General comments

The manuscript by Xu et al. presents a scRNA-seq atlas of immune cells in the mouse small intestine. It then focuses on the role of the α-CGRP peptide in controlling ILC2s proliferation and regulating type 2 immunity activity. The second part of the paper describing the follow-up experiments examining the role of α-CGRP is well developed, and overall there is not much that is technically wrong with the paper, except for some methodological concerns about the scRNA-seq atlas part of it. However, as a whole is generally not very well put together and quite difficult to follow, does not present any new methodological advances and is focused on a fairly narrow aspect of immune function in a mouse model system, thus I am not sure how much of an interest it will be to a general audience.

Specific comments

1. One methodological concern I have with the manuscript has to do with the batch correction approach used. While it does not affect the follow up experiments carried out, it is the foundation of the cell type classification analyses, but the way it is done was glossed over in quite unfortunate way. Apparently, the authors used projections of the scRNA-seq data onto bulk microarray datasets from more than a decade ago, removed the first eigenvector and then retained the next 100 eigenvectors. Why this procedure should be trusted is not entirely clear despite the obvious concerns about it having to do with how well a (possibly quite disparate itself) microarray dataset would serve as a basis for batch correction of scRNA-seq data. The authors themselves acknowledge that more sophisticated methods for scRNA-seq batch correction have become recently available, but dismiss those with the following sentence:

   > More recent methods (Korsunsky et al., 2018; Lin et al., 2018; Stuart et al., 2018; Welch et al., 2018) might help merge cells from different experiments but were published when this analysis was long completed.

   It is rather remarkable to see a statement like this in such a high-profile manuscript. Ideally the authors should have run the classification analysis using the best state-of-the-art tools available to them prior to submission.

2. The bulk RNA-seq data is said to have been processed by mapping with Bowtie against the mm10 mouse reference genome, then quantified with RSEM. Of course, RSEM works in transcriptome space (and Bowtie does not do spliced alignments anyway), so it cannot be correct that this is how the data was processed (given that differential expression analysis was also later carried out and looked at).

3. There are multiple occasions on which the manuscript appears to not have been carefully written. This applies both to the introduction of the subject as a whole, which could be written much better, and to the more concrete textual level. Some examples:

   - The abstract says that:

     > Among the key transcripts associated with an inflammation-induced program in intestinal KLRG1$^+$ ILC2s was exon 5 of *Calca*, which encodes the alpha-calcitonin gene-related peptide (α-CGRP).

     Of course, "exon 5" cannot be a "transcript", and this is not how alternative splicing of *Calca* works, as α-CGRP and calcitonin are both produced from transcripts containing multiple exons.
   - p. 3, line 2: "respond antigens" should be "respond to antigens"
   - p. 3, line 8: IgE is listed as a cytokine the way the sentence is phrased
   - p. 3, line 8: "tightly regulated" $\rightarrow$ "by tightly regulated"
   - p. 4, line 9: "and highlighting in particular" $\rightarrow$ "and highlight in particular"