OPINION

regarding the dissertation for the acquisition of the scientific and educational degree "doctor" (PhD)

on the topic "IMPORTANCE OF THE ENDOMETRIAL IMMUNE PROFILE FOR THE SUCCESS OF ASSISTED REPRODUCTION",

of Rumyana Rumenova Ganeva, part-time doctoral student in the Department of Cellular and Developmental Biology, Faculty of Biology, Sofia University, in the scientific field 4.3. Biological Sciences, Department of Cellular Biology

supervised by Assoc. Prof. Dr. Vesselina Svetoslavova Moskova-Dumanova, Head of the Department of Cellular and Developmental Biology, Faculty of Biology, Sofia University "St. Kliment Ohridski"

by Prof. Dr. Tanya Ivanova Topuzova-Hristova, Faculty of Biology, Sofia University "St. Kliment Ohridski"

Data about the doctoral student and doctoral studies.

Rumyana Rumenova Ganeva graduated with a Bachelor's degree in Molecular Biology from the Faculty of Biology of Sofia University in 2016 and a Master's degree in Developmental Biology from the same faculty in 2018. Since 2016, Rumyana Ganeva has been working as a biologist in the Research Laboratory at the Nadezhda Hospital. Since January 2022, she has been enrolled as a part-time doctoral student in the Department of Cell Biology at the Department of Cell Biology and Developmental Biology, Faculty of Biology, Sofia University, in the scientific direction 4.3. Biological Sciences with Order No. RD-20-84/18.01.2022. During the doctoral studies, the required number of exams were taken and the necessary credits were acquired according to the doctoral student's individual plan. Doctoral student Ganeva was finished ahead of schedule with the right to defend her thesis, and all deadlines according to the Regulations on the conditions and procedure for acquiring scientific degrees and holding academic positions at the Sofia University have been met. The minimum national requirements according to the ZRASRB have also been met.

Data about the dissertation.

The topic of the dissertation "IMPORTANCE OF THE ENDOMETRIAL IMMUNE PROFILE FOR THE SUCCESS OF ASSISTED REPRODUCTION" faithfully reflects its content. The dissertation covers a total of 160 pages of main text, to which are attached an informed consent form and three approvals from the ethics committee for conducting research with patient samples, as well as one clinical study in connection with the dissertation (making the volume a total of 193 pages). The research in connection with the dissertation was conducted in the Research Laboratory at the Nadezhda Hospital.

The main parts of the dissertation follow the generally accepted plan for such work and include: Literature review – 57 pages, Aims and objectives – 1 page, Materials and methods – 18 pages, Results – 41 pages, divided into two stages and including a discussion for each stage, Conclusions – 1 page, Conclusion – 1 page and contributions – 1 page. There are a total of 40 figures and 19 tables for the individual chapters.

The literature review provides an overview of the modern views on the role of the endometrium and the immune system in the processes of implantation in reproduction or in reproductive pathologies. In separate points, attention is paid to the morphology and role of the endometrium, the role of T and B lymphocytes, macrophages and natural killers in the endometrium and implantation, the main reproductive pathologies and methods for diagnosis and immunotherapy in recurrent implantation failures. The lack of sufficiently reliable biomarkers for the prediction of implantation success is emphasized, which also determines the goal of the dissertation work to establish immune indicators of endometrial receptivity, which would assess the effectiveness of local immunotherapy in in vitro patients with recurrent implantation failures.

The formulated goal and objectives logically follow from the review, and the materials and methods used are described correctly and clearly, and are illustrated with the necessary tables and figures. The studies are divided into two stages, for each of which the criteria are clearly formulated and a diagram of the experimental design is presented.

The results are well illustrated and explained, allowing the derivation of 6 clearly formulated conclusions regarding the two groups of studies - on the immunological status of the endometrium in women with recurrent implantation failures and on the changes after immunotherapy with autologous lymphocytes. A discussion of the results was also made in view of the data known in the scientific literature after each group of studies.

Scientific apparatus

343 sources are cited, mostly from recent years, including 84 publications after 2020 (over 24%). All sources are adequately selected and have a direct bearing on the research topic, which shows the excellent awareness of the doctoral student. The citations are made in compliance with the established standards for citing scientific literature.

Abstract

The abstract contains 58 pages and fully reflects the content of the dissertation. The main results are correctly presented, illustrated with a total of 14 figures and 9 tables, which include graphs, color microphotographs and original schemes. The conclusions are presented correctly.

Publications

The main results of the dissertation have been published in two articles in prestigious scientific journals (with an impact factor of 2.02 and 2.7, respectively) with a quartile of Q1. In one article, the doctoral student is the first author, and in the other - the second author, which reflects the significant contribution to their development. According to the requirements of the Academic Staff Development Act, the two publications carry a total of 50 points, which exceeds the required minimum of 30. In addition to these publications, R. Ganeva has attached a list of 1 additional one in a journal without an impact factor, as well as 18 participations in scientific forums. This significant publication activity characterizes the doctoral student Rumyana Ganeva as a well-established and active young scientist with excellent prospects for future development.

Scientific and scientific-applied contributions

Methodological and applied contributions of the dissertation work are the determination of biomarkers with predictive value in assessing the risk of implantation failures, as well as those for assessing the results of immunotherapy with intrauterine administration of autologous PBMCs for assessing endometrial receptivity.

As a contribution of a scientific nature that is relevant to the fundamental knowledge of the implantation process, there is a comparison of the immune profile of the endometrium in patients with successful and unsuccessful embryo implantation.

Conclusion

In conclusion, the determination and introduction of appropriate biomarkers in the assessment of an appropriate implantation window and the diagnosis of endometrial receptivity is particularly relevant in view of the modern aspects of personalized medicine. This makes this dissertation work relevant and of high applied value. Based on the presented materials, I believe that the doctoral student fully meets the requirements of the ZRAS for awarding the scientific and educational degree "doctor" and I give my positive opinion to award the scientific and educational degree "doctor" in the scientific direction 4.3. Biological Sciences to Rumyana Rumenova Ganeva.

10.07.2025

City of Sofia /prof. dr. Tanya Topuzova-Hristova/