Reviewer 2 v.1

Comments to the Author

In this MS authors were tried to elucidate the role of lncRNA cancer susceptibility candidate 2 (CASC2) and their possible molecular targets like miR-18/IG1 in the Chronic obstructive pulmonary disease (COPD) model. For that, they used serum of subjects as well as cigarette smoke extract (CSE)-induced 16HBE cells as a model. The following comments/suggestions will improve the quality of this work.

Major Comments:

1. Authors used only CASC2 expression level in serum, what about the CASC2 expression level in lung tissues. We can use serum level for non-invasive diagnostic purposes, but the tissue expression level is critical for COPD phenotype. Authors should show tissue CASC2 level in either qPCR or histochemistry method.

2. Are all subjects under the same GOLD stage or from different GOLD stages. This will indicate that weather CASC2 associate with the early onset of COPD or at later stages.

3. What is the source of research-grade cigarettes used in this study.

4. What is the expression level of CASC2 in overexpressed condition (Fig.2B) without CSE

5. In this study authors focused only inflammation as a phenotype of COPD, what about others, and how it's associated with lncRNA CASC2.

6. In the methods section authors mentioned both student t-test and ANOVA were used in this study, but results/fig legends did not mention where they used t-test / ANOVA.

Minor comments:

1. On page 10 lines 8-10 there was no clarity in the sentence.

2. On page 11 line 25 authors used ‘CSE-induced cell viability inhibition', authors should correct this sentence.

3. The expansion of CASC2 should mention in the abstract rather than discussion.