

Dear editor,

There are four points to answer the comments of reviewer. The contents of answer had been underlined.

This short review deals with quite interesting topics. The topic is of high interest. This paper can be improved in following points. English writing is not good. There are numerous grammatical issues in nearly all sentences. This needs to be edited, possibly by professional editing service.

(1) The English editing of this manuscript had been performed and the certification would be uploaded.

Interactive roles of statin, microbiome, and immune cells should be discussed. There are also influences of germline and somatic genetic variations on both cellular signaling. Those gene-by-environment (i.e., statin use) interactions should be discussed.

(2) In the paragraph prior to the conclusion, the microbiota can be used for selection of pancreatic adenocarcinoma patients suitable for statin treatment. The association between gut dysbiosis and pancreatic adenocarcinoma was discussed. There will be a favorable outcome of statin use for the dysbiosis. The gene was not discussed because this article focusing on clinical viewpoints. The detailed analysis of gene will be belonging to the basic study field.

Related to the above points, as a future direction, research on statin, diet, genetics, microbiome, immunity, and molecular tissue biomarkers is needed.

(3) The Bact2 dysbiotic microbiome constellation is a possible biomarker for further microbiome researches to precisely select patients suitable for statin treatment.

The authors can discuss molecular pathological epidemiology (MPE), which can investigate those factors in relation to molecular pathologies, immunity, and clinical outcomes in cancer. MPE, its strengths and challenges have been discussed in Gut 2011, Annu Rev Pathol 2019, etc. The authors can discuss that MPE research can be a promising direction

(4) The following paragraph will be added into the manuscript.
The treatment of pancreatic adenocarcinoma can be approached by the

molecular subtypes of cancer tissue as well as the genotype-oriented intervention. The application of molecular pathology can be used in predicting treatment response, risk of distant metastasis.

Thank you very much.

With best regards

Chung-Tsui Huang