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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 5482
Title: Abnormal endocrine cells in the ileum of patients with irritable bowel syndrome
Reviewer code: 00843082
Science editor: Cui, Xue-Mei
Date sent for review: 2013-09-12 16:11
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] 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

The authors present a well conducted and written histologic study of enteroendocrine cell types in the ileum of IBS patients, correlating cell densities wtih symptoms and comparing them to control subjects. This is an observational and correlative study, and does not address possibly pathophysiology that would explain the findings. The groups are well matched and there are no ethical issues. Two comments should be addressed. First, the quantification of cells is done over a cross sectional area of tissue represented between groups. The number of enteroendocrine cells will be varible based on the height of sampling along the crypt-villus axis, and the number of crypts counted, rather than based on the cross sectional area of the slide surveyed. For this reason, some methods of quantification of such cells would be based on a denominator of a standardized number of crypt cross sections (xx cells/10 crypt cross sections). How did the investigators assure that the height along the crypt-villus axis was similar and the amount of epithelium being investigated was similar. As an example, Figure 2 shows twice as many cryps cross sections in 2b as in 2a, something that would skew the results. Second, the authors might comment on how these findings might be explained in the context of the disease. For instance, Wang et al (NEJM 2006) described and cloned the NGN3 gene in patients with different infantile diarrheas, demonstrating that these diseases were a result of abnormal cellular differentiation due to mutations at the point of stem cell differentiation into the secretory subtypes. Alternatively, Fishbein et al (AJT 2008) found depletion of enteroendocrine cell precursors appeared to cause diarrhea among rejecting transplants of the ileum, and presumably due to depletion. Can the authors similarly propose how ther findings are consistent with an understanding of the pathophysiology of IBS?

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
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Title: Abnormal endocrine cells in the ileum of patients with irritable bowel syndrome
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] 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
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

The manuscript by El-Salhy et al. addresses the interesting areas of endocrine cells in ileum and irritable bowel syndrome (IBS). However, it is not clear why the authors did not investigate the endocrine cells in the colonic biopsies. Based on the data they have shown they cannot draw a conclusion on the relationship between the decrease in serotonin expressing cells and visceral hypersensitivity in IBS subtypes, and between the increased density of PYY cells and C-IBS. In Figure 2 crypts cross sections are more in 2b compared to 2a which may raise question on the results. In addition, serotonin synthesis in gut is regulated by two rate limiting enzyme. In endocrine cells tryptophan hydroxylase 1 (Tph1) regulates serotonin synthesis and in enteric neurons tryptophan hydroxylase 2 (Tph2) regulates serotonin synthesis. The authors only assessed endocrine cells. The serotonin production in enteric neurons might not be the same as in endocrine cells and that might influence visceral hypersensitivity. The authors could include discussion on this.