

Opponent's report of the doctoral thesis:

Mgr. Hana Tykalová: „Interaction of tick-borne encephalitis virus with host and vector cells.”

The doctoral thesis of Mgr. Hana Tykalová is written in a “cumulative way” and is based on five scientific articles. All of them are published in recognized international journals while at least two of them are in high-ranking journals with impact factors higher than 7 and 9. Mgr. Tykalová served as a shared first author only in one of them what might seem as a bit underwhelming. On the other hand, I see it as a downside of contribution to important, influential studies involving international partners. Moreover, her important contribution is clearly documented by respectably high authors' contribution percentage values which were confirmed by the key co-authors of the studies. I also greatly appreciate student's dedication to the scientific work as she clearly had to overcome major obstacles such as long maternity leave followed by the COVID-19 pandemic.

The thesis is focused on various aspects of tick-borne encephalitis interaction with host and vector cells what is highly relevant and important topic. The quality of the research needs no review as it was thoroughly reviewed in peer-reviewed journals. It is a respectable collection of high-quality papers focused on tick-borne encephalitis infection on the cellular level, with the special emphasis on the immune response elicited by the host cell and virus immune evasion strategies. The thesis covers considerable range of knowledge associated with a broad spectrum of applied highly advanced molecular biology methods combined with classical virology and corresponding soft skills. Obviously, the student had to learn all aspects of scientific work and there is no doubt that she is capable of independent, high-quality research in her scientific future.

Because of the cumulative character, the thesis is written in a concise and easy-to-read style. The first part, consisting of the first 33 pages, contains introduction which is well-written and due to its depth also very useful for the reader. My only criticism here would be that just for the graphical stylistic reasons, the capitalized titles were difficult to follow if they contained shortcuts such as SFRNA instead of sfRNA. Aims of the study are clearly formulated. The actual results of the thesis are then presented in the form of the particular manuscripts as they were published. They are then followed by the Summary and future perspectives chapter which on six pages provides a concise summary but also author's own perspective on her work. Altogether, the thesis consists of 167 pages divided into 8 main

chapters. The thesis is written in English. Even though it is obvious that it is not author's mother-language, the readability is very good.

I have few questions for the student which should stimulate the discussion and do not in any way doubt or criticize the obtained data or conclusions.

- Two of the presented papers (manuscripts 2 and 4) are based on comparative transcriptomic analyses. You present those data as a starting point or a baseline for future studies. What were the highlights from the transcriptome analyses which you would like to follow in your scientific future.
- The major finding of the manuscript 3 that TBEV specifically reduces POLR1 rRNA transcripts is highly valuable. Do you have any hypothesis about the mechanism of this phenomenon?
- In the manuscript 3, you observed a series of mutations generated during long-term virus adaptation to specific cell lines. In the discussion chapter, you critically discussed which of them are most likely biologically relevant. How could the biological relevance of the particular mutations be evaluated and do you intend to continue this research direction.

In conclusion, the thesis fulfills all requirements for a PhD thesis. I fully recommend the thesis for the defense and, after the successful defense, to award Mgr. Hana Tykalová the academic degree of "Philosophiae doctor" ("PhD.").

Bratislava, 14. 10. 2022



RNDr. Boris Klempa, DrSc.