**Reviewers' comments:**  
  
  
  
**Reviewer #1:**  
Manuscript Summary:  
The present study examined the impact of gene inhibitor in human and mouse myeloid cells. The paper is not well written, and the results are not presented in a clear manner, there are a number of significant issues that need to be addressed.

Major Concerns:  
1. In Abstract, the authors should list the important findings of this work.

*> We thank the reviewer for spotting this deficiency. We have now addressed this comment, in both the short- and the long- abstract.*  
2. It would be useful to determine the effect of key genes on TNF-a production by RNAi.

*> Here, TNF-a production was used as a readout to compare the impact of MALT1 on CLLR and TLR signaling pathways. Therefore, we have focused our work on the effects of MLT-827, a well-characterized inhibitor. The aim of this short manuscript was to describe protocols for testing MLT-827. It was not to investigate the biology of the signaling pathways beyond involvement of MALT1 and the CBM complex.*  
3. In REPRESENTATIVE RESULTS, there are many places that are difficult to follow. The reviewer cannot understand the difference between Figure 2 and 3. This should explained in detail.

*> We have now added information in the legends for these two figures to guide the reader.*  
4. In Figure 2, the authors should employ other marker(s) in addition to TNF-a.

*> TNF-a was used as a first line, robust cytokine readout. We also monitored other cytokines and the results are presented in Fig. 3B.*  
  
  
**Reviewer #2:**  
This study shows that in both human and mouse cells MALT1 paracaspase activity controls C-type lectin-like receptor, but not TLR4, induced cytokine  
production, including TNF-α. Collectively, these data provide solid evidence corroborating the key and selective contribution of the CBM signalosome downstream of C-type lectin-like receptors, which was unveiled by earlier studies. The data is worth of publication.  
  
  
**Reviewer #3:**  
Manuscript Summary:  
The authors use a selective inhibitor of MALT1 in human and mouse myeloid cells to demonstrate the important role of this protein in the signaling cascade downstream CLRs. The protocol is well detailed and will serve a useful resource in the field. This reviewer recommends publication with minor revisions below.  
  
Major Concerns:  
None  
  
Minor Concerns:  
Dectin-1 signals via a single copy tyrosine signaling module termed the hemi-immunoreceptor tyrosine-based activation motif (hemITAM) - please see Marakalala & Ndlovu, Plos Pathogens 2017 or Bauer & Steinle, Sci Signal, 2017. This is not exactly the same as ITAM, and it should be accurately depicted in the cartoon and legend in Figure 1.

*> We thank the reviewer for this valuable insight. We corrected Fig. 1 accordingly.*  
  
It will be helpful if the authors indicated the statistical significance (as it was done in figure 2B) of the results/ individual points in Figure 4A and B.

*> We have added any missing information in the figure legends.*