Reviewer report

On doctoral dissertation entitled
„Physiological and Pharmacological Perspectives of Monoamine Regulation in the Fetoplacental Unit.“

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Reviewer: Professor Stanislav Mičuda, MD., PhD., Charles University, Faculty of Medicine in Hradec Králové, Department of Pharmacology

This is a high-quality dissertation that meets all scientific and formal requirements.
The assessed dissertation contains all the necessary elements and is submitted in the form of an annotated set of four original papers, in accordance with the rules of the Faculty of Pharmacy of Charles University in Hradec Králové. The work contains a brief introduction (three pages), a theoretical background (15 pages), the goals of the work divided into three categories, methods (5 pages), comments on individual publications (10 pages), summary (4 pages), a list of other outputs of the candidate including the declaration of foreign six-month scientific internship and awards, a list of used literature (contains 268 cited works, mostly very recent), and enclosed scientific papers of the author. The information presented is logically linked.

Regarding scientific results, the dissertation is divided into two closely related areas. The first is an analysis of the presence of the main transporters and enzymes for biogenic amines turnover in the placenta using different advanced models, starting from cell models such as Bewo and JEG-3 cells through the isolated human trophoblast model to the human or rat placenta at various stages of pregnancy. The second part of the results consists of works focused on the evaluation of the influence of antidepressants and the antidiabetic drug metformin on the transport of biogenic amines in the placenta. Again, the involvement of a set of suitable models and a sophisticated experimental design can be appreciated here. This approach led to obtaining essential data for understanding the mechanisms of biogenic amine turnover in the placenta and their changes during pregnancy. It also identified the risks associated with the inhibitory effect of antidepressants and metformin on OCT3 transporters during pregnancy. At the same time, it was also important to identify differences in the results of the models used - for example, in changes in the expression of the OCT3 transporter between placenta and BeWo cells. Consequently, in summary, the author demonstrated the ability to relate her work's implications to basic research and potential clinical applications in maternal-fetal medicine.

The author's publication activity meets the criteria for the defense of the dissertation.

- The applicant is the first author of three original papers (2x Q1 and 1x Q2 according to Article Influence Score) and is the co-author of another four original papers in highly impacted journals. According to Scopus, these works have already found 41 citation responses with an h-index of 3. This is undoubtedly a highly superior publishing performance.

Comments and questions:

- Is it currently known how the expression of transporters for biogenic amines in the placenta is regulated, and what is behind the changes in expression during pregnancy?
- Were there any changes in these transporters described because of gestational diabetes itself?

Conclusion:
The submitted dissertation meets all the formal and scientific requirements for a qualification file of this category. The author participated in creating seven original scientific papers published in journals with a high impact factor, including three first-author publications, which more than fulfills the requirements for the defense of a dissertation at the Faculty of Pharmacy of Charles University in Hradec Králové. M.Sc. Veronika Váchalová has thus demonstrated the ability to carry out high-quality research with outstanding scientific rigor and advanced presentation and writing skills.

Based on the excellent quality of the dissertation, I recommend it for defense and, after its successful completion, the award of the Ph.D. title to MSc. Veronika Váchalová.

Hradec Králové, October 13th, 2024

Professor Stanislav Mičuda, MD., PhD.