Peer Review File
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Review comments-Reviewer A

Comment 1：1）First of all, because of the low specificity of the two biomarkers (0.629 and 0.629), IL-17 and sB7-DC, this is a failed study on the predictive accuracy of the two biomarkers. The current findings are not deserved to be reported as a predictive study. The authors should combine the two biomarkers to test their predictive accuracy to see whether the predictive value is satisfactory. Otherwise, the current study cannot answer the clinical question of predictive accuracy.

Reply 1：Thank you for your valuable comments. we are fully aware of the shortcomings of our research. Although the specificity of IL-17 and sB7-DC is 0.629, the sensitivity of sB7-DC is higher than that of IL-17. In addition, we will test the predictive accuracy of these two biomarkers in the clinical diagnosis of RMPP in the follow-up study to better describe the role of sB7-DC in the diagnosis of RMPP.

Comment 1：2）Second, the abstract needs some revisions because it is not adequate. The background did not describe the clinical importance of the correct diagnosis of RMPP and why soluble B7-DC is potentially accurate for the differential diagnosis between GMPP and RMPP. The methods did not describe the inclusion criteria and gold diagnosis of GMPP and RMPP. The results need to briefly describe the clinical characteristics of the study sample, and the predictive accuracy parameters such as AUC, sensitivity and specificity. The conclusion is overstated and need to be tone down and have comments for the clinical implications of the findings.

Reply 2：Thank you for your comments. We have revised the part of background description in the “abstract”. Because of “abstract” word limit, the inclusion criteria and gold diagnosis of GMPP and RMPP are described in the “method” part (page 5,line 138-153). In the results, the clinical characteristics of the study samples and prediction accuracy parameters such as AUC, sensitivity and specificity were supplemented. We also revised the conclusion.
Changes in the text: We have revised the part of background description in the “abstract” (page 2, line 35-39). The results are supplemented (page 2, line 52-54, 62-65). We revised the conclusion (page 2, line 66-68).

Comment 1：3）Third, the introduction of the main text needs to review what has been known about the factors and biomarkers associated with RMPP, the limitations and accuracy available predictive models for RMPP, and explain why B7-DC is potentially accurate for the differential diagnosis between GMPP and RMPP.

Reply 3：Thank you for your comments. We have supplemented the second paragraph of the introduction according to your comments (page 4, line 105-106, 108-112). The second paragraph of the introduction describes the factors related to RMPP and the known situation of biomarkers, as well as the limitations and accuracy of available prediction models for RMPP (page 4, line 106-

118). In the third paragraph of the introduction, we explained why we studied sB7-DC (page 4, line 119-128).

Changes in the text: We have supplemented the second paragraph of the introduction according to your comments (page 4, line 105-106, 108-112).

Comment 1：4）Fourth, in the methodology of the main text, please accurately describe the clinical research design, sample size estimation, and ethics approval for this study. In statistics, please describe the threshold values of AUC, sensitivity and specificity for a good predictive model. As I commented above, please consider to combine the two biomarkers to improve the predictive accuracy.

Reply 4：Thank you for your comments. In the first sentence of the first paragraph of the manuscript method, we describe the data collection time range, clinical sample size and data collection location of this retrospective experiment (page 4-5, line 133-136). In addition, we describe the data collection methods and research methods when conducting this study (page 5-6, line 136-169). In the second paragraph of the methodology section, we describe the ethical approval for conducting this study (page 5, line 153-156). In the statistical analysis, we modified the role of AUC threshold, sensitivity and specificity (page 6, line 189-191).

Changes in the text: In the statistical analysis, we modified the role of AUC threshold, sensitivity and specificity (page 6, line 189-191).

Review comments-Reviewer B

The manuscript is well-written, the experiments are described in sufficient detail and the figures and tables are clear. I think that the findings should be of particular interest to the audience of this journal.

Review comments-Reviewer C

1. Please unify the hospital name below.

159 This retrospective study comprised 20 normal individuals and 65 children who
160 were diagnosed with MPP during their hospitalization at the Children's Hospital of
161 Soochow University between January 2017 and December 2018. The study was
162 conducted at the Children's Hospital of Suzhou University. Before entering the study,

Reply 1: Thank you for your comments. We have revised it in the manuscript (page5, line 138).
Change in the text: The study was conducted at the Children's Hospital of Soochow University (page5, line 138).

2. Reference 7 and 11 are duplicate references in your Reference list. Please check and revise.

Reply 2: Thank you for your comments. We have made changes to the reference part of the

manuscript and the references in the manuscript.

3. Please check if any more references need to be added in the below 3 sentences since you mentioned "Studies", but only one reference was cited. If not, "studies" should be changed to "a study/a previous study".

138 chemokine 10 (CXCL10) /IP-10 may be potential biomarkers of RMPP (12-14). Studies
139 have shown that interleukin (IL)-17, interleukin (IL)-8, and tumor necrosis factor alpha
140 (TNF-α) cytokines in the bronchoalveolar lavage fluid of patients are increased, the
141 increase of IL-17, IL-8, and TNF-α is greater in RMPP patients than general
142 mycoplasma pneumoniae pneumonia (GMPP) patients, and an increase in the IL-17
143 level is associated with an increase in lung lesions (15). However, these cytokines still

312 25). Previous studies have shown that B7-DC, IFN-γ, and IL-13 are involved in
313 regulating the allergic asthma phase (26). Other studies have shown that B7-DC is
314 involved in the asthma response phase, and promotes the development of pathogenic
315 type II helper T cells and their migration and activation to the lungs (24). The

Reply3: Thank you for your comments. We have revised it in the manuscript (page 4, line 114; page9, line 282,284).

4. Table 1:
The data below are wrong. 16+19=30?

6 Table 1 Clinical and laboratory characteristics of the GMPP and RMPP patients

Variables	GMPP (n=30)	RMPP (n=35)	P value
Characteristics			
Male/female	16/19	14/16	0.939

Reply4: Thank you for your comments. We have revised it in the manuscript (page16, table 1).

5. Table 2:
The data below in your main text is inconsistent with your Table 2.

233 results showed that the level of sB7-DC was positively correlated with the IFN-γ and
234 IL-17 levels (Spearman r=0.386, P<0.05; Spearman r=0.441, respectively, P<0.0001,
235 Table 2).

476 **Table 2 Correlation analysis of the serum B7-DC level with IgG, IgM, CD3-CD19+,**

477 **CD19+CD23+, IFN-γ, and IL-17**

	IgG	IgM	CD3-CD19+	CD19+CD23+	IFN-γ	IL-17
Spearman r	0.152	0.184	–0.219	–0.116	0.363	0.441

Reply5: Thank you for your comments. We have revised it in the manuscript (page7, line 230).
Change in the text: Spearman r=0.363, P<0.05; Spearman r=0.441, respectively, P<0.0001, Table 2 (page7, line 230).

6. Figure 2:
Please indicate the meaning of **, ***, **** and ns in the legend.
Reply6: Thank you for your comments. We have revised it in the manuscript (page19, line 529-530).
Change in the text: **P<0.01, ***P<0.001, ****P<0.0001, ns means no significance (page19, line 529-530).

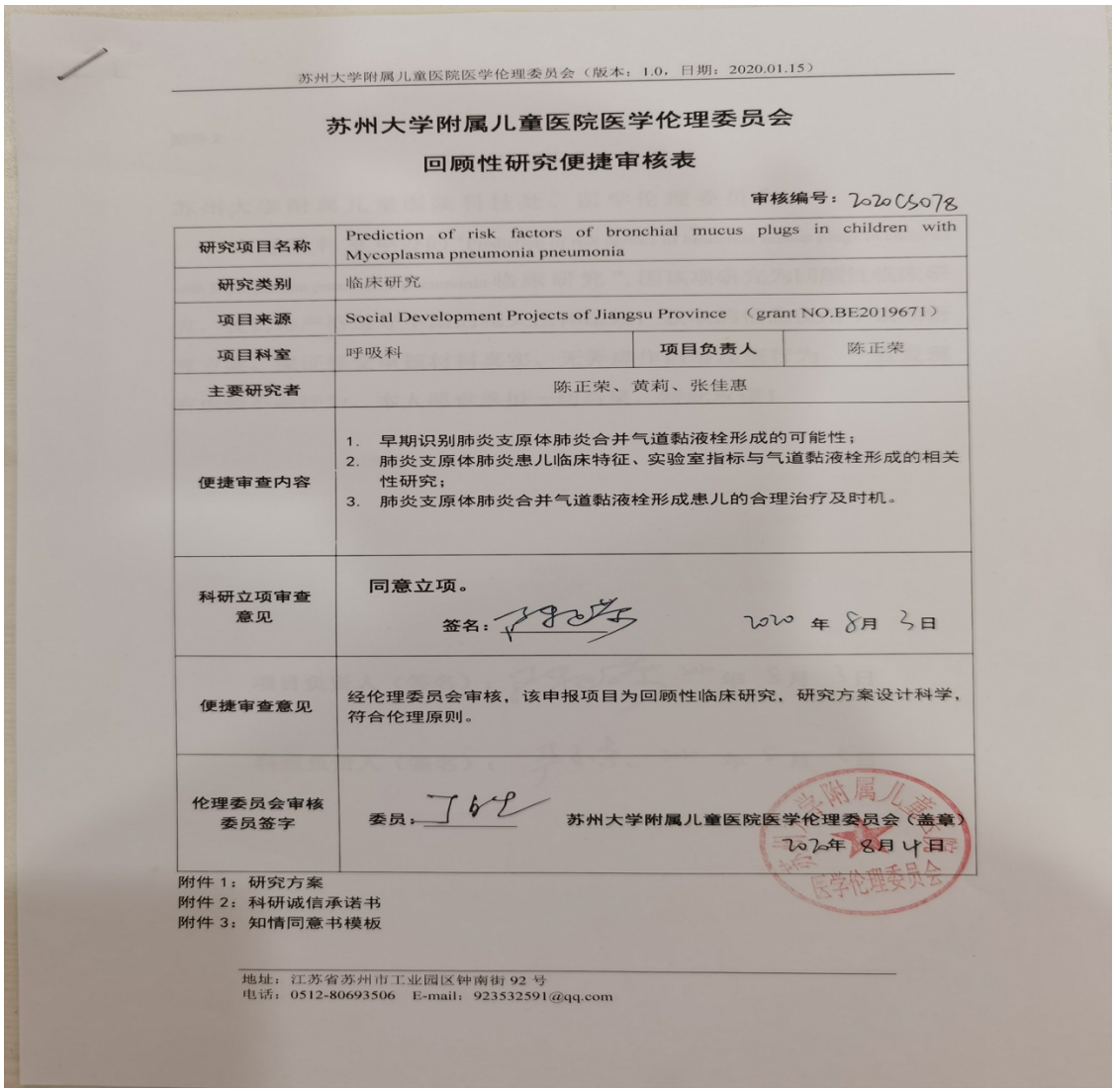
7. **Ethics**:
Your Ethical approval number 2020CS078 has appeared in other two published articles (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8161875/; https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-05765-w). Usually, one Ethical number can only be used in one study. Please explain and provide the certificate of ethical approval to us.

162 (5). The study was conducted in accordance with the Declaration of Helsinki (as revised
163 in 2013). This study protocol was approved by the Ethical Review Committee of the
164 Children's Hospital of Soochow University (reference number 2020CS078). Written
165 informed consent was obtained from the parents or their legal guardians prior to their
166 being included in the study.

Reply7: Regarding the ethical approval of this manuscript, I would like to explain: the ethical approval used in our manuscript is the ethical approval of "Social development projects of Jiangsu Province (approval number: no. BE2019671)". The research content of our manuscript is related to the research content of "Social Development Projects of Jiangsu Province (Approval number: no. BE2019671)", which is a subproject of this project, so we use the same ethics approval. If the same ethical approval cannot be used, we will apply for a new ethical approval from Children's Hospital of Soochow University, but the time may be a little long.

In addition, since this project has been completed, it was not included in the funding section.
If this project needs to be added to the funding section, please give us the chance to revise it.
If you need us to provide another new ethical approval, please give us a chance to revise the manuscript again, and we will apply for a new ethical approval. We have provided you with an

ethical accreditation certificate (see the picture). Thank you very much for your valuable comments on our manuscript.



苏州大学附属儿童医院医学伦理委员会（版本：1.0，日期：2020.01.15）

苏州大学附属儿童医院医学伦理委员会

回顾性研究便捷审核表

审核编号：2020CS078

研究项目名称	Prediction of risk factors of bronchial mucus plugs in children with Mycoplasma pneumonia pneumonia		
研究类别	临床研究		
项目来源	Social Development Projects of Jiangsu Province （grant NO.BE2019671）		
项目科室	呼吸科	项目负责人	陈正荣
主要研究者	陈正荣、黄莉、张佳惠		
便捷审查内容	1. 早期识别肺炎支原体肺炎合并气道黏液栓形成的可能性； 2. 肺炎支原体肺炎患儿临床特征、实验室指标与气道黏液栓形成的相关性研究； 3. 肺炎支原体肺炎合并气道黏液栓形成患儿的合理治疗及时机。		
科研立项审查意见	同意立项。 签名：　　2020 年 8月 3日		
便捷审查意见	经伦理委员会审核，该申报项目为回顾性临床研究，研究方案设计科学，符合伦理原则。		
伦理委员会审核委员签字	委员：　　苏州大学附属儿童医院医学伦理委员会（盖章） 2020年 8月 4日		

附件 1：研究方案
附件 2：科研诚信承诺书
附件 3：知情同意书模板

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