Dear Editor Prof. Dr. Fang-Fang Ji,

We are pleased that you are interested in our review manuscript entitled "**Fasciculation and elongation zeta proteins 1 and 2: From structural flexibility to functional diversity**" , by M.B. Teixeira, M.R. Alborghetti and J. Kobarg , and that you consider it ś publication, pending revision.

Please see below our answers to the minor suggestions raised by the 2 reviewers.

Point-by-point reply:

1. Reviewer # 03865268, wrote:

"The manuscript should have prepared according to author guidelines. The authors should be said "Authors in year" e.g. Bloom & Horvitz in 1997. Otherwise, remove year."

Answer: We changed this and other citations in the text so that the adhere to the author guidelines.

2. Reviewer # 00183460, basically raised the following three points:

I) The part of the article regarding the molecular structure and expression profile of the discussed proteins is it is written clearly and in interesting way, but in my opinion would much benefit from more schematics.

Answer: We agree with the reviewer here. We elaborated three additional figures. One (the new figure 2) on the esquematic structure and domain organization an the relation of the latter with the interacting proteins and where in FEZ they are docking, whenever this is Known. The second new figure presents a model/hypothesis for the formation of the FEZ/kinesin complex and how it "walks " on the microtubule (new figure 5). The third figure is the new figure 6, which represents a new model for the possible nuclear function of FEZ1 in cooperation with nuclear receptors. All figures and tables have been edited to explain abbreviations and original editable files have been attached. With these new and additional figures the review became more attractive.

II) In the following chapters of the article the authors clearly focused on the participation of FEZ proteins and their analogues in neurodegeneration and viral infection, especially HIV-1. And again, in my opinion, some of the described mechanisms could be presented in a graphic form. In addition, the disproportion between part concerning neurodegeneration and HIV-1 infection it is striking.

Answer: We do not agree with this comment. The fact that the virus related section is larger than that of the neurodegeneration simply resulted from the fact that the literature of the former is much more extensive and brought important mechanistic insights in FEZ proteins molecular functions. Also the major player in the case of neurological degenerative disorders are other proteins , such as the FEZ interactor DISC1, and the role of FEZ proteins is not yet well understood. We did not change the section therefore.

III) The authors did not take into account the potential role of the discussed proteins in the process of **tumorogenesis**, **especially in the nervous system**. In my opinion, it is rather a mini-review, which can be successfully expanded including role of FEZ and its analogues in cancerogenesis.

Answer: This is a very important suggestion, although it is probably based on a misunderstanding. Let us explain: There is another transcription factor /protein called nowadays: LZTS1 (**L**eucine **z**ipper putative **T**umor **S**uppressor **1**), whose past synonym was FEZ1 (which stood for: "**F**37

/**E**sophageal cancer-related gene-coding leucine **Z**ipper motif **1**"). This protein is frequently confused with the FEZ1 of this review article, and it is a transcription factor of 596 amino acids length, involved in several tumors, especially brain tumors. Probably the reviewer also knows this protein and thought that both proteins are the same, although they are neither functionally nor sequencially related. This raised the very important point that we need to introduce a small section in our review to clarify that we are only talking on the proteins of the FEZ1/2 family (also called Zygins, FEZ for Fasciculation and elongation zeta/zygin; FEZ1: Acession number: Q99689 (392 aa length), FEZ2: Q9UHY8; UNC-76: Q7JL62 – C. elegans), and not about the FEZ1/FZTS1 (Q9Y250, 596 amino acids length). We now included a new section at the end of the discussion to explain these facts.

Although there is a truly vast literature on LZTS1 (/"FEZ1") and its involvement in cancer and brain tumors, on the other hand there is almost nothing known about the role of "our" FEZ1/2 in tumorigenesis. Therefore our review is quite complete and nothing in relation to cancer is missing .
We than the reviewer to bringing up this point , which was probably based on the false impression of the synonym that Fez1/LZTS1 are of the same protein family as FEZ1/2 , described here. But this is not the case, it ś just a coincidence.

In summary we addressed all point raised by the editor and the two reviewers and present you here a much improved review manuscript. We hope you agree to its acceptability in the WJBC.

Thank you
Best wishes

Prof. Jörg Kobarg –

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