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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5887
Title: Inflammation and colorectal cancer, when microbiota-host mutualism breaks
Reviewer code: 00504462
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-29 15:28
Date reviewed: 2013-10-13 04:04

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Dear Sir, Human gut microbiota has become a key point to understand the health and disease process not only for diseases related to the gut but in several other organs of our body. As it is stated in your manuscript most of the information is partial. I want to congratulate you as you make an extensive and complete revision of the literature. For the future I hope to hear more about your achievements, and hopefully to hear more about the process of prevention as well the interrelation of the different bacteria in order to maintain a stable environment as well to prevent the colonization of harmful bacteria. Thank you for the opportunity to review your manuscript.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5887
Title: Inflammation and colorectal cancer, when microbiota-host mutualism breaks
Reviewer code: 00227418
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-29 15:28
Date reviewed: 2013-11-06 01:30

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
Candela and colleagues provide a clear and thorough review of the relationship between microbiota and colon cancer, which is a relevant issue. The manuscript is well outlined and does an excellent covering of the literature.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5887
Title: Inflammation and colorectal cancer, when microbiota-host mutualism breaks
Reviewer code: 00506058
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-29 15:28
Date reviewed: 2013-11-07 23:26

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
This paper reviews the mechanisms involved in the bacteria-mediated carcinogenesis, specifically colorectal cancer. The paper is well written and covers novel aspects of the topic. Some typing and language mistakes needs to be corrected.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5887
Title: Inflammation and colorectal cancer, when microbiota-host mutualism breaks
Reviewer code: 00058387
Science editor: Gou, Su-Xin
Date sent for review: 2013-09-29 15:28
Date reviewed: 2013-11-09 19:47

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[Y] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

The authors present a comprehensive overview of how microbiota contribute to intestinal inflammation and colorectal cancer development. The review is well written and covers recent developments in this field. However, I still have the following comments and remarks: 191: the authors mention APC end CTNNB1 as driver mutations in CRC development. It is now appreciated that in contrast to spontaneous CRC development, colitis associated cancer (CAC) is characterized by late mutations in APC. Given the interplay between NF-kB and Wnt signaling in IECs (Schwitalla et al., Cell 2013), and the inherent pro-survival/proliferation effect of NF-kB activation, microbiota induced NF-kB activation in IECs may bypass the requirement of early mutations causing hyperactive Wnt signaling during colorectal cancer development. At multiple sites in the review, the authors describe changes in microbiota in CRC patients, or specifically at cancerous mucosa compared to healthy mucosa. Could the authors elaborate briefly on the mechanism by which cancerous epithelium can harbor specific bacteria. How can the tumor create a specific microbial niche? (difference in epithelial adhesion, reduced mucin/anti-microbial peptide production at tumor sites,…?). How could passengers show competitive advantage in the tumor micoenvironment? In chapter 4 the authors suggest different mechanisms involved in microbial CRC promotion. When discussing the role of inflammation and NF-kB, it is worth stressing the cell type specific function of NF-kB in IECs (anti-apoptotic) versus myeloid cells (pro-inflammatory). In this respect, the landmark paper of Greten et al., Cell 2004 is very informative. It is also worth mentioning a few important tumor promoting inflammatory cytokines, like IL6 and TNF. The authors mention a few examples of TLR and colorectal cancer, but do not mention the importance of inflammasomes. Mice deficient for inflammasome components (casp1, nlrp3, nlrp6,…) have increased susceptibility to CRC

development (largely due to lack of IL18). Inflammasome dysfunction also causes dysbioses, which contributes to CRC sensitivity (transmissible!) via epithelial IL6 signalling. Therefore I believe inflammasomes should be discussed briefly in this chapter. 365: explain what the abbreviation ATM stands for 370: change (REF) with appropriate reference 378 and 382, psk+ should be pks+ 380: typo: has been recently proven 408 …innate immune adaptor Rip1-Rip2. Rip1 and Rip2 are not adaptor proteins but kinases, which act in distinct signaling pathways 427 maybe consider to refer to Tbet instead of TBX21 (less frequently used) Genetic studies in IBD patients and mouse studies have identified autophagy as a critical cellular mechanism for intestinal immune homeostasis. Therefore it is worth briefly mentioning proper handling of intracellular bacteria by autophagy in the context of intestinal inflammation (ATG16L1, NOD2,…) 463 quotation mark missing "benificial