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8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00004011

Reviewer's country: Greece

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-03 17:35

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

Very interesting and well documented manuscript



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00035901

Reviewer's country: Japan

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-04 14:15

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 checked="" 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 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

The authors reviewed recent advances of proteomic biomarkers in diagnosing and managing IBD, especially in the clinical field. The present paper was well written and will give us important information. I have no claim in the present form.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00009530

Reviewer's country: Italy

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-05 23:48

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 type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" 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

The paper deals with a very interesting issue and is well documented and well written. Only minor comments, mostly related to table 1: there are no data on sensitivity and specificity of ANCA; the word "fecal" lacks both for lactoferrin and for calprotectin in the section "Marker of disease activity"; in the section "predicting course" I would add that pANCA may predict aggressive course and risk for pouchitis after surgery in UC and a "UC-like" behavior in CD. In the section "predicting relapse" I would cite the combined Brignola score (Brignola et al, Gastroenterology 1986). In Table 2 I would put Kanmura paper at the second position, similarly to what is in the text. In the discussion, it should be underscored that almost no spontaneous experimental model of IBD exist and that cell cultures as well are quite far from disease pathophysiology. Last: there are typographical errors here and there.



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http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 02520738

Reviewer's country: Italy

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-07 22:58

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 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

To: Professor Lian-Sheng Ma Editor board World Journal of Gastroenterology Title: "Current Application of Proteomics in Biomarker Discovery for Inflammatory Bowel Disease" Dear Editor, We have read through the manuscript and we think that the paper is good and well written as it stands.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00038879

Reviewer's country: United States

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-09 03:08

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 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

In this review Dr.Chan and colleagues examine the current status of IBD proteomics research especially as it relates to clinical applications such as diagnosis, disease activity, disease course and therapeutic response. The field of proteomics is rapidly growing. At least in theory, in the future it could potentially provide tools to improve IBD diagnosis and management. These are my comments: 1. By contrast with the authors' premise that "proteomics provides a powerful means of addressing major challenges in IBD today..." (page 2) the overall impression from their review is that: a. No conclusions of relevant clinical or scientific meaning can be drawn from current studies. b. By the authors' admission (page 19) most of these studies are small and not properly designed. c. Even supposing that the current findings in the field - highlighted by the authors - are confirmed by future studies none of these discoveries seem to be superior to current noninvasive markers, most notably stool markers. 2. In addition to deal with a field which currently has no clinical impact the reader is dealing here with a paper that is not well written and organized. a. The English is often incomprehensible. These are just some examples: 1. Abstract: "...improve diagnostic and

management...” 2. Core tips: “...disease biomarkers for numerous disease...” this mistake is not a typo since it is repeated many times (page 3: “...many disease...”) (page 9: “...biomarkers are present...and becomes...”) and many more 3. Page 6: description of MS (fifth line from top) comes out of the blue, without a premise. 4. Page 8: “...the application of proteomics...accumulating at the discovery phase...” This is totally unclear. 5. Page 9: “...biological fluid that is closer to the diseased tissue...” Closer than what? 6. Page 9 “..examining for protein variations...” what do you mean? 7. Page 10: “...governed by an scoring...” 8. Page 11: “...an area that has yet been addressed...” 9. Page 11: “...additional investigation into validity...” b. The abbreviations are an option in this manuscript – sometimes they are present most often they are not (see figure 2, figure 3 and all the tables) c. The paragraph on MS should be re-written in a more comprehensible way for the standard clinician (e.g.one wonders what is a “triple quadrupole”) d. Tables and figures: table 1 appears to be a summary of a summary (i.e. reference 10) whilst it really should list the individual references. Figure 1 should be labeled as “ideal or potential uses of biomarkers in IBD” not “application of biomarkers” – especially as it relates to pre-clinical screening. Figure 2 is entitled “Quantitative methods in proteomics” when it should really be labeled “quantitative (word misspelled in the artwork) MS”. Figure 3: Verification: “selected”; 2DE: abbreviation; “number of candidate markers” is this a proportion or an absolute number? It is unclear to the reader. e. The paragraph and the entire table 4 epitomizes the confusing presentation of this paper – we don’t discuss this... no,actually we do, in part...but only with the table... In my opinion either you discuss it properly or you eliminate paragraph and table. f. Perhaps even more importantly the authors fail to draw any attention on the findings they discuss – no reference at all to any mechanist aspect of these discoveries. The reader is essentially left with a dry list of studies and authors – and hardly any take home message.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology
ESPS manuscript NO: 22518
Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease
Reviewer's code: 02520845
Reviewer's country: Croatia
Science editor: Shui Qiu
Date sent for review: 2015-09-02 10:19
Date reviewed: 2015-09-10 21:07

Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various evaluation criteria like 'Grade A: Excellent', 'Priority publishing', 'Google Search', etc.

COMMENTS TO AUTHORS

Title: Current Application of Proteomics in Biomarker Discovery for Inflammatory Bowel Disease
This review provides an overview of current and possible proteomic biomarkers in the diagnosis and evaluation of therapeutic responses in the inflammatory bowel disease (IBD). The author methodically described the process of introducing biomarker candidates in pre-clinical and clinical management, described the mass spectrometry, and its application to IBD. Further, they described the current biomarkers in IBD management and gave a list of proteomics studies for discovering IBD diagnostic biomarkers and pathogenesis of IBD. Finally, they offer future guidelines for verification and validation of IBD proteomic biomarkers. The text is accompanied by appropriate tables. References are not completely written according to the WJGP guidelines (journal abbreviations instead of the full name of journal). In conclusion, this is a very interesting review which provides a view of the problem in screening and testing new proteomic biomarkers in the diagnosis and management of IBD.



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http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00009064

Reviewer's country: India

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-12 22:41

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 checked="" 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 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

Very comprehensive review and well written.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Pathophysiology

ESPS manuscript NO: 22518

Title: Current application of proteomics in biomarker discovery for inflammatory bowel disease

Reviewer's code: 00004594

Reviewer's country: France

Science editor: Shui Qiu

Date sent for review: 2015-09-02 10:19

Date reviewed: 2015-09-20 15:01

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 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 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

In this review, the authors examine the current state of IBD proteomics research, in particular relating to clinical applications such as the development of diagnostic markers. They also discuss the challenges of translating proteomic research into clinically relevant tools. This proteomic approach has many implications for a better understanding and management of IBD. This is an interesting and well written manuscript in an innovative field in the domain of IBD. I have some comments which need to be addressed: - Medical therapy of IBD is not so much different for Crohn's disease (CD) and ulcerative colitis (UC): if 5-ASA are essentially active in UC but not in CD, the rest of the treatment is the same for UC and CD; corticosteroids, immunosuppressants, anti-TNF and anti-integrins (Vedolizumab) have been validated for both diseases. - Monitoring of IBD is clinical, biological, morphological (ultrasonography, CT scan, MRI, endoscopy). Fecal calprotectin is a very useful tool that we currently use in practice (diagnosis, therapeutic follow-up, post-operative recurrence for CD...). Endoscopic procedures are important for the initial diagnosis but patient are more and more reluctant to endoscopies and noninvasive imaging such as ultrasonography and/or MRI are more



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and more used. CRP is not a good marker for UC and is normal in 20-30% of CD. Fecal calprotectin is more accurate for the colon than the small bowel. - If “proteomics could play a potentially significant role towards improving the clinical management of IBD” the tools that we have presently are very interesting and have improved the clinical diagnosis and management of IBD. - As stated by the authors IBD proteomics remains in its infancy and requires further investigations. The cost, availability, reproducibility... is also a matter of debate. At the time where the management of IBD is more and more personalized (e.g. treatment), IBD proteomics should be of interest.