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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 5698

Title: Role of Intestinal Microorganisms in Pathogenesis and Therapy with Probiotics and Prebiotics in Treatment of Inflammatory Bowel Disease

Reviewer code: 00506548

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-09-22 19:08

Date reviewed: 2013-10-09 16:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input checked="" type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This is a full review article - although I am a microbiologists, you need a specialist like a medical health practitioner or somebody specializing in this field. I was not aware this is a review article and therefore I will not be able to assist you with a proper assessment on this topic.

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Title: Role of Intestinal Microorganisms in Pathogenesis and Therapy with Probiotics and Prebiotics in Treatment of Inflammatory Bowel Disease

Reviewer code: 02529070

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-09-22 19:08

Date reviewed: 2013-10-10 08:45

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Orel and Trop present a review of the literature describing the use of pro- and pre-biotics for the treatment of IBD. Overall I thought that the amount of background reading that has gone into producing this review was impressive, and the authors have been quite thorough. Indeed, the review is so thorough that it does sometimes become a bit of an effort to read through in parts. Especially those where you are faced with long lists of studies, often with conflicting results, so it is difficult to come away with an overall impression. I therefore wondered if it would be better to perhaps reduce the length of some of the text and present the findings in a Table format instead? Certainly I think it would be helpful for the reader if the authors could condense down information into a table where they list each of the microorganisms/mix of microorganisms that have been used as probiotics and briefly summarise the findings for each of them. For example list VSL#3, Lactobacillus rhamnosus GG etc and summarise studies for each of them in one easy to look over place? This is not a necessary requirement but I do think it would help the reader. I would also say that it is a sometimes a little bit optimistic about the efficacy of probiotics. While the authors do give some examples of studies where negative results or no effect was observed I do think it is worth stating somewhere in the text that positive results bias likely exists in the literature, simply because people are less likely to report negative results. Indeed, many of my clinical colleagues no longer bother using VSL#3 because they have not found it to have significant benefit for their patients. Of course, this does not end up getting written up into manuscripts, only the positive results. In addition, it would not hurt to mention that most of the studies they report on suffer from a similar limitation,

namely that they involve too few participants. Bigger trials are sorely needed. Beyond these points I had no other major comments. Note though that there are a large number of minor factual errors and grammatical mistakes throughout the text and these will need to be corrected. I have listed them in the order they appear on the text below. For future reference it would be easier for the peer reviewer if the authors were to include line numbers! Minor comments: Page 1, Abstract, line 4 – should read “probably play a central role” Page 1, final paragraph, 1st line – should read “The normal human gut...” Page 2, first paragraph – There are a few mistakes in this paragraph. First of all, *Bacteroides uniformis* does not produce butyrate so should be removed from the list of “butyrate-producing bacteria”. Secondly, it is now well established that there are no species that are present in all individuals, therefore it is not really appropriate to call these “key members”. Next, the list of “predominant” genera is not really accurate as it reflects older thinking before improved taxonomy in the light of sequence data. I would recommend reading Lawley TD, Immunology, 2013 for a more up to date list of abundant genera in the healthy gut. Finally, I think they should delete the percentages listed at the end of the paragraph since the composition of the microbiota is unique to each individual it is meaningless to give proportions since these will vary greatly depending on the person. Page 2, 2nd paragraph, 6th line – should “division” be “diversion”? Page 2, 2nd paragraph, 16th line – should read “..were raised in a sterile environment...” Page 3, 1st paragraph, 2nd line – should read “The intestinal mucus barrier...” Page 3, 2nd paragraph, 1st line – should read “Despite much evidence ... are required for triggering and perpetuating inflammation in IBD...” Page 3, 3rd paragraph, 1st line – “particularly serious” is not really right, perhaps change to “particularly marked”? Page 3, 3rd paragraph, 4th line – “Mycobacteria” should be “mycobacteria” and not in

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Title: Role of Intestinal Microorganisms in Pathogenesis and Therapy with Probiotics and Prebiotics in Treatment of Inflammatory Bowel Disease

Reviewer code: 00381580

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-09-22 19:08

Date reviewed: 2013-10-11 10:11

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is a very comprehensive review on the role of the microbiota in IBD and a second part that details the published literature on the use of prebiotics and probiotics for UC, Crohn's, and pouchitis. Major points: This is a long review and the second part can be a bit hard to follow with the numerous studies that are mentioned. To improve readability, I recommend constructing a table that has all the studies for UC, CD, and pouchitis for probiotics and prebiotics and that includes all the pertinent information such as type of study, number of patients, endpoints, results. In the text of the review, I would mention maybe only the best studies for each category of IBD. Minor points: 1) Please have this reviewed carefully for English grammatical errors that are throughout the review and too numerous for me to detail. 2) Treatment of active UC- first paragraph- Would take out the part about fecal transplantation which will be covered in another review in the same journal 3) Treatment of active UC- for VSL#3- sometimes the dosage is listed as cfu and sometimes as mgs. Can this be just one, preferably cfu? 4) Top of page 9- the remission (defined as UCDAI < or = 2) was achieved in 53%,- I think you mean "response" not remission 5) Page 15- please check the doses listed for VSL#3- there seems to be a large range listed in the various studies 6) Page 17- section of Crohn's- when at all possible, I would put what type of crohn's the patients had in the various studies 7) Page 18- second paragraph- you mention Bifidobacterium as a prebiotic, should be probiotic 8) Page 19- second paragraph does not make sense at all