Review of: "Regulation of Follicular Atresia by WIP1-Mediated Apoptosis and Autophagy"

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Potential competing interests: The author(s) declared that no potential competing interests exist.

In the manuscript by Su Zhou and colleages, they explored the effects and the underlying mechanisms of WIP1 phosphatase on ovarian follicular development in mice. By using WIP1 phosphatase inhibitor GSK2830371 and siRNA mediated knockdown, the authors showed that decline WIP1 expression promotes granulosa cells apoptosis and autophagy via WIP1-p53 and WIP1-mTOR signal pathway. They also declared that up-regulation of WIP1 may delaying the decline of ovarian reserve. The experiments itself were mostly sound. The results were clearly presented. Functional studies were also quite interesting. However, there are some problems to be solved.

Specific comments:

1. Language needs to be reedited.
2. The title”Regulation of Follicular Atresia by WIP1-Mediated Granulosa Cells Apoptosis and Autophagy” is much better. Because, apoptosis and autophagy tests were based on the granulosa cells.
3. The authors declared that downregulation of WIP1 expression accelerates follicle atresia via WIP1-p53 and WIP1-mTOR signal pathway related apoptosis and autophagy. The got this conclusion only based on figure 6E. In my opinion, this support data is very weak. Additional work needs to be carried out. For example, the apoptosis and autophagy assay after p53 and mTOR knock down. Indeed, there are several studies have reported that p53 and mTOR are involved in the cellular apoptosis and autophagy, and it will be more convincing if the authors performed these experiments in mouse granulosa cells. Does any relationship between p53 and mTOR? This also need to be clarified.
4. Fig.5. How many follicles and oocytes were used in this experiment, please give details.
5. As known that GSK2830371 is a specific inhibitor of WIP1 (by inhibits WIP1phosphatase activity). As shown in Fig. 3C, western blot assay, why the WIP1 protein levels were decreased in response to GSK2830371 treatment?
6. What is SQSTM1? It should be mentioned and introduced in article. Why the authors detect it in this study□It is confused. The authors declared that SQSTM1 expression in follicle granulosa cells was weak, and highly expressed in ovarian stroma. The total SQSTM1 expression in GSK groups was significantly higher than that in Veh group. As shown in Fig 4 C&D□this data is also confused.
7. In Fig.6A, The morphology of mouse granulosa cells after siRNA transfection. What’s the meaning of the two figures in each group? Different enlargement factor? Add the figures with scale bars.

8. In Fig.5B, what’s the meaning of “*” labeled behand different concentrations of GSK□
9. The English language of the manuscript should be carefully revised.
10. Therefore, my decision is “Major Revision”.