

October 14, 2022

To
Assoc. Prof. Eva Novakova
Program director of PhD studies in Parasitology

Dear Prof. Novakova:

I herewith summarize my evaluation of Mgr. Hana Tykalova's PhD thesis.

SUMMARY:

Tick borne encephalitis virus (TBEV) is a medically important virus of global health concern. The primary research theme described in the PhD thesis focuses on characterizing mammalian and tick cell responses to TBEV infection. Multiple molecular and bioinformatic analyses, including proteomics and transcriptomics are utilized/described to investigate responses to TBEV infection in human neurons, astrocytes, and tick cells. The data provided in this thesis document have been published in peer-reviewed journals. The candidate provides a bird's eye view introduction to TBE virus biology, epidemiology, and innate immunity. This is followed by describing the overall objective of the thesis and list of publications. The final thesis chapter summarizes the findings described in the manuscript. Though there are minor editorial mistakes, the thesis is well written for clarity. I do not have any major concerns with the data, as they have all been peer-reviewed and published. I only have some minor concerns or comments to the candidate.

GENERAL QUESTIONS TO THE CANDIDATE:

1. Though tick cell lines offer convenience to generate TBEV infected cells and downstream investigations, would it not be ideal [natural infection model] to infect *Ixodes ricinus* ticks to investigate vector response to TBEV infection? This is particularly important when investigating adaptations of viruses in different host environments and the existence of Quasispecies. Would your results be different if you had conducted this study with natural tick vector species?
2. Langat virus, a tick-borne flavivirus, is an attenuated virus, and not known to cause any productive infection in mammals. How could you correlate/extrapolate the results obtained from Langat virus to a highly virulent and lethal virus such as TBEV.
3. Central European/Western European strains of TBEV are used in the studies described in the thesis. However, it is well known that the far-Eastern and Siberian subtypes of TBEV are more virulent and neuroinvasive than the Central European/Western European subtypes. It would have been ideal to incorporate these subtypes in this study and compare the mammalian and tick responses. At the least, this could have been discussed in the summary/future directions section.

Suggestions to add to the thesis:

4. Introduction chapters: The introductory chapters are rather brief and does not provide in-depth description. It would be good to have detailed and in-depth description.
5. Final chapter: What are the final conclusions, and how could this study's findings lead to countermeasure development?
6. Final chapter: What are the future directions for the studies described in the thesis?

RECOMMENDATION:

I recommend the dissertation of Mrs. Hana Tykalová to be awarded the academic title 'Doctor' in short Ph.D based on its defense.

Sincerely,



Saravanan Thangamani