Reviewer's code: 03647279

Name of Journal: World Journal of Gastroenterology Manuscript Type: OBSERVATIONAL STUDY Circulating MicroRNAs as Biomarkers for Detection of severe acute pancreatitis (SAP) assiciated with acute lung injury (ALI): An observational study Notes to authors: The study entitled "Circulating MicroRNAs as Biomarkers for Detection of severe acute pancreatitis (SAP) assiciated with acute lung injury (ALI): An observational study" aims to identify circulating miRNAs as biological markers for prediction of SAP with ALI. Acute pancreatitis (AP) is globally wide phenomena with widespread complications and high mortality rate. Acute lung injury (ALI) is serious complication of AP, hence timely diagnosis and treatment are crucial. miRNAs are small noncoding RNA molecules with mostly regulatory roles and can serve as potential diagnostic markers for all different pathological processes. There are only several minor comments that are necessary to address: 1. Check abstract for abbreviations. At the first mention it is always necessary to write full word. 2. Reduce results section of abstract. 3. Please explain in the manuscript why patients gave only verbal informed consent. 4. It would be nice to put etiology of AP in these patients if possible. 5. Discussion part of manuscript is long. Manuscript would be improved if discussion part is reduced with focus on only couple of most important miRNAs and their role in other pathological processes. 6. It is necessary to completely check manuscript for grammar. Some sentences make no sense, in some parts is hard to understand what authors wanted to say. I recommend that manuscript is checked again before next submission. 7. Check references to include all the latest research. In conclusion, this observational study is novel, interesting and has potential clinical application and I recommend to accept it with minor changes.   Respectfully submitted, Ivan Zaja, MD

Response to reviewer 1:
1. Check abstract for abbreviations. At the first mention it is always necessary to write full word.
Response: According to the reviewer's comments, we checked abstract for abbreviations. All of abbreviations have written full word at the first mention.

2. Reduce results section of abstract.
Response: As suggested by reviewer, we reduce results section of abstract.

3. Please explain in the manuscript why patients gave only verbal informed consent.
Response: That may be due to poor English expression and writing. All of the patients gave written informed consent in the course of clinical study. So we changed "All of the patients signed the informed consent " in manuscript to "All of the patients gave written

informed consent" in patients section of Materials and Methods part in revised manuscript.

4. It would be nice to put etiology of AP in these patients if possible.
Respone: According to the reviewer's comments, we put etiology of SAP in table 1, and also gave statistical processing of the data.

5. Discussion part of manuscript is long. Manuscript would be improved if discussion part is reduced with focus on only couple of most important miRNAs and their role in other pathological processes.
Respone: As suggested by reviewer, we cut down the Discussion part of the manuscript from 1131 words to 997 words. In addition, we focused on some of significantly differentially expressed miRNA and their role in pathological processes in second and third paragraph of Discussion part in revised manuscript.

6. It is necessary to completely check manuscript for grammar. Some sentences make no sense, in some parts is hard to understand what authors wanted to say. I recommend that manuscript is checked again before next submission.
Respone: As suggested by reviewer, we check manuscript for grammar carefully. In addition, we have done the language modification through MedE Editing Group: http://meditorexpert.com and provided a language editing certificate, which verifed that the language of the revised manuscript has reached Grade A.

7. Check references to include all the latest research.
Respone: In accordance with the reviewers' comments, we added the four latest research in 2016 and 2017.

Reviewer's code: 03699916

General comments: 1, severe acute pancreatitis (SAP) associated with acute lung injury (ALI)is critical situation in the clinics, therefore it is important to find relevant biomarkers for Detecting SAP associated with ALI in the patients. In the   present study, authors demonstrated that 12 circulating MicroRNAs are associated with SAP patients with ALI. Compared with SAP patients without ALI, 5 MicroRNAs are up-regulated and 7 MicroRNAs are down-regulated in the SAP patients with ALI. Therefore, these 12 circulating MicroRNAs may be used as biomarkers for prediction of ALI in SAP patients. This manuscript is relevant for WJG. 2, However, the authors are not so clear to indicate the association about these 12 circulating MicroRNAs with ALI in SAP patients, that

may be due to poor English expression and writing. Authors have to improve the English writing for the manuscript. 3, Author in the manuscript should clearly indicate the hypotheses for the study. Furthermore, authors should avoid the repetitions between Methods section and Results section, and between Results section and Discussion section. 4, In the discussion authors reference a lot of literatures, however most of them are not so relevant with the present study. Authors should focus on the circulating MicroRNAs in relation to prediction of ALI in SAP patients. 5, Authors should explain in more detail for methods such as the quantitative real-time PCR and the online software TargetScan, MiRanda, and PicTar because a lot of readers in WJG may not know so well about them. 6, The discussion section is not so well written, please make major revision with citing relevant literatures.   Minor comments: 1, Normally the abbreviations, such as SAP and ALI should not be used in the abstract, they should spell out.   2, Please add a sentence to indicate the hypothesis for the study in last paragraph of Introduction. 3, In the result section of KEGG pathway enrichment analysis and miRNA-KEGG-network, some words such as "et al" are not correctly used. They should be replaced by "etc".   4, In the second line of first paragraph in the Discussion, "e.g." should be replaced by "such as". 5, please add error bar in Figure 2.

Response to reviewer 2:
General comments:
1, severe acute pancreatitis (SAP) associated with acute lung injury (ALI)is critical situation in the clinics, ...This manuscript is relevant for WJG.
Respone: no

2, However, the authors are not so clear to indicate the association about these 12 circulating MicroRNAs with ALI in SAP patients, that may be due to poor English expression and writing. Authors have to improve the English writing for the manuscript.
Respone: As suggested by reviewer, we introduced some new literatures for enhancing association about these 12 circulating MicroRNAs with ALI in SAP patients. In addition, we have done the language modification through MedE Editing Group: http://meditorexpert.com and provided a language editing certificate, which verifed that the language of the revised manuscript has reached Grade A.

3, Author in the manuscript should clearly indicate the hypotheses for the study. Furthermore, authors should avoid the repetitions between Methods section and Results section, and between Results section and Discussion section.
Respone:
Respone: In accordance with the reviewers' comments, we clearly indicate the

hypotheses for the study in third paragraph of Introduction part in revised manuscript.

4, In the discussion authors reference a lot of literatures, however most of them are not so relevant with the present study. Authors should focus on the circulating MicroRNAs in relation to prediction of ALI in SAP patients.

Respone: According to the reviewer's comments, we deleted some old literatures with little relevance with the present study, and added some new relevant research literature with the present study in revised manusript.

5. Authors should explain in more detail for methods such as the quantitative real-time PCR and the online software TargetScan, MiRanda, and PicTar because a lot of readers in WJG may not know so well about them.

Respone: According to the reviewer's comments, we made a very detailed description for methods such as the online software TargetScan, MiRanda, and PicTar etc in Materials and Methods and Discussion parts in revised manuscript. It enables readers to better understand them.

6, The discussion section is not so well written, please make major revision with citing relevant literatures.

Response: As suggested by reviewer, we made a lot of revision in all paragraphs in Discussion part, and cited many latest relevant literatures. In addition, we improved the English writing by MedE Editing Group.

Minor comments:

1, Normally the abbreviations, such as SAP and ALI should not be used in the abstract, they should spell out.

Response: According to the reviewer's comments, we checked abstract for abbreviations. All of abbreviations have written full word at the first mention in the Abstract.

2, Please add a sentence to indicate the hypothesis for the study in last paragraph of Introduction.

Response: we add a sentence to indicate the hypothesis"The present study was designed to test the hypotheses that circulating miRNAs are closely related to the incidence of SAP associated with ALI, and they may be involved in a variety of pathophysiological processes of ALI, and be used as a circulating marker to predict the disease" in last paragraph of Introduction.

3, In the result section of KEGG pathway enrichment analysis and miRNA-KEGG-network, some words such as "et al" are not correctly used. They should be replaced by "etc".

Response:In revised manuscript, we have deleted the "et al" in the result section of KEGG pathway enrichment analysis and miRNA-KEGG-network.

4, In the second line of first paragraph in the Discussion, "e.g." should be replaced by "such as".

Response:As suggested by reviewer, the "e.g" has replaced by "such as" in the first paragraph in the Discussion.

5, please add error bar in Figure 2.

Response:According to the reviewer's comments, we added error bar in Fiugre2.