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Reviewer Assessment of the dissertation of **PharmDr. Jana Uhlířová**

The role of Nucleoporin TPR in cell functioning and differentiation.

The dissertation covers Mgr Uhlířová's research on TPR nucleoporin protein. It is based on 3 published papers in peer-reviewed international journals and one manuscript in preparation. In three of them is Mgr. Uhlířová co-author and in one of the published papers is PharmDr. Uhlířová first author.

The dissertation has 3 main aims, each of which has been fully addressed.

The first aim focuses on the nuclear distribution of TPR and its structure and function in nucleoplasm, which have been mainly covered by publications in the Journal of Cell Science and in Cellular and Molecular Life Science and in the manuscript in preparation, with PharmDr. Uhlířová as a co-author. Both published publications provide high-quality research and novel methods for image analysis of immunofluorescence staining in respect to the nuclear periphery and to measure and count TPR filaments in the nucleoplasm. One of the conclusions from this part of the work is that TPR may contribute to the formation of nucleoskeleton, which is supported mainly by the structural analysis of TPR in the nucleoplasm. *Could you comment on which experiments should be done in the future to confirm and decipher its function within the nucleoskeleton?*

The second aim focuses on the epigenetic landscape associated with the TPR-defined heterochromatin exclusion zones and on the mechanism of regulation of gene expression by TPR. The research presented in the dissertation clearly shows that TPR associates among others with genes linked to myogenic differentiation and muscle cell functioning. *Has this kind of analysis been done in other cell lines such as HeLa cells, used in some of the co-authored publications? Do you expect that TPR could regulate another specific set of genes in other cell type(s)?*

The third aim "Is TPR involved in the myogenesis? How?" has been addressed in a recent paper in Cells, where Mgr Uhlířová the first author. In the discussion is mentioned that the role of TPR in myogenesis *in vivo* is needed to clarify the significance of its effect. *Could you suggest some future experiment that could allow elucidation of TPR function in myogenesis in vivo?*

The dissertation is well and clearly written. The introduction thoroughly covers current knowledge about nucleopores and their component TPR. Within the dissertation the author uses adequate references,

however the number of figures accompanying the text in the introduction should be higher to make the text easier to comprehend. The dissertation contains some grammatical or other errors, especially in the introduction part. The presented research data are of high quality. Some confirm already published results - these are used as a positive control to confirm reliability of the methods used to generate novel data. The new data and the new methods generated within this work are a valuable contribution to the basic research within the field of myogenesis, nucleopores and-or chromatin structure. The experiments are done and repeated thoroughly with proper statistical analysis.

In conclusion, the work proves the ability of PharmDr. Jana Uhlířová to carry out an independent and creative scientific work, fulfills the requirements for a dissertation in the given field and allows awarding the Ph.D. title after the name. I strongly recommend the dissertation for defense.

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