Reviewer's report

Title: LncRNAs regulating gene transcriptions may connect ubiquitin-proteasome system with infection-inflammation pathways in preterm birth and preterm premature rupture of membrane

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Reviewer: Ramkumar Menon

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LncRNAs in regulating gene transcriptions

The manuscript by Luo X describes a novel epigenetic mechanisms that can determine the pathways resulting in adverse pregnancy outcomes line preterm birth and pPROM. The concept of LncRNA is novel and the authors have already published one report in PLoS One earlier this this year describing the mechanism of LncRNA.

1. One of the major concerns related to this paper is the source of the material. Placenta are heterogeneous and the exact site of sampling is not clear for the manuscript. The site heterogeneity can significantly confound the data presented in this manuscript. Authors should address this issue and may provide an explanation for any regional variations that are expected in epigenetic mechanisms.

2. Placental cellular type is also heterogeneous. Like miRNA and Methylation, tissue and cell type variations may be factor in such studies. Having 10 samples may not be adequate to determine the cellular heterogeneity. Please explain how such changes will affect this data.

3. An ideal sample for pPROM evaluation is not placenta but fetal membrane itself. It is not clear why authors chose placenta to study pPROM although fetal membrane environment may cause altered LncRNA expressions in placenta. But without such a correlative analysis of both placenta and fetal membranes, an argument membrane – placental interactions are hard to explain.

4. How multiple testing is controlled in this study?

5. Many of the LncRNA functions seems to control infection and inflammatory pathways and it is expected. How many subjects had intraamniotic infection and treated? How does antibiotic, steroid and tocolytics interventions impact LncRNA?

6. With several unknown factors that are not controlled in this study, it may be better to change the title to more of a generic title.

7. It will be easier to read the figures and tables if authors change A vs B and AC vs BD etc to actual name of these groups.