

REVIEW

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on the thesis of

ASSOC. PROF. NIKOLAY TODOROV EVTIMOV, PhD

"THE NGF AND BDNF ROLE(NERVE GROWTH FACTOR and BRAIN-DERIVAD NEUROTROPHIC FACTOR) , AND THEIR RECEPTORS TRKA, TRKB AND P75 NT R FOR THE INVENTION AND METASTASIS OF THE PROSTATE CARCINOMA."

for awarding a scientific degree

"DOCTOR OF MEDICAL SCIENCES"

on the scientific specialty

"UROLOGY"

I. INFORMATION ABOUT THE PROCEDURE

The dissertation work was developed in the form of an independent doctorate at the Clinic of Urology at the University Hospital "St. Anna ", Varna and the Department of Pathology at the University Hospital "St. Marina ", Medical University, Varna. The procedure is in the professional field 7.1. "Medicine" and scientific specialty "Urology". The presented set of materials on the protection and the actions to it comply with the requirements of the Law on the Development of the Academic Staff in the Republic of Bulgaria (ZRARSR), the Rules and Procedures of the Bulgarian State Agency for Research and Development and the Regulations on the Terms and Procedure for Acquiring Scientific Degrees in Medical University, Varna. The preparation of the review complies with the requirements of the above mentioned normative documents.

II. BIOGRAPHIC DATA

Assoc. Prof. Dr. Nikolai Evtimov, was born in 1960. In 1984 he graduated from the Medical Faculty of the Medical University of Varna. Since 1998 he has been awarded the "Urology" specialty. In 2013 Dr. Nikolay Evtimov defends dissertation on the topic: "Systemic inflammatory response in laparoscopic and classical radical prostatectomy in prostate carcinoma. Surgical and Functional Comparison ", for the award of the Doctor's educational and scientific degree. In 2017 he was awarded the Academic Position "Associate Professor" at the Department of Surgical Diseases, Medical University, Varna. The professional development of Assoc. Prof. Nikolay Evtimov is connected to the Clinic of Urology at the *University Hospital "St. Anna "* in the city of Varna. His professional qualifications include courses and specializations in university centers in Germany and Austria, Romania and Bulgaria, for laparoscopic and robot assisted surgery, transplantology, urology and andrology. He speaks English, German, French and Russian. In the documents submitted for participation in the competition, the applicant has provided a detailed up-to-date reference for his professional development, qualification, as well as for his teaching, scientific and public activities

III. ACTUALITY OF THE THESIS

The prostate cancer is a topic in urology that, despite the historical advances over the years in terms of diagnosis and treatment, seems to be becoming more and more relevant and widely embedded in scientific research on a global scale. This unceasing interest is dictated by both the high frequency and social importance of the disease and the variety of diagnostic and treatment tools that provide us with modern medical science. Unfortunately, the results associated with early diagnosis of the disease, despite the definite progress in this direction in recent years, are still unsatisfactory. There is no contemporary large scientific forum or specialized scientific forum dedicated to the diseases of the prostate gland, which does not address the problem of prostate cancer in its various aspects in terms of biological nature and manifestation, diagnostics, medical, surgical, radiological treatment, as well as the complications associated with these healing methods. Prostate carcinoma is the second most

frequent cancer in men. The identification of risk factors for the development of prostate cancer and factors influencing the progression of the disease is of utmost importance for early diagnosis and timely treatment. The identification of growth factors, substances and receptors associated with the mechanisms of tumour growth, neoangiogenesis and metastasis, allow for a precise understanding of the pathogenetic mechanisms related to the carcinogenicity and the progression of the disease and their potential therapeutic response.

IV. ANALYSIS OF THE THESIS

The structure of the dissertation corresponds to the requirements of the Regulations and contains all the necessary sections. It is written in the correct Bulgarian language on 231 pages and is illustrated with 58 figures and 44 tables. The bibliography contains 290 titles, of which 27 in Bulgarian and 263 in English. Key and up-to-date publications on the topic are presented, which allow a fair comparison and commenting on the results of the study. The book review is written in 69 pages and looks at the role of NHG and BDNF, neurotropic receptors and other etiological factors for prostate cancer. Benefits for dissertation work are formulated at the analysis of literature discussable issues related to the expression of growth factors and the role of their receptors in the development of prostate carcinoma. This helps to formulate a study objective and tasks related to the analysis of the surgical results of the laparoscopic and open radical prostatectomy, and the correlation and prognostic significance of neurotrophin NGF and BDNF (Brain-Derivad Neurotrophic Factor) as well as tyrosine - kinase receptors Trk, (TrkA, TrkB, p75NTR) with various preoperative and intraoperative parameters.

In the section **Material and Methods** Assoc. prof. Nikolay Evtimov, presents systematized and summarized clinico-statistical data from retrospective, and on individual parameters prospective, non-randomized study on 257 patients with prostate cancer, operated in laparoscopic and classical surgical methods at the clinic of Urology of hospital "St. Anna " in the town of Varna for a period of 6 years. It have been described the detailed methods used to diagnose and treat patients and to demonstrate the expression of neurotrophins in histological preparations. The study was developed on its own clinical

material, with special attention being paid to surgical techniques and methods of histological examination of the active substances. The methods used are up-to-date, effective and allow the objectives and tasks to be achieved.

The **Results and Discussion** sections of the dissertation are presented with sufficient tables, figures and a textual part. The results are statistically processed and the author establishes correlations between different preoperative characteristics of patients and the expression of neurotrophin in the operative preparations. A comparative analysis of the two surgical techniques - laparoscopic and open surgical techniques - has been made in terms of oncology results, safety and expression of growth factors. All this gives the opportunity to make reliable and concrete real comparisons and conclusions. The published results are of original character and have a strong scientific and scientific-practical contribution to the Bulgarian medical science and practice.

The detailed analysis of the data in the results section of this scientific study provides an opportunity for Assoc. Prof. Nikolay Evtimov to make a thorough and detailed discussion of the own results in the context of topical publications on the topic in the international scientific press.

As a result of competent and critical mapping of methodologies, approaches and achieved results, Assoc. Prof. Nikolay Evtimov formulated 12 conclusions, which determine the scientific contribution and scientifically applied benefits of this dissertation work. The conclusions logically follow the results obtained and the discussion made and I accept them as well justified and justified. The 8 contributions of the dissertation work demonstrate its qualities of recent scientific research, conducted on a contemporary problem of utmost importance and results with a marked benefit for the Bulgarian medical science and practice.

V. PUBLICATIONS IN REFERENCE TO THESIS

Assoc. Prof. Nikolai Evtimov has participated in international and national congresses and symposiums and publications in the periodical medical press, covering the national requirements and the requirements of the Medical University of Varna Regulations for awarding the Doctor of Medical Sciences degree. 24 publications in reference national and

foreign scientific journals and collections published in the period 2012-2018 focused on the problem of prostate carcinoma and the role of growth factors in the pathogenesis of the disease. The scientific analysis shows a very good publicity value of the dissertation work of Assoc. Prof. Nikolai Evtimov.

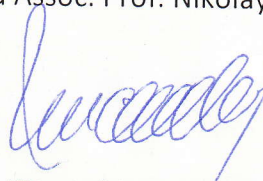
VI. CONCLUSION

Dr. Nikolay Evtimov's thesis on "The role of NGF, BDNF and their receptors TrkA, TrkB and p75 NT R for the onset and metastasis of prostate carcinoma" summarizes a complex study of prostate cancer patients and offers interesting and original contributions to the role of growth factors in the pathogenesis of the disease and their correlation with various preoperative factors. Therefore, it brings the qualities of current and in-depth scientific research and has a certain scientific and scientific-practical contribution. Dissertation work is planned and developed in depth and precision. It is structured properly and is written in an academic style. Its purpose is clearly formulated and the assigned tasks contribute to the realization and achievement of the objective. Dissertation work meets the requirements of the ZRAEB and the regulations for its application at the Medical University of Varna.

Having in mind everything written above, reflecting the scientific value and importance of the developed dissertation work, the personal and professional qualities of Assoc. Prof. Nikolay Evtimov, as a specialist urologist and scientist, I give my positive vote and recommend to the Members of the Scientific jury to award Assoc. Prof. Nikolay Evtimov, scientific degree "Doctor of Medical Sciences".

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Sofia



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