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## PEER-REVIEW REPORT

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

**Manuscript NO:** 36452

**Title:** Increased intestinal mucosal leptin levels in patients with diarrhea-predominant irritable bowel syndrome

**Reviewer's code:** 02860590

**Reviewer's country:** Brazil

**Science editor:** Yuan Qi

**Date sent for review:** 2017-09-30

**Date reviewed:** 2017-10-13

**Review time:** 13 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
<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"/> No	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		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 study proposed to measure leptin levels and analyse the relationship of leptin with clinical features, visceral sensitivity, mast cells, and nerve fibres. My specific queries and comments are below: 1. Abstract: The characteristics of the patients and controls are not well described such as age, sex, characteristics (type/severity) of baseline disease and presence of other comorbidities. Were the controls age- and sex matched with the patients? What were the criteria adopted to establish the diagnosis of IBD-D? 2. Page 6, Measures (line 11). Could the authors add the reference related to the validated questionnaire? 3. Were the specific questionnaires validated in the Chinese population? Could the authors add the reference related to the specific questionnaires? 4. Please, Could the authors revise the tables' titles? 5. In the tables, legends should contain sufficient information to provide an adequate understanding of the table by the reader



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without reference to the text. 6. Authors should be more careful with the details of the figures. They should be improved as well as the legends. 7. There is a limited discussion regarding the strengths, weakness and limitations of the study. 8. The manuscript should be described in a more concise and substantial manner. 9. Reviewer conclusion: Accept but needs revision (both major and minor).



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## PEER-REVIEW REPORT

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

**Manuscript NO:** 36452

**Title:** Increased intestinal mucosal leptin levels in patients with diarrhea-predominant irritable bowel syndrome

**Reviewer's code:** 00009420

**Reviewer's country:** Belgium

**Science editor:** Yuan Qi

**Date sent for review:** 2017-09-30

**Date reviewed:** 2017-10-15

**Review time:** 15 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

In their study, the authors investigate the expression of leptin and the leptin receptor in serum and mucosal biopsies of IBS-D patients and healthy controls. Based on mainly immunohistochemical stainings the authors relate the leptin profiles to mast cells and neurons and correlate the findings to visceral hypersensitivity measurements, symptom scores and QoL. Major remarks 1. The authors should provide much more details on the immunohistochemical results. In my opinion the stainings are not clear at all or mistakes are present in the legends. The stainings presented not always support the statement/conclusions of the authors in my opinion. For instance in figure 2 (and all other figures) the authors should mention which samples are from IBS-D patients and which from controls. If I understood it correctly the leptin immunoreactivity shown in part a is from an IBS-D patient showing less intense staining than part b which is a



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control according to the legend? 2. Also the mast cell activation rate should be demonstrated in much more detail. How did the authors score this parameter: using a present/absent or a more continuous scale, or using a scoring system, ... It is not clear from figure 1 what exactly in the stainings accounts for the difference in activation rate. 3. Please also clarify the co-localisations in figures 3-4. Indicate with arrows and/or asterisks which mast cells show co-staining with leptin and which mast cells don't. If the mast cell activation rates are different I wonder whether tryptase is a reliable marker to study this research question. One could wonder whether the tryptase stainings per se were not different between controls and IBD patients. 4. Looking at table 1 the authors indicate that the IBS scales were not determined in the controls, why not? 5. The authors conclude that the increased levels of mucosal leptin interact with mast cells and the nervous system. This seems an overstatement to me as the immunohistochemical stainings are the only basis for this statement and they are not that clear to me. Besides the authors only used PGP 9.5 as a neuronal marker, why didn't they study more specific neuronal markers investigating for instance the colocalisation with afferent nerve fibers? Please change the word 'interacting' in your final conclusion in abstract and discussion. 6. Were the observers for the histological data analysis blinded for the two groups as well as the investigator investigating the visceral hypersensitivity? 7. Do the authors have any data on the power of their study? Minor remarks 1. The authors used only one reference gene (GAPDH) where normally three reference genes are used according to the guidelines. Could the authors at least show that the reference gene remained stable in their analyses. 2. In the discussion the authors link the leptin expression to CRH and cortisol while this is not studied at all in their paper. 3. Page 15 comments - background line 5 'Leptin instead of leptin' 4. Page 23 legend figure 1. 'Metachromatically instead of metachromatically'