Reviewer's report

Title: Carbon monoxide-Releasing Molecule-2 (CORM-2) attenuates acute hepatic ischemia reperfusion injury in rats

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Reviewer: Bingwei Sun

Reviewer's report:

Major Compulsory Revisions.

The manuscript by Yunwei Wei, et al. entitled “Carbon monoxide-Releasing Molecule-2 (CORM-2) attenuates acute hepatic ischemia reperfusion injury in rats” is presented for review.

The obtained results indicate that CORM-2-released CO protected the liver from I/Ri by a reduction of AST and ALT, upregulated the expression of Bcl-2 protein, inhibited the activation of NF-#B, reduced the cytokines production, and attenuated the PMN accumulation in the liver after I/Ri.

The proposed experiments are straightforward and well controlled. The findings of the present study seems interesting, however, the major concern with the manuscript is the dose of CORM-2 administrated in this study. The CORM-2 concentration used in the current study (i.e. 8mg/ml) was originally described and used in mouse model of sepsis (Sun BW, et al. “Attenuation of Leukocytes Sequestration by CO-releasing Molecules -liberated CO in the Liver of Thermal Mice” J Burn Care Res. 2007#28#1##173-181 and Cepinskas et al. “Carbon monoxide liberated from carbon monoxide-releasing molecule CORM-2 attenuates inflammation in the liver of septic mice” Am J Physiol Gastrointest Liver Physiol 294: G184–G191, 2008). However, why the authors used the same dose of CORM-2 for the study in rats? Did the authors measure the COHb level in the rats under the administration of CORM-2 with the dose of 8mg/ml?

This issue should be properly addressed.

Additional points to consider:

1. Carbon monoxide (CO) is well known to have anti-inflammatory, anti-oxidative and cytoprotective effects. In this study, the authors observed the anti-inflammatory effects of CO in the liver I/R model in rats. However, they did not rule out the effects of other products (i.e. bilirubin) of HO-1 activity. Therefore, it is necessary to use HO-1 inhibitor to know pure effects of CO in the liver I/R model in rats.

2. Abstract Results, line 7: should be “….of the adhesion molecule ICAM-1 in the endothelial cells of liver.”

3. Materials and methods section: liver NF-#B activation:15mg protein was used?
4. Why the authors design the time point of CORM-2 treatment at the time of reperfusion, not at the time of ischemia?

**Level of interest:** An article of limited interest

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.