



STATEMENT

On the submitted works for participation in a competition for the academic position of "Associate Professor" in the field of Higher Education 4. Natural sciences, mathematics and informatics, Professional area 4.3. Biological sciences (Biochemistry), announced by Medical University-Varna in State Gazette, issue No. 7/23.01.2024

Reviewer: Svetla Dimitrova Petrova PhD,

Professor of Biochemistry at the Department of Biochemistry, Faculty of Biology, Sofia University "St. Kliment Ohridski"

Member of the Scientific Jury, according to order No. P-109-119/22.03.2024 of the Rector of Medical University - Varna, in a competition for the academic position "Professor", Professional area 4.3. Biological sciences (Biochemistry), Higher education field 4. "Natural sciences, mathematics and informatics", published in SG No. 7/23.01.2024 for the needs of the Faculty of Pharmacy, Department of Biochemistry, Molecular Medicine and Nutrigenomics

Candidate: Deyana Georgieva Vankova PhD

Chief assistant professor at the Department of "Biochemistry, Molecular Medicine and Nutrigenomics", Faculty of Pharmacy, Medical University Varna – the only candidate who submitted documents for participation in the announced competition for the academic position "Associate Professor"

According to the documents presented by the "Career Development" Department, Dr Deyana Vankova has more than 19 years of work experience in the biology speciality and fully satisfies the requirements set out in the Law for the Development of Academic Staff in the Republic of Bulgaria (LDASRB), and the Regulations for its application, as well as an acquired speciality in Biochemistry as an additional condition for the competition. The materials submitted by the applicant are precisely prepared and completed in accordance with the legal requirements. I declare that I have no common publications with the candidate submitted for this competition.

1. Brief biographical details of the applicant

Dr Deyana Vankova graduated from SU "St. Kliment Ohridski" majoring in "Molecular Biology" (professional qualification Molecular Biologist) in 2002, and in 2004 she graduated as a "Master" in "Human and Animal Physiology". She defended her PhD thesis in "Biochemistry" entitled: *"Study the role of genetic factors and lifestyle on the appearance of obesity and metabolic syndrome in a sample of the Bulgarian population"* at the Medical University - Varna in 2015. The same year Dr Vankova completed her studies with an additional specialization in medical biochemistry, required by medical universities. The professional development of Dr Deyana Vankova goes through: a medical representative in "Tchaikapharma - high-quality drugs" Inc; a laboratory specialist in SGS-Bulgaria Ltd; and since 2009 her professional career is closely related to the Department of Biochemistry, Molecular Medicine and Nutrigenomics at MU "Prof. Dr. Parashev

Stoyanov" -Varna, where she works as an assistant and chief assistant. She is assigned an important administrative activity in the Department - chief administrative assistant.

2. General assessment of the applicant scientific activity

In the competition for the academic position "Associate Professor", Dr. Deyana Vankova submitted an Academic Reference of scientific works that fully cover both, the National and those of the Medical University - Varna requirements, including 16 publications (14 referred and indexed in Scopus and Web of Science with IF, cited 27 times), 1 monograph, 2 book chapters, 2 published university textbooks (after 2016), 1 dissertation and 22 presentations and posters in national (13) and international (9) scientific forums.

- ✓ indicator group A1 (50 pts) - PhD thesis;
- ✓ indicator group B3 (100 pts) - monograph - "*Role of some adipokines in the pathogenesis of socially significant diseases*" PC Clinic, ISBN 978-619-91772-5-9;5
- ✓ indicator group Г7 (225t.) - 14 scientific publications, referred and indexed in Scopus and Web of Science - 1 publication - Q1 (*J.Mol.Sciences*), 4 - Q2 ; 4 - Q3; 5 - Q4 (all beyond those equivalent to habilitation work);
- ✓ indicator Г8 (30 pts) - 2 published book chapters (1 chapter - Q3 in *Medical toxicology*) and 1 chapter in an issue without IF.
- ✓ indicator Д11 (54 pts) – 54 citations of the presented scientific publications
- ✓ indicators E14-E18 – participation in scientific and educational projects (10) (1 international, financed by FP7- European Union, 4 financed by NSF and 5 financed by "Science" Fund MU-Varna).
- ✓ indicator E20 – 2 participations in published University textbooks

The list of Deyana Vankova's scientific works includes also 3 publications (published in the scientific journal of MU-Varna) above the requirements. She has presented her research work at 9 international and 13 national scientific forums. All listed publications prove that the candidate as an established scientist with knowledge in various areas of modern biology.

3. Assessment of scientific and applied research activities

The scientific activity of Dr. Deyana Vankova is summarized in thematic areas, which include interdisciplinary experimental approaches, methods and analyzes (biochemical, molecular-biological, cell-biological, physiological, immunological, histological, clinical), requiring the candidate to have integral knowledge of various biological areas. This is absolutely necessary for the scientific and teaching activity of Dr Vankova but is also a requirement for contemporary molecular biological education and research in Medical universities, elevating medicine to a higher level becoming translational, integral, modern and more efficient. Thematic areas are:

A. Biomarker research in socially significant diseases

- In this area (Г7.14), which is a continuation of Dr. Vankova's doctoral thesis and her research experience, she proves that in patients with metabolic syndrome, *the expression levels of the transcription factors NF-kB, Nrf2 and the enzyme HO -1 (heme-oxygenase-1) in PBMCs were significantly higher than in controls, allowing Nrf2, NF-kB and the NOS inhibitor – ADMA to be used as biomarkers in the assessment of endothelial dysfunction in clinical practice.*

- in studies of cardiovascular pathological conditions, it has been found: a relationship and dependence between the expression of the matrix Gla protein (inhibitor of vascular mineralization) in PBMCs and impaired regulation of lipid metabolism (Г7.8); *biochemical relationship between statins and vascular calcification* (Г7.7); *relationship between increased calcium concentration* (Г7.9) *and vitamin D deficiency, which is accepted as a cardiovascular risk factor.* Significantly lower levels of non-carboxylated matrix Gla protein have been demonstrated in patients with coronary calcium deposits.

B. Investigation of the antioxidant and anti-inflammatory properties of medicinal plants and biologically active substances *in vitro* and *in vivo*.

In vitro research in this area is related to the use of mouse cell line J774A.1 - macrophage-like, cancer line with high metabolic activity and expression of IL-1 and lysozyme. It is easy to follow the change in metabolic activity and cytotoxicity caused by different pharmacologically active plant fractions, and in the course of these studies certain regularities have been established:

- in a model system of induced cytotoxicity (with tertiary butyl alcohol, $\Gamma 7.2$), hydrophilic and anthocyanin fractions from *Sambucus ebulus* reduce toxicity and protect macrophages;

- in a model system of induced inflammation (cell line J774A.1), molecular mechanisms of action of the homeopathic remedy Ferrum phosphoricum D12 on proliferation and mRNA expression of genes (related to iron metabolism, antioxidant defense and inflammation) were analyzed. Even at low concentrations FP D12 (0.025 mg/mL), stimulated the proliferation of J774A.1 cells and induced an increase in mRNA expression of ferritin light chain (up to 8-fold), β -2-microglobulin (2.5-fold), iron-binding protein-2 (up to 4 times) and glutathione peroxidase (1.27) times compared to untreated cells ($\Gamma 7.4$);

- in a model system (cell line J744A.1 ($\Gamma 7.10$), the role of elevated plasma uric acid levels as a risk factor for metabolic syndrome was analyzed. The cells were treated with pathophysiological concentrations of uric acid and their antioxidant cellular response was evidenced by increased transcription of genes encoding enzymes of glutathione (GSH) metabolism, GCL (glutamate-cysteine ligase), GPx1 (glutathione peroxidase 1), GR (glutathione reductase) and GS (glutathione synthetase). Studies clearly show that glutathione metabolism in macrophages is subject to tight regulation to maintain certain concentration levels of GSH;

- *in silico* prediction of the metabolism of Br-oxph-1 (5-ethyl-5-methyl-4-bromo-2-N-butylamido-2,5-dihydro-1,2-oxophosphole-2-oxide) and analysis of the quantum chemical and physicochemical characteristics of Br-oxph-1 show that the compound has potential for drug development ($\Gamma 7.5$) - at a concentration of 0.25 mg/mL it strongly affects the expression of glutamate cysteine ligase (8x) and glutathione peroxidase 1 (magnification 3x), while a higher concentration induced cytotoxicity to J774A.1 macrophages;

- *adaptogenic and anti-inflammatory effect* of *Agrimonia eupatoria* extract was established when treating 3T3-L1 preadipocyte cell line – it was demonstrated a significant reduction in the expression levels of the pro-inflammatory monocyte chemoattractant protein-1 (MCP-1) (full text publication beyond the minimum requirements).

- *in vivo* experiments - experimental animals as a model system (Wistar rats) in a study for potential application of plant extracts (antioxidant activity) in metabolic disorders. The main achievements are based on the application of an aqueous extract of *Agrimonia eupatoria* in conditons of lipid metabolic disorders. It was demonstrated that it regulates total cholesterol and triglyceride levels by modulating gene expression in adipose tissue. Inhibition of triglyceride synthesis and induction of mobilization of triacylglycerols stored in adipose tissue have been proposed as a mechanism ($\Gamma 7.11$).

- *in human* – scientific project "Study of the molecular mechanisms of action of sulfur-containing mineral waters from Varna reservoir on human metabolism with a view to their use as medicinal and drinking resource". Investigations proved the healing effect of sulfur mineral waters which significantly increased levels of total GSH, total -SH thiols and increased gene expression levels of the antioxidant enzymes γ - glutamyl-cysteinyl ligase and sICAM-1 ($\Gamma 7.1$).

I could like to emphasize Dr. Vankova's participation in two joint projects with SU "St. Kliment Ohridski" on algotoxins and cyanoprokaryotes that prove their cytotoxicity on Hs27 human skin cell line ($\Gamma 7.3$) and a high potential of cyanoprokaryotes and their metabolites to be a risk factor for

animals and human health in the studied water reservoirs (Г 7.3; Г 8.1). Such joint research is extremely important for integrating biological knowledge from different areas in elucidating the molecular mechanisms of pharmacological effects and creating new drug forms.

C. Applied contributions - innovative nanotechnological approaches and methods for creating medicinal forms

- *Nanostructured lipid carriers with included hyperforin* (from *Hypericum perforatum*) have been created for local application and enhanced wound healing (Г7.13). This scientific area with high applied potential is closely linked to the objectives of the Faculty of Pharmacy and the Department of Biochemistry, Molecular Medicine and Nutrigenomics.

The monograph, written by Dr. Vankova (B3 -117 pages): "*Role of some adipokines in the pathogenesis of socially significant diseases*", is an in-depth review of one of the most common metabolic regulatory disorders in adipose tissue, related to the integral role of adipokines (leptin, adiponectin, resistin, visfatin and retinol-binding protein 4) as modulators of biological processes (direct or indirect) throughout the organism, influencing neuroendocrine and immune functions with an impact on metabolically active tissues (liver, skeletal muscles and brain). Elucidating the molecular mechanisms of modern diseases such as obesity, cancer, cardiovascular pathologies, diabetes, etc. is one of the most modern biomedical fields and it requires an interdisciplinary approach and solid knowledge of biochemistry, molecular biology, genetics and immunology. The monograph includes the results of Dr. Vankova's scientific activity, and her courage to shed light on such complex and interdependent processes (from an extremely large number of factors) shows both scientific and creative writing growth, which confirms the readiness of Dr Vankova for habilitation.

The scientific activity and lab experience prove Dr. Vankova's abilities as a researcher and her transition to a new stage in career development with more teaching and lecturing activities and responsibilities, becomes a necessity.

4. Assessment of the educational and pedagogical activity

Dr. Deyana Vankova is an active teacher and as chief assistant has a high academic classroom workload (reference from the academic department attached) - ~400 hours/year, of which ~380 are practical exercises and ~10 hours of delimited lectures, both for bulgarian and foreign students. As an associated professor, Dr Deyana Vankova will give lectures in Biochemistry for students from different majors at the Faculty of Pharmacy.

I accept the certificate for fulfillment of the minimum national requirements under Art. 2b of Law for the Development of Academic Staff in the Republic of Bulgaria (LDASRB), for the Higher Education fields 4. Natural sciences, mathematics and informatics, Professional area 4.3 Biological sciences (Biochemistry), in which the chief asst. prof. Dr Deyana Vankova exceeds the points for a group of indicators Г, Д, Е.

5. Conclusion

As a member of the Scientific Jury for the announced competition, I support chief assistant professor Deyana Vankova PhD for academic growth and habilitation.

The scientific and applied contributions of Dr Vankova's research and highly rated publications exceed the requirements for awarding the academic position of "Associate Professor", referred to in the normative documents. The high teaching activity and participation in various scientific projects show that Dr. Vankova possesses the competencies and skills to be leader of scientific activity, she gained experience in training of doctoral students and working in team, which is an absolute necessity after habilitation and managing of her own research group with individual scientific expertise and

capacity. I confidently give my **positive opinion** and recommend the Scientific Jury to choose chief ass. prof. Dr. Deyana Vankova for academic position "Associate professor" in professional area 4.3. Biological Sciences, with a scientific speciality "Biochemistry" at the Department of "Biochemistry, Molecular Medicine and Nutrigenomics" of the Faculty of Pharmacy at the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

Prof. Svetla Petrova, PhD – member of the Scientific Jury

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

20th of May 2024

Sofia