

Reviewer Report

Title: Single-cell transcriptome analysis illuminating the characteristics of species-specific innate immune responses against viral infections

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Reviewer Comments to Author:

This paper gives a good introduction on bats as reservoirs of several viral infections, which studies have shown is due to the uniqueness of their immune system. They and others suggest that bats immune system is dampened exhibiting tolerance to various viruses. This gives the study a good rationale as to why study the bats immune system, compared to other mammals. They also give a good rationale as to why they used single-cell sequencing, to allow the identification of various cell types and the differences in these cell types. From their finding the main conclusions are that differences in the host species are more impactful; than those among the different stimuli. They also suggest that bats initiate an innate immune response after infection with DNA viruses through an alternative pathway. For example, the induction dynamics of PRRs seems to be different in their dataset. They also suggest this could be due to the presence of species-specific cellular subsets.

1. Interesting model system and a good comparison of bats with other mammals.
2. Good technique in using single-cell sequencing, with a clear rationale as to why it was chosen. This advances knowledge on what was already known about bats immune system, but the species-specific cellular subsets are new.
3. Interesting technique to go through the bulk transcriptomic data in four species and four conditions. This allowed findings of the most important genes/pathways.
4. Good rationale / flow of experiments from one to another
5. I liked that they investigated stimuli from different pathogens , including DNA, RNA virus and bacteria and still show that bats had a different immune system, in the different stimuli.

Minor comments

1. Do they speculate this occurrence in is this just in Egyptian Fruit bats or all species of bats?
2. Mentioned in the introduction why they used the egyptian fruit bats - which are a model organism, but this could help people who are not in this field understand exactly why use these bats. Advantages? Location? Proximity to the various viruses based on the fact they are mostly found in endemic regions such as Africa etc.
3. Can they include viral load in each species?
4. It is not clear which scRNAseq tools were used for data analysis in identifying the types of cells. Or did they use already established database based on markers?

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

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