Poznań University of Life Science

Prof. Krzysztof W. Nowak, PhD DSc
corresponding member of Polish Academy of Science

Assessment of the doctoral dissertation

Karolina Wołodko, MSc entitled "The influence of maternal obesity on leptin signaling in the ovary and the influence on the regulation of oocytes and cumulus cells in mice"

performed at the Department of Reproductive Immunology and Pathology, Institute of Animal Reproduction and Food Research Polish Academy of Sciences in Olsztyn,

under the supervision of António Miguel Galvão, VMD PhD DSc

Obesity has in recent years become one of the most important medical problems affecting many life functions and at the same time being a major economic problem. One of the medical problems related to energy storage is the dependence of the proper functioning of the ovary on the accumulated reserves. It is known that in order to start the cyclic function of the ovary, it is necessary to store an adequate amount of energy in the adipose tissue, on the other hand, excessive amount of adipose tissue causes disturbances in the ovarian function. The main sign of the amount of energy deposited in the tissue is its hormone, leptin. Leptin secretion is proportional to the amount of adipose tissue and it is a signal for the hormonal axis. In addition to its impact at the hypothalamus level, leptin also affects peripheral tissues, including endocrine tissues.

The doctoral dissertation submitted for evaluation consists of two publications (an experimental work and a review article) published in indexed journals and a descriptive part divided into chapters. The entire work, with the exception of the Polish abstract, is in English. In both attached publications, the Candidate is the first author with 45% and 60% shares.

The reviewed doctoral thesis concerns the influence of obesity on the elements of the ovarian leptin signal transduction system. Hyperleptinemia was caused by diet-induced obesity and administration of exogenous leptin. The series of analyses were conducted on stimulated ovaries in early (4 weeks) and late (16 weeks) obesity stimulated by diet and after 16 days of exogenous leptin administration. A wide variety of methods were used to analyse the component of the leptin signaling pathway (Western blot, RT-PCR, immunostaining, transcriptome analysis) and NMR was used to verify the amount of adipose tissue.

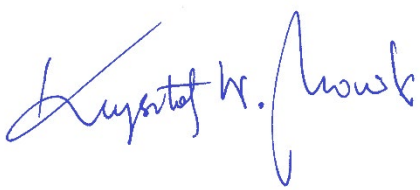
Department of Animal Physiology, Biochemistry and Biostructure
Faculty of Veterinary Medicine and Animal Science
Poznań University of Life Science
35 Wołyńska Street, 60-637 Poznań, Poland
phone: 61 846 6082, fax: 61 8487197
e-mail: kwnowak@up.poznan.pl
www.kwnowak.pl

Assessing a dissertation based on published papers is much easier for a reviewer because these papers have already been assessed by independent reviewers and probably "matured" throughout the publishing process. I believe that the issues raised are of great cognitive and application significance. Adequate and modern research methods were used in the work, and their diversity proves the good scientific skills of the PhD student. The review article that is part of the doctorate is a comprehensive study of the current state of knowledge on leptin signaling during folliculogenesis and oocyte maturation in obesity.

The authors examined the expression of 10 mRNA proteins from the signal transduction cascade, and Western blotting of 12 proteins, including six phosphorylation sites. They also compared cumulus cell transcriptomes in early and late obesity and after leptin loading. The most important result of the study is the demonstration of the ovarian leptin resistance that develops with obesity for the first time. This condition is documented by marked changes in the expression of elements of the signal transduction cascade, mainly an increase in SOCS3 expression and a decrease in the phosphorylation of the leptin receptor on Tyr985 and Janus kinase 2. Moreover, very large differences in the transcriptome of cumulus cells in early and late obesity and in mice loaded for 16 days with leptin have been shown in relation to the control groups. These profiles are almost completely opposite in all cases.

Summing up, I would like to state that the PhD student has demonstrated knowledge in the area of research, good and varied research techniques and the ability to analyse the results and interpret them.

Therefore, I can say with full conviction that the doctoral dissertation presented for evaluation by Karolina Wołodko entitled "The impact of maternal obesity on leptin signaling in the ovary and effects on oocyte and cumulus cells regulation in mice" meets the requirements of Art. 187 OF THE ACT of July 20, 2018 LAW ON HIGHER EDUCATION AND SCIENCE (Journal of Laws of 2021, item 478) and I request the Senate of the Medical University of Bialystok to admit the PhD student to further stages of the doctoral dissertation.



Poznań, August 24, 2021