



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 47598

Title: Colorectal Cancer: The Epigenetic Role of Microbiome

Reviewer's code: 03887097

Position: Editorial Board

Academic degree: MBBS

Professional title: Doctor

Reviewer's country: Singapore

Author's country: Saudi Arabia

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-05-16 12:09

Reviewer performed review: 2019-05-18 10:46

Review time: 1 Day and 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review is relevant and shares some interesting insights. However, some areas of the



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manuscript could be further developed and the writing style could be more polished. Specific comments: - There is a recent review written on the same topic (see: ncbi.nlm.nih.gov/pmc/articles/PMC6087872/). This was not referenced in the current manuscript. Authors should make reference where relevant and try to avoid areas for overlap. - Please avoid the use of superfluous and imprecise language in scientific writing. Descriptions such as "Gut microbiota is an enhancer to our second brain; the intestine" and "With millions of proteins expressed by the microbiota's arsenal, human could make use of various kinds of dietary ingredients, that otherwise will be rubbish-in/rubbish-out" can be tautological; they are redundant 'padding' words that add no meaning to the sentence; or your meaning might be clearer by using a verb instead of abstract nouns. - Please change "in inducing CRC will help attaining reliable strategies to precisely diagnose and treat this fatal disease" to "in the pathogenesis of CRC will help in diagnosis and management". - I am not really sure how understanding the role of the microbiome will help in diagnosis. Please make this link to diagnostic strategies clearer in your article. - Please change "most prevailed" to "most prevalent". - Please change "It is well established that gut microbiota plays critical role in the progression of CRC either via their metabolites or interaction with their host intestinal epithelial cells" to "It is known that gut microbiota plays a role in the progression of CRC either via their metabolites or interaction with their host intestinal epithelial cells." I would not use the word "critical" as genetics may probably plays a more significant role. - What is "a hasty shift in the gut microbiome"? Please be more scientific and specific. - Dietary polyphenols, which are often indigestible, may also positively influence gut microbiota (citation: ncbi.nlm.nih.gov/pubmed/30248988). In Sprague Dawley rats with hepatic steatosis (induced by a high-fat diet), curcumin not only restored intestinal barrier integrity (increased expression of tight junction proteins ZO-1 and occluding), it markedly altered the overall composition of the gut microbiota, towards that of lean rats



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maintained on a normal diet (citation: ncbi.nlm.nih.gov/pubmed/28341485). - It is incorrect to say that "Gut bacteria can attack the intestinal epithelial cells to cause inflammation". Rather, microbial dysbiosis is associated with impaired epithelial barrier, bacterial translocation, decreased regulatory T cells in the gut mucosa and has been shown to promote inflammation (citation: ncbi.nlm.nih.gov/pubmed/24310267). - Please change "the recent researches that addresses causal link between gut microbiota and CRC onset and progression. Meanwhile, the epigenetic changes underlie CRC and its microbial root will be also described" to "the recent studies addressing the causal link between gut microbiota and CRC onset and progression. The epigenetic changes underlying CRC and the host microbiome will also be discussed." - Also important to mention would be that the intestinal mucosa is part of a complex enteric immune system and consists of a large variety of immune cells. The intestine mucosal immune system consists of three different mucosal lymphoid structures: Peyer's patches, the lamina propria and the epithelia. The intestinal mucosa is the main site for microbiome-host interactions. Exposure to food, bacteria, parasites, and viruses may contribute to sensitization of the enteric immune system and activation of the inflammatory cascade (citation: ncbi.nlm.nih.gov/pmc/articles/PMC6159811). - A recent study showed that IgA in the feces significantly increased after treatment with prebiotics, while the expression of pro-inflammatory factor in the mesenteric lymph nodes and Peyer's patches was significantly reduced. Additionally, the IL-10, CXCL-1 and Mucin-6 genes were up-regulated, while the colonic mucosa 4, IFN- γ , GM-CSF and IL-1 β genes were down-regulated in the ileum (citation: ncbi.nlm.nih.gov/pubmed/25811034). Quantitative PCR analysis of different bacterial groups revealed significant changes in Lactobacillus population. These results indicate that the gut microbiome affects intestinal mucosal immune balance. - In Table 1, it is important to explain that *H. pylori* may also have a hypothetical role in the pathogenesis of CRC, especially *cagA*-positive strains.



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One study found an association between cagA seropositivity and an associated increased risk in gastric and colonic cancer. Shmueli et al. reported cag-positive H. pylori strains were associated with a 10.6-fold increased risk of CRC compared to cagA negative strains (citation: [ncbi.nlm.nih.gov/pubmed/11774957](https://pubmed.ncbi.nlm.nih.gov/11774957/)). - Some present areas of limitations and avenues for future work should be mentioned. For example, it is important to highlight that the strongest evidence for a role of the microbiome in immunity and homeostasis comes from animal studies. There is need for the concepts generated in animal models to be translated to the human in the future. There are also existing gaps in knowledge regarding the interaction between the microbiome and the host in vivo - and the pathway of its metabolites - and how their metabolites influence the microenvironment. Further mechanistic studies involving "omics" technologies, as adapted from previous studies (citation: [ncbi.nlm.nih.gov/pubmed/30056340](https://pubmed.ncbi.nlm.nih.gov/30056340/)), might help shed light on these questions. - Please specify if any funding/external grants were received.

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 47598

Title: Colorectal Cancer: The Epigenetic Role of Microbiome

Reviewer's code: 00058573

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor

Reviewer's country: India

Author's country: Saudi Arabia

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-05-21 05:33

Reviewer performed review: 2019-05-21 07:14

Review time: 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

There is NO Manuscript File. In the link of manuscript file, there is Non-Native



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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 47598

Title: Colorectal Cancer: The Epigenetic Role of Microbiome

Reviewer's code: 02728137

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's country: Georgia

Author's country: Saudi Arabia

Reviewer chosen by: Jia-Ping Yan

Reviewer accepted review: 2019-05-16 09:47

Reviewer performed review: 2019-05-21 18:06

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SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear authors, It is very nice manuscript.



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