

## Comments to Authors

**03976790**

**Conclusion:** Minor revision

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade A (Priority publishing)

Comments on the manuscript entitled “Elevated Levels of IL-1 $\beta$ , IL-6, TNF- $\alpha$  and VEGF in Patients with Knee Articular Cartilage Injury” The study presented in this manuscript is to explore the expression profiles of IL-1 $\beta$ , IL-6, TNF- $\alpha$  and VEGF in cases of knee cartilage injury. The purpose is to evaluate their significance in this disease, and to use them such as biomarkers of the disease. The study has been correctly done; nevertheless, the manuscript needs any improvements.

Patients and methods: - Patients The total number of patients is given, but it would be useful to know the number of males and females. What were the parameters of blood centrifugation? Number of g? Duration?

**Response:** The number of males (n=26) and females (n=29) has been provided as well as the centrifugation speed (x 2000 g) and time (for 20 min) in the revised manuscript.

- Immunohistochemical staining The technique is described but several specificities lack. - After blocking: what is blocked? The endogenous peroxidases? - What is the method used? Reading the text, it seems to be an indirect immunohistochemical staining with a secondary antibody labeled with enzyme, probably peroxidase for DAB is used such as a chromogen. But this method must be specified: how the secondary antibodies are labeled? With peroxidase? With avidin-biotin complex? How is obtained the staining? - what are the origins of primary and secondary antibodies? - what is the mounting medium used for stained sections?

**Response:** More details have been added into the immunohistochemical staining method including the issues mentioned by the reviewer.

Results It would be useful to add a figure with micrographs of at least a single marker (chosen by the authors) with the different aspects in different grades.

**Response:** We thank the reviewer for this comment and agree with the reviewer that it would be more useful to provide a figure with micrographs. Unfortunately, the compute system has been updated several weeks ago and the data are lost.

Figure 5: In the legend, indicate what is A and B.

**Response:** This has been indicated.

**01299180**

**Conclusion:** Minor revision

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

This is a nice piece of research: very well-written and the data are well-organized. Fig. 3. It is hard to imagine that the differences of IL-6 as shown in Fig.3 are actually significant.

**Response:** We thank the reviewer for this comment. Even if there was a small difference of IL-6 among different groups, the difference was significant.