

STATEMENT
BY PROF. DR. PETRANKA PETROVA TROYANOVA, DM
DEPARTMENT OF NUCLEAR MEDICINE, RADIATION AND MEDICAL
ONCOLOGY, FACULTY OF MEDICINE, MU, SOFIA
MEMBER OF THE SCIENTIFIC JURY APPOINTED BY ORDER OF THE RECTOR
OF MU- VARNA No. P-109-516/30.11.2023.

Subject: Competition for the academic position "Professor" in the field of higher education 7. Health care and sports, professional direction 7.1. Medicine and scientific specialty "Oncology" for the needs of the "Oncology" Department, Faculty of "Medicine" at the Medical University-Varna, announced SG No. 83 of 03.10.2023.

To participate in the competition within the legal deadline, only one candidate submitted documents - Associate Professor Nikolay Vladimirov Tsonev, MD, Department of Oncology, Medical University - Varna. The documents and materials submitted by the candidate have been carefully and systematically prepared and fully meet the requirements of the Law on the development of the academic staff in the Republic of Bulgarian and the Rules for the development of the academic staff in the Medical University "Prof. Dr. P. Stoyanov" - Varna.

I have not found any violations in the course of the contest so far. I declare that I have no scientific works in common with the candidate and my participation in the present scientific jury does not give rise to a conflict of interest. I have not found data on plagiarism and unreliability in the materials provided.

I. CANDIDATE CAREER PROFILE DATA

Associate Professor Dr. Nikolay Vladimirov Tsonev graduated from secondary education at the "St. Kliment Ohridski" - city of Silistra with "Biology" profile. In 2002, he graduated from the University of Economics - Varna - Bachelor of Economics, specialty "Commodity Science". In 2009, he graduated as a Master of Medicine at the Medical University of Varna, majoring in "Medicine".

In 2010, he started working as a specialist in medical oncology at the Medical Oncology Clinic, "St. Marina" - Varna. In 2015, he acquired the clinical specialty "Medical Oncology". Since 2016, he has been a medical oncology specialist at the Medical Oncology Clinic, Saint Marina UMBAL, and since 2018 he has been the head of the same clinic. Since 2019, he has been the head of the "Oncology Clinics" department at the Saint Marina UMBAL.

In 2013, he was appointed as a part-time assistant in the "Propaedeutics of Internal Diseases" Department at the Medical University - Varna. Since 2017, he has been a full-time assistant, and since 2018, he has been the main assistant at the Department of "Propaedeutics of Internal Diseases" at the Medical University - Varna. In 2018, he was habilitated and held the academic position of "Docent" in the Department of "Propaedeutics of Internal Diseases", and since 2020 he is an associate professor at the Department of "Oncology".

Since 2019, he has been the head of the "Oncology and Rare Diseases" department at the Research Institute of the Medical University of Varna - Varna.

In 2016, he defended a dissertation for the acquisition of the ONS "Doctor" in the scientific specialty "Medical Oncology" on the topic: "Microribonucleic acids miR-17, miR-21, miR-29a and miR-92 as potential markers for risk assessment of relapse after adjuvant chemotherapy in patients with colon carcinoma'.

Associate Professor Nikolay Tsonev has numerous participations in various master courses of the European School of Oncology (ESO), as well as continuing medical education courses at ESMO, etc. among which are Qualification Course/Seminar on Organization, management and conduct of a clinical trial, November 2012, specialized course on Antiangiogenesis treatment, Belgium (2014), Antiangiogenic therapy in recurrent platinum-sensitive ovarian carcinoma and Masterclass in Molecular Oncology, Prague, Czech Republic in 2015.

Associate Professor Tsonev is a member of numerous Bulgarian and international scientific organizations, his participation in ESMO (European Society for Medical Oncology) and ASCO (American Society of Clinical Oncology) being particularly important.

Associate Professor Tsonev is a highly qualified expert in the field of oncology. He is a member of the Expert Council on Medical Oncology at the Ministry of Health.

He is a reviewer and member of the editorial boards of numerous scientific journals. He is a reviewer of a number of competitions for acquiring an academic position.

II. CANDIDATE CAREER PROFILE DATA

Associate Professor Dr. Nikolay Vladimirov Tsonev graduated from secondary education at the "St. Kliment Ohridski" - city of Silistra with "Biology" profile. In 2002, he graduated from the University of Economics - Varna - Bachelor of Economics, specialty "Commodity Science". In 2009, he graduated as a Master of Medicine at the Medical University of Varna, majoring in "Medicine".

In 2010, he started working as a specialist in medical oncology at the Medical Oncology Clinic, "St. Marina" - Varna. In 2015, he acquired the clinical specialty "Medical Oncology". Since 2016, he has been a medical oncology specialist at the Medical Oncology Clinic, Saint Marina UMBAL, and since 2018 he has been the head of the same clinic. Since 2019, he has been the head of the "Oncology Clinics" department at the Saint Marina UMBAL.

In 2013, he was appointed as a part-time assistant in the "Propaedeutics of Internal Diseases" Department at the Medical University - Varna. Since 2017, he has been a full-time assistant, and since 2018, he has been the main assistant at the Department of "Propaedeutics of Internal Diseases" at the Medical University - Varna. In 2018, he was habilitated and held the academic position of "Docent" in the Department of "Propaedeutics of Internal Diseases", and since 2020 he is an associate professor at the Department of "Oncology".

Since 2019, he has been the head of the "Oncology and Rare Diseases" department at the Research Institute of the Medical University of Varna - Varna.

In 2016, he defended a dissertation for the acquisition of the ONS "Doctor" in the scientific specialty "Medical Oncology" on the topic: "Microribonucleic acids miR-17, miR-21, miR-29a and miR-92 as potential markers for risk assessment of relapse after adjuvant chemotherapy in patients with colon carcinoma".

Associate Professor Nikolay Tsonev has numerous participations in various master courses of the European School of Oncology (ESO), as well as continuing medical education courses at ESMO, etc. among which are Qualification Course/Seminar on Organization, management and conduct of a clinical trial, November 2012, specialized course on Antiangiogenesis treatment, Belgium (2014), Antiangiogenic therapy in recurrent platinum-sensitive ovarian carcinoma and Masterclass in Molecular Oncology, Prague, Czech Republic in 2015.

Associate Professor Tsonev is a member of numerous Bulgarian and international scientific organizations, his participation in ESMO (European Society for Medical Oncology) and ASCO (American Society of Clinical Oncology) being particularly important.

Associate Professor Tsonev is a highly qualified expert in the field of oncology. He is a member of the Expert Council on Medical Oncology at the Ministry of Health.

He is a reviewer and member of the editorial boards of numerous scientific journals. He is a reviewer of a number of competitions for acquiring an academic position.

III. GENERAL DESCRIPTION OF THE COMPETITION SUBMITTED MATERIALS AND REFLECTION OF THE CANDIDATE'S PUBLICATIONS IN NATIONAL AND FOREIGN LITERATURE (PUBLICATION IMAGE)

For the competition, the candidate Assoc. Professor Tsonev submitted, in addition to a dissertation, another 61 titles, of which:

- 12 real publications in scientific publications, which are referenced and indexed in world-renowned databases with scientific information, equivalent to a habilitation thesis
- 33 original articles and reports published in scientific publications, referenced and indexed in world-famous databases with scientific information;
- 12 original articles and reports published in non-refereed peer-reviewed journals or published in edited collective volumes;
- 4 articles in scientific journals and anthologies, beyond the minimum scientometric requirements for holding the AD "professor";

Prof. Tsonev has 56 scientific developments presented at scientific forums (in Bulgaria - 8 and abroad - 48).

The works of Prof. Tsonev have been evaluated by the scientific community as significant. The serious interest shown in his scientific publications is proved by the large number of citations. 749 citations or reviews in scientific publications, referenced and indexed in world-renowned databases of scientific information or in monographs and collective volumes are presented.

Quotes as of 10.2030:

- Scopus - 1,604; h-index 8
- Google Scholar – 2274; h-index 14; i10-index 18.

The candidate has active scientific profiles in:

Google Scholar	https://scholar.google.com/citations?user=xvP_he4AAAAJ
ORCID	0000-0003-2641-8635
SCOPUS AID	6508132535
ResearcherID	AAR-8444-2021
ResearchGate	https://www.researchgate.net/profile/Ilina-Micheva

Dissertation on: MICRORIBONUCLEIC ACIDS miR-17, miR-21, miR-29a and miR-92 AS POTENTIAL MARKERS FOR ASSESSING THE RISK OF RECURRENCE AFTER ADJUVANT CHEMOTHERAPY IN PATIENTS WITH COLON CANCER.

The dissertation was published in Bioscience trends - an international journal with an impact factor and was cited 45 times in international journals. The results of the research were presented at a prestigious international congress - SMO Copenhagen 2016.

Associate Professor Tsonev has publications in leading journals directions in the field of oncology and internal medicine, implemented in the period 2018-2023 with a total impact factor of 1276.168. The very high IF of the candidate is impressive, which speaks of the importance of scientific works and their adequate implementation in appropriate publications.

Prof. Tsonev participated in a number of scientific projects as an expert and scientific supervisor, which were successfully completed, and their results were published in various scientific journals:

1. Study of expression levels of immunohistochemical markers for necroptosis in breast carcinoma. Period: 19.12.2019 – 20.12.2021. Organization: MU-Varna. Position: Research supervisor.

2. Investigation of the influence of specific carboxylesterase inhibitors on the effectiveness of chemotherapy with Capecitabine. Period: 19.12.2019 – 20.12.2021. Organization: MU-Varna. Position: Expert.

Scientometric indicators presented for occupying the academic position "Professor" from the presented academic reference	
GROUP OF INDICATORS A: Dissertation thesis for obtaining the educational and scientific degree "Doctor (PhD)" - Conev N. "Microribonucleic acids miR-17, miR-21, miR-29a and miR-92 as potential markers for assessing the risk of relapse after adjuvant chemotherapy in patients with colon cancer."	(50 points)
GROUP OF INDICATORS C: Habilitation work = scientific publications (not less than 10) in publications that are referenced and indexed in world-renowned databases of scientific information.	(100.67 points)
GROUP OF INDICATORS D: Publications and reports published in scientific journals, referenced and indexed in world-renowned databases of scientific information, publications and reports published in non-refereed peer-reviewed journals or published in edited collective volumes.	(315.22 points)
GROUP OF INDICATORS E: Citations.	(11 235 points)

GROUP OF INDICATORS F: Guidance of a successfully defended doctoral student.	(100 points)
GROUP OF INDICATORS F: Acquired medical specialty.	(40 points)
GROUP OF INDICATORS F: Participation in a national scientific or educational project.	(15 points)
GROUP OF INDICATORS F: Management of a national scientific or educational project.	(30 points)
Additionally provided articles beyond the minimum scientometric requirements for occupying the academic position "Professor" - 3 pieces	

The presented academic reference shows that the minimum scientometric requirements for occupying the academic position "Professor" have been met.

IV. THEMATIC AREAS AND CONTRIBUTIONS OF SCIENTIFIC RESEARCH ACTIVITY

Associate Professor Nikolay Tsonev began his scientific activity in 2012, and his output includes a number of original scientific articles, literature reviews, presentation of medical clinical cases and summaries of participation in scientific forums. Tracking over time the scientific output of Prof. Tsonev, his gradual, stable, progressive and upward scientific development and growth in the field of oncology is clearly noticeable. In the publications of recent years, the author works with multicentric, multidisciplinary teams, both from Bulgaria and abroad. It should be noted the interrelationship between scientific and scientific-applied contributions, which allowed him to obtain many original and confirmatory results of theoretical and applied importance.

The scientific research activity of Prof. Tsonev, independently and in the composition of research teams, as well as the contributions of the achieved results, are concentrated in the following main directions:

1. Investigation of small non-coding RNAs as prognostic and predictive markers in cancer patients (B4.5, B4.6, B4.8);
2. Markers for response to immunotherapy treatment in solid tumors (B4.9, B4.11);
3. Association of time perception with distress in cancer patients; Association of the perception of time with other indicators for the assessment of the psychological state of oncological patients; Creation of ultra-rapid distress assessment tools (B4.7, B4.10, B4.12);

4. Assessment of access to facilities that offer oncology care and treatment outcomes (B4.3);

5. Study of circulating histones as markers for monitoring oncological diseases (B4.1);

6. Analysis of the CASPIAN study and its long-term results (B4.2, B4.4).

The contributions of Prof. Tsonev's scientific works are from various areas of oncology and cover a very wide spectrum, which are reduced to the following thematic areas:

1. Investigation of small non-coding RNAs as prognostic and predictive markers in cancer patients - dissertation plus (B4.5, B4.6, B4.8)

Microribonucleic acids miRNAs are small RNA molecules made up of about 21-25 nucleotides that do not code for proteins, but have an important function for regulating gene expression. A number of evidences have been accumulated for the involvement of miRNAs in diverse biological processes, such as regulators of cell proliferation, differentiation, apoptosis and other phenomena related to oncogenesis. Recent studies have shown different levels of miRNA expression in tissues, serum, and other body fluids.

Dissertation thesis entitled: "Microribonucleic acids miR-17, miR-21, miR-29a and miR-92 as potential markers for the assessment of risk of recurrence after adjuvant chemotherapy in patients with colon cancer" with original contributions nationally and globally. Single nucleotide polymorphisms (single nucleotide polymorphisms SNPs) are genetic variations that are involved in various functional processes affecting individual susceptibility to certain oncological diseases. The article Single Nucleotide Polymorphisms in microRNA Genes and Colorectal Cancer Risk and Prognosis provides an in-depth review of various SNPs that have been studied to assess CRC risk, prognosis and response to treatment.

The article Circulating miR 618 Has Prognostic Significance in Patients with Metastatic Colon Cancer reports an analysis of the prognostic role of circulating miRNA 618 in patients with metastatic colon cancer and whether the miR 618 gene rs 2682818 (single nucleotide polymorphisms) is associated with cancer susceptibility of the colon and with the expression levels of mature miR 618.

The article New Circulating Circular RNAs with Diagnostic and Prognostic Potential in Advanced Colorectal Cancer examines the study of plasma expression levels of four circRNAs: has_circ_0001445, hsa_circ_0003028, hsa_circ_0007915 and hsa_circ_0008717 in CRC patients and their association with clinicopathological features and clinical outcome of patients.

SCIENTIFIC CONTRIBUTIONS

1. For the first time, the distribution of allelic and genotypic frequencies of SNPs in the Bulgarian population of individuals in patients with CRC was investigated;

2. Circulating miRNA 618 has been found to be useful as a prognostic biomarker in CRC. Patients with the AC rs 2682818 genotype had a reduced risk of colon cancer compared to patients with the CC and AA genotypes;
3. The levels of has_circ_0001445, hsa_circ_0003028, hsa_circ_0007915 and hsa_circ_0008717 were found to be significantly increased in the plasma of CRC patients. The median overall survival of patients with high median expression of hsa_circ_0001445 was significantly higher compared to the median OS of patients with low expression. Low levels of hsa_circ_0001445 were also associated with shorter survival. Prognostic significance of hsa_circ_0001445 was found in patients with metastatic CRC.

2. Markers of response to immunotherapy treatment in solid tumors (B4.9, B4.11)

The article Sarcopenia and high NLR are associated with the development of hyperprogressive disease after second line pembrolizumab in patients with nonsmall cell lung cancer reviews the results of a multicenter retrospective study that assessed the incidence of hyperprogressive disease (after second line treatment with pembrolizumab in patients with metastatic nonsmall cell lung cancer (whose tumors express Programmed cell death ligand 1), and also identified hematological and imaging biomarkers associated with its development.

The article Neutrophil to lymphocyte ratio as a potential predictive marker for treatment with pembrolizumab as a second line treatment in patients with non-small cell lung cancer examines the results of a multicenter retrospective study that evaluated the predictive and prognostic value of the neutrophil to lymphocyte ratio (the platelet-lymphocyte ratio) and their dynamics in patients with non-small cell lung cancer (treated with pembrolizumab as second-line therapy).

SCIENTIFIC CONTRIBUTIONS

1. A high NLR (neutrophil lymphocyte ratio) before immunotherapy and the presence of sarcopenia were found to be potential risk factors for the development of hyperprogressive disease;
2. NLR 5 was found to be a potential predictive marker that could identify patients suitable for immunotherapy as a second-line treatment.

3. Association of time perception with distress in cancer patients; Association of the perception of time with other indicators for the assessment of the psychological state of oncological patients; Creating ultra-rapid distress assessment tools (B4.7, B4.10, B4.12)

The article One minute time interval estimation as a novel ultrashort tool for distress screening examines the subjective time interval estimation as a screening test for distress among cancer patients. This test is an easy-to-administer, time-saving and non-intrusive ultrashort

screening tool that is suitable even for patients who do not wish to disclose their level of distress through direct questionnaires.

The article Fast time perception is associated with high levels of anxiety in cancer patients prior to starting chemotherapy examines the subjective assessment of time as a screening test for emotional instability among cancer patients. This test is an easy-to-administer, time-saving and non-intrusive ultrashort screening tool that is suitable even for patients who do not wish to reveal their level of emotional instability through direct questionnaires.

SCIENTIFIC CONTRIBUTIONS

1. Created a subjective time assessment test equivalent to The National Comprehensive Cancer Network Distress Thermometer, Problem List and reproduced their results. This test is an easy-to-administer, time-saving, non-intrusive, ultra-brief screening tool that is suitable even for patients who do not wish to reveal their emotional state through direct questionnaires.

4. Assessing access to facilities that offer oncology care and treatment outcomes (B4.3)

"Impact of travel burden on clinical outcomes in lung cancer" in this retrospective study found significant differences in the overall survival of patients with lung cancer depending on the distance and time of travel to an oncology facility. Despite similar clinical and pathologic characteristics (sex, stage at initial diagnosis, histologic subtype), median overall survival was significantly lower in these subgroups of patients with higher travel burden.

SCIENTIFIC CONTRIBUTIONS

1. For the first time in national clinical oncology, such a comprehensive analysis of patients with lung cancer was performed, focused on proving the role of distance and travel time to the oncology center as prognostic factors.
2. For the first time in Bulgaria, correlations between clinico-pathological characteristics of patients with lung cancer and the distance and time to reach the oncology center are sought.
3. For the first time worldwide, an association between travel time and distance to the cancer center and survival of patients with histologically verified lung cancer is demonstrated using an analysis based on such a large patient cohort.

5. Investigation of circulating histones as markers for monitoring oncological diseases (B4.1)

+The review Circulating Histones to Detect and Monitor the Progression of Cancer reviews the current knowledge of circulating histones in hematologic malignancies and solid tumors, with an emphasis on their role in cancer propagation, monitoring, and tumorigenesis.

SCIENTIFIC CONTRIBUTIONS

1. The review analyzes recently developed strategies to identify the origin of tumor tissue in blood plasma based on nucleosome positioning inferred from nucleosomal DNA fragmentation.

Analysis of the CASPIAN study and its long-term results (B4.2, B4.4)

In this study, Associate Professor Nikolay Conev participated as a reviewer of the results and subsequent analyzes of exploratory targets in more than 25 articles and reports at international scientific forums.

Additional developments in the field of radiation therapy

Research has identified markers that are predictors of response to radiation therapy and has also examined levels of distress among cancer patients undergoing radiation therapy.

Additional developments in the field of pulmonology

A new tool - "Time Assessment" has been created as a powerful ultrashort tool for screening depression in patients with COPD.

Measuring stress levels among cancer patients with COVID 19 infection

Distress levels have been reliably found to be higher among cancer patients with COVID 19 infection.

For the first time in Bulgaria, a retrospective analysis of the effectiveness of drugs for the treatment of colorectal carcinoma beyond the second line was conducted: Penkova M, Stoyanov D, Panayotova T, Donev I, Petrova M, Conev N. Regorafenib and trifluridine/tipiracil efficacy and safety in chemorefractory metastatic colorectal cancer patients: A single Bulgarian centre retrospective study. *Ann Oncol.* 2020 Jul;31(Suppl 3):S100–S100.

V. EDUCATIONAL AND TEACHING ACTIVITY

Associate Professor Nikolay Tsonev has a long teaching experience as an assistant and associate professor in the Department of "Propaedeutics of Internal Diseases" and the Department of "Oncology" at the Medical University - Varna. He conducts practical exercises and lectures on Medical Oncology and Propedeutics of internal diseases for students of medicine, dentistry and pharmacy and conducts training in Bulgarian and English. The study load for the last academic year 2023-2024 is 212 hours.

Associate Professor Nikolay Tsonev participates in postgraduate training through theoretical lectures to interns and specialists; thematic courses for specialists; individual trainings in internal medicine and oncology for specialists and specialists.

He is a member of examination committees for students and specialists.

The complex, qualitative evaluation of the teaching-methodical and pedagogical work, incl. scientific guidance of students, doctoral students, specialists, proves the high level of the teaching activity of Prof. Tsonev.

VI. CONCLUSION

The scientific works presented by Assoc. Dr. Nikolay Tsonev, published in prestigious Bulgarian and international scientific publications, the number of citations and other quantitative scientometric indicators, fulfill and exceed the requirements for occupying the academic position "Professor", specified in the Regulations for Terms and Conditions for acquiring scientific degrees and occupying academic positions at MU-Varna. The scientific activity of the candidate is extremely wide-ranging and is carried out within small teams or in the course of large-scale scientific projects. Associate Professor Nikolay Tsonev's participation in multidisciplinary teams, both at the scientific and expert level, make him a recognizable and referenced specialist in medical oncology.

This, as well as the significant scientific and teaching activity, the national and international recognition and authority in the field of oncology, are reasons I am convinced to recommend to the honorable scientific jury to support the candidacy of Associate Professor Nikolay Tsonev to be elected to the academic position "Professor" in scientific specialty "Oncology" for the needs of the "Oncology" Department of MU-Varna.

February 19, 2024

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

Prof. P. Troyanova, dm