OPINION

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About the competiton for the **Academic position "Associate Professor"**,
Announced in the **State Gazette, issue 69 from 16.08.2024**
Higher education Area: **4. Natural sciences, mathematics and informatics**
Professional field: **4.3. Biological Sciences**
Scientific specialty: **Biophysics**
For the needs of **Lipid-protein interactions Department, IBPhBME**

candidate: ***Assistant Professor Rusina Lachezarova Hazarosova, Ph.D***

I. REVIEW OF THE CONTEST MATERIALS PROVIDED FOR THE OPINION

By Ordinance No. 1350/14.10.2024 of the Director of the Institute of Biophysics and Biomedical Engineering — Bulgarian Academy of Sciences (IBPhBME-BAS), I have been appointed as a member of the Scientific Jury in connection with a competition for the Academic position of "Associate Professor" where the only candidate is ***senior assist. prof. Rusina Lachezarova Hazarosova, PhD.***

At the first meeting of the Scientific Jury, I have received the following documents: (1) Package of materials for participation in the competition; (2) Copies of the applicant's publications.

The candicate has attached in an very diligent and logical manner the full set of required documents. The procedure for opening and conducting the competition has been followed, as the documents have been prepared in accordance with the requirements stipulated in the Act on the Development of the Academic Staff in the Republic of Bulgaria (ADASRB), as well as the Regulations of the Council of Ministers, BAS and IBFBMI - BAS for its implementation.

II. SHORT CANDIDATE BIOGRAPHY

Rusina Hazarosova obtained her Master's Degree in "Cell Biology and Pathology" at the Faculty of Biology, Sofia University "St. Kliment Ohridski" in 2003. She began her scientific career as a biologist at the IBPhBME - BAS (2004), and for the period 2013 - 2016 she successfully developed and defended a PhD thesis for the educational and scientific degree "doctor" on the topic: "Influence of the biologically active molecules on the membrane organization", in the scientific specialty "Biophysics", "Lipid-protein interactions" department - IBPhBME. In 2017 Rusina Hazarosova has been chosen for the academic position "senior assistant professor" in the same department, where she works till now.

III. SCIENTIFIC RESEARCH ACTIVITY OF THE CANDIDATE

The scientific research activity of senior assist. prof. Hazarosova are simultaneously focused on current fundamental scientific problems of membrane biophysics, as well as an applied research studies. The main scientific research topic of the candidate is focused on investigations of the role of biologically active molecules on the membrane organization (composition and structure), in particular lipid rafts, as well as their importance for the cellular processes in norma and pathology. The investigation of specific molecular mechanisms of action and the relation between molecules, studied by assist. prof. Hazarosova and the native biological membranes and/or biomimetic model membranes, are of great importance for the detailed elucidation of their action, protective and therapeutic effects, as well as for the development of new biomedical approaches in the treatment and prevention of a number of diseases.

IV. PUBLICATION/ LECTURING ACTIVITIES & PROJECT PARTICIPATION

The candidate has provided a list of a total of 23 scientific papers for the entire period of her creative work (total impact factor: 56.108 for 18 publications and 5 with impact rank), of which 19 papers for the participation in the competition for the academic position "Associate Professor". H-index of the candidate is 5 (based on the publications included in the scientific information database). According to the provided scientific autobiography, some of the assist. prof. Hazarosova's research have been popularized among the scientific community with a total of 44 participations in national and international scientific forums. It is also provided a information for total participations in 2 international, 12 national projects, as well as for project-management of 1 national project.

The included 19 publications indicated for the participation in the contest are distributed as: total impact factor: 41.019 - 14 are in impact factor journals (5 in Q1, 5 in Q2, 3 in Q3 and 1 in Q4) and 5 in SJR journals (2 in Q3 and 3 in Q4). Overall quartile distribution: 5 in Q1, 5 in Q2, 5 in Q3 and 4 in Q4. The total number of observed citations is 48 (without self-citations of all authors). In the reference for the fulfillment of the minimal reqiurements, it can be seen that 6 scientific publications are included into the "Habilitation part". According to indicators B (117/100 fulffiled/required), G (231/220) and D (96/60), it completely covers, and on some of the indicators it exceeds the required number of points, legally determined by the Low for holding the position of "Associate professor".

V. ANALISYS OF MAIN FUNDAMENTAL AND APPLIED RESEARCH CONTRIBUTIONS IN THE FIELD

The main scientific contributions of the candidate are formulated as contributions with fundamental and applied character and they are framed at 2 groups: contributions included in the Habilitation work and those outside it.

Fundamental and applied contributions from the Habilitation work: This group summarizes fundamental and applied contributions related to detailed investigation and verification of new aspects in the mechanism of action of natural antioxidant agents. The effectiveness and activity of two naturally active substances - Myconoside (publications 2 & 3 - B4) and Resveratrol (publications 1, 4, 5 & 6 - B4) have been qualitatively studied in detail on cell lines and model lipid membrane. The antitumor, antioxidant and membrane organization modulating effects have been successfully demonstrated for the tested substances. A lipid environment dependent mechanism of action has been proposed for the both type of substances. All the obtained data are of great importance for a deeper analysis of bioactive compounds and their potential pharmacological actions in the context of prevention and treatment of pathological conditions.

Fundamental and applied contributions beyond the Habilitation work: There are 8 different categories of contributions in this group:

- The relationship between certain membrane-bound receptors (lipid raft-associated integrins) and specific lipid components of the rafts has been investigated. The role of these receptors in the formation and stabilization of cholesterol-rich raft domains has been demonstrated and elucidated.
- The molecular mechanisms of Halothane's action on lung cell line have been studied. The ultrastructural changes, proliferation, and ability of alveolar A549 cells to recover after Halothane treatment are thoroughly investigated. A genotoxic and cytotoxic effect on alveolar cells *in vitro*, after administration of Halothane in clinically significant concentrations, has been demonstrated, and a hypothesis of a relationship with stress-induced apoptosis and subsequent modulation of lung functions has been suggested.
- A different effect of the oxidized lipid palmitoyl-oxovaleroyl-phosphatidylcholine (POVPC) on membrane organization in mono- and polyunsaturated lipid matrices has been demonstrated. Based on the obtained data, it is suggested that the Ω-3 fatty acid DHA is able to compensate for the changes caused by the presence of oxidized lipids in the membranes and demonstrates a model of a structural protective role against the generation of oxidized lipids during the membrane-bound oxidative processes in the cell.
- A molecular mechanism of interaction of Chitosan-based nanoparticles with biological membranes is proposed - with fundamental and applied importance.
- An effect of oxidized lipids on the lipid order and activity of secretory phospholipase A2 has been demonstrated. For the first time, the lipid hydration and mixing protocol for the formation for model systems

composed of polyunsaturated and oxidized glycerophospholipids was found to be a critical parameter for establishing the lateral membrane organization and activity of sPLA2.

- The effect of the biologically active VV-hemorphin-5 (Valorphine) and its analogues on the structural organization, mechanical and electrical properties of the lipid membrane has been thoroughly investigated. It has been proven that the established effects on the molecular organization and physicochemical parameters of lipid bilayers are related to the membrane-mediated mechanisms of interaction of Valorphine with cells and subcellular structures (the basis for the development of liposome-based strategies involving hemorphins as therapeutic agents and biomarkers in neuropharmacology/ oncology).
- A different effect of nanomaterials on pathogenic bacteria - the most common causes of nosocomial infections - has been proven. In summary, the most cytotoxic for the tested bacteria are Se NPs, followed by Au-PVP (gold nanoparticles with polyvinylpyrolidone) and Au NPs. The SiO_2 NPs and Fe_2O_3 NPs can be successfully used as a drug delivery system, but at higher concentrations and as antibacterial agents.
- The importance of biochemical and biophysical structural and functional changes in lipid membranes (fatty acid composition and lipid arrangement) of red blood cells in the prognosis and treatment of coronary artery disease has been demonstrated.

I consider the so formulated contributions from candidate as an original and reflecting her overall scientific research activity. I am convinient, that all the contributions are essential for the development of the field of research - membrane biophysics, in the context of in-depth studies of the activity of bioactive compounds on the structural organization and biophysical/biochemical properties of cell membranes, adhesive contacts and cell viability, which occupy an important place in modern biomedical sciences. As another independent testimony for the quality of the excellent research results achieved with an active candidate's participation could be accepted the high number of the citations on the Hazarosova's research works.

VI. PERSONAL IMPRESSIONS

I have personally known senior assist. prof. Rusina Hazarosova for more than 10 years as a colleague from IBPhBME. My impressions of her are of a positive person, responsible and hardworking young scientist, with motivation for scientific work and potential for academic development. The candidate always shows a desire and readiness to participate in joint projects with her scientific expertise acquired over the years. I believe, that with her professional experience and competence, candidate contributes to increasing the authority not only of the "Lipid Protein Interactions" department, but also of IBPhBME-BAS in the field of natural sciences.

VII. CONCLUSION

All described above presents the candidate in the competition for academic position "Associate professor" – senior assist. prof. Rusina Hazarosova, PhD as a highly qualifiled and established scientist in the field of membrane biophysics and modern biomedical research. It is clearly shown, that she represents herself as a highly productive scientist, with extensive experience in project activity, able to work effectively in a research team, as well as to increase scientific output in accordance with generally accepted high international standards.

With respect to all the presented documents, the candidate meets all the requierments set by Low for holding the academic position "Associate professor". On the basis of the provided concourse materials and all publications, which provide visibility of the obtained results, as well as on the basis on the notability of the included scientific contributions, I recommend to the respected members of the Scientific Jury to propose to the Scientific council of IBPhBME – BAS to vote for the promotion of Rusina Lachezarova Hazarosova to the academic position "Associate professor" in professional field 4.3. Biological Sciences, Scientific specialty: Biophysics.

Date: 18.11.2024

Signature: ...

Sofia

/Assoc. Prof. Severina Semkova, PhD/