

STATEMENT

By Corresponding Member Prof. Ivan Gergov Mitov, Medical University, Faculty of medicine, Sofia

Regarding: Competition for the academic position "Associated Professor", Scientific field - Biological Sciences (Microbiology), announced in the State Gazette issue 47/22.05.2020

Dr. Violeta Valcheva Ruseva completed her biological education at Sofia University "St. Kliment Ohridski", Sofia, in speciality "Biotechnology" in 2002. In 2003-2005, she continued her education and received Master's degree in Microbiology and Microbiological Control. In 2005 she entered the Institute of Microbiology - BAS as a doctoral student and defended her dissertation "Molecular genetic characterization of *Mycobacterium tuberculosis* strains isolated from different regions of Bulgaria" and obtained the educational and scientific degree "Doctor of Microbiology". Since 2009, she continued to work at the same institute as Assistant Professor. In 2005-2019, she improved her professional qualification through specializations and courses in the field of tuberculosis and mycobacteria at the Central Children's Hospital - Beijing, Pasteur Institute in St. Petersburg, Institute Pasteur - Guadeloupe, France, Centre Pasteur - Hong Kong, Institute Pasteur - Athens, Center for Disease Control in Shanghai, etc. She is a member of a number of scientific societies such as the European Society of Mycobacteriology, Federation of European Microbiological Societies, Union of Scientists in Bulgaria, International Society of Infectious Diseases, European Society of Clinical Microbiology and Infectious Diseases. Her scientific competence is recognized with the invitations at national and international conferences and the preparation of over 130 peer-reviews of scientific articles, projects and opinions. She is fluent in written and spoken English, French and Russian.

Dr. Violeta Valcheva Ruseva participates in this competition with 24 scientific papers as follows:

- Dissertation on "Molecular genetic characterization of *Mycobacterium tuberculosis* strains, isolated from different regions of Bulgaria."
- Articles in international journals with a total impact factor of 39,214; Total of 15 articles, including papers in peer-reviewed journals such as *Molecular Phylogenetics and Evolution*,

Infection, Genetics and Evolution, Antimicrobial Agents and Chemotherapy, European Journal of Medicinal Chemistry, International Journal of Antimicrobial Agents.

- Articles in referenced international journals without impact factor - 1
- Articles in referenced Bulgarian sources -
- Chapters in international books - 2
- Proceedings of national forums with foreign participation, published in full text - 1
- First author in 7 publications.

The results of the scientific production have become available to the scientific community and with participation in 44 scientific events, 30 of which abroad.

The works of Dr. Violeta Valcheva Ruseva are widely known to the international scientific community. A list of 241 citations of 28 articles is presented, of which 238 in foreign sources and 3 in Bulgarian sources.

In the period 2006 - 2019, her research was supported by participation in 14 research projects and consortiums funded by BAS, NSF, COST (International Consortium for Nucleum Research), FATE (Fight Against Tuberculosis in Central and Eastern Europe) , Council of Medical Science of MU-Sofia, National Diagnostic and Research Veterinary Medical Institute, 7th Framework Program, NATO.

For her active research activity Dr. Valcheva was awarded with three prestigious awards: for best scientific publication of a young Bulgarian microbiologist for 2008 from "Foundation Prof. Dr. Stefan Angeloff" and awards for High scientific achievements of a young researcher, Union of Scientists in Bulgaria, Section "Microbiology" in 2009, 2011.

The research activity of Dr. Valcheva and her contributions are focused on the study of microbiology, molecular biological characteristics, mechanisms of drug resistance and epidemiology of *M. tuberculosis* and *M. bovis* and antimycobacterial activity of new compounds suitable for development as drugs. A wide range of classical and modern microbiological, molecular biological and genetic methods have been used in the studies, such as PCR, RLFP fingerprinting, spoligotyping, MIRU-VNTR, DNA sequencing and others.

The most significant of her outstanding contributions to the advancement of science are as follows:

Identification and molecular genetic studies on the causative agents of tuberculosis in animals.

- The first for Bulgaria study of the genetic diversity of *Mycobacterium bovis* strains circulating in Bulgaria in the field of animal husbandry was conducted.
- For the first time in the country the presence and circulation of *Mycobacterium caprae* strains has been established.

Molecular epidemiology, drug resistance, phylogenetics and evolution of *M. tuberculosis*.

- It has been proven that the migration of the human population is a major factor shaping the phylogeography of *M. tuberculosis*.
- A low frequency of Latin American and Mediterranean (LAM) phylogenetic family of *M. tuberculosis* in Bulgaria has been established.
- The population structure of *M. tuberculosis* in Bulgaria is heterogeneous and it is dominated by several globally widespread international (ST53, ST47, ST34) and Balkan (ST125, ST41, ST284) spoligotypes, which is not associated with the development of drug resistance. The *M. tuberculosis* spoligotype ST125 is specific for our country.
- *M. tuberculosis* in prisons in Kyrgyzstan has significant similarity to the causative agents in Northwest Eurasia (mainly Russia) and low similarity to those in East Asia.
- IS6110-inverse-PCR and VNTR (by applying hypervariable loci) are effective in detecting and identifying subtypes of strains of the Beijing family.
- Population-based analysis and drug resistance studies of *M. tuberculosis* strains circulating in the Beijing region show that Beijing strains, subdivided into ancient and modern sublines, predominate. A stronger connection with resistance is observed in the ancient sublines.

Studies on L-forms in mycobacteria and staphylococci.

- A molecular genetic method (spoligotyping) for identification and typing of L-forms of *M. tuberculosis* strains has been optimized. The ability of L-forms to grow faster than classical tuberculosis bacteria has been confirmed.
- In susceptible (*mecA*-negative) and heteroresistant (*mecA*-positive) strains of *Staphylococcus aureus*, the conversion to L-forms has been demonstrated and the presence of methicillin resistance has been demonstrated. The development of methicillin resistance in strains with the *mecA* gene does not affect their adaptation to environmental changes.

Methicillin-sensitive strains within the heterogeneous population without the *mecA* gene respond to adverse environmental factors by transforming them into L-forms.

Development of new compounds with antimycobacterial activity.

- New 2H-chromium or coumarin bound acylhydrazones have been synthesized. Molecular modeling proved the role of certain structural fragments for their antimycobacterial activity.
- More than 110 new chemical structures have been synthesized, including more than 50 compounds derived from natural terpenoids and camphor scaffold. Several of the amide derivatives, structurally close to the anti-tuberculosis chemotherapeutic ethambutol, show significantly higher activity compared to the reference strain *M. tuberculosis* H37Rv. The role of the configuration of the obtained compounds for their bioactivity is proved.
- The high antimycobacterial activity of compounds with (R) -2-amino-1-butanol and (S) -2-amino-1-butanol, square acid amides, heterocyclic camphor derivatives are suitable for further development of new anti-tuberculosis drugs.

Along with the extensive scientific activity, Dr. Violeta Ruseva also conducts educational activities. She was a research consultant to two successfully defended PhD students and a second research supervisor of a student who prepared an MS thesis.

CONCLUSION

The presented scientific production confirms that Dr. Violeta Valcheva Ruseva is an established and recognized specialist in research on tuberculosis in humans and animals using a wide array of modern molecular biological methods. She participates in this competition with a significant number of scientific papers in scientific periodicals with a very high impact factor and a considerable number of citations by foreign and Bulgarian authors, many times exceeding the requirements of the Law of the Development of the Academic Compositions in the Republic of Bulgaria and the Rules for its application at the Institute of Microbiology, BAS. All this gives me a reason to strongly support the academic position "Associate Professor" in Microbiology to Dr. Violeta Valcheva Ruseva

11/09/2020

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/Corresponding Member Prof. Ivan Mitov/