

STATEMENT

by

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Regarding: The doctoral dissertation entitled *"Analysis of the Expression of Hormonal Receptors and the Biomarkers p53 and Ki-67 in Endometrial Polyps in Pre- and Postmenopausal Women"* by Dr. Krum Stefanov Vladov, submitted for the award of the educational and scientific degree "Doctor" in the field of Higher Education: 7. Health and Sports, Professional Field 7.1 Medicine, Doctoral Program "Obstetrics and Gynecology," in accordance with Order № P-3342/01.07.2025.

I. BRIEF BIOGRAPHICAL INFORMATION

Dr. Krum Vladov was born in 1992. In 2011, he graduated with honors from the High School of Mathematics and Natural Sciences "Konstantin Velichkov" in Pazardzhik. He obtained his Master's degree in Medicine in 2017 from the Medical University of Plovdiv. Between 2017 and 2021, he was a resident at the Clinic of Obstetrics and Gynecology at University Hospital "St. George" – Plovdiv, and in January 2022 he completed his specialty in Obstetrics and Gynecology. Since 2020, he has served as an assistant professor at the Department of Obstetrics and Gynecology at the Medical University of Plovdiv.

Dr. Vladov has successfully completed several postgraduate trainings, including obstetric and gynecological ultrasonography, pregnancy monitoring under the "Maternal Health" program, diagnostic laparoscopy, colposcopy with targeted biopsy, and hysteroscopy.

He is proficient in English and actively participates in the instruction of international students in Medicine, Dental Medicine, and internship programs. He is

also competent in using Microsoft Excel, Word, PowerPoint, Office 365, Teams, Zoom, among others.

Dr. Vladov is a member of several professional associations: the Bulgarian Medical Association (BMA), the Bulgarian Society of Obstetrics and Gynecology (BSOG), the Bulgarian Association of Oncogynecology (BAOG), and the Bulgarian Association for Minimally Invasive Gynecologic Surgery (BAMIGS).

II. RELEVANCE OF THE TOPIC

The topic of the dissertation addresses a highly pertinent, clinically significant, and contemporary issue.

Endometrial polyps represent one of the most common benign lesions within the uterine cavity. Due to advancements in diagnostic modalities, they are frequently discovered as incidental findings, particularly in pre- and postmenopausal women. Their pathogenesis remains a subject of debate. However, it is thought to involve an imbalance in the expression of endometrial steroid hormone receptors (estrogen and progesterone) and elevated serum estradiol levels, along with disruptions in the mechanisms governing cellular proliferation and apoptosis.

A particularly important consideration is the potential for malignant transformation of endometrial polyps, especially in light of the fact that endometrial carcinoma ranks second only to breast cancer among malignancies affecting women (National Cancer Registry). Therefore, the investigation of specific biomarkers as potential predictors of malignancy is of considerable relevance to gynecological practice. Analysis of serum estradiol levels, immunohistochemical expression of steroid receptors, and the biomarkers p53 and Ki-67 may yield valuable insights into unresolved aspects of this pathology. Accordingly, I consider the selection of this dissertation topic to be particularly appropriate.

Aim of the Study: To analyze the expression of estrogen and progesterone receptors, as well as the biomarkers p53 and Ki-67, in endometrial polyps among pre- and postmenopausal women.

The candidate delineates five specific research objectives:

1. To analyze the demographic characteristics of the study population.
2. To perform a comparative analysis of serum estradiol levels among three groups: women with endometrial polyps, endometrial carcinoma, and atrophic endometrium.
3. To assess and compare the expression of estrogen and progesterone receptors among these groups.
4. To compare the expression levels of biomarkers p53 and Ki-67 across the studied groups.
5. To evaluate the correlations between hormonal receptor expression, biomarker expression, serum estradiol concentrations, and the incidence of endometrial polyps.

III. STRUCTURE OF THE DISSERTATION

The dissertation follows a classical structure and comprises 210 standard pages, supplemented by 56 figures and 82 tables.

The literature review spans 38 pages and includes 196 references—15 in Cyrillic and 181 in Latin script.

Materials and Methods: A cross-sectional study was conducted on 120 women hospitalized at the Clinic of Obstetrics and Gynecology at University Hospital "St. George" – Plovdiv. Participants were divided into three groups based on defined inclusion and exclusion criteria. The study period extended from December 2022 to December 2024. A wide array of methods was employed, including questionnaires, clinical and paraclinical assessments, laboratory and histological analyses, imaging techniques, and statistical evaluations. Data were processed using IBM SPSS v.26.0, with statistical significance set at $p < 0.05$.

Original Results: The results are rigorously analyzed and concisely summarized following each research objective: Endometrial polyps were most prevalent among overweight premenopausal women aged 41–50; Endometrial carcinoma was most

common among obese postmenopausal women aged 51–60; Among premenopausal women, serum estradiol levels positively correlated with increased BMI and were associated with the risk of polyp formation; Endometrial polyps demonstrated strong expression of both estrogen and progesterone receptors across all tissue components, with no statistically significant difference between pre- and postmenopausal women; Menopausal status influenced the proliferative potential of endometrial polyps: Ki-67 expression was significantly higher in premenopausal women, whereas p53 levels showed no significant variation.; Expression of both biomarkers in endometrial polyps exhibited significant positive correlations with hormonal receptor levels.

Of the six conclusions presented, I would particularly emphasize the scientific and practical significance of conclusions 4, 5, and 6.

Contributions of the Dissertation: The dissertation provides original, confirmatory, and applied scientific contributions: This is the first comprehensive analysis conducted in Bulgaria assessing risk factors, serum estradiol concentrations, steroid receptor expression, and the cellular biomarkers p53 and Ki-67 in women with endometrial polyps, endometrial carcinoma, and atrophic endometrium.; The author formulates novel hypotheses regarding the etiopathogenesis of endometrial polyps in pre- and postmenopausal women.; A practical model for risk stratification in endometrial polyps is proposed, based on a composite approach integrating clinical, hormonal, and metabolic parameters with immunohistochemical findings.

IV. CONCLUSION

The dissertation by Dr. Krum Vladov constitutes a modern, in-depth, and clinically significant investigation. The candidate has demonstrated adequate scientific output through publications and conference participation, thereby fulfilling the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, its implementing regulations, and the internal regulations of the Medical University – Plovdiv.

Based on the foregoing, I fully support and recommend that the esteemed members of the Scientific Jury vote affirmatively for the awarding of the educational and scientific degree "Doctor" to Dr. Krum Stefanov Vladov.

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Prepared by: 

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