Reviewer's report

Title: Enhanced upper genital tract pathologies by blocking Tim-3 and PD-L1 signaling pathways in mice intravaginally infected with Chlamydia muridarum

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Reviewer: Qing He

Reviewer's report:

Chlamydia trachomatis is a major infectious bacterial agent that causes sexually transmitted disease (STD) in the industrialized and developing nations. Chlamydia can cause severe health consequences for women, including pelvic inflammatory disease (PID), ectopic pregnancy, chronic pelvic pain, and infertility. The vaccine strategy is the most reliable and cost effective, having the greatest potential impact in controlling Chlamydia infections and the associated complications in the human population. A major challenge in Chlamydia vaccine effort is that a Chlamydia infection not only induces protective immunity but also immunity-mediated pathology. The mechanism(s) underlying this immunopathology are not fully understood. Authors investigated the role of Tim-3 & PD-L1 signaling pathways in chlamydial infection Chlamydia muridarum model and found that negative regulation of Tim-3 and PD-L1 did not significantly suppress immunity against chlamydial infection. However, the double blocking of TIM3 and PD1 significantly enhanced the upper genital tract pathologies following C. muridarum infection. Those findings indicated that there are multi-factors that play a role in immuno-mediated pathology during chlamydial infection and TIM3 or PD1 may not major player in immunomodulation of chlamydial infection. The concept is novel. Despite this novel observation the paper has several issues that need to be addressed. Here are the specific comments.

1. Materials and method need to be organized. Author should reference their previous publications to replace the detailed description of experiments.
2. Figures are not easy to read and need to simplified, especially figure 1.
3. Reduce number of pages.
4. can authors give a explanation why double blocking of these two pathways did not alter C. muridarum infection time course

Minor Essential Revisions

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**

I declare that I have no competing interests