

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35838(37443)

**Title:** Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases?

**Reviewer's code:** 00034437

**Reviewer's country:** Japan

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-08-29

**Date reviewed:** 2017-09-04

**Review time:** 5 Days

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

## COMMENTS TO AUTHORS

This manuscript showed the expression of GLUT2, SGLT1, and GLUT5 in large intestinal mucosa in patients with IBD, colorectal cancer and healthy control only by immunohistochemistry study. Overall, data shown in this manuscript is all phenomenon. This reviewer strongly suggests that the authors should do more additional experiments regarding what mechanisms regulate expression of GLUT2, SGLT1, and GLUT5 in colonic mucosa in the inflamed and non-inflamed mucosa.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35838(37443)

**Title:** Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases?

**Reviewer's code:** 02520845

**Reviewer's country:** Croatia

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-09-20

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**Review time:** 8 Days

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 checked="" 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"/> 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"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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

ESPS Manuscript NO: 35838 Title: Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases? The authors investigated the expression of the members of the GLUT family of membrane proteins in the human colorectal mucosa in inflammatory bowel disease. The manuscript is readable and presentable, but there are a few minor comments. Results & Discussion: The data is clearly presented and the discussion is well organized. The immunohistochemical data which is not presented, it would be specified as "data was not shown" (page 14). Also, I suggest decreasing the number of Figures on the way to select the representative figures for the most important results and throw out the figures which did not show difference between the investigated groups; in the Fig.7 summarize the most important findings in the figure legend. In literature review, recent

researches are listed to this topic. In conclusion, this is an interesting study which highlights the role of GLUT5 expression in inflammatory bowel disease associated with atypical aggregation of lymphatic vessels.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35838(37443)

**Title:** Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases?

**Reviewer's code:** 01047616

**Reviewer's country:** Taiwan

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-09-20

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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"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input 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 type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" 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

The authors investigated the expression patterns of GLUT2, SGLT1, and GLUT5 in the mucosal biopsies of control subjects and IBD patients by using immunohistochemistry and immunofluorescent staining. The study aim is straightforward and the results showed novel findings of glucose transporters expression in the human colonic mucosa of IBD patients. While the technical difficulties of tissue collection and rareness of the human biopsies are well recognized, a number of concerns regarding the inclusion of patients must be corrected. Major concerns are listed below. Major points: 1. The control subjects included those who had a history of colorectal surgery (n=4 out of 20). These post-surgical patients are not proper controls and should be excluded from analysis. It is known that intestinal adaptation such as upregulation of glucose transporter occurred in brush border of remnant intestine in animal models of short

bowel syndrome (Martin GR et al., Am J Physiol 2014). Moreover, both inflamed and non-inflamed areas obtained from the control subjects were included in the analysis (Table 2). The inflamed tissues should not be considered as controls. 2. The immunostaining pattern of glucose transporters in each intestinal segment appears to be in cluster forms on the epithelial surface and only 5-33% of biopsies are positively stained. Since no difference in pattern or percentage could be definitely identified for the glucose transporters and the n number of patients are relatively low, the title is far-reaching by suggesting “ a missing ring in the pathogenesis of colonic diseases”. This should be deleted. 3. Has the author tried peptide competition assay to ensure the specificity of antibodies used for staining of glucose transporters? The authors have to show the absence of non-specific staining by antibody since the conclusion is mainly based on immunohistochemical staining. Fig 9: Gold-labeled TEM is recommended to show if GLUT5 is localized to lymphatic vessels . Fig 10 and 11: Stainings of GLUT5 and LYVE-1 (a lymphatic vessel endothelium marker) were not co-localized. GLUT5 seems to be present on certain cell types, lymphocytes? 4. The stainings are mostly based on immunohistochemistry or immunofluorescence. The use of real-time PCR would be beneficial for quantification of overall expression levels.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 35838 (37443)

**Title:** Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases?

**Reviewer's code:** 02441737

**Reviewer's country:** Mexico

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2017-09-20

**Date reviewed:** 2017-10-04

**Review time:** 14 Days

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
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Comments to the manuscript 35838 entitled: Glucose transporter expression in the human colon: the missing ring in pathogenesis of colonic diseases? From the authors Merigo F., et al. It is a very interesting descriptive study to be innovative in daily clinical practice, although it is advisable that the authors respond to the following comments. Methodology: It is recommended that the authors describe in detail the statistical procedure for determining sample sizes for the groups studied (sample size and precision for estimating a population proportion). Because this is a descriptive study, the following statistical parameters should be considered: a) confidence level, b) expected proportion of patients expressing glucose transporters in colorectal mucosa in healthy subjects and subjects with inflammatory bowel disease, and c) the accuracy of the test. It would be of interest to describe clearly the clinical characteristics and the diagnosis of



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the patients who formed the control group. This, because this group was formed by patients with very different symptomatology and / or diagnosis. Patients who underwent colonoscopy for prevention of colorectal cancer or were followed-up after polypectomy or had history of colorectal surgery or lower gastrointestinal symptoms were designated as the control group. The BMI of the patients has a very wide range, could present the results of the expression of glucose tracers stratifying patients according to their BMI (obese and non-obese). The above, because the age and BMI of patients and controls vary significantly between groups, which could influence the presented results. It would be of interest if the researchers compared the results among the groups of subjects: 1) who underwent complete colonoscopy, biopsies were obtained from all 6 portions of the colon-rectum (cecum, ascending colon, transverse, descending, sigmoid colon, rectum) and those which the biopsies were obtained only from the endoscopically. Results In Figure 1, it is recommended that the authors highlight the microscopically findings of using arrows. Make the correction at the foot of Figure 7, since these are bar graphs, they are not histograms.