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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 25873
Title: Inflammatory bowel disease and airway diseases
Reviewer's code: 00009530
Reviewer's country: Italy
Science editor: Ya-Juan Ma
Date sent for review: 2016-03-25 18:03
Date reviewed: 2016-04-05 06:30

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

I have read with interest the paper by Vutcovici et al. which is focused on a rather unknown but yet important and stimulating topic in IBD. The review is complete and updated. Since the association of NOD2 with Crohn's disease is the most relevant genetic observation in IBD, I think that the observation that similar mutations are observed in COPD would deserve more comments, also focused on the role that this mutation may have in bacterial recognition.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 25873
Title: Inflammatory bowel disease and airway diseases
Reviewer's code: 00189619
Reviewer's country: Israel
Science editor: Ya-Juan Ma
Date sent for review: 2016-03-25 18:03
Date reviewed: 2016-04-16 23:55

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
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[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is a nicely written manuscript that reviews the literature for epidemiologic and etiopathogenesis association between IBD and airway diseases. The authors attempt to find similarities between IBD and airway diseases and state that they focus on "IBD occurrence in patients with airway diseases". Major comments: 1. The review should begin with the last section that actually describes the epidemiological occurrence of IBD in patients with airway diseases and only after this section the authors should discuss the similarities between the diseases. As the authors state- this is the actual topic of the review and therefore it should be more detailed and findings that are nicely put in the table should be thoroughly discussed and referred to in the rest of the manuscript. For instance, in the two largest studies that evaluated the occurrence of asthma in IBD, one of the studies demonstrated an association with UC while the other did not. 2. Despite the comprehensive review of the literature, the message of the review is not entirely clear and in some sections, statements are too general and more details are required. It would be more convincing to try and discuss common pathways that may drive both diseases rather than looking at general similarities that may be true also other disease such as skin and rheumatic diseases. Is there a common pathogenesis between

airways diseases and IBD? This should be discussed with regard to each of the airway diseases that have been associated with IBD (asthma, COPD and bronchiectasis) and not mentioned in a general manner. For instance, are there common dysbiotic bacteria? Are there common immunological pathways? Can these support the greater association of asthma with CD as opposed to UC? Minor comments: 1. The hygene theory should be mentioned as a model that tries to explain the surge in asthma and IBD. 2. Page 4- Pathogenesis- "Autoimmunity is yet another characteristic that IBD…"- IBD is not considered an autoimmune disease, but a disease that is characterized by immune dysregulation. 3. Page- 6- Airways disease in IBD- "It is estimated that 40-60% of IBD patients have some degree of subclinical lung involvement". This is based on references from more than 10 years ago. Are there more recent data? What is the degree of subclinical lung involvement in the general population? And most important- what is the clinical significance of these associations? 4. Page- 7- Airways disease in IBD- The authors should at least mention the IBD medications that are associated with lung diseases (e.g. sulfasalazine, methotrexate, etc) and what is their clinical manifestations. 5. The authors mention that exposure of animals to air pollutants may be associated with increased intestinal permeability, but are there animal models of airway diseases that support increased tendency to develop actual enteritis and vice versa- has there been shown that in animal models of colitis there is an airway injury? 6. Are there any recommendations to the clinician- in terms of screening for IBD in patients with airways diseases or vice versa? 7. Should IBD patients who are about to be treated with mediations that may compromise the airways, undergo pulmonologic evaluation? 8. Are there specific recommendations to patients who are about to be treated with anti-TNF agents, especially in the setting of cigarette smoking and Crohn's disease. It has been demonstrated that anti-TNF may be harmful for patients with COPD.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 25873
Title: Inflammatory bowel disease and airway diseases
Reviewer's code: 02441672
Reviewer's country: Brazil
Science editor: Ya-Juan Ma
Date sent for review: 2016-03-25 18:03
Date reviewed: 2016-04-28 23:26

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The article is a concise and practical review and introduces innovative concepts to gastroenterological clinic, arousing the interest in the research of the interaction between the respiratory and digestive immune mucosal systems and its possible clinical consequences. I would suggest that the authors could include a discussion about this mucsal interrelation observed and published by our research group in patients with IBS. This subject is a future challenge for clinical science: Soares, R. L., Figueiredo, H. N., Santos, J. M., Oliveira, R. F., Godoy, R. L., & Mendon?a, F. A. (2008). Discrepancies between the responses to skin prick test to food and respiratory antigens in two subtypes of patients with irritable bowel syndrome. World Journal of Gastroenterology?: WJG, 14(19), 3044–3048. http://doi.org/10.3748/wjg.14.3044 Soares RL, Figueiredo HN, Maneschy CP, Rocha VR, Santos JM. Correlation between symptoms of the irritable bowel syndrome and the response to the food extract skin prick test. Braz J Med Biol Res. 2004;37:659–662. Soares RL, Figueiredo HN, Moreira Filho PF, Oliveira RF, Gon?alves CD, Micuci AJQR, Parada BA, Brand?o IB, Rodrigues CC. The prevalence and clinical characteristics of atopic manifestations in patients with irritable bowel syndrome in a Brazilian urban community. Gastroenterol Ins. 2010;2:p. e11.