To the attention of:
Prof. Dr. Varban Ganev, DBSc,
Chairman of the Academic Jury
Faculty of Medicine at Sofia University "St. Kliment Ohridski"
city of Sofia

STATEMENT

by Prof. Dr. Vili Krasteva Stoyanova, MD

Department of Pediatrics and Medical Genetics, Medical University, city of Plovdiv, external member of an Academic jury, appointed by Order of the Rector of Sofa University "St. Kliment Ohridski", city of Sofia- № RD 38-601/16.12.2020.

Regarding: a competition for holding the academic degree of "Associate Professor" in academic field 7.1. Medicine, major "Medical Genetics" for the needs of the Faculty of Medicine at Sofia University "St. Kliment Ohridski", city of Sofia, announced in State Gazette, ed. 88 date: 13.10.2020.

Only one applicant has submitted documents for participation in the competition- **Dr. Radoslava Vasileva Vazharova.**

The presented materials for the competition have been prepared in compliance with the requirements of the Law for the Development of the Academic staff in the Republic of Bulgaria and the Regulations for its application at Sofia University "St. Kliment Ohridski".

Professional development

Dr. Vazharova has more than 25 years of experience as a lecturer in Medical Genetics. She acquired the major of Medicine at the Medical Faculty of the Medical University, city of Sofia in 1994 (Diploma № 012341, reg. № 41201/27.12.1994). Since then she has been working consecutively in leading university departments in our country: Department of Medical Genetics, Faculty of Medicine, Medical University, Sofia (1994-2008), Department of Obstetrics and Gynaecology, Faculty of Medicine, Medical University, Sofia (2008-2012), Department of Biology, Medical Genetics and Microbiology, Faculty of Medicine, Sofia University "St. Kliment Ohridski", city of Sofia (since 2012 till present).
She has an acquired major in Medical Genetics since 2000 (certificate Series AS № 006691, reg. № 004828/10.02.2000). Besides being a lecturer since 2012, Dr. Vazharova has also been working as a geneticist at a private clinic "Dr. Malinov". Her distinguished academic career began in 2016 when she successfully defended a dissertation for the educational and academic degree Doctor in Genetics with topic "Analytical approach for detection of genetic disorders in rare diseases via new generation of DNA sequencing (diploma Series MUS № 000486, reg № 429-D/20.07.2016).
Dr. Vazharova conducted a few courses for an additional qualification: FISH analysis - December 2007, Department of Genetic Ecotoxicology, The Institute of Experimental Medicine, Prague, Czech Republic; ArrayCGH analysis - November 2008, BlueGnome, Cambridge, UK; November 2009 - Genetic Laboratory of Gustave Roussy Institute, Paris, France; May 2010, OGT, Oxford, Begbroke,UK.
Besides her direct responsibilities as a lecturer, Dr. Vazharova has proved her excellent qualities as an accurate researcher in serious studies - participation in 4 research projects: as a co-author and

participant in 1 international project with topic "Functional role of follicular helper and regulatory T cells for the production and maintenance of the levels of SARS-CoV-2 neutralizing antibodies" and three projects funded by the NSF, MES - as a leader of one of them with topic "Innate immune response to RNA-viral pathogens. Evaluation of the role of variants in genes of RLRs /TLRs signal pathways of the host using a model of SARS-CoV-2 invasion" (KP-06PN-43/31) and as a member of the research team in two others: "Characterization of longevity genes via genomic and target sequencing" (DN03/7 (18.12.2016) as well as "Comparative characteristics of genomic/exomic spectra and antibody repertoire in Bulgarian patients with Alzheimer's disease, with frontotemporal and unspecified dementia" (KP-06PH33/5 date: 13.12.2019).

Dr. Vazharova is a respected and renowned specialist in Medical Genetics. Her prestige is proved by her membership in the Bulgarian Society of Genetics and Genomics; Bulgarian Alliance for Precise and Personalized Medicine; Union of Scientists in Bulgaria; European Society of Human Genetics.

Academic- research activity

Dr. Vazharova presents for an assessment of her research activity 51 true publications, 3 of which are correctly derived, presented and reviewed for acquiring the educational and academic degree of "Associate Professor" (1 with IF).
She participates in the competition for acquiring the academic position of "Associate Professor" with 48 true publications (beyond the dissertation work):
- 22 in journals referred and indexed in world-famous databases with academic information (20 of them with IF - total impact factor 37,756)
- 26 publications in non-referred journals with academic review (5 of them in international journals).

Furthermore, the applicant has 49 participations in academic forums. 33 of them are beyond those for acquiring the academic degree Doctor: 29 at international academic forums (2 spoken presentations and 27 posters) and 4 at national academic forums. The abstracts of 27 participations in international congresses (without full text) have been published in academic journals with impact factor.

Most of the publications in journals with IF are prepared by research teams. In three of them Dr. Radoslava Vazharova is the first author, in 4 – the second one and in 15- third and consecutive. She is the first author in 9 published reviews out of 33 total.

Studying the academic work of Dr. Vazharova, an impressive trend of a searching and skillful researcher emerges. An indirect but reliable criterion for the quality of the publications are the 208 citations (according to SCOPUS and Web of Science databases) of all publications (without auto-citations).

Dr. Vazharova's research is in the following main directions:
- Rare genetic diseases: mechanisms of occurrence, variability of phenotypic expression, approaches for genetic diagnosis, screening and prevention;
- Application of modern methods for genetic diagnosis - microarray, massive parallel sequencing in patients with congenital anomalies, malformative syndromes and intellectual deficits;
- Genetic predisposition to psychiatric diseases;
- Genetic factors for longevity.

10 articles published in journals with impact factor (total impact factor 11,719) are presented as habilitation work. 4 of these publications have been cited 41 times, 19 of the citations were in the last

5 years. These publications address problems in the field of rare chromosomal and monogenic diseases in humans and the approaches to their diagnosis – pre- and postnatally. The diverse etiology, the variability of the clinical manifestations and the low population frequency of the individual nosological units classified as rare diseases make them a difficult object to study.

Dr. Vazharova works with modern genetic methods which she successfully applies for:
1/ clarification of the etiology and phenotype-genotype correlation of rare chromosomal/microdeletion/microduplication syndromes, malformative syndromes and intellectual deficit (№4; №5; №6; №7);
2/ clarification of the genetic defect of extremely rare monogenic diseases in humans: infantile epileptic encephalopathy type 13; one of the rare forms of 5-alpha reductase deficiency and PMM2-CDG. Early detection of the etiology of these rare genetic diseases gives patients a chance for a proper plan treatment (if possible) and their families to be able to plan reproduction and avoid giving birth to children with disabling incurable diseases. (№1; №2; №3; №10);
3/ for detection of fetal aneuploidies via DNA fragment analysis of polymorphic STR markers (№8; №9).

Dr. Vazharova's publications are up-to-date and innovative. They prove her professionalism as a specialist in Medical Genetics.
The analysis of the academic work shows a wide range of topics which did not prevent the applicant to achieve in-depth and academic-applied results with pointing out numerous contributions leading to a large number of citations.

The most significant are the applicant's achievements in studying the clinical and genetic characteristics of congenital anomalies - polymalformative syndromes; monogenic and chromosomal disorders. Dr. Vazharova is one of the leading researchers in the country who has contributed to the development and implementation of innovative methods for genetic analysis - SNParray, arrayCGH, massive parallel sequencing of an eczoma which allow high-resolution comprehensive genome screening to improve both genetic diagnosis of congenital anomalies as well as genetic counseling and development of strategies for prevention and treatment. She contributed to the identification of new variants associated with monogenic diseases: two new variants in the CYP11B1 gene have been identified (both mutations have not been previously reported as pathogenic in the literature) in nonclassical 11β-hydroxylase deficiency (№16). She expanded the knowledge of neurofibromaosis type 1 by presenting patients from families with NF1 and sporadic cases with clinical heterogeneity including rare symptoms (№32); a rare microdeletion 2p24.3-25.1 was found in a child with severe mental and physical retardation (№24).

The results of the genetic research in cardiovascular diseases are also significant: mutations in the ACTA2 gene have been found in patients with large vascular pathology (№28); in a patient with a complex phenotype (Fallot's tetralogy, Meckel's diverticulum, microvesicular steatosis and hepatic hypotrophy, etc.). New, unreported in the literature and one known, extremely rare variant in the CPT2 gene were found (№23); in the study process of genetic variants associated with ischemic heart disease (IHD) five variants were identified with priority as related to IHD in the studied Bulgarian extract (№19).

The achievements in detection of phenotype-genotype associations in psychiatric diseases are also serious:
- Through a comprehensive genomic associative study (GWAS) followed by a replicative study, the genetic etiology of bipolar affective disorder (BAD) was analyzed in the Bulgarian population.

Results of an associative study type "cases-controls" of BAD in which 191 SNPs were genotyped suggest that the HTR5A gene might play an important role in the pathogenesis of BAD for our population (№13; №14).
- The genetic predisposition to schizophrenia was studied. A comprehensive genomic associative study was performed and a significant association was found between schizophrenia and intron SNP rs7527939 in the HHAT gene which is proposed as the strongest indicator of predisposition to schizophrenia in the Bulgarian population (№20; №21; №25).

An extremely valuable contribution of academic-applied nature are the 14 extremely rare gene variants with phenotypic significance (pathogenic, probably pathogenic, VUS) which are deposited in the ClinVar database.

The gained experience of the applicant in the use of avangard methods for genetic analysis allows her to offer modern approaches to genetic diagnosis of idiopathic mental retardation; microdeletion syndromes; lysosomal diseases (№29; №30; №31; №34).

Dr. Vazharova not only knows, studies in details and shares her results but she can also be considered a mature and promising scientist.

Teaching activity

Dr. Vazharova has an extremely large teaching activity. According to the presented reference (Appendix 6) in the last 5 years the study workload of the applicant is over 1600 hours annually. This includes conducting exercises in Medical Genetics (in Bulgarian and in English) to students in Medicine and participation in semester exams. She participates in the preparation of 2 textbooks and has 4 publications in edited collective works.

The presented reference for meeting the minimum national requirements for the respective academic field (400) and the real points of Dr. Radoslava Vazharova (3508,71) show that the applicant covers and exceeds the quantitative scientometric indicators according to the approved regulations and criteria.

Conclusion: Dr. Vazharova is a skilled creative personality. She is aspiring and capable researcher with significant academic achievements, academic-applied contributions widely covered in international and national journals with impact factor and good citation of publications. She has detailed knowledge in various fields of Medical Genetics which she successfully applies in practice. She has great prestige among colleagues, patients and students.
Based on the materials provided in the competition, I can say that Dr. Radoslava Vasileva Vazharova fully meets the requirements of the Law for the Development of the Academic Staff in the Republic of Bulgaria and the Regulations for its application at Sofia University "St. Kliment Ohridski" for holding the academic position of "Associate Professor" in the academic degree of Medicine, major Medical Genetics.
I highly recommend that the members of the respected Academic jury award Dr. Radoslava Vasileva Vazharova the academic position of ASSOCIATE PROFESSOR in the academic degree of Medicine, major Medical Genetics for the needs of Sofia University "St. Kliment Ohridski", city of Sofia.

03.02.2021

Written by:
/Prof. Dr. V. Stoyanova, MD/