

Review of PhD thesis by Mikołaj Kocikowski titled: "Of dogs and men. Tracing immune checkpoint signatures across cancers and unleashing the potential of canine PD-1 antibodies".

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Review: This is a very interesting thesis, and clearly meets the requirements for a doctoral dissertation.

My review of this thesis is organized around the three criteria outlined in Art. 190 par. 3 of the Act of July 20, 2018.

1) An assessment along with an explanation whether the doctoral dissertation presents general theoretical knowledge of the person applying for granting a doctoral degree in a specific discipline or disciplines.

The thesis demonstrates that Mikołaj has an excellent knowledge base related to cancer, immunotherapy, immune checkpoints, and immune checkpoint inhibitor therapy. I appreciate how he started at a broad high-level view of the field and then narrowed down to details most relevant to his work. Mikołaj also demonstrated the ability to distill complex information into a practical working knowledge of the field, and the ability to direct his research towards clinically-important questions. One example of this is the three objectives he considered most important for one area of his thesis: assessing the abundance of immune checkpoints (IC) across the canine cancer types, comparing those IC profiles with those found in human cancers, and when possible analyzing the IC patterns of human cancer subtypes and individual patients. The inclusion of the canine-human comparisons was important as information learned from one species will allow investigators to uncover previously unknown information in the other species. The similarities and differences across species are both important in advancing the scientific understanding of cancer and how to control or eradicate it.

It is readily apparent that Mikołaj directed his work at establishing an essential foundation that can be further built upon in the future. His approach was broad, and that was the appropriate strategy for the state of the field, and the best approach to define the IC landscape across cancer types. I appreciate Mikołaj's comments about his work making it possible to delve more into more specific patient populations in the future. These could include segregating gliomas into astrocytoma or oligodendrogliomas and into those with different grades (high or low), as well as segregating prostatic carcinoma into urothelial carcinoma or adenocarcinoma as better markers for these become available. Similarly, different types of sequencing data and aligning sequencing data with immune cell identity specifically in the dog is an evolving field. Importantly, Mikołaj's thesis provides a firm foundation to build on in the future. Without this foundation, the field cannot advance.

2) An assessment along with an explanation whether the doctoral dissertation demonstrates the ability for independently conducting scientific or artistic work by the person applying for granting a doctoral degree.

The thesis demonstrates that Mikołaj has the ability to independently conduct scientific work. It is readily apparent that Mikołaj is aware of research challenges in the field, that he considered multiple approaches, and that he proposed logical solutions.

Some of the gaps he identified in the field that he worked to address were:

- The landscape of immune checkpoints (ICs) in canine cancers and its relation to human cancer
- Antibodies targeting canine PD-1
- Canine cancer ICB therapeutics

For the first gap, it is impressive that he assembled data from >400 canine cases to work with and that he paid attention to aligning orthologs or sequences of genes between canine and human samples. One challenge beyond his control was that the rigor by which the earlier investigators assembled the samples that he ended up using, such as rigor in diagnosis and defined subgroups, varied from study to study, but having the larger numbers aided in increasing the validity of the results. Similarly, larger numbers of human samples will be available in the future compared to those available when Mikołaj conducted his work.


Mikołaj's work related to the PD-1 antibody was thorough and compelling, and it is likely that this required trouble shooting and the ability to update methods, providing evidence for Mikołaj's critical thinking skills and independence. The figures look very good including those for Western blot and immunohistochemistry.

The decision to start with the phage display approach to develop the PD-1 antibody and the persistence in this approach indicate Mikołaj's independent thought. Yet, the recognition for the need to move to a more traditional hybridoma approach demonstrated his adaptability, an important characteristic of successful researchers.

3) An assessment with justification whether the doctoral dissertation constitutes an original solution to a scientific problem, an original solution in the field of applying the results of own scientific research in the economic or social sphere, or an original artistic achievement.

Mikołaj's thesis demonstrates original thinking and an original solution(s) to a scientific problem in that no other investigator or group has reported similar work. This is especially the case for the comparison between canine and human data, and the comparison across cancer types. The approach to examine ICs in this broad way is unique and has allowed Mikołaj to study cancer in the context of the IC landscape rather than by traditional means. This also opens the door to therapies directed at cancers that share an IC landscape.

Therefore, I am applying to the Council of the Biotechnology Discipline for admission of Mikołaj Kocikowski to further stages of the doctoral procedure.



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