Reviewer's report

Title: Indoxyl sulfate, a uremic toxin, downregulates renal expression of Nrf2 through activation of NF-kappaB

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Reviewer: Wenpeng Cui

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Bolati et al. demonstrated that indoxyl sulfate downregulates renal Nrf2 expression and function by activation of NF-kB, and AST-120, an oral sorbent, upregulates Nrf2 expression and function by reducing serum indoxyl sulfate. This is an interesting study, however, there are some comments should be considered.

Major Compulsory Revisions,

1. For in vivo study, the authors used two animal models: spontaneous hypertension rat model and 4/5-nephrectomy CKD rat model. Why do you choose different animal models for in vivo study? Appropriate reasons should be given.

2. The quality of immunohistochemical staining (Fig.4 and Fig.6) was poor. Please change these photos.

Minor Essential Revisions,

1. “…… HO-1, a downstream gene of Nrf2 and an antioxidant gene, ……” this sentence has been repeated several times in this article.

2. Abbreviations should be used appropriately.

   (1) Page 2. In abstract, “HK-2 cells” should be used as “human proximal tubular cells” comes out the first time.

   (2) Page 5. For introduction part, “epithelial-mesenchymal transition (EMT)” is no need to be used, because this term was used only one time in this article.

   (3) Page 7. “Human proximal tubular cells” should be given together with “HK-2 cells”.

3. Page 2, In abstract, “Nrf2 and its related genes is downregulated.” Here “is” should be changed with “are”.

4. Page 5, “The expression of Nrf2 and its related genes is impaired in kidneys of CKD rats [20].” Here “is” should be changed with “are”.

5. Page 7. The concentration of insulin-transferrin-selenium should be given.

6. Page 8. The authors mentioned “indoxyl sulfate (200mg/kg of indoxyl sulfate in water)”, is this dose (200mg/kg) for one day?
**Level of interest:** An article whose findings are important to those with closely related research interests

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests