Reviewer’s report

Title: Downregulation of SAV1 plays a role in pathogenesis of high-grade clear cell renal cell carcinoma

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Reviewer: Junbo Hu

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The manuscript by Keiko Matsuura et al., describes a new function for the human Salvador (SAV1) as a potential tumor suppressor involved in the pathogenesis of high-grade ccRCC.

The authors used CGH array to show SAV1 downregulated with copy number loss at 14q22.1 in RCC. They go on to show that knockdown or forced overexpression of SAV1 enhances or inhibits cell proliferation, respectively. Furthermore, using reporter assay and immunohistochemical analysis they find the downstream molecule, YAP.

This is an interesting report that sheds new light on the function of hSav1 in the pathogenesis of high-grade ccRCC.

Major Compulsory Revisions

1. The authors should provided the data to prove the difference between the normal kidney tissue and RCC in the protein level of SAV1 not just mRNA.
2. Fig 2, Re-expression of SAV1 inhibits cell proliferation and colony formation. Could you show the consequent protein changes of YAP and p-YAP?
3. Fig 3, it’s said in the manuscript ‘Knockdown of SAV1 induces cell proliferation and promotes apoptosis.’ (page 24), however, the figure shows Knockdown of SAV1 inhibits apoptosis. The author using a cell death ELISA kit to detect cell apoptosis, please show me the consequent protein changes of apoptosis, such as cleaved caspase 3/9, PARP et al.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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.