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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23142

Title: Serum vitamin D and colonic vitamin D receptor in inflammatory bowel disease

Reviewer's code: 00227449

Reviewer's country: United States

Science editor: Ze-Mao Gong

Date sent for review: 2015-10-26 19:05

Date reviewed: 2015-11-11 00:14

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This very small observational study (total 20 subjects, 10 IBD patients, 10 control) reported several outcomes. 1. More vitamin D deficiency/insufficiency in IBD patients despite the fact that the control subjects were older because they were selected from normal colonoscopy patients. This is not a new observation. Micronutrient deficiencies among IBD patients have been reviewed (Curr Opin Clin Nutr Metab Care. 2015 Nov;18(6):576-81). 2. They found more inflammation in intestinal tissues from IBD patients than from control. This is why IBD is considered an inflammatory disease and thus not a new observation. 3. They found negative correlation of inflammation and VDR expression in the intestine. The significance of this correlation is unclear and the analysis needs to be repeated in a larger study (see Fig. 3 for large variations in VDR expression among Control samples). Because of the small sample size and a lack of in-depth tissue analysis, we cannot be sure of the presence of causal relationship. Was the expression of other genes affected in IBD intestine samples? The authors performed numerous statistical analyses on a limited set of data and the increased chance of false positive was not discussed.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23142

Title: Serum vitamin D and colonic vitamin D receptor in inflammatory bowel disease

Reviewer's code: 00070280

Reviewer's country: Sri Lanka

Science editor: Ze-Mao Gong

Date sent for review: 2015-10-26 19:05

Date reviewed: 2015-11-11 03:18

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" type="checkbox"/> No	<input checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is an interesting article. However, they should not conclude the results apply to IBD as their were only 3 UC patients. They should consider using only CD patients or using equal number of patients with UC.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23142

Title: Serum vitamin D and colonic vitamin D receptor in inflammatory bowel disease

Reviewer's code: 02529831

Reviewer's country: Australia

Science editor: Ze-Mao Gong

Date sent for review: 2015-10-26 19:05

Date reviewed: 2015-11-11 08:29

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

COMMENTS TO AUTHORS

This is an interesting study, but significantly compromised by the few numbers of patients and biopsy samples studied. The conclusions drawn are not supported by the data presented. There are multiple miscalculations in the statistics presented, and the p values presented do not seem to be accurate. VDR IHC scores were (non-significantly) higher amongst inflamed tissue than non-inflamed tissue in patients with IBD, yet negative correlation is demonstrated with inflammation scores. How is this explained? Why was inflammation scored amongst controls? Why is this relevant, and what does this add to our knowledge?



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23142

Title: Serum vitamin D and colonic vitamin D receptor in inflammatory bowel disease

Reviewer's code: 00503587

Reviewer's country: New Zealand

Science editor: Ze-Mao Gong

Date sent for review: 2015-10-26 19:05

Date reviewed: 2015-11-05 15:51

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" 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 checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" 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

This work focused on a small group of subjects with and without IBD, and elucidated relationships between gut inflammation, Vit D and VDR staining. Specific Comments 1. Although the authors noted differences in key outcomes the work included only 20 subjects in total. Detailed understanding beyond this pilot work would need to include larger numbers of subjects 2. The Introduction is about twice as long as it needs to be. 3. There are numerous errors of English language word usage or grammar that must all be corrected 4. It is unclear why the authors expected the age of the patients with IBD to be less than that of the control subjects. Also, why were controls not recruited to be age-matched? 5. What was the ethnic make-up of the 20 individuals included? 6. In regards the subjects with IBD, there are many aspects not included: were these patients all newly diagnosed or did they have long-standing disease? In a related fashion, what was the length of their disease? Were these subjects in remission or did they have active disease at the time of assessment? Which medications were being prescribed for the 20 individuals - and did these correlate with the outcomes of interest? 7. The comment about the risk of colitis-associated cancer in the context of IBD needs to be qualified. The risk of cancer in the setting of colitis reflects other factors, such as the



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length of active disease.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23142

Title: Serum vitamin D and colonic vitamin D receptor in inflammatory bowel disease

Reviewer's code: 02529166

Reviewer's country: France

Science editor: Ze-Mao Gong

Date sent for review: 2015-10-26 19:05

Date reviewed: 2015-11-08 00:32

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In the present study, Abreu-Delgado et al. show that VDR expression in normal mucosa correlates with serum vitamin D levels, and that VDR expression inversely correlates with inflammation in IBD patient-inflamed mucosa. This report supports many clinical and pre-clinical findings about the important role of active vitamin D in disease severity, especially in IBD. Moreover, they highlight the clinical relevance for vitamin D supplementation in Porto Ricans patients. The introduction is a bit long but recapitulates quite well the previous research on vitamin D and IBD. Even if the low number of patient limits the high impact of the study, as underline by the authors, the results are clear and the conclusion not over-interpreted. However, few points need to be addressed: 1) Statement made page 2 line 2 of the introduction part need to be corrected. Effectively, ChIP-seq experiments reveal the presence of Vitamin D response element in the promoter region of VDR in intestine and bone, and thus contribute to the regulation of VDR expression (PMID: 24466413). 2) A decreased of Vitamin D-mediated activity in colorectal cancer is due to an increased expression of CYP24A1, the enzyme responsible of Vitamin D catabolism (PMID: 23674869). Moreover CYP24A1 overexpression increases aggressiveness and proliferative potential of colorectal tumors (PMID: 26238339). Please



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insert these works. 3) Insert representative H&E staining of a normal and an inflamed mucosa. 4) Where is located VDR in normal and inflamed mucosa? Representative IHC are required to identify subcellular localization of VDR (immune cells, epithelial cells or other). Please also discussed this point. 5) Functional relevance of a decreased VDR expression needs to be address. CYP24A1 and DEF?/HBD2 staining on adjacent section will be informative. Minor point: - Please state in the introduction that the main role of VDR is intestinal calcium absorption and regulation of serum calcium and phosphate levels. - Scatter dot plot representation will be more informative than bar graphs. - Introduction page 1 line 20: delete "can" and line 28: substitute "that" by "and"