

Dear Editor-in-chief Prof. Dr. Ma

We are very pleased, that our Review article entitled : “The complex interactomes and post-translational modifications of the regulatory proteins HABP4 and SERBP1 suggest pleiotropic cellular functions”, by Carolina Colleti, Talita D. Melo-Hanchuk, Flávia M. da Silva, Ângela Saito and Jörg Kobarg is acceptable for publication after thorough revision.

We submit herewith a carefully revised version in which we addressed all points raised by all three reviewers and by the editor, regarding the format and style, too.

Please, see below a point by point reply to all raised issues:

Reviewer # 02932624 raised the following two points:

1. The description of phosphorylation modification is relative less when compared to other PTM.

Answer: We don not agree. The three different parts on phosphorylation, methylation and sumoylation are roughly of the same size. Also there is not so much known on the functional consequences of phosphorylation, limiting thereby the size of this section.

2. The resolution of the figures, especially figs 3 and 4, is too low.

Answer: We agree. We increased the resolution of all figures.

Reviewer # 02447901 , had three concerns:

1. Figure 2 should include information on the functional consequences of the shown post-translational modifications.

Answer: We do not agree with this. The main function of figure 2 is to show the distribution of the potential Post-translational modification sites in the both proteins sequences and their high degree of conservation. In figure 3 we elaborate in great detail the effect of phosphorylation and methylation on the subcellular distribution of the proteins. Additionally a straight connection between individual modified residues as shown in fig 2 and functional differences as shown in fig 3 cannot be made because the latter depends on the overall phosphorylation level of the proteins and not on specific residues , in most cases. Thereby a junction of both figures would be misleading.

2. The potential biological consequences of interactions of the protein in their respective protein networks should be provided.

Answer: We discuss throughout the review the potential functional roles as deduced from the protein interaction network, citing all relevant literature. Examples: pages 9 to 12. We also provided the figure 4 which groups the most relevant interactors in regard to the domain of interaction and whether the interaction partner is specific or common to HABP4 / SERBP1.

3. The prognostic roles of the proteins should be mentioned.

Answer: Unfortunately, there are virtually no comprehensive data available yet which we could incorporate in a beneficial fashion. Work from our group is ongoing and will hopefully be published in the near future.

Reviewer # 0347635 had two additional points of criticism:

1. The scale bar and arrows for Ki-1 staining may be added in figure 5.

*Answer: We added a white scale bar, which represents 1 micro meter. In the high resolution figure provided now the labeling of the gold atom labeled Ki-1 antibody can be seen as individual black dots.*

2. Some references seem to have not been cited.

*Answer: We checked this carefully and found only one citation in format of author name [Saito et al]] that was now corrected to the number format e.g. [13]*

We trust that we addressed all raised issues appropriately and that our manuscript is now much improved.

We look forward to hear from you.

Best wishes,

Jörg Kobarg