

REFERENCE STATEMENT

within the call for **Professor position** in Biological sciences (Application of the principles of cybernetics in various branches of science (*in silico* study of bioactive compounds)) published in the Bulgarian State Newspaper, vol. 18 from 28. 02. 2020

by Prof. Dr. **Anela Nikolova Ivanova**
Sofia University, Faculty of Chemistry and Pharmacy,
member of the scientific jury appointed with Order № 198 from 16. 04. 2020
of the Director of the Institute of Biophysics and Biomolecular Engineering
of the Bulgarian Academy of Sciences

There is a single applicant for the position – Assoc. Prof. Dr. Ivanka Milosheva Tsakovska. She has been employed for more than 11 years as an Associate Professor in the group „QSAR and molecular modelling“ of the Institute of Biophysics and Biomolecular Engineering of the Bulgarian Academy of Sciences (IBPhBME-BAS). All required documents are available, together with information on additional criteria related to the selection procedure.

Dr. Tsakovska is a co-author of 66 scientific articles, among which 37 published in international peer-reviewed journals (Source: Web of Science), and of 3 book chapters. She has submitted for the selection procedure 24 publications (3 book chapters and 21 articles, 20 thereof published in international peer-reviewed journals). None of these has been used for the position of Associate Professor or for the PhD degree. Hence, in line with Art. 29, Sec. 1, P. 3, 4 of the Law for promotions in academia in Bulgaria (LPAB), they are used to evaluate the scientific contributions of the candidate. Dr. Tsakovska is first author in 4 of the papers and last one – in one of them. All articles are published in journals specialized in the area of the call, some of them being especially renowned in the field of research on bioactive compounds: Drug Resistance Updates (2 papers), Toxicology (2 papers), Antioxidants (1 paper), Phytomedicine (1 paper). The publications submitted for assessment have been cited 134 times in international peer-reviewed journals. The total number of independent citations of the publications of Dr. Tsakovska is 479 (Source: Scopus). The applicant has participated in the coordination of at least 5 European research projects, coordinated 2 and taken part in 6 more national research projects. She has had 2 long-terms post-docs abroad. Dr. Tsakovska has co-supervised 1 successfully defended and one ongoing PhD thesis. She is the recipient of 3 national awards in the period 2002-2004. The fact that she is an acknowledged scientist is corroborated by the fact that Dr. Tsakovska is a reviewer of manuscripts submitted for publication in more than 20 international scientific journals and member of the editorial board of 2 of them. She is also an evaluator of European and national research project proposals. Since 2008 Dr. Tsakovska has been teaching „QSAR and molecular modelling“ in the M. Sc. program „Computational Chemistry“ of Sofia University „St. Kliment Ohridski“ with excellent feedback from the students.

Dr. Tsakovska presents the following achievements to fulfill the minimum national criteria and the additional requirements of IBPhBME-BAS for occupying the Professor position:

- indicators group A - defended PhD thesis - 50 points out of minimum required 50;
- indicators group C – 9 publications in Q1 standing for a habilitation thesis, devoted to combatting multidrug resistance and elucidating the structure and interactions of the PPAR γ

receptor - 225 points out of minimum required 100;

- indicators group D - 15 publications different than those for the habilitation work, 5 of which in Q1, 2 - in Q2, 1 – in Q4, 3 – in journals with SJR, and 3 book chapters - 252 points out of minimum required 220;

- indicators group E - 134 citations of the publications submitted for evaluation - 268 points out of minimum required 120;

- indicators group F – co-supervision of 1 PhD student, coordination of 2 national projects (with secured third-party funding) and participation in 6 national and 3 international projects – 431 points out of minimum required 150.

It is evident from the above summary that the applicant either fulfills or goes beyond the minimum national requirements in all groups of indicators. The overall scientific metrics is in compliance with the general requirements of LPAB, the statutes for its application, and the additional recommendations of IBPhBME-BAS.

The research of Dr. Tsakovska is in the following directions:

- design of drugs to overcome multidrug resistance (papers 1, 2, 3);
- toxicity prediction, mainly by the discovery of compounds activating the receptor PPAR γ (papers 4, 7, 8);
- development of new pharmacophore models and study of the structure and interactions within bioactive receptor-ligand complexes (papers 5, 6, 9, 12, 15, 16, 18, 20, 21).

There are also several methodological publications (papers 10, 11, 14, 17, 19). The book chapters (papers 22-24) summarize the applicability of various *in silico* methods or structural representations of molecules for studying the biological activity of several classes of compounds.

The works employ diverse QSAR methods including both 2D and 3D techniques, in order to obtain a more comprehensive description of the intermolecular interactions. Combining the theoretical predictions with specially designed experiments is an advantage and in one case the experiments confirm the hypothesis predicted first by the computations. The predominant usage of structure-based methods for modelling is also commendable because they provide more accurate results. The synchronous utilization of QSAR and molecular dynamics simulations is very advanced. All computations are carried out at high level of expertise. The successful collaboration of the applicant with colleagues from other research groups in Bulgaria and abroad should be noted, too.

As a result of the research, new ligands are suggested, which inhibit or activate the following receptors: PPAR γ , the estrogen receptor- α , or P-gp, and the ligand-receptor interactions are explained better by structure-based design. A broad range of bioactive compounds of natural or synthetic origin are investigated and the most suitable ones for a given receptor are outlined. The areas of applicability of two molecular modelling approaches are delineated – docking and intercriteria analysis. The outcome of the studies enhances the understanding of the mechanisms of action of the target receptors and provides stable QSAR/pharmacophore models, which may be used to predict biological activity (molecular initiating events, toxicological/pharmacological pathways, toxicity) of a set of substances. The habilitation summary clearly presents the scientific merits contributing new knowledge and aiding the solution of the selected complex and timely problems.

Overall, the applicant has specialized very profoundly during the last decade in the direction of the call and I am convinced that she has the required scientific competence to continue advancing in the perspective research areas mentioned above. Her h-factor 12 (Sources: Web of Science и Scopus) is in support of this.

In summary, the materials submitted for the evaluation comply with all requirements of the law and with the additional recommendations of IBPhBME-BAS for a Professor position. This motivates me to assess positively the applicant Associate Professor Dr. Ivanka Tsakovska and to vote for her appointment as a Professor.

September 4, 2020

Member of the scientific jury:

/ Prof. Dr. Anela Ivanova /