In this manuscript, Dr. Klett and colleagues have conducted a comprehensive bioinformatics and clinic-pathological analysis to identify a multi-gene biomarker diagnosis and prognosis panel for pancreatic cancer. The investigation was designed perfectly with the combination of computer scientist and biologist with the perspectives on feature selection and gene ontology strategy. The authors collected large number public genome-wide gene expression dataset and apply Meta-analysis to identify several different panels with great performance on cancer prediction. What’s more, a 17-gene classifier/panel was validated with different study design/aims. From the result section, I notice the prediction performance is quite good, especially the author proof all the biomarkers they identified have strong evidence that are differentially expressed in solid cancer tissue and serum samples from pancreatic cancer patients. The study was performed rigorously and the findings are interesting. In general, I really enjoy the study strategy and manuscript draft.

**Major Compulsory Revisions**

1, For the dataset V4, only several of cancer types were enrolled in the study, there are almost 20+ different cancer type in TCGA, I wonder to know how to determine which cancer types were filter out.

2, The description of the feature selection in line 112 is not very clear, more detailed would be helpful.

3, The description of the meta-aggregation in line 131 is not very clear, more detailed would be helpful.

4, The description of the feature selection in line 134 and 135 is not very clear, more detailed would be helpful.

5, In the Figure 3, how to combine gene rankings could be given more details. Meanwhile, how to determine gene number in optimization should be described.

6, Availability of data and materials is another problem. The R scripts are recommended to be shared with GitHub.

7, It should be okay to apply the 17-biomarker for the diagnosis and prognosis in solid tissues, however, do you think there will be some problem for the serum plasma detection since some other cancer might also have the two markers in the study.

8, I am not confident what kinds of prediction method/approach was applied between line 215-217. Meanwhile, did you check if you put normal pancreas input the data matrix, what’s the performance?

9, I am not confident what kinds of prediction method/approach was applied between line 218-227