Response letter (*invited resubmission with minor revisions* ***jcm- 1083627)***

Dear Reviewers,

we would like to thank you for your valuable comments on our paper *"Soluble Pecam-1 as a Biomarker in Periprosthetic Joint Infection".*
With this blinded response letter, we would like to take the chance of resubmission for potential publication of our article in The Journal of Clinical Medicine.

We appreciate all of the reviewers' comments and are pleased to address all raised issues after the minor revision process with the attached detailed point-by-point response. With gratitude, we'd like to thank the reviewers for their specific comments which helped us to further improve our manuscript. All of the below mentioned comments, corresponding remarks and corrections were implemented in the revised manuscript.
The manuscript text has been edited accordingly and, as clearly stated in your submission guidelines, track-changes were used.

We confirm that all authors have read the revised manuscript and approved its resubmission. With this minor revision, we hope to meet the reviewer's expectations and would like to thank you once again for your time and effort regarding the substantial improvements of our manuscript.

Please do not hesitate to contact us if you have further questions.

Yours sincerely,



The Corresponding Author
On behalf of all authors

Point-by-point response to the comments of **Reviewer 2** on the manuscript *"Soluble Pecam-1 as a Biomarker in Periprosthetic Joint Infection"*

*(invited resubmission with minor revisions **jcm- 1083627**)*

Specific comments **Reviewer 2:**

1.) **Reviewer 2**:

First is the susceptibility of the new biomarker to storage time and temperature.

Second, there is a relatively low number of patients included and it should be extended prospectively for further conclusions.

Response: *Thank you for mentioning this point. As you clearly pointed out and according to the stated limitations, sPecam-1 is susceptible to storage time and temperature.*
In line with this issue, we suggest an immediate analysis after sample acquisition within 24 hours.

Addressing this very valid point of low patient numbers, we would like to pass on the information that we are currently investigating a larger group of patients, also in the "aseptic" group that showed slightly elevated quantities of sPecam-1, to analyze a potential predictive character of the molecule. We plan to further analyze the diagnostic potential in a prospective multicenter study. Currently, we work on the according study design.
At this stage though we felt that it was already of high value for the scientific community to reveal the potential of sPecam-1 in PJI diagnostics.

2.) **Reviewer 2**:

Additionally, there are some errors found in the manuscript, which should be corrected before publication; Several times in the text there is an error mentioned, because the reference source is not found. (line 84, 96, 120, 133, 149, , 159, 173, 296,) - please clarify that. Additional there are some mistakes in the text in the discussion section, which have to be corrected. (line 199, 210, 267)

Response: *Thank you for this valuable comment and the meticulous reading of our manuscript. Indeed, there was a mistake regarding reference 15, which was*

*accidentally implemented in the originally submitted manuscript. This work (Sah et al.) has no relevance within this manuscript and was therefore deleted. The above mentioned corrections have been made (Line 80, 81, 88, 89, 96, 100). The new editing slightly changed the line numbers. Therefore, we changed line 273-275 according to your suggestions ("*However, patient numbers are relatively low in this approach and need to be prospectively extended for further conclusions").

3.) **Reviewer 2**:

Furthermore I would recommend to add a recent paper to the introduction section, concerning the role of established inflammatory markers for diagnosing periprosthetic joint infections. (*Inferior performance of established and novel serum inflammatory markers in diagnosing periprosthetic joint infections. Sigmund IK, Holinka J, Staats K, Sevelda F, Lass R, Kubista B, Giurea A, Windhager R.Int Orthop. 2020 Nov 27. doi: 10.1007/s00264-020-04889-z. Online ahead of print.)*

Response: *Thank you for this interesting cause for thought. The authors agree that the above mentioned work clearly underlines the importance of local biomarker evaluation in PJI. The introduction was changed accordingly by implementing the respective publication (Line 43-44: "*Despite established evaluations of serum inflammatory markers, synovial fluid analysis can be seen as the diagnostic mainstay").

4.) **Reviewer 2**:

Due to the originality and novelty of this study and the importance of this paper for the scientific community, I would recommend this paper for publication after considering the minor revisions mentioned above.

Response: *Overall, we are delighted to meet the reviewer's expectations and thank you for your suggestions which helped us to improve the manuscript. The stated minor revisions have been made.*