In the manuscript by Pent et al entitled “Enhanced upper genital tract pathologies by blocking Tim-3 and PD-L1 signaling pathways in mice intravaginally infected with Chlamydia muridarum”, the authors evaluated the effect of antibody-mediated simultaneous inhibition of Tim-3 and PD-L1 pathways on Chlamydia muridarum infection in mice. Tim-3 and PD-L1 are inhibitors of Th1-dominated cell-mediated immunity thought to be critical for the development of protective immunity against chlamydial genital tract infection. Previously, it has been shown that antibodies for Tim-3 and PD-L1 are effective in inducing anti-tumor immunity and thus tumor growth inhibition, and are also able to reverse the inhibition of CTL activity. Thus, inhibition of Tim-3 and PD-L1 may exert a beneficial effect in chlamydial infection. However, the authors found no inhibition of chlamydial growth by the antibodies, even though the same treatment regiment is effective in inhibiting tumor growth. Furthermore, they found that the treatment may worsen the pathology in upper genital tract following chlamydial infection. Therefore, they suggest that Tim-3 and PD-L1 signaling may play an inhibitory role in the development of pathological changes caused by chlamydial infection. Overall, the manuscript is well written; the results are carefully analyzed and properly discussed. The work merits publication after the following comments are addressed:

1) The rationale of selecting BALB/c mice instead of other mouse strains should be given.

2) Although antibody treatment resulted in the worsening of hydrosalpinx, the effect is somewhat mild, and caution should be taken to not overstate the effect.

3) Medroxyprogesterone treatment prior to chlamydial infection is to achieve a synchronized estrous cycle in mice, not the “menstrual cycle” as stated by the authors in p5. The latter term is for primates only.

4) p11, “during intravaginal infection with Chlamydia muridarum” should be deleted or be changed to “after…”.

5) p14, the effect of Tim-3 and PD-L1 antibody treatment should be referred as restoration of in vitro cytotoxicity towards HCV-bearing hepatocytes instead of inhibition of viral replication.

6) A few typographical errors should be corrected.
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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.