

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32199

Title: Diet and microbiota in IBD: the gut in disharmony

Reviewer's code: 02462498

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2016-12-29 14:08

Date reviewed: 2017-01-12 22:09

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Publication Name: World Journal of Gastroenterology Number ID: 01589311 Manuscript Type: Review This is a nice review on diet, microbiota and IBD. There are two comments on article: 1. If the journal cannot accept so long manuscript, authors need shorten it. 2. As for the treatment on IBD using microbiota/bacteria, FMT should be the most important therapy. However, the authors only use very limited literature evidence to support it and even said there was no controlled study. The only supporting evidence is the review published in 2012 (Anderson JL, et al. Alimentary pharmacology & therapeutics 2012). Actually the recent published clinical studies should be strong supportive to highlight the therapeutic role of remodeling microbiota in IBD. Research articles on RCT or the largest samples, instead of review, listed as following: Moayyedi P, Surette MG, Kim PT, Libertucci J, Wolfe M, Onischi C, Armstrong D, Marshall JK, Kassam Z, Reinisch W, Lee CH. Fecal Microbiota Transplantation Induces Remission in Patients With Active Ulcerative Colitis in a Randomized Controlled Trial. Gastroenterology. 2015 Findings From a Randomized Controlled Trial of Fecal Transplantation for Patients With Ulcerative Colitis. [Gastroenterology. 2015] Cui B, Li P, Xu L, Zhao Y, Wang H, Peng Z, Xu H, Xiang J, He Z, Zhang T, Nie Y, Wu K, Fan D, Ji G, Zhang F.



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Step-up fecal microbiota transplantation strategy: a pilot study for steroid-dependent ulcerative colitis. *J Transl Med.* 2015 Cui B, Feng Q, Wang H, Wang M, Peng Z, Li P, Huang G, Liu Z, Wu P, Fan Z, Ji G, Wang X, Wu K, Fan D, Zhang F. Fecal microbiota transplantation through mid-gut for refractory Crohn's disease: safety, feasibility, and efficacy trial results. *J Gastroenterol Hepatol.* 2015

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32199

Title: Diet and microbiota in IBD: the gut in disharmony

Reviewer's code: 03661119

Reviewer's country: China

Science editor: Yuan Qi

Date sent for review: 2016-12-29 14:08

Date reviewed: 2017-01-13 20:02

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The is a nice review focuses on the relationship of dietary components, epigenetics, immune system and gut microbiota. It starts with an introduction of the host immunity and IBD, followed by a thorough discussion of gut microbiota, dysbiosis, IBD and some diet components. While diet will certainly influence gut microbiota, the connection from diet to IBD is still lacking. This can be further discussed. I suggest discussing different types of dysbiosis in page 14, paragraph 2 ("Whether dysbiosis consists of a primary or secondary phenomenon in IBD is a question that remains unanswered", "dysbiosis alone is not sufficient to induce IBD"). Different types of diet have differential effects on epigenome. Do these further correlate with the incidence of IBD? The review is focused more on specific components including retinoic acid, iron, vitamin D, folic acid, choline, selenium as well as antibiotics, prebiotics and probiotics than on different types of diets. I suggest further expanding on different types of diets such as fat-enriched diet and carbohydrate-enriched diet. What kinds of dietary intervention can we anticipate in the end? Some minor errors: Page 8, paragraph 1: predominantly localized "at" epithelial and immune cells -> "in" Page 8, paragraph 2: Alimentary fibers are not digested by the human gastrointestinal tract but, instead, they are



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“modified” in the gut by bacteria -> bacteria ferment fibers, which in turn modify gut microbiota.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 32199

Title: Diet and microbiota in IBD: the gut in disharmony

Reviewer's code: 01490743

Reviewer's country: Sweden

Science editor: Yuan Qi

Date sent for review: 2016-12-29 14:08

Date reviewed: 2017-01-17 01:18

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input 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"/> The same title	<input type="checkbox"/> High priority for publication
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COMMENTS TO AUTHORS

Comments on Diet, Microbiota and IBD The article is well written and provides an comprehensive overview of the field and what is currently known. The review makes it possible to get a quick insight in the intriguing mechanisms that may contribute to IBD. However, I have some comments that could be worth while to consider. Major The choice of dietary factors is obscure to me. How have they been chosen among the multtude of factors that have been discussed over the years. See the bottom of this reveiw for reference suggestions In general the taxonomic rank is not mentioned thus making the interpretation of the message somewhat more difficult. It is not necessary but it could be worth contemplating the possibility to further clarify the rank of the different organisms mentioned (whether it is about phylum, class, order, family, genus, species etc). Minor Page 9, last paragraph, first sentence (Network-based studies of microbial communities performed with faecal samples of several mammalian species confirmed that diet does determine bacterial diversity, which increases from carnivore to omnivore to herbivore, whereas microbial communities diversify concomitantly with their hosts) is somewhat unclear. In this sentence two ways for microbial development is described. Are they correlated? Is the second one over time? Page 10,

four lines from bottom (more than 160 genetic risk loci) is now more than 200. Page 13, in the last last paragraph (In CD, for example, immune reactivity against microbial-derived antigens has long been reported, characterized by several different circulating serum antibodies [64-66].) reference 64 is about ASCA that comes from yeast, reference 65 is appropriate but the substances referred to in reference 66 seems – as far as I can understand – to come from fruit (?). In this context the antibodies against pseudomonas could also be mentioned if further references about bacterial antigens should be warranted. Page 13, last paragraph, 8 lines from bottom (about *Faecalibacterium prausnitzii*) mentions a reference 71 referring to the occurrence of this bacteria in the postoperative state and risk for relapse. As I see it there are several other more appropriate references that could be used. Page 14, last paragraph, about UPR – this type of response could be explained by one sentence (or two) for those readers not fully familiar with this phenomenon. Page 15, second last paragraph (Furthermore, the interaction between single nucleotide polymorphisms of ATG16L1 and IRGM also has been demonstrated in CD [94], indicating the probable integration of defective autophagy with mitochondrial dysfunction and apoptosis) deals with mitochondrial dysfunction but without explaining it. Some kind of explanation could be valuable. Page 16, second last paragraph, ref 101 is about maltodextrin, that is one putatively harmful additive. There are other suspects on the crime scene. For example read the articles by Lerner about the seven possibly harmful additives that could contribute to the present autoimmune epidemic. Although many of these substances have not been definitively proven to be hazardous to man they could maybe be mentioned as possible contributors. Page 16, second last paragraph, about sun light, check out Dopico from 2015 about summer and winter genes providing evidence that it is not only about vitamin D. It is outside IBD but worth mentioning. The part about folic acid is contradictory as both high and low levels increase the risk for cancer. This ought to be explained in a more thorough way. About the choice of dietary factors When it comes to dietary micronutrients vitamin A, iron, selenium and folic acid are discussed. How have these specific factors been chosen? The list is not complete. It must be explained why only these factors have been chosen. How about zinc that has impact on the risk for both IBD in mice as well as diabetes? How about fat, espe