

Comments to the Author

In this manuscript, Sun et al. discuss the potential connection of IL-7 gene fusion and idiopathic pulmonary fibrosis. The authors use a robust approach in analyzing 91 RNAseq data-sets to determine gene fusion events, and associate them with overall changes in gene expression and functional pathway analysis. The authors identified a particular gene fusion event, IL7=AC083837.1 (a lncRNA) which was associated with IPF. The authors describe the association of this gene-fusion event with differential gene expression patterns and ontologies. While this study uses a rather robust approach, analyzing 91 data-sets, and find an interesting event which may be associated with IPF pathogenesis, there are a number of concerns regarding the presentation and discussion of the data generated.

Major concerns:

General concern – Unfortunately, the manuscript is poorly written, making it very difficult to understand the methods, results and discussion. Much of the text has incorrect grammar, contradicting statements and typos (even in the title: "involves" should be "is involved"). The manuscript will need major editing and likely English proof-editing if available. Many of the statements made are repetitive and do not make sense. Overall the description of results and discussion lacks coherent speculation on the overall findings (e.g. the association of this fusion event with biological processes indicated by GO terms).

The authors also make statements such as “Our study shows that IL7=AC083837.1 gene fusion was associated significantly enhanced gene expression related to NK cell- mediated cytotoxicity, which, according to the latest studies, will further activate the fibrosis process and exacerbates patients’ respiratory impairment. We have little clue about the mechanism of this impact; thus, more studies in this area is required.”

It would be better to discuss particular genes which are related to NK-cell cytotoxicity and speculate on possible mechanisms which could contribute to the pathogenesis of IPF.

It would be advantageous to try to demonstrate some functionality of the loss of IL-7 or IL-7R using an in vitro assay. For example, how NK-cell cytotoxicity could induce epithelial or endothelial cell apoptosis, as discussed in lines 489-506.

In terms of the figures presented, there are a number of concerns, in most of the figures it is unclear what is actually being presented.

Figure 4 may be better suited to be listed as a table.

Figure 5 is difficult to understand what is actually being presented and the “blue” is not discernable.

From Figure 6 onward, it is unclear what actual data is being presented. Showing GO-term node connections like this does not inform the reader of much. Please consider presenting this data more clearly. Tables could be very helpful.

Overall this manuscript will need significant revision before it will be suitable for publication.