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Reviewer’s code: 02856239
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Associate Professor
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Author’s Country/Territory: Germany

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Scientific quality

[ ] Grade A: Excellent  [Y] Grade B: Very good  [ ] Grade C: Good
[ ] Grade D: Fair  [ ] Grade E: Do not publish

Language quality

[ ] Grade A: Priority publishing  [Y] Grade B: Minor language polishing
[ ] Grade C: A great deal of language polishing  [ ] Grade D: Rejection

Conclusion

[ ] Accept (High priority)  [ ] Accept (General priority)
[Y] Minor revision  [ ] Major revision  [ ] Rejection

Re-review

[Y] Yes  [ ] No
SPECIFIC COMMENTS TO AUTHORS

The authors wrote a quite interesting review on colo-rectal cancer. This is generally of interest. Following things should be addressed and the authors should improve the paper. Prevention should be the top topics. It is currently hidden in the middle. The authors should discuss more prevention and early detection as main topics since they are important in reducing the cancer burden much more effectively than treatment. The authors should discuss the importance of diet and lifestyle for not only prevention but also survivorship. Indeed there are many environmental, dietary, and lifestyle factors that influence the microbiome (in both intestine and other tissue), immune system, pathogenic mechanisms. The authors should discuss factors other than diet too, eg, smoking, alcohol, obesity, diabetes, bowel habits, etc. There are also influences of germline genetic variations on both immune system and microbiota. Gene-by-environment interactions should be discussed. In these lines, research on dietary / lifestyle factors, microbiome, immunity, and personalized molecular biomarkers in tumor is needed for prevention and treatment research. The authors should discuss molecular pathological epidemiology research that can investigate those factors in relation to microbiome, molecular pathologies, immunity, and clinical outcomes. Molecular pathological epidemiology research can be a promising direction. Strengths and challenges of molecular pathological epidemiology (J Pathol 2019, Ann Rev Pathol 2019, Curr Colorectal Cancer Rep 2017, etc.) should be discussed. Currently, despite use of the term “multidisciplinary”, the authors mainly discuss surgery and oncology only. The authors should discuss epidemiology, nutrition, pathology, genetics, microbiology, immunology, gastroenterology, and integration of
these fields.