We would like to thank the reviewer for taking the time and the effort to review and provide valuable feedback regarding our manuscript. We have reviewed most of the reviewer comments and incorporated changes to reflect most of the suggestions.
However, given the complexity of some of the reviewer's comments and recommendations we have found it more adequate to retain some aspects of the review with modifications to explore the reviewer point of view.

Reviewer 2: Comments and Suggestions for Authors

The current review titled "Immunological Insights into Cigarette Smoking-Induced Cardiovascular Disease Risk", highlights the impact of cigarette smoking on the immune, cardio, pulmonary and vascular systems. The authors discussed the molecular mechanisms of how Smoking effects both the structure and function of major organs (lungs and cardiovascular system). They have highlighted that smoking plays an important role in maintaining the homeostasis of the immune system any alterations in these pathways elicits inflammatory responses leading to autoimmune, inflammatory diseases and cancer. Most of the content discussed are not very novel. Several important points should be addressed before considering the article for publication.

Major comments –

1. Why did not the authors talk about the biochemical markers associated with cardiac injury?

   We have introduced a brief description of biochemical markers associated with cardiac injury that are fluctuated during smoking.

2. The authors discussed how CS effects on the innate immune system in a general way. It would be better to highlight the biomarkers of cardiovascular diseases (such as C-Reactive peptide (CRP), IL-6, ICAM-1, and CCL-2).

   We thank the reviewer for this comment. It is important to note that CRP, IL-6, ICAM-1 and CCL2 are not biomarkers of cardiovascular disease, but markers of systemic inflammation. We concur that cardiovascular might imply and inflammatory response that is highlighted by the aforementioned markers, however, these markers are not specific for cardiovascular disease and therefore are not deemed to be titled as such. Nonetheless, we found it constructive to explore these pathways further in the appropriate parts of the review.

3. Why did not the authors mention about the current challenges and future directions in association with cardiovascular disease risk caused by using Cigarette smoke.

   We have modified the conclusion to answer some changes brought by the reviewer

4. As the authors highlighted about the effect of CS mainly on pulmonary, CVD and innate immune system. It would be better to make separate tabular discussing about the impact of CS on each organ. In the tabular column discus about the pathological, physiological, and metabolic effects of CS.

Although we agree with the reviewer, this step requires a dramatic rewrite of the entire review, rearrange, and reattribute specific paragraphs to accommodate the comment. It is a major overhaul and would require additional review time.