

Opinion

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*on: Dissertation assignment for awarding of NSA "Doctor of Sciences" of
Assoc. Prof. Nikolay Todorov Evtimov, PhD*

dissertation topic: *"The role of NGF and BDNF and their receptors Trk-A, Trk-B, p 75 for the onset and metastasis of prostate carcinoma"*

By Order No P-109-662 / 14.12.2018 on the grounds of Art. 4, para. 2 of the Law on the Development of the Academic Staff in the Republic of Bulgaria I have been appointed for the preparation of an opinion on the procedure for obtaining a scientific degree “Doctor of Sciences” by the candidate Assoc. Prof. Dr. Nikolay Todorov Evtimov on the topic “The role of NGF and BDNF and their receptors Trk-A, Trk-B, p 75 for the occurrence and metastasis of prostate carcinoma” in the field of higher education 7. Health and Sports, Professional Field 7.1 Medicine, Precision" Urology".

The presented dissertation thesis by Assoc. Prof. Dr. Nikolay Todorov Evtimov is properly structured. It contains 232 pages. It is illustrated with 58 figures and 44 tables. The bibliographic reference includes 290 titles, of which 27 in the Cyrillic alphabet.

The concept of cell growth factors – the differentiation and functions of various cell types are regulated by specific signal proteins called cell growth factors. Today, cell growth factors are more than 50 in number and occupy central locations in the pathogenesis of many diseases. In recent years, research has also addressed the demand for intercellular interactions between stromal cells and epithelial cells of the prostate gland.

Assoc. Prof. Evtimov has set a clear goal to establish and evaluate the immunohistochemical density of neurotrophin expression NGF and BDNF as well as their tyrosine kinase receptors TrkA, TrkB, p75 that regulate stromo-

epithelial interactions and their fundamental role in the onset and progression of prostate carcinoma and has formulated 14 tasks in order to achieve this goal.

For the period 2010-2016 in the Urology Clinic of "St. Anna-Varna" performed 257 radical prostatectomies in patients with localized prostate carcinoma. Patients are divided into two groups depending on the PSA and Gleason score. Tissue preparations have been routinely processed. 257 patients with prostate cancer were examined with sample size and relative ratio being determined. Ten biopsy cylinders were obtained and were examined histologically and immunohistologically. All preparations were treated with monoclonal antibodies and the expression of growth factors and their receptors was determined. By a formula based on 20 arbitrarily selected fields and statistically processed, a semi-quantitative analysis of the expression of the neurotrophins and their specific receptors was performed, and a correlation was made between the two groups of patients, depending on the PSA values > 20 ng / ml, clinical stage pT2 > <pT3-4, Gleason score > <7, prostate volume > 60 g, patient age <60 years and pathoanatomic stage G2 > <G3-4. The intensity of expression in carcinoma tissue relative to the expression level in benign prostate tissue is compared.

The results are arranged and illustrated in 40 tables and 19 figures. They are statistically credible and originally written by the author.

In the discussion, the two main groups of parameters monitored during the study were analyzed: clinical and immunohistochemical. The correlation analysis of all parameters demonstrates a relationship between BMI, prostate volume, PSA, Gleason Score and neurotrophic expression density and their use in combination. These dependencies lead to the creation of prognostic models with a high positive predictive value.

The author attempts and presents a hypothesis about a likely pathoatomic pathway for the occurrence and metastasis of prostate carcinoma. It also proposes the possible introduction in the clinical practice of another extremely sensitive and subjective method for diagnosis and prognosis of this insidious disease by immunohistochemical examination of NGF and BDNF and quantitative analysis of their blood levels perioperatively. It also expresses the view of potential therapeutic potential by suppressing the growth factors it studies or blocking its specific receptors as a probable healing strategy.

On the basis of the study, the author made 11 credible conclusions and has 8 contributions of an original nature, of which 4 are confirmatory.

In conclusion Assoc. Prof. Evtimov is a urologist who won the trust and respect of his colleagues. In his scientific work he proves and analyzes the expression of

BDNF and NGF in prostate carcinoma. In his study he suggested that strong expression of NGF and BDNF was probably associated with increased invasiveness of the neoplastic process, indicating increased proliferative activity. This makes it increasingly possible to use target therapy to treat neoplastic processes. His dissertation work is the result of many years of scientific research, some of which he presented to the Bulgarian urological community. There are the necessary scientific publications in our and foreign urological scientific journals.

The present scientific work is entirely the author's work and possesses all the qualities and requirements for awarding the educational and scientific degree "Doctor of Medical Sciences" of Assoc. Prof. Dr. Nikolay Todorov Evtimov, PhD. Therefore, internally convinced, I recommend to the members of the honorable scientific jury to vote positively for the award of the scientific degree "Doctor of Sciences" to Assoc. Nikolay Todorov Evtimov dm.

Assoc. Prof. Tosho Yordanov Ganev

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City of Varna