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**ESPS Peer-review Report**
**Name of Journal:** World Journal of Gastroenterology
**ESPS Manuscript NO:** 8438
**Title:** Predictive proteomic biomarkers for colitis-associated cancer; where are we now?
**Reviewer code:** 00050427
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-12-28 18:37
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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 | [ ]Rejection |
| [ ] Grade D (Fair) | [ ] Grade D: rejected | BPG Search: | [ ] Minor revision |
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| | | [ ] No records | |

**COMMENTS TO AUTHORS**
Check for punctuation at places

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**ESPS Peer-review Report**
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| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
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| [Y] Grade C (Good) | [Y] 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**

This is a worthwhile review, although this field of proteomics in IBD is still in its infant stages and thus is there is not really much literature on which to base a review! Comments for authors to please address: 1. The review is difficult to read, as in many sentences throughout the manuscript there are errors in English grammar/ syntax which detract from the paper. A native English speaker or writing assistant will be needed to correct this issue prior to publication. 2. The introduction focuses on IBD and its molecular diagnosis, but the review, and therefore the introduction, should be more specific and directed to biomarkers for colitis-associated cancer, rather than IBD overall. A brief discussion of IBD in general in the first paragraph of the introduction should then be followed by a more focussed introduction of the topic of colitis-associated cancer and proteomics associated with this entity. 3. Equally, the next two sections under subheadings "Current status of biological markers in IBD" and "Classic serological or fecal marker in IBD" again are too broad and these biomarkers have been reviewed in detail (over and over!) elsewhere. These sections add nothing to the topic of proteomics or colitis-associated cancer either as introduction or providing perspective, and thus should be removed/ drastically shortened from this review article. 4. The sections under subheadings "Colitis-associated cancer; pathogenesis and biomarker for prediction" and "Molecular pathogenesis of CRC and CAC" are more appropriate as introductory paragraphs than the current introduction and thus should be incorporated in or replace the current introduction. 5. The section beginning on page 5 under subheading "Proteomic biomarker in IBD" could then be moved to more logically follow the above paragraphs as mentioned in point (4) above. Also, for a non-molecular biologist like myself, passing reference is made to the techniques of "Matrix-assisted laser desorption/ionization

time-of-flight (MALDI-TOF) mass spectrometry (MS) and "surface-enhanced laser desorption/ionization (SELDI)-TOF MS" but there is insufficient explanation of their application with reference to the topic of the review in simple to understand language for the clinician reader (like myself!). Why are these techniques worthy of mention in this field and how will they advance our understanding of molecular prediction of colitis-associated cancer in IBD? These questions should be addressed rather than the rather non-explanatory sentence in this paragraph [quote] "With these applications, analyses of serum or plasma by MALDI-TOF MS provide new information mainly about small proteins and peptides with high molar abundance suggests value for applications such as assessment of IBD, UC or CD, respectively, candidate for potential disease markers." 6. The paragraph with subheading "Label free quantification analysis to pull out potential biomarkers predicting CAC risks in 16 patients with IBD" somewhat appears out of the blue and there needs to be explanation of why this technique and how this study mentioned here relates to the preceding discussion and studies mentioned in the previous paragraph entitled "Proteomic biomarker for CAC in IBD". This will greatly improve the flow of the article here. 7. The Figures are nicely presented but I am confused by the apparent discrepancy between the sentence on page 10 "Applying label free quantification analysis to discover proteomic biomarkers in patients with different type and different stage of 16 IBD patients, comparative analysis was done in 8 patients with UC, 8 patients with CD, and 8 patients with irritable bowel syndrome (IBS)" versus the Figure 1 legend which suggests the analysis was done on "8 patients with UC, 8 patients with CD, and 8 patients with CAC." The latter makes more sense to me – which one is it? 8. Also, the proteomics analyses appear to have been done on the basis of the conferred risk of known clinical risk

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**ESPS Peer-review Report**
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| | | [ ] No records | |

**COMMENTS TO AUTHORS**

This is an interesting review with some new evidence. However, and since proteomics in IBD are not extensively studied it is questionable a review with such limited literature. In addition, there are several points requiring correction or clarification, in order the m/s will be suitable for publication, such as: 1. There are many errors in English grammar/ syntax. The authors should read carefully, word by word, all the text and correct. Moreover, most of the sentences are very long and difficult to read. 2. The introduction should be more focused on biomarkers. The sections "Colitis-associated cancer; pathogenesis and biomarker for prediction" and "Molecular pathogenesis of CRC and CAC" should be incorporated in the general introduction. 3. The application to the topic of specific chemical/biochemical techniques should be more explained. The reader of the journal is not interested to the possible biomarkers that could be recovered by applying such methodology, but what means the presence or absence of a putative biomarker. 4. The fig. 1 legend (8 patients with UC, 8 patients with CD, and 8 patients with CAC) differs with the text (8 patients with UC, 8 patients with CD, and 8 patients with irritable bowel syndrome). 5. It is not correct to describe proteoglycans as "filling" substances of the extracellular matrix. Most of the proteoglycan molecules participate in specific interactions, regulate growth factors' activity, or provide the milieu for cell spreading and proliferation, depending on their structure.

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| [ Y] Grade E (Poor) | | [ ] Existed | [ ] Major revision |
| | | [ ] No records | |

**COMMENTS TO AUTHORS**

With interest I have read the manuscript by Park et al, entitled: "Predictive proteomic biomarkers for colitis-associated cancer; where are we now?". It is a mix of a literature review and presentation of new own data. The manuscript is generally rather difficult to read as the level of English is poor in terms of grammar and sentence construction. Furthermore, the manuscript is at times unstructured and repetitive. The molecular subtyping of IBD is an interesting topic on its own and still a lot is unknown in this regard. Large proteomic studies in IBD are lacking and in this regard there is not a lot of data to review. The introduction is largely focused on IBD and novel molecular techniques. The title would suggest however more emphasis on colitis-associated cancer and predictive biomarkers. The proteomics techniques could be better explained. A figure illustrating the different techniques would help in this regard. A clinically diverse test cohort of only 24 patients seems largely insufficient to generate a robust predictive signature. A power calculation is lacking. No validation study was performed. Data remains therefore highly speculative. It is not explained why a proteomics based prediction signature would be superior to a DNA or (micro)RNA based signature. Figure 1 mentions 8 patients with CAC, the text mentions 8 patients with IBS. This should be clarified.