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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
Ms: 243
Title: Tumor budding as a potential histopathological biomarker in colorectal cancer: hype or hope?
Reviewer code: 00061675
Science editor: x.z.huang@wjgnet.com
Date sent for review: 2012-09-19 14:51
Date reviewed: 2012-09-25 04:53

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[Y] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[Y] No records	

COMMENTS

Major comments:
This is an epidemiological paper with statistical analysis. Thus the factors used in this research should be cleared.
1. The author should show the definition of pathological diagnosis such as SCG, SACG, MACG and MCG. The definition depends on what guidelines? (Sydney system? or …) It is unclear. Thus, it is very difficult to evaluate the results and compare with other epidemiological reports previously described in world-wide.
2. Regarding to Table.2; Table shows 71 isolates. But I calculated; a sum of total is 73 isolates. What data do I believe?
Furthermore, I do not understand the explanation of "*There is no pathologic data for 9 isolates" showed in the foot note. The author should separately summarize the data according to endoscopic diagnosis and pathological diagnosis. I confuse to understand the summarized data.
3. As you know, H. pylori has highly genetic diversity and the mixed infection is observed in same stomach. How many colonies did you check per patient? At least few colonies of H. pylori should be analyzed per patient (stomach) to clarify the genetic diversity and mixed infection.
Thus, I can not evaluate the results due to these ambiguous explanations and expressions.

Minor comments:
1. Number of patients participated in this study should be shown in "material and methods"

2. As risk factors, aging definitely influences the presence (onset) of diseases. Age match is necessary to analyze the statistical significance.
3. "Duedenitis" is not correct, maybe "Duodenitis"? in foot note of Table 2.

Specific comments;
Title and Introduction are OK.
Abstract is needed to be revised according the comments mentioned above.
Materials and Methods;
The authors should show the information of patients such as number, age (average) and sex.
Results, Tables and Discussion;
The authors should rewrite the contents under the comments mentioned above for the reader.
References;
The references are appropriate.

CLASSIFICATION OF THE MANUSCRIPT
Grade E

LANGUAGE EVALUATION
Grade B

Comments to authors
The paper focuses on finding the genetic diversity of H. pylori isolates from Iranian patients and the relationship between the genetic features and gastro-duodenal diseases as epidemiological research. I understand the strategy of research project and objective in this paper. These results are helpful to understand the geographical differences in terms of the prevalence of H. pylori genotype and its association with clinical manifestation of gastro-duodenal disorders. The manuscript is relative legibly written and this research has no ethical problem. However, there are some critical problems in the view of epidemiological research paper as below.

Major comments:
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1. The author should show the definition of pathological diagnosis such as SCG, SACG, MACG and MCG. The definition depends on what guidelines? (Sydney system? or …) It is unclear. Thus, it is very difficult to evaluate the results and compare with other epidemiological reports previously described in world-wide.
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[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
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COMMENTS

General comments:
The submitted entitled “Vast diversity of Helicobacter pylori genotypes in Iranian patients with different gastro duodenal disorders” reports It deals with the important question of association between certain H.pylori genotypes and specific pathologies, and with the problem of predictive value of H.pylori infection genotyping. Although the question of H.pylori genetic diversity in Iranian population was already addressed in at least two publications (Dabiri et al., 2010; Hosseini et al., 2012), in the submitted manuscript this issue is dissected in fine details and using quite extensive clinical material, thus providing novel and more reliable data. The research complies with the standard ethic regulations. The paper is rather well written, though with a lot of typing errors scattered around the text, but somewhat poor and cryptic in the graphic presentation of the results. Therefore, I would suggest that the authors make an effort at presenting the data on genotype diversity and association with pathology in a more careful and comprehensive way.
Specific comments:
Results section:
The authors managed to get 71 isolates from 177 biopsies. Neither in the Methods, nor in Results sections it is indicated, why the success rate was only 40%. Were other patients (60%) H.pylori-negative by other diagnostic tests? What was the rate of mixed infection (presence of several different genotypes of H.pylori in a single patient, which is quite typical for H.pylori)? Please provide explanation.

Discussion section:

1. For genotyping for vacA gene 4 markers were used – s1, s2, m1, m2. At the same time, in the Discussion section authors state, that intermediate (i-) region of vacA is an important determinant of H.pylori pathogenicity. Why did the authors deliberately skip genotyping for this marker? If they dispose of the data for vacAi-divesity in the same 71 isolates – it would be valuable to show them as well, in the Table 2, for instance.

2. In the Discussion section, the authors claim that the analysis of association of individual genes with clinical outcomes is more useful than combined genotypes. At the same time, major data analysis (Table 2, Fig.1 and 2) are based on analysis of combined genotypes. This leads to some kind of confusion. It would be helpful, if the authors could follow more strictly the approach they found more reliable – single or combined genotype – and to state it more distinctly in the Conclusion section.

3. As far as the work deals with geographic peculiarities of H.pylori genotype occurrence, it would be valuable if the authors provide accurate and detailed comparison of their results from Iranian population with the published data on Asian, European and American populations. It will put the work into the global framework of H.pylori genetic diversity research.

Tables and figures:

Generally, I would recommend the authors to make more specific headings and legends for the tables and figures.

1. Table 2 demonstrates association or OCCURENCE of genotypes in different pathological conditions. According to the legend, asterisk indicates "there is no data for 9 isolates", but labels only 4 isolates. It is not clear as well, for what kind of analysis P-value is indicated in the very right column, and why only for one raw. Please make the legend more comprehensive.

2. In my opinion, Figures 2 and 3 are worth being fused to one (Fig.2a,b) to be seen side by side. The use of 3D-columns seems to be needless. Being flat the diagrams will be easily read. Please label the axes, at least the Y- one.

3. Just from the point of readers view, it would be helpful to see the strongest pathology-associated genotype (cagA, vacAs1/m1, iceA2, babA2) to be highlighted in the Table 2 and Fig.2

Finally, there are typographical errors and spelling mistakes throughout the text which should be corrected.

Dear Ms. Ling Jiang,

thank you for your letter. It is a pleasure to see the manuscript well and accurately revised. In my opinion, it is now much easier to understand and to follow the message. I have no more questions or criticism, and would recommend to publish the paper after some final language and typesetting polishing in the manuscript.

Best regards,

Sincerely,
Alexander Klimovich

Alexander Klimovich, PhD.
Christian-Albrechts-Universität zu Kiel
Zoologisches Institut - Abt. Allgemeine Zoologie Am Botanischen Garten 1-9
24118 Kiel
Phone: ++49-431-8804174; Mob.: 01577-1827253; Fax: ++49-431-8804747
Email: aklimovich@zoologie.uni-kiel.de

2012/10/12 l.jiang <l.jiang@wjgnet.com>:
> Dear Dr. Klimovich,
>
> Thank you very much for your peer review to the manuscript Vast
> diversity of Helicobacter pylori genotypes in Iranian patients with
> different gastro duodenal disorders for World Journal of Gastroenterology on 9th September.
> The authors received your review comments and they have revised the
> manuscript according to it. Now their revised manuscript returned and
> we would very much appreciate you could agree to check it again which
> will help us to make further consideration or a conclusion to this
> manuscript. Thanks so much for your time and effort again.
>
> Please free to contact if you have any problem.
>
>
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