2 22501-Answering reviewers

Dear reviewers

Thank you for the comments. We have revised the manuscript according to the comments.

1 Comments of reviewer 1

This is a very interesting article. Analyses are good overall. Please improve on following points. The largest study on fusobacterium in >1000 colorecal carcinomas has been published by Mima K et al. in Gut 2015. Fusobacterium is a poor prognostic factor. Lack of other tumor molecular changes is a weakness. The authors should discuss molecular changes in colorectal cancers, reviewed by D Colussi et al. Int J Mol Sci 2013; K Bardhan et al. Cancers 2013; F Zoratto et al. Tumour Biol 2014. Gut microbiota is influenced by diet and lifestyle factors. The authors should discuss the emerging science of molecular pathological epidemiology (MPE) (S Ogino et al. Gut 2011; S Ogino et al. Mod Pathol 2013; F Bishehsari et al. World J Gastroenterol 2014), which links risk factors to molecular features of cancers (such as fusobacterium). In the future, diet or medications can be used to alter microbiota for prevention of cancers.

Reply: We have revised the manuscript according to your suggestion. Data from Mima's study, and the updated sciences of molecular pathways and molecular pathological epidemiology (MPE) (with the references) have been added to the Discussion section, which greatly improves the quality of the manuscript. The revisions are labeled in red. We hope the reply meets your requirement.

2 Comments of reviewer 2

In this study the authors have investigated the relationship between Fusobacterium nucleatum infection with colorectal cancer in Chinese patients. Although an interesting association of the presence of F. nucleatum and the worse prognosis was described, an important data is missing to strongly support the conclusion of the present study. Were F nucelatum specifically enriched in these tumors or were the data

just a mere reflect of enhanced invasion of the tumor for all intestinal bacteria?

Reply: We have revised the manuscript according to your suggestion. A rational interpretation of the data is of crucial importance. We provide additional evidences to support F. nucleatum to be a cause of CRC. We also offer additional data from our ongoing study and from literature to infer that F. nucelatum is specifically enriched in CRC and enhance CRC invasiveness. The limitation you noted is explained in Discussion section. We hope the revisions (labeled in red) are helpful for understanding the paper, and our reply meets your requirement.

With best regards

Authors

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