Review of: "Timing of transcriptomic peripheral blood mononuclear cell responses of sheep to Fasciola hepatica infection differs from those of cattle, reflecting different disease phenotypes"

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

The paper submitted by Niedziela et al entitled “
Timing of transcriptomic peripheral blood mononuclear cell responses 1 of sheep to *Fasciola hepatica* infection differs from those of cattle, 2 reflecting different disease phenotypes” describes an exhaustive analysis of differentially expressed genes by PBMC in acute and chronic sheep infected by F. hepatica. The major weakness of this paper it is the low originality/novelty, since transcriptomic analyses of PBMC from infected ruminants have already been published. However, one of its strengths is that the analyses is profound, visualized by the detailed comparison between previous transcriptomic analyses from F. hepatic cattle and sheep, including their own, and from acute versus chronic fasciolosis. Other strength of this paper is that it demonstrates the importance of including PBMC from control animals in this type of analysis, as in one recently publication by the same group studying hepatic draining lymph nodes: (https://www.frontiersin.org/articles/10.3389/fimmu.2021.687579/full).

Concerned comments by this review
Lines 217 to 230
Authors describe the experimental model, and in particular parasite-specific antibodies at 9 wpi. These data are complemented with faecal F. hepatica eggs, eosinophil counting and liver fibrosis. They cite a very recent published work of them, describing the same experimental infection and focusing on hepatic lymph nodes (https://www.frontiersin.org/articles/10.3389/fimmu.2021.687579/full). However, the information given in that paper for egg count is at 15wpi (Figure 1A) and not at 9 wpi.
“After experimental infection, animals in the infected group showed the presence of *F. hepatica* eggs 220 in their faeces by 9 wpi, and eggs were detected in all 8 infected animals by the end of the 221 study. No eggs were detected in the control animals.”

Lines 251 to 264
In the “Cell composition” paragraph, the authors use cell specific surface markers genes as in Finotell et al 2019 to detect different populations of leukocytes present in PBMC. I firmly recommend to highlight at which these markers were since in Supplementary Figure 1 nothing is explained in the figure legend. Also,

this reviewer thinks it is quite ambitious to define a cell type according to gene expression. Indeed, gene expression does not guarantee protein activity, and thus, cell differentiation. Last but not least, how did authors define regulatory T cells? The cited paper (Finotell et al 2019) defined regulatory T cells according the expression of CD4 and FOXP3 using human tumor cell lines. It is proven the regulatory role of gamma-delta T cells, which I firmly suggest be explored in this article and comment about it.

“Numbers of T regulatory 260 cells appeared higher in the infected group than in the control group at 2 wpi; however, the 261 difference was not significant.”