

REVIEW

by

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member of the Scientific Jury

(Order No P-109-232 from 02.06.2021 of the Rector of the Medical
University - Varna)

according to announced in the State Gazette, issue 27 from 02.04.2021 by the
Medical University of Varna - **competition for academic position**
"Associate Professor" in the field of higher education 7. Health and sports;
professional direction 7.1. Medicine; specialty Nervous diseases

Subject: The candidacy of **Dr. Detelina Stoilova Zhelyazkova, PhD** in
the competition for academic position "Associate Professor" announced by the
Medical University of Varna

One candidate, *Dr. Detelina Stoilova Zhelyazkova, PhD*, who fulfills all
the requirements of the announced competition in accordance with the Rules
for Implementation of the Law on The Development of the Academic

Composition in the Republic of Bulgaria (LDACRB) and the Development Regulations of the Academic Staff of the Medical University of Varna, has appeared in the announced competition, namely:

1. Scientific degree "Doctor of Medicine" from 2013;
2. Recognized Specialty in Neurology since 2002;
3. Teaching activity since 2002 consecutively as an assistant, senior assistant and chief assistant in the Neurology Clinic at University Hospital "Alexandrovska"; and since 2011 as chief assistant in the Neurology Clinic at the University Hospital "St. Ivan Rilski", Sofia;
4. Outlined profile of the scientific activity in the context of cipher 03.01.19 Neurology, professional direction 7.1. Medicine;
5. A sufficient number of scientific publications:
 - 5.1. Dissertation on the acquisition of educational and scientific degree "Doctor" (2012);
 - 5.2. One single-author monograph (2019);
 - 5.3. A total of 30 scientific work;
 - 5.4. List of 22 publications in publishers of the National Reference List and in edited collective works;
 - 5.5. Participation in 4 neurology textbooks, of which one is in English;
 - 5.6. Total Impact Factor 5.0 from 6 publications in scientific journals, referenced and indexed in a global database;
 - 5.7. Applied number of citations - 7 in international journals, indexed in world databases (Scopus and Web of Knowledge);
6. In 33% of the submitted publications Dr. Detelina Stoilova Zhelyazkova, PhD is the first author and in 29% of them – a second co-author.

These data fully meet the scientific-metric criteria set by the Rules of Development of the Academic Staff of the Medical University - Varna and thus Dr. Detelina Stoilova Zhelyazkova, PhD fully meets the requirements for participation in the announced competition.

SCIENTIFIC AND RESEARCH ACTIVITY AND RELATED CONTRIBUTIONS

The presented scientific materials indicate a comprehensive competency of the candidate in the field of neurological diseases. The greatest part of the scientific production is in the field of autoimmune diseases of the CNS and in particular in multiple sclerosis - immunopathology, clinical aspects and management. Dr. Detelina Stoilova Zhelyazkova, PhD, is an established specialist in the field of multiple sclerosis. On this topic are devoted her main publications: dissertation thesis ("*Clinico - immunological correlations in patients with multiple sclerosis /profile of cytokines, chemokines and adhesion molecules – influence of interferon-beta immunomodulatory treatment/*"); and her single-author monograph "*Immunopathogenesis and treatment of multiple sclerosis*", as well as 12 of the presented articles.

Indeed, as a broad-profile specialist-neurologist some of her scientific papers are related to other areas of neuroscience, such as neuro-ophthalmology, neuro-oncology, infectious diseases of the nervous system, etc.

The dissertation work of Dr. Detelina Stoilova is a large-scale clinical-immunological study on a total of 227 patients with relapsing-remitting

Multiple sclerosis. Such a complex clinico-immunological examination on a large contingent of patients with MS is carried out for the first time in our country. For the first time in Bulgaria, a study of chemokines and adhesion molecules in serum and in cerebrospinal fluid of MS patients was conducted. A comparative analysis of the levels of a large group of cytokines, chemokines and adhesion molecules (11 indicators in total) in serum and in cerebrospinal fluid was carried out, assessing the presence of a correlation between their concentration, disease activity and the therapeutic effect of IFN- β . For the first time, serum CCL17 concentration was studied in MS patients undergoing IFN- β therapy. There was established a significantly lower serum concentration of CCL17 in patients receiving IFN- β therapy compared to the non-treated group. An original contribution is also the comparative study of the immunological profile of patients on IFN- β 1b therapy versus these on IFN- β 1a therapy; no significant difference was found within the studied immunological markers. The conducted immunological studies confirm the validity of hypothesis concerning the significant impact of IFN- β immunomodulatory therapy on the profile of cytokines, chemokines and adhesion molecules. In a scientific-applied aspect, Dr. Detelina Stoilova suggests that the sICAM-1 examination can be used as a biomarker to assess the therapeutic response to IFN- β . The therapeutic effect of IFN- β has also been studied in a large contingent of patients with relapsing-remitting MS within a 2-year period after the start of therapy. The clinical studies conducted confirm the beneficial therapeutic effect of IFN- β in terms of reduction in the frequency of relapses and delay in the progression of disability. For the first time in Bulgaria, a comparative analysis of the clinical effectiveness of IFN- β 1b versus IFN- β 1a SC was carried out in patients with relapsing-remitting

MS. When comparing the results for patients on IFN- β 1b treatment and these on IFN- β 1a SC treatment, a significant difference was found only by the indicator number of relapse-free patients ("relapse free status") at the end of the 2-year follow-up period.

The monograph of Dr. Detelina Stoilova, PhD, "Immunopathogenesis and treatment of Multiple sclerosis" is a well-structured and in-depth scientific work in the field of demyelinating diseases, written by a specialist with extensive experience in the field of diagnosis and treatment of the condition. For the first time in Bulgaria, the knowledge on immunopathogenesis of MS is systematized and summarized in the form of a single-author monograph. An original author's analysis of the relationship between them is exposed. Furthermore, an analysis of the nowadays knowledge in the field of immunopathogenesis of MS has been carried out; the most important cell populations and the related inflammatory mediators are presented and summarized; the various immune processes, determining the therapeutic effect of immunomodulatory drugs have been also discussed. The monograph also includes an interesting discussion about modern therapeutic strategies in relapsing-remitting MS, with author's own critical analysis of therapeutic algorithms (escalating or induction strategy, early high-effective immunomodifying therapy), analyzed through the rich practical experience of the author. The complex presentation of all immunomodulating drugs with their mechanism of action, therapeutic efficacy, method of administration and adverse drug reactions, makes the monograph of Dr. Detelina Stoilova the first comprehensive guide for MS treatment, intended to help the neurology specialists in Bulgaria.

As scientific contribution can be considered also the other scientific publications of Dr. Detelina Stoilova, devoted to the studies and analyses in the field of multiple sclerosis: study of the cognitive status of patients with relapsing-remitting MS, in particularly the working memory; the executive control and attention; study of levels of antiphospholipid antibodies (anticardiolipin, anti-beta-2-glycoprotein-I and anti-annexin V) in patients with relapsing-remitting MS versus patients with Systemic Lupus erythematosus; development of a neurorehabilitation algorithm in MS patients, including physiotherapy, cryotherapy, ergotherapy, pulse magnetic field, electrostimulations and training in daily activities. Publications related to the differential diagnosis of MS and in particular to Tropical Spastic paraparesis and to Progressive Multifocal leukoencephalopathy are also of contributory value.

In conclusion, it can be summarized that with her scientific achievements and her clinical activity Dr. Detelina Stoilova Zhelyazkova, PhD can be considered as one of the most experienced specialists in Bulgaria in the field of immunology, clinical aspects and MS management.

Another field, in which Dr. Detelina Stoilova has scientific interests is neuro-ophthalmology, where she has a professional qualification. Her research in this area includes a collective study of the method of automated perimetry in the early diagnosis of brain neoplasms. A large contingent of patients have been examined: 73 patients with chiasmal and 29 with retrochiasmal tumors. The study found a high sensitivity of the method in the early detection of brain neoplasms. In addition, she participated in a team of researchers conducting the largest in the country study and follow-up of neuro-ophthalmic symptomatology in orbital brain tumors. The analysis includes a total of 246

patients with different space-occupying processes in the orbital region, each of them operated and histologically verified. The study was published in Neuro-ophthalmology journal.

Dr. Detelina Stoilova, PhD, in collectives, participates in studies of some rare neurological diseases, such as: a rare case of spinal malignant melanoma, manifested clinically with bilateral papilledema; Myasthenia gravis with disseminated dermatophytic pseudomycetomas; dural sinus thrombosis; polychondritis, etc. Two of the study results are published in recognized international magazines.

TRAINING AND TEACHING ACTIVITIES

The teaching experience of Dr. Detelina Stoilova Zhelyazkova, PhD, dates back to 2002, when she was appointed as an assistant professor in the Neurology Clinic at University Hospital "Alexandrovska". She has consistently gone through the senior and chief assistant degrees. In 2011 she was appointed as Chief Assistant in the Neurology clinic at University Hospital "St. Ivan Rilski", where she currently works and teaches. The teaching activity of Dr. Detelina Stoilova, PhD, of 130 hours per year for the last five years, meets the requirements of the Development Regulations of the Academic Staff at the Medical University of Varna.

Dr. Detelina Stoilova participates as a collective member in writing of several textbooks on Neurology:

- Textbook in Neurology, ARSO, Sofia, 2001
- Neurology, ARSO, Sofia, 2004

- Neurology, ARSO, Sofia, 2010
- Neurology, ARSO, Sofia, 2015 (English edition).

CONCLUSION

On the basis of the examination and analysis of the scientific and teaching activities of the applicant, I have every reason to propose to this respected Scientific Jury the approval of Dr. Detelina Stoilova Zhelyazkova, PhD, for the academic position "Associate Professor" in the professional direction "Medicine", scientific specialty "Nervous Diseases".

Her scientometric data fully meet the criteria for the position, in accordance with the requirements of the Law and the Rules of Development of the Academic Staff at the Medical University of Varna.

This decision of mine is based on the following grounds:

1. Dr. Detelina Stoilova Zhelyazkova, PhD, has 20 years of experience as a lecturer and neurology specialist at the University Hospitals "Alexandrovska" and University Hospital "St. Ivan Rilski", Sofia;

2. She has gone through all academic positions from assistant to chief assistant;

3. The scientific production of Dr. Detelina Stoilova Zhelyazkova, PhD, meets all the criteria required by the Law and the Rules of Development of the Academic Staff at the Medical University of Varna. It includes the dissertation for the ESD "Doctor", monograph and articles published in foreign and Bulgarian magazines with the necessary impact factor and citations;

4. Dr. Detelina Stoilova Zhelyazkova, PhD, has participated in the writing of several subtitle chapters in: "Textbook on Neurology" 2001, two editions of "Neurology" (2004 and 2010) and in "Neurology" (2015, English edition);

5. Dr. Detelina Stoilova Zhelyazkova, PhD, is an established Neurology specialist in the field of Multiple Sclerosis. She leads the Specialized Center for Research and Treatment of MS at University Hospital "St. Ivan Rilski", Sofia.

On the basis of all these facts, I confidently give *my positive review* and I do suggest the members of the esteemed Scientific Jury to vote positively for the award of *Dr. Detelina Stoilova Zhelyazkova, PhD*, to the academic position "*Associate Professor*" in the professional field "Medicine", scientific specialty "*Nervous Diseases*".

17.07.2021

REVIEWER:

(Prof. P. Shotekov, M.D., D. Med. Sc.)

