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Annex No. 11 to the MU Directive on Habilitation Procedures and Professor Appointment Procedures

HABILITATION THESIS REVIEWER'S REPORT

Masaryk University	
Faculty	Faculty of Science MUNI
Procedure field	Animal Physiology
Applicant	RNDr. Alena Hyrslova Vaculova, Ph.D.
Applicant's home unit, institution	Faculty of Science MUNI
Habilitation thesis	Novel molecular mechanisms of cancer cell death regulation
Reviewer	Prof. Boris Turk, PhD, PhD
Reviewer's home unit, institution	Department of Biochemistry and Molecular and Structural Biology, Jozef Stefan Institute, Jamova 39, Ljubljana, Slovenia…

The Thesis of Dr. Alena Hryslova Vaculova is nicely written, but I feel that it could have been improved. The first suggestion is that it could have been written in a more balanced way. While the TRAIL-related part is very elaborated, the initial Introduction on the mechanisms of apoptosis induction and its role in cancer is too basic for this level. I also miss some introduction to other cell death modalities to set up the ground for the whole thesis. In addition, molecular mechanisms are known to be a bit more complex now, so I would add the other molecules involved and the extra roles of some of the molecules involved. Similarly, since the Thesis is playing around anticancer therapies based on apoptosis-involved proteins, I would expect the candidate to elaborate more on the current status of apoptosis-related therapies, where currently the only one, which was shown to work, is the anti-Bcl-2 therapy in certain leukemias, and of the reasons for the relatively low success.
The TRAIL part is very elaborate, but could perhaps be more condensed and I am again missing the part on its translation into clinics and an analysis of the current status of the field. In addition, the potential of the combination therapies, which was investigated in the thesis, could have been improved with describing more rationale for particular combination and potential risks.
Looking through the performance of the candidate, I can say that she has clearly demonstrated that she is capable of independent research and leadership. For the Thesis, she included 19 papers, which were published in very solid journals, and she is a corresponding author of 6 of them and the first author of another 5. I have totally found in the Pubmed 41 papers by the author (last one published in 2017) that were totally cited almost 1000 times in Web of Science, which is an excellent achievement for this stage of career. She is very active in teaching students for a number of years. In addition, she has been also successfully supervising several PhD students (4 concluded, 1 still ongoing), demonstrating excellent pedagogical skills. I have seen only 1 grant listed in the system, which is maybe not everything, but could perhaps be improved in future. In conclusion, with such performance, she would clearly fulfil all the requirements for the Associate Prof. position at my University (University of Ljubljana).

Reviewer's questions for the habilitation thesis defence

1. I would like the candidate to further elaborate why have TRAIL-based therapies failed in clinical trials for cancer therapy and how would the combination therapies proposed by the candidate overcome the hurdles?
2. It seems that most in not all of the results were obtained in cellular models. So how would they translate into *in vivo* models? Which animal cancer models would be the best to evaluate the findings obtained in cellular studies taking into account the roles of TRAIL in immune system? What would be pros and cons for using syngeneic mouse models vs. xenograft mouse models?
3. What are the scientific and research career plans of the candidate? Would she continue with the current studies or would she also look into other directions? What does she think about further translational efforts and what should have been done to go in this direction?

Conclusion

The habilitation thesis entitled Novel molecular mechanisms of cancer cell death regulation by RNDr. Alena Hyrslova Vaculova, Ph.D. **fulfils** requirements expected of a habilitation thesis in the field of Animal Physiology.

Date: October 1, 2019 Signature: