Reviewer's report

**Title:** Podocyte specific knock out of selenoproteins does not enhance nephropathy in streptozotocin diabetic C57BL/6 mice

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**Reviewer:** Vadim Gladyshev

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**Comments for authors:**

The manuscript entitled "Podocyte specific knock out of selenoproteins does not enhance nephropathy in streptozotocin diabetic C57BL/6 mice" by Blauwkapm et al. describes the development of a mouse model which lacks selenoproteins specifically in podocytes and studies potential role of selenoproteins in the development of diabetic nephropathy. Even though oxidative stress has been implicated in contributing to the pathogenesis of diabetic nephropathy, results of this study demonstrate that severe deficiency in the expression of selenocysteine-containing antioxidant enzymes in podocytes does not affect progression of this diabetic complication. The findings of this study raise the possibility that other antioxidant enzymes or protective mechanisms may compensate for the lack of selenoproteins and will be of importance in understanding the contribution of oxidative stress as well as micronutrient selenium to the development of diabetes. The manuscript is recommended for publication with the following revisions:

1. The authors hypothesized that "selenoproteins as a group protect against diabetic nephropathy, and that deletion of all selenoproteins would reveal their importance by preventing compensatory effects". The function of all selenoproteins in the mouse genome is not known. Whereas some selenoproteins demonstrate antioxidant activities such as glutathione peroxidase 1 and thioredoxin reductase 1, functions of several other selenoproteins remain to be established. In turn, their activities may affect diabetes associated nephropathy by other, unidentified mechanisms.

2. The authors state that "selenoproteins are not important in the protection against diabetic nephropathy, or that remaining antioxidant mechanisms can compensate". Is there any evidence that expression and/or activities of other antioxidant enzymes such as catalase and superoxide dismutase, or detoxification enzymes such as glutathione S transferase, are increased in podocytes that lack selenoprotein expression?