper is well written ad describes an important novel technique of rat hepatic ischemia and reperfusion.  
1. The authors should provide H&E staining of the liver tissue following ischemia and reperfusion.

In our experience using this and similar models the one hour long period of ischemia and two hour long period of reperfusion is not of sufficient duration to produce dramatic histologic changes, although as demonstrated here there is clearly a significant impact on biochemical markers.

2. The authors should discuss if the model is suitable for tumor cell injection in specific liver lobes.

Although we believe that this model could be used for tumor cell injection, our lab is not tumor focused and we have not experimented with this in particular. This would certainly be an area for further adaptation of the model described here and a fruitful area for further experimentation.

3. Beal et al should discuss possible implications for the investigation of liver regeneration.

This model is not directly designed to test liver regeneration, but short-term response to ischemia-reperfusion injury. With longer ischemic times there would likely be increased and injury and it may be possible to study liver regeneration. A sentence in regards to this has been added.   
  
*Additional Comments to Authors:*  
N/A

Additionally, we updated the acknowledgement statement to more accurately reflect the funding support.

Thank you,

Eliza W. Beal, MD