MUNI

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
Procedure field	Animal Physiology
Applicant	MVDr. Martin Anger,CSc.
Applicant's home unit, institution	Masaryk University, Faculty of Medicine
Habilitation thesis	Control of chromosome segregation in mammalian female meiosis
Reviewer	Karen Schindler, PhD
Reviewer's home unit, institution	Rutgers University, NJ, USA

After reviewing the habilitation thesis of Dr. Martin Anger, I **enthusiastically support his habilitation and promotion**. For reference, I am an Associate Professor of Genetics at Rutgers University in the USA where my lab focuses on understanding the molecular and genetic causes of aneuploidy in the female germline. Therefore, I am very familiar with Dr. Anger's research and the research field at large. I came to know Dr. Anger through interactions at professional conferences (Society for the Study of Reproduction and Gordan Research). We both conducted our postdoctoral work with Dr. Richard Schultz at the U. of Pennsylvania, but did not overlap during our training periods. Please note that I do not have knowledge about his teaching and service to the University and am therefore only qualified to comment on his research contributions to the field.

Dr. Anger has developed his research program focused on understanding how chromosome segregation during female meiosis in mammals is controlled. He is taking a multi-pronged approach by evaluating difference aspects that control chromosomes including, spindle formation, cell size, cohesin biology, and genetics. As a postdoc in the Schultz lab, he laid the foundation for working with mouse oocytes and investigated the role of a protein known to control DNA replication but surprisingly found a new requirement in spindle formation. This publication in *Biology of Reproduction*, a leading speciality journal in the field, **set the precedent** for a connection between DNA replication and spindle formation that was later replicated in other organismal systems. As of May 2019, the article was cited an impressive 36 times. Dr. Anger then completed a second postdoc with Dr. Kim Nasmyth, a leader in cohesin biology using yeast. There, Dr. Anger established the mouse work and high-resolution live cell imaging microscopy that Dr. Nasmyth continues today. He works were highly significant, developing new mouse genetic models (conditional Separase and Bub1 knockouts, Rec8-myc transgenic, and Rec8-cleavage site mutants). These manuscripts are published in **high impact, general interest journals** such as *Molecular Cell* (116 citations, IF 14.9), *Journal of Cell Science* (58 citations), Current Biology (123 citations, IF 10.4) and *Cell* (141 citations, IF 34.3). Given his outstanding impact on the field of chromosome and oocyte biology as a postdoc, Dr. Anger would have been competitive on the academic job market in the US, but he chose to return to the Czech Republic to support the training of Czech students and the country's growing research infrastructure.

As an independent investigator, Dr. Anger has continued in this line of research interest and expanded into **making connections between mouse and pig with that of relevant**

problems in the human IVF setting. To do so, he has capitalized on differences between mouse strains. For example, he evaluated aneuploidy in commonly used mouse strains (inbred and outbred) and found differences in the frequency of "predivision" between strain. These differences indicate that there is genetic causes underlying aneuploidy and strength of the cell to recognize these defects. This brief, but significant finding was published in *Chromosome Research*, and has since been supported by others' work in human reproductive genetic studies that are published in journals such as *Science* and *Nature* and even some of my own translational research. This work also led him to evaluate differences in spindle building and regulation. He found fascinating differences in how spindles are built when meiosis occurs in vitro compared to in vivo, sensitivities to low temperature, weaknesses in sensing mechanisms. Collectively, this body of work has contributed to strategies to human IVF conditions, developed new assays adopted by researchers in the field, and improved our knowledge of understanding basic mechanisms that cause aneuploidy in the female germline.

To summarize, I fully support Dr. Anger's promotion with enthusiasm and no reservations. This body of work would be supported here in the US for receiving tenure at R1 institutions like Rutgers and in Animal Science departments. I fully anticipate Dr. Anger will continue to contribute to the knowledge of understanding sources of maternal aneuploidy and making the critical translational connections to the clinic to improve human reproductive outcomes.

Reviewer's questions for the habilitation thesis defence (number of questions up to the reviewer)

1. Why do you think spindle building, specifically a requirement for Eg5 differs between in vivo vs in vitro meiosis in mouse oocytes? Can you explain how these differences could be important in our interpretation of human oocyte studies that are conducted from the in vitro setting?
2. Cryopreservation of human eggs is a common procedure for fertility preservation. Given your studies, what concerns should IVF clinics have when fertilizing these gametes?
3. In considering genetic differences in humans, what genes and potential SNPs in these genes would you suggest clinicians evaluate in their patients?

Conclusion

The habilitation thesis entitled "Control of chromosome segregation in mammalian female meiosis" by MVDr. Martin Anger,CSc. **fulfils** requirements expected of a habilitation thesis in the field of Animal Physiology

Date: October 22, 2019 Signature: