

STATEMENT

from

Assoc. Prof. Dr. Rositsa Valerieva Karalilova, DMSc

Department of Propaedeutics of Internal Diseases

MU Plovdiv, Faculty of Medicine

of a dissertation for awarding the educational and scientific **degree 'doctor'**

professional direction 7.1. Medicine from the field of higher education 7. Health care and sports

doctoral program Nephrology

Author: Irina Yavorova Zdravkova

Form of doctoral studies: independent preparation

Department: Second Department of Internal Medicine

Topic: Specific serum and deposited autoantibodies and immunoglobulins in membranous nephropathy and their significance for the therapeutic approach

Scientific supervisors:

Assoc. Prof. Dr. Eduard Emil Tilkiyan, MD, PhD
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1. General presentation of the procedure and the doctoral student

The presented set of materials on paper /electronic is in accordance with Art. 70 (1) of I. Sec. Acquisition of educational and scientific degree "DOCTOR" in MU-Plovdiv; Regulations of MU-Plovdiv from 28.01.2021

Dr. Irina Yavorova Zdravkova was born on September 19, 1982 in Odessa, Ukraine. She completed her secondary education at the "Exarch Antim I" Science and Mathematics High School with intensive study of the English language, the city of Vidin in 2000, with excellent success. In 2001 began to study medicine in Romania, Cluj-Napoca at the Medical University Iuliu Hatcieganu, until the 3rd year - 2004. In

2004, she continued her studies at the Medical University of Plovdiv and graduated in medicine in 2008. From 11.2008 to 01.2009 she worked at CSMP-Plovdiv as a resident doctor. From 01.2009 to 10.2009 she worked as an assistant personal physician in the Outpatient Clinic for Individual Practice for Primary Medical Care. October 2009 started working at the Nephrology Clinic of UMBAL „Kaspela”, where she has been working until now. In 2018, she acquired the clinical specialty "Nephrology". Since 2015 after a competition, she was appointed to the position of assistant at the Department of Propedeutics of Internal Medicine. She is fluent in Russian, English and Romanian, has good communication and presentation skills, as well as the ability to work in a team.

2. Relevance of the topic

The problem developed in the dissertation is relevant in a scientific and scientific-applied sense. Membranous nephropathy is a glomerulonephritis with an immunological pathogenesis, which is characterized by a high thromboembolic risk, resistance to therapy, frequent relapses, treatment complications. Reaching end-stage renal disease within 10 years, despite pathogenetic treatment and relapses in transplanted patients.

For more than 50 years, the efforts of many researchers to clarify the etiology and pathogenesis of this disease have continued. Despite the discovery of the main target antigen - PLA2R, characteristic of the primary form of this disease, it is still not clear what triggers the development of an autoimmune response and the formation of antibodies to it. Things become even more complicated with the discovery of many other antigens and antibodies to them. The ambiguity of etiopathogenesis also stems from the fact that these antibodies are positive in primary and in different percentages in secondary forms of the disease, which makes diagnosis and treatment even more difficult.

In her dissertation work, Dr. Zdravkova weaves in one: the study of antibodies in serum to the main target antigen, the study of the same antigen by immunohistochemistry on material from kidney tissue, which is performed on paraffin blocks, i.e. before carrying out pathogenetic treatment. Adds examination of MBL again by immunohistochemistry in order to confirm/disprove the involvement of the lectin pathway of complement in the pathogenesis of the disease. Finally, an analysis is made and the therapeutic combinations leading to complete clinical remission, as well as their alternatives, are highlighted.

3. Awareness of the problem

The in-depth literature review of the doctoral student makes an impression, which, despite the fact that it does not exceed the permissible volume, includes the most recent and current statements and discoveries on the subject, as well as older ones, but viewed from the perspective of the new knowledge we have about the disease. Also presented are

the activation pathways of the complement system, especially the lectin pathway and its higher frequency of activation in patients with diabetes mellitus. The conclusions of the literature review are up-to-date and make a smooth and safe transition to the next part of the dissertation.

4. Research methodology

The scientific research methods and statistical processing used are modern and adequate and allow a precise analysis of the obtained results.

5.Characterization and evaluation of the dissertation work and contributions

The dissertation is written on 163 standard typewritten pages and contains 19 tables, 31 figures and 10 images. Its structure corresponds to the rules for building a dissertation work: introduction - 1 page, literature review 53 pages, goal and tasks - 2 pages, materials and methods - 7 pages, results - 40 pages, discussion - 20 pages, conclusions - 2 pages, contributions - 2 pages and bibliography - 25 pages. The bibliography contains 180 authors, of which six in Bulgarian and 174 in foreign languages, most of which have been published in refereed and indexed journals.

The purpose of the dissertation work is formulated precisely and clearly. There are eight tasks and they are set specifically and comprehensively, according to the achievement of the goal.

Results - the chapter is organized according to the requirements and according to the order of the tasks, and the results are illustrated through well-understood and accessible graphs, tables, and images. Dr. Irina Zdravkova studied the deposition of the three indicators not separately, but together, and brought out the most common combinations: triple, double and positive for one indicator in the various types of MN. It brings to the fore which combinations are definitive for the presence of pMN, which are predominant in iMN and examines the type of deposits in sMN.

Examines patients with diabetes mellitus separately, which is the most common type of MN in them and the type of ICH deposits.

The dissertation work has contributions in a scientific aspect, confirming the activation of the lectin pathway of complement, confirming the importance of the main antigen for the diagnosis, comparing it with the presence of antibodies in serum and their importance in diagnosing, follow-up and treatment of patients. The contributions in the scientific and applied aspect, the conclusions regarding the most appropriate therapy and the guidelines in the correct categorization of the type of MN are also significant. The diagnostic role of KB in patients with diabetes mellitus, the need for screening for other pathology and the need for pathogenetic treatment despite the presence of DM are confirmed.

In conclusion, the doctoral student presents his pathogenetic model of MN, which, although it is hypothetical, makes distinguishing the type of MN easy and has a great practical application for the correct clinical-immunological treatment of patients, facilitates the categorization of the type of MN and, accordingly, guidelines for the type of therapy required, for MN or the disease that led to it, and if necessary, both.

6. Evaluation of the publications and personal contribution of the doctoral student

Dr. Irina Zdravkova has 15 publications in Bulgarian collections and refereed journals, in 3 of which she is the first author and participation in 21 reports and posters at Bulgarian scientific forums. She is a member of the Bulgarian Nephrology Society and BLS.

The doctoral student himself provided the antibodies necessary for conducting immunohistochemistry, actively participated in the provision and delivery of the solutions and systems necessary for the processing of the puncture material, and the formulated contributions and obtained results are his personal credit.

Critical remarks and recommendations: The tasks set are many and very diverse: antibody research by immunohistochemistry, antibody research in serum, tracking how many patients, what type of therapy they have had, what type of MH they have and bringing to the fore the most suitable therapeutic approach. This made the evaluation of the dissertation difficult to a certain extent, and this most likely made it difficult for the dissertation student as well.

7. Abstract

The abstract is structured precisely and according to the requirements. It presents the main and illustrated research results, a summary discussion and main contributions.

CONCLUSION

The dissertation *contains scientific, scientific-applied and applied results, which represent an original contribution to science* and meet the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRASRB), the Regulations for the Implementation of ZRASRB and the Regulations of the MU-Plovdiv. The presented materials and dissertation results **fully** correspond to the specific requirements adopted in connection with the Regulations of the MU - Plovdiv for the application of the ZRASRB.

The dissertation shows that the doctoral student Irina Yavorova Zdravkova **possesses** in-depth theoretical knowledge and professional skills in the scientific specialty of Nephrology, **demonstrating** qualities and skills for independent conduct of scientific research.

Due to the above, I confidently give my *positive assessment* of the conducted research, presented by the above-reviewed dissertation work, abstract, achieved results and contributions, and *I propose to the honorable scientific jury to award the educational and scientific degree "doctor"* to Dr. Irina Yavorova Zdravkova in a doctoral program in Nephrology.

09.08.2022

Statement prepared by:

Assoc. Prof. Dr. Rositsa Karalilova, DMSc

Заличено на основание
Чл.5 §1, б. "В" Регламент (ЕС)2016/679