Review of: "Loss of SUMO-specific protease 2 causes isolated glucocorticoid deficiency by blocking zonal transdifferentiation"

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In this paper, the authors generated mice with adrenal-specific SENP2 loss, and they identified that disruption of SENP2 activity in steroidogenic cells leads to specific hypoplasia of zF, which is a blunted response to ACTH and isolated glucocorticoid deficiency. They studied the molecular mechanism and found that SENP2 deletion shifts the balance between ACTH/PKA and WNT/β-catenin signaling leading to repression of PKA activity and ectopic activation of β-catenin, thus blocks the transdifferentiation of zona glomerulosa cells into zF cells and premature apoptosis. They concluded that the SUMO pathway is critical for adrenal homeostasis and stress response. Overall, the content of the article is completed and the logical relationship is clear, and the current results are solid to support the conclusion.
There are a number of concerns with this study which include the following:

1. Since DRP1 is considered the primary driver of mitochondrial fission and fusion, it may be interesting to see whether the morphology of mitochondria was affected by SENP2 knockout.
2. The mRNA abundance of SENP3 looks much more than SENP2 in figure S1B, does it mean that SENP3 may also play important roles?
3. The balance of the ACTH/PKA and WNT/β-catenin pathways were disrupted, what is the relationship between these two pathways that affected by SENP2 knockout?
4. The number of mice studied in each group is better to be clarified in every experiment.
5. The internal control was missing in some figures, including figures 3H and 7D.
6. It looks like that there is no significant enhancement of SUMO1 and SUMO2/3 modification after SENP2 knockout in figures S1G-H.