

TO THE ATTENTION OF THE MEMBERS  
OF THE SCIENTIFIC JURY DETERMINED  
BY ORDER P-109-276/25.05.2023 of the RECTOR OF THE MEDICAL  
UNIVERSITY "PROF. DR. PARASKEV  
STOYANOV", VARNA

**Subject:** Submitted documents for participation in the competition of the Medical University of Varna (announced in State Gazette No.28/28.03.2023 ) for the academic position of Associate Professor in the specialty "Virology", professional field 4.3., Biological sciences, field of higher education 4. Natural Sciences, Mathematics and Informatics for the needs of the Department of Microbiology and Virology, Faculty of Medicine, on the ground of art. 4q par. 1 and para. 2 of the Academic Staff Development Act of the Republic of Bulgaria (ASDA) and Art. 1 and para. 2 of the Regulations for the Implementation of the Law on Academic Staff Development , art. 6, para. 1, art. 127, para. 1 and para. 2 of the Regulations for the Development of the Academic Staff at the Medical University - Varna to **D-r Denitsa Todorova Tsaneva-Damyanova Ph.**

According to the Protocol 3/15.05.2023 of the meeting of the Faculty Council of the Faculty of Medicine at MU-Varna and by the order R-109-276/25.05.2023 of the Rector of MU-Varna I am appointed as a member of the Scientific Jury (SJ). According to the protocol 1/06.06.2023 from the first meeting of the SJ I am appointed to prepare **an opinion** on the above procedure for filling the academic position, with the only candidate **D-r Denitsa Todorova Tsaneva-Damyanova Ph.**

**STATEMENT**

by Assoc. Prof. **D-r Liliya Ivanova Ivanova, PhD, Associate Professor SMDL "City Lab"**  
Varna

**Brief biographical data:**

D-r Denitsa Todorova Tsaneva-Damyanova was born in 27.02.1983 in Varna. In 2001 she graduated from the III Natural and Mathematical High School "Academician Metodiy Popov"-Varna (profile - biology with advanced study of English) and from the V Language High School "John Exarch" with an equivalency exam in English, for which she provided the relevant certificates. She obtained a Master's degree in Medicine at the Medical University "Prof. Dr. Paraskev Stoyanov"- Varna in 2007 with a professional qualification of a doctor. In 2021 she obtained a Master's degree in Health Management and Medical-Social Care. She worked successively as a paramedic and a medical resident at the Medical Center - Varna and a sales representative at UCB-The Allergy company (2007-2008). Since 01.02.2012 till now he is a Doctor-Virologist, Head of Virology Laboratory at MDL "Status", Varna. Since 2015 she has been appointed as Honorary Assistant Professor at the Department of Microbiology and Virology of MU-Varna, and since 2016 - as a full-time Assistant Professor at the same Department. Since 2019 she has been a senior assistant professor at the Department of Microbiology and Virology of MU-Varna. D-r. Tsenitsa Tsaneva Damyanova is a full-time clinical resident in virology from 2008 to 2011. She obtained her medical specialty in Virology in 2012. From 2016 to 2019 she is a PhD student at the Department of Microbiology and Virology of MU-Varna; specialty. In 2019, he successfully defended his educational and scientific degree "Doctor" in the scientific specialty

"Virology" and dissertation work on "Clinical and laboratory study on the prevalence of viral hepatitis B and D in the general population and in patients with chronic liver diseases in Northeastern Bulgaria. Duration of HBV-postvaccinal immune response in vaccinated persons". D-r Tsaneva-Damyanova continues to improve her qualifications over the years. She has participated in Introductory Computational Biology course - Medical University - Varna (2021), Course "Pedagogical and Andragogical Competence for Teachers and Doctoral Students (2022)", in 23 Training (on-line, webinar) seminars mainly related to the Covid-19 pandemic (2020 - 2023). Dr. Denitsa Tsaneva-Damyanova participated in 4 research projects, 3 of which were funded by the Science Fund of MU-Varna and one by the National Program "Young Scientists and Postdoctoral Researchers" of the Ministry of Education and Science.

She speaks English fluently, French at a very good level and German at a beginner level.

### **Teaching activity**

D-r Denitsa Tsaneva-Damyanova's teaching activity is significantly above the required minimum. For the last years she has between 280 and over 300 hours of annual teaching load with practical classes and lecture course with the students in the faculties of medicine, dentistry and pharmacy at MU-Varna in the discipline "Microbiology and virology", taught in Bulgarian and mainly in English.

### **Science metrics:**

In the period 2015 - 2023 D-r Tsaneva-Damyanova developed and successfully defended her dissertation on "Clinical and Laboratory Study on the Prevalence of Viral Hepatitis B and D in the General Population and in Patients with Chronic Liver Diseases in Northeastern Bulgaria. Duration of HBV-postvaccinal immune response in vaccinated persons" (indicator A1 - 50 points).

Developed a habilitation thesis on "Hepatitis D virus (HDV) satellite in the orbit of chronic hepatitis B virus" - review and own data (100 points). A total of 14 scientific publications (indicator D7, articles D7 - 1 - D7 - 14 in the academic transcript) in journals refereed and indexed in world-known databases of scientific information (Web of Science and Scopus) are presented in the academic transcript, of which in 2 scientific publications he is an independent author.

One of the independent scientific publications has an IF of 2.116. She is co-author of a book chapter (index G8, paper G8-1). Total indicators G5 - G10 - 207 points against the required 200 points. Submits a list of 26 citations (indicator D11 - 52 points total). Out of 3 full-text publications in scientific journals and collections beyond the minimum scientific requirements for the academic position of Associate Professor, 2 are chapters from the Manual for Students of Medicine, Dentistry, Pharmacy and Medical College Varna (2011, Zograf Publishing House - Varna, ISBN 978-954-15-0226-6) and 1 - full-text publication in a scientific journal refereed and indexed in world-known databases of scientific information Web of Science and Scopus (Hepatitis A and Hepatitis E virus in patients with acute hepatitis - a three-year hospital-based, retrospective study, 2022, Acta Microbiologica bulgarica) - 12 points. Participated in a total of 14 international and national scientific forums with 14 papers and poster presentations, mainly in English.

### **Evaluation of research activities and contributions:**

The candidate D-r Denitsa Tsaneva-Damyanova has developed significant research activity in the period 2015 - 2023. The main topics of the scientific publications and the scientific contributions are grouped in 4 areas:

***Hepatitis viruses- HBV (hepatitis B), HDV (hepatitis D), HCV (hepatitis C) (Monograph B3; Publications G.7.6; G7.7; G7.9; G8.1).***

Viral hepatitis continues to preoccupy the scientific community both diagnostically and therapeutically. Parenterally transmitted hepatitis viruses (HBV, HCV, HDV) are highly significant viruses causing infections in diverse populations. Dr Tsaneva-Damyanova's research in the field of **viral hepatitis** is extremely thorough and covers many aspects of infections with certain hepatotropic viruses: they contribute greatly to focusing attention on them. Infection with these viruses is defined and in comparative aspect with previous studies, determined the tendency to reduce their spread due to mass immunization and awareness of citizens and the medical community that led to mass testing of hospital and outpatient patients. The role of occult, "serologically quiet" HBV infections – a serious problem in transplantation and immunosuppression – has also been defined very thoroughly. HBV and HCV reactivation was found in immunosuppressed patients with a sharp increase in viral replication. A large-scale study of HBV-post-vaccinal immunity in immunized individuals is one of the first in the country and shows that only about 1/3 of them have a detectable immune response after the age of 15.

This inevitably requires a revision of the immunization calendar and determining risk groups for re-immunization. Isolation, sequencing and genotyping of the hepatitis D virus has been carried out for the first time in Bulgaria in order to define the dominant HDV genotype circulating in Bulgaria.

Particular attention should be paid to the monographic work /Monograph B3/ of Dr. Tsaneva-Damyanova. The main focus is on the most unique human virus – HDV, the only satellite of HBV. An overview is made on existing data from literature, history of virus detection, classification, morphology, biological properties and unique replication of this virus. Own data from the studies were included, with emphasis on chronic double HBV/HDV infection and its consequences. The monographic work was particularly precisely written and was a significant contribution to medical science and practice. For the first time in Bulgaria, a detailed description of the existing legislation and surveillance regarding chronic diseases has been made in the section on the prevention and control of chronic viral hepatitis. For the first time in Bulgaria, a survey is presented among patients with chronic hepatitis D, taking into account their awareness of the disease, as well as its impact in everyday life - disease management, combating stigma and discrimination

***Herpes viruses - EBV (Epstein-Barr virus), CMV (cytomegalovirus) (Publications G7.1; G 7.2; G7.3; G7.5; G7.8; G7.10; G7.11; G7.12; G7.13).***

Large scale seroepidemiological studies have been performed on the prevalence of the most massive latent viral infections induced by CMV and EBV depending on age and sex. The onset and incidence of primary infections is defined, as well as the degree of infection with advancing age. The role of these viruses in the most at-risk groups such as women of childbearing age, pregnant women and newborn children is defined. Many modern methods of diagnosis and a combination of them (various ELISA tests, Western blot analysis) have been used to define primary infection, particular forms of primary infection and reactivation of infection. An outstanding contribution is the use of various additional laboratory methods, the capabilities of which are thoroughly analyzed in the presented scientific publications.

The IgG avidity of EBV infection prescription, anti EBNA 1 for differentiating acute from pre-existing EBV infection, immunoblot for defining acute EBV infection and PCR techniques in immunocompromised patients help diagnosis and prognosis.

For the first time in the country, a molecular biological (PCR) method has been applied for the diagnosis of primary EBV infection and relatively with serological markers - in defining reactivation of infection in patients with Hodgkin's disease, non-Hodgkin lymphomas and other immunosuppressed patients. A competent assessment of the importance of each of them was made and criteria were formulated to improve the diagnosis of EBV and establish viral reactivation in potentially at-risk patients.

**Viral infections in transplanted and immunocompromised individuals. (Publications G7.9; G7.10; G7.12; G7.13; G7.14; G8.1).**

In recent decades, the number of immunocompromised individuals is growing rapidly due to more intensive antitumor therapy, transplants and concomitant immunosuppressive therapy, increasing HIV positivity. Immunosuppressed patients are very often affected by nosocomial infections in hospitals and infections in society. The viruses involved in this process are many in number, but Epstein Barr virus (EBV) one of the leading ones Cytomegalovirus (CMV), Herpes simplex viruses (HSV1, HSV2), Varicella zoster (VZV), hepatitis B virus (HBV), hepatitis C virus (HCV) and human polyomaviruses (BKV, JC).

The established high seroprevalence and respectively infection in a general population with EBV unequivocally reflects in the need to introduce into routine practice methods for establishing the reactivation of these latent viral infections in patients under immunosuppression for the underlying disease, after transplantation of solid organs and hematopoietic stem cells. With immune deficiency, this reactivation leads to a disease with a much longer course and a complicated outcome.

In this section, the risk of developing EBV-induced lymphoproliferative diseases in immunosuppressed patients is defined as a possible marker of viral reactivation. In a seroepidemiological study in patients with non-Hodgkin lymphomas, a higher than average for northeastern Bulgaria and the country frequency of HBsAg and anti-HCV positivity was found, with HBV markers being more prevalent compared to those of HCV.

In another study in patients at risk-Hodgkin's lymphoma, non-Hodgkin's lymphoma, patients under immunosuppression (acute myeloid leukemia) and patients with primary infection (infectious mononucleosis), a comparative analysis of the primary immune response against major antigens (VCA) and EA (D) was performed to determine the antibody response to the early EA (D) antigen as a marker of reactivation.

It was applied for the first time in the EBV-Real time PCR method compared to serological markers in immunosuppressed patients. The applied PCR techniques in different groups of patients at risk prove that this is the method of choice in monitoring the severity of infection and determining a specific treatment.

Study (G7.14) analysed the most common clinical symptoms leading to the search for and demonstration of HIV seropositivity (pneumonia not amenable to conventional treatment, lymphadenopathy, hepatitis, mononucleosis-like syndrome, chronic diarrhoea and weight loss, neurological symptoms, recurrent Herpes zoster, arthralgia with rash. Patients living with HIV in the study were most infected with syphilis and/or had active CMV infection.

**SARS-CoV-2 virus (COVID-19). (Publication G7.4).**

The current SARS-coV-2 is not overlooked in the scientific research activity of D-r Tsaneva-Damyanova. In a large-scale study of 586 serum samples of outpatients, a seroepidemiological screening assay for carrying specific antibodies to the virus was performed. Screening tests are

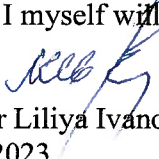
essential to define the spread of the virus, the formation of herd immunity, prevention and algorithms for the treatment of infection.

The candidate D-r Denitsa Todorova Tsaneva-Damyanova presents in this competition as a major part of her research and practical activity contributions divided into several directions listed above. I fully accept the submitted scientific papers (Monographic work and publications) and references, which the candidate for associate professor presents because:

1. Contain results and analyses based on personal studies useful for scientific knowledge, laboratory diagnosis and clinical practice, especially in the field of chronic and latent viral infections.
2. Present consistent and in-depth information on the regional spread of a wide range of viral agents and laboratory diagnostic options for determining the status of viral infection and the need for specific antiviral therapy in patients with chronic HBV/HDV infections, immunosuppressed and immunocoprometed patients.
3. The habilitation monographic work "Hepatitis D virus (HDV) satellite in the orbit of the chronic hepatitis B virus". The review and own data represent the first for the country extremely thorough and precisely written analysis of this little-known virus. The monographic work is extremely useful for specialists with different medical focus, mainly: virologists, microbiologists, gastroenterologists, infectionists, as well as medical students and postgraduates, public health officials, as well as researchers with a deeper interest in the field of hepatology.
4. Show scientific production and educational activity that meet the quantitative requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria (RASA) and the Rules for the Development of Academic Staff at the Medical University – Varna.

**Conclusion:** On the basis of the materials provided to me for the preparation of an opinion on the application for JSC "Associate Professor", after a careful analysis of all documents, I accept as fully appropriate the candidacy of D-r Denitsa Todorova Tsaneva-Damyanova, taking the liberty of politely recommending to the honorable members of the Scientific Jury at MU-Varna to vote positively, as I myself will do.

Signature:

  
Ass. Prof. D-r Liliya Ivanova Ivanova, MD, PhD  
Varna 25.07.2023