

REVIEW

by

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for Member of a Scientific Jury

With relation to: Competition for holding the academic position of "Associate Professor" in the field of higher education 7. "Health and Sports", professional field 7.1 "Medicine", specialty "Social Medicine and Health Management" announced for the needs of the Department "Health policies analysis and accreditation procedures", Directorate "Health promotion and disease prevention" in the State Gazette, issue 14 of 18.02.2022.

The competition announced for the academic position of "Associate Professor" is for **two places** to meet the needs of the Department "Health Policy Analysis and Accreditation Procedures" at the Directorate for Health Promotion and Disease Prevention. Two candidates are participating in the competition, one of whom is **Atanas Radinov Radinov, MD, PhD**.

The review was prepared in accordance with the requirements of the Act on the Development of Academic Staff in the Republic of Bulgaria (ADASRB) and the Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at the National Center of Public Health and Analyses (NCPHA).

General presentation of the procedure and candidate's received materials

In connection with the procedure, a set of materials on electronic media is presented, which includes the required documents, as follows: European curriculum vitae (CV) format; a notarized copy of the diploma for the educational and scientific degree "Doctor"; medical certificate; criminal record certificate; copy of employment record book; certificate of the last place of work; list of scientific papers; reference for fulfillment of the minimum national requirements and the relevant evidence (monographs, books and chapters, copies of scientific publications and reports, referenced and indexed in world's most popular databases with scientific information, citations or reviews in peer-reviewed and indexed scientific journals, in monographs and collective volumes with scientific peer-review, and in non-peer-reviewed journals with scientific peer-review); reference for the collected points by indicators according to the minimum requirements for the position of "associate professor"; reference to the citations of the publications; reference for the impact factor of publications; list of

participations in scientific forums and copies of materials from participations in scientific forums; summaries of scientific papers other than those submitted for acquisition of educational and scientific degree "Doctor"; habilitation extended reference for scientific contributions; evidence of participation in a research project; reference for study load; diplomas for specialties in internal medicine and clinical hematology, master's degree in health management.

The presented set of documents is in accordance with the requirements of the Regulation for awarding the academic position "Associate Professor" at the NCPHA. All required documents are available and arranged, which allows easy access and analysis.

Curriculum vitae of the candidate

Atanas Radinov Radinov was born on February 25, 1962. In 1988 he graduated in medicine from the Higher Medical Institute in Varna. From 1989 to 1994 he specialized in "Internal Medicine", and from 1995-1997 in "Clinical Hematology" at the Medical University in Sofia. From 1989 to 1990 he worked as the head of a military medical unit - Pomorie, then until 1995 - as head of the laboratory of immunology at the Center for Immunology of the Military Medical Academy (MMA), Sofia. From 1995 to October 2003 he worked at the Clinic of Hematology, Chemotherapy and Oncology of the MMA, Sofia, and since 2000 he has been appointed Chief Assistant Professor. After a year of training in London, he started working at the IV Multiprofile Hospital of Active Treatment (MHAT), Sofia as a therapist and at the XXV Diagnostic Consultative Center (DCC) - as a hematologist. From 2006 to 2014 he worked first as head of the Hematology Department, and then as medical director of Tokuda Hospital, Sofia. Since December 2014 he has been appointed Head of the Department of Hematology at the University MHAT "St. Ivan Rilski", Sofia.

In 2015 he obtained a master's degree in health management at the University of National and World Economy - Sofia, and in 2021 - an educational and scientific degree "Doctor" in the scientific specialty "Social Medicine and Health Management".

Dr. Radinov has improved his qualifications in a number of courses in the country and abroad. He has specialized in the Department of Immunology at the University Hospital of Antwerp, Belgium, under the direction of Professor Dirk Van Bockstal, as well as in Tokyo and Osaka. He has participated in numerous clinical studies aimed at clinical hematology and medical oncology, as well as a medical doctor of the Bulgarian contingent in the NATO-led Stabilisation Force (SFOR) mission in Bosnia and Herzegovina and an international observer at the Organization for Security and Co-operation in Europe (OSCE) in Bosnia and Herzegovina and Kosovo.

He is a member of the Bulgarian Medical Association (BMA), Expert Council on Clinical Hematology at the Ministry of Health, Bulgarian Medical Society of Hematology.

Educational and teaching activity

The educational and teaching activity of the candidate is mainly related to the training of specialists in clinical hematology, medical oncology, gastroenterology, endocrinology and others. During the last 7 years, 9 doctors have been trained as specialists in clinical hematology at the Clinic of Hematology at the University MHAT "St. Ivan Rilski" as in 4 of them the candidate was the head of the specialization (2 of the physicians have successfully passed the specialty exam). He conducted the necessary colloquia for all of them (a total of 32). 49 people have passed the module "Hematology", some of whom have also held colloquia. The report received from the University MHAT "St. Ivan Rilski" for study load shows that in the period 2019-2021 he gave a total of 40 hours of lectures and 180 hours of exercises.

Assessment of the presented materials

Quantitative indicators

The candidate's scientific publications follow the stages in his professional development. Their total number, other than those related to the dissertation, is 105, 39 of which are publications in Bulgarian and English, 13 of which in prestigious foreign journals with high impact factor (IF - 229,905) and numerous citations, 26 are in refereed Bulgarian editions, and 3 are chapters from monographs. In addition, 1 research project won funding from the Bulgarian National Science Fund, 17 participations in world congresses and 37 participations in national congresses and conferences, 1 publication in an unrefereed journal and 7 participations in regional scientific meetings were presented.

The total number of points on indicators A to E is **22211.61** (Table 1), with a minimum required number of 400 for "Associate Professor", according to the Rules of the NCPHA. The scientometric indicators of the candidate in the competition significantly exceed the required number of points.

Table 1. Information on the collected points by indicators according to the minimum requirements for the position of associate professor (400 points)

Group of indicators	Indicators	Requirements of the NCPHA Regulations	Scores achieved by the candidate
A	1. Dissertation work for awarding the educational and scientific degree "Doctor"	50	50
C	4. Habilitation work, in the form of scientific publications (not less than 10) in publications that are referenced and indexed in world-famous databases of scientific information (only Scopus and Web of science);	100	102.28
D	7. Publications and reports published in scientific journals, referenced and indexed in world-famous databases of scientific information (only Scopus and Web of science)		110
	8. Publications and reports published in non-peer-reviewed journals with scientific review or published in edited collective volumes n = number of authors		130.41
	9. Published chapter of a collective monograph n = number of authors		38.92
	p.7+p.8+p.9	200	279.33
E	10. Citation and/ or reviews in scientific journals, referenced and indexed in world-renowned databases of scientific information (only Scopus and Web of science)		1430x15=21450
	12. Citation and / or reviews in non-peer-reviewed journals with scientific review		10x5 = 50
	p.10+p.12	50	21550
F	15. Acquired medical specialty		2x40=80
	18. Management of a national scientific or educational project		1x30=30
	22. Training of interns, postgraduates and doctoral students (seminars/workshops and practical classes)		4x30=120
	p.15+p.18+p.22		230
TOTAL POINTS	A+C+D+E+F = 50+102.28+279.33+21550+230		22211.61

Scientific contributions

The presented reference for the scientific contributions of the works of At. Radinov, MD, PhD covers the period from 1990 to 2021 and includes areas of scientific, scientific-applied, clinical-diagnostic and clinical-therapeutic nature.

Scientific contributions are divided into the following areas:

1. Clinical studies and their importance for patients' access to innovative therapy.
2. Fundamental and clinical immunology, implementation and application of immunological methods in clinical practice.
3. Quality of life in cancer patients and management of chemotherapy side effects.
4. Main problems in the diagnosis and treatment of patients with oncohematological diseases.
5. Public health, crises and pandemics, Covid-19 pandemic.

1. Clinical studies and their importance for patients' access to innovative therapy

In this field the candidate has achieved significant scientific and scientific-applied contributions, especially as a leader of numerous clinical trials conducted in the country. In the period 2003-2006, At. Radinov, MD, PhD in parallel with taking the exams for a license to work in the UK (IELTS, PLAB 1 and PLAB 2), gained experience in various hospitals of the National Health Service (NHS) in England, mainly at the Guy's Hospital Hematology Clinic, where a significant percentage of patients receive the most innovative therapies.

As a principal investigator, the candidate has conducted clinical studies on: herpes vaccine in patients with hematological and oncological diseases, epoetin alfa therapy in anemic patients with low-risk myelodysplastic syndrome, the results of which were published in 2018 in *Leukemia* (10), treatment of essential thrombocythemia (ET) patients with first-line drug anagrelide, the results of which were published in 2019 in the *British Journal of Hematology* (13) and others.

Excellent results in clinical research enable the candidate to work in collaboration with teams of world-renowned scientists. The results obtained have been published in many prestigious publications, such as *Lancet* (16), *Leukemia* (10, 17, 19), *British Journal of Hematology* (13), as well as presented on the forums of the *European Hematology Association (EHA)* (57, 58, 60, 62, 64), *American Society of Hematology (ASH)* (65, 66), *American Society of Clinical Oncology (ASCO)* (59, 63). Of particular value is the study of the effect of the use of selinexor in combination with bortezomib and dexamethasone in

patients with multiple myeloma, published in *Lancet* (16), the study of the efficacy and safety of ruxolitinib in patients with myelofibrosis and anemia, published in *Leukemia* (17), the effect of the combination of pevonedistat plus azacitidine in patients with high risk myelodysplastic syndrome (MDS), Chronic myelomonocytic leukemia (CMML) or Acute myeloid leukemia (AML) with a low percentage of blasts published in *Leukemia* (19).

The candidate's contributions in this field are proof of his professional knowledge and skills in the field of health management, especially in addressing such important socially significant diseases that are in the field of his clinical and managerial activities.

2. Fundamental and clinical immunology, implementation and application of immunological methods in clinical practice

During the period 1990-1995 the candidate carried out research at the MMA Center for Immunology, where he learned about the most modern immunological diagnostic methods and their importance for the diagnosis and follow-up of many diseases, especially in the field of clinical hematology, medical oncology, otorhinolaryngology and others.

After a one-month specialization in the Department of Immunology at the University Hospital of Antwerp, Belgium, the candidate mastered the method of flow cytometry cell cycle analysis using propidium iodide DNA staining, which he successfully implemented at the MMA Center for Immunology using a laser flow cytometer (FACSort) (20). The device, one of the most modern for its time, in addition to enabling flow cytometric DNA analysis with propidium iodide, it also makes it possible to perform immunophenotyping of lymphocyte populations using monoclonal antibodies conjugated to various dyes such as fluorescein isothiocyanate (FITC) and phycoerythrin (PE), as well as phagocytosis studies. The method of immunophenotyping allows extremely accurate diagnosis of lymphocyte populations, using monoclonal antibodies to identify them according to the expression of surface receptors cataloged in the cluster of designation (CD) system. This method is currently common and an accurate diagnosis of malignant haemopathy (lymphoma or leukemia) is not possible without immunophenotyping.

Based on the abovementioned possibilities of flow cytometry in clinical medicine, Dr. Radinov developed a research project on "Correlative relationships between the immunophenotype of the main lymphocyte populations and DNA status during the neoplastic process" (49). With this project № MU-14-MED/1993 he won funding from the Young Scientist Fund within the Bulgarian National Science Fund, used for research in the field of oncological diseases. The results are presented in two scientific papers, as well as in presentations in several scientific forums (50, 67, 68, 69).

The possibilities of flow cytometry are extremely large in the study of the effectiveness of the oral polybacterial immunomodulator Dentavax developed by National Centre of Infectious and Parasitic Diseases (NCIPD), as the co-authored studies are presented in publication (7) and at scientific forums in the country and abroad (50, 68, 69, 71, 77).

In the field of otorhinolaryngology, using a wide arsenal of methods for the study of humoral immunity, as well as the flow cytometric method of immunophenotyping, DNA analysis and phagocytic activity of immune cells from peripheral blood and tonsillar suspension, a number of studies have been conducted, which are co-authored in a number of publications - (23, 24, 25, 26, 29, 30) and at various scientific forums abroad and in the country (51, 52, 53, 54, 55, 78, 79, 80, 81).

The great advantage of the clinic where the candidate worked - the Clinic of Hematology, Chemotherapy and Oncology at the Military Medical Academy, was the opportunity provided to patients for complex treatment. The accumulated knowledge is the background of his personal management contribution to the establishment of similar clinics at Tokuda Hospital in 2008 and at University Hospital "St. Ivan Rilski" in 2014, which he still manages. The successful development of these clinics confirms the managerial qualities of the candidate, who since 2015 has a master's degree in health management.

3. Quality of life in cancer patients and management of chemotherapy side effects

Medical oncology is the other important area of the candidate's research activity. Already in his work as an immunologist, he has explored the possibilities for clinical application of flow cytometric DNA analysis in oncology practice. During the period 1995-2003, together with Professor Raynov, they studied the most common side effects of chemotherapy - emesis, as well as the most effective means of controlling the act or instance of vomiting.

Quality of life is one of the most significant health problems in cancer patients. It is based on patients' perceptions, encompassing their social, financial, psychosocial and physical activities. In this regard, an evaluation was performed according to EORTC-QoL-Q30, before and 7 days after highly emetogenic chemotherapy (HEC) including cisplatin in patients with lung, head and neck and genital tract cancer. Metoclopramide and setrons (ondansetron, tropisetron, granisetron) were compared, demonstrating the high efficacy and advantage of the latter over metoclopramide, especially at the psychological level. A number of publications (8,9, 28, 34, 37) and presentations at scientific forums have been co-authored (56, 83, 85, 86).

4. Main problems in the diagnosis and treatment of patients with oncohematological - diseases

A significant part of the candidate's research is focused on the diagnosis and follow-up of patients with oncohematological diseases. A significant scientific contribution is the study of the possibilities for the diagnostic and prognostic significance of flow cytometric DNA analysis in malignant hemopathy. A number of publications and presentations at scientific forums on the treatment of non-Hodgkin's lymphomas have been co-authored (11, 22, 75, 95, 96, 97) and Hodgkin's disease (40, 94), cytogenetic studies in multiple myeloma (34, 39, 82), cytogenetic studies in chronic myeloid leukemia (14, 18, 89, 90, 91, 93), myelofibrosis (15, 45, 60, 88) myelodysplastic syndrome (19, 42) non-lymphoblastic leukemias (27, 31, 32, 35, 36, 84), as well as chronic lymphocytic leukemia (38). Interesting cases of patients with rare diseases such as Gaucher disease (41) and osteopetrosis (87) have also been co-authored.

5. Public health, crises and pandemics, Covid-19 pandemic

In 2011, after the accident at the Fukushima nuclear power plant in Japan, Dr. Radinov began an in-depth study of the consequences of the nuclear incident and the actions of the Japanese authorities to deal with them. In this regard, he developed a dissertation on "Organization and management of the elimination of the consequences from radiation contamination of the population as a result of terrorist acts and other radiation incidents" (1), which the candidate successfully defended. In addition to the purely organizational activities it offers in terms of first aid, triage and follow-up, it also focuses on the psychological consequences in the event of a radiation accident. These studies are presented in publications related to the dissertation (2-6, 103). Researches in this area are of significant scientific and applied nature and offers organizational solutions in the event of such a scenario.

The COVID-19 pandemic has changed the world in the last 2 years. In addition to the psychological aspects of the problem, there has been a significant deterioration in health indicators of morbidity and mortality, often due to difficult access to treatment for patients with cardiovascular, oncological and oncohematological diseases. Working actively in the field of clinical studies, the applicant is studying the impact of the COVID 19 pandemic on clinical trials and the treatment of multiple myeloma and other haematological diseases (43). A review of the data on the growing influence of the microbiome in hematological malignancies has been published in co-authorship (44).

CONCLUSIOS

Based on the documents submitted for review, I believe that Atanas Radinov, MD, PhD is a successful scientist and top expert in the field of clinical hematology, medical oncology and health management.

The scientometric indicators fully meet the requirements of the Regulations on the terms and conditions for obtaining scientific degrees and holding academic positions at the NCPHA, ADASRB and its Regulations, which gives me convincing reason to vote positively and strongly recommend to the esteemed scientific jury to award the academic position of "Associate Professor" to Atanas Radinov Radinov, MD, PhD in the field of higher education 7. "Health and Sports" in professional direction 7.1. "Medicine" in the scientific specialty "Social Medicine and Health Management" for the needs of the Department "Health policies analysis and accreditation procedures" at the Directorate "Health Promotion and Disease Prevention".

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